Drug Free Australia series – Media suppression of alarming cannabis harms

Episode 1 – Known for decades

DRUG FREE AUSTRALIA

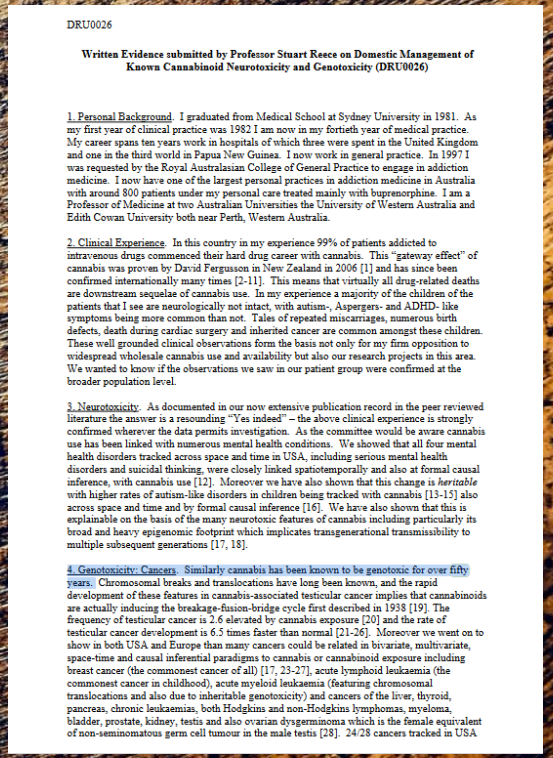
Known for decades

- From a world authority on cannabis and its harms:

  " . . . cannabis has been known to be genotoxic for over fifty years."

  Dr Stuart Reece

- So why is our media suppressing the latest studies showing that cannabis, used recreationally or medicinally, is causing unprecedented harm?



DRU0026

Written Evidence submitted by Professor Stuart Reece on Domestic Management of Known Cannabinoid Neurotoxicity and Genotoxicity (DRU0026)

1. Personal Background. I graduated from Medical School at Sydney University in 1981. As my first year of clinical practice was 1982 I am now in my fortieth year of medical practice. My career spans ten years work in hospitals of which three were spent in the United Kingdom and one in the third world in Papua New Guinea. I now work in general practice. In 1997 I was requested by the Royal Australasian College of General Practice to engage in addiction medicine. I now have one of the largest personal practices in addiction medicine in Australia with around 800 patients under my personal care treated mainly with buprenorphine. I am a Professor of Medicine at two Australian Universities the University of Western Australia and Edith Cowan University both near Perth, Western Australia.

2. Clinical Experience. In this country in my experience 99% of patients addicted to intravenous drugs commenced their hard drug career with cannabis. This "gateway effect" of cannabis was proven by David Fergusson in New Zealand in 2006 [1] and has since been confirmed internationally many times [2-11]. This means that virtually all drug-related deaths are downstream sequelae of cannabis use. In my experience a majority of the children of the patients that I see are neurologically not intact, with autism-, Aspergers- and ADHD- like symptoms being more common than not. Tales of repeated miscarriages, numerous birth defects, death during cardiac surgery and inherited cancer are common amongst these children. These well grounded clinical observations form the basis not only for my firm opposition to widespread wholesale cannabis use and availability but also our research projects in this area. We wanted to know if the observations we saw in our patient group were confirmed at the broader population level.

3. Neurotoxicity. As documented in our now extensive publication record in the peer reviewed literature the answer is a resounding "Yes indeed" – the above clinical experience is strongly confirmed wherever the data permits investigation. As the committee would be aware cannabis use has been linked with numerous mental health conditions. We showed that all four mental health disorders tracked across space and time in USA, including serious mental health disorders and suicidal thinking, were closely linked spatiotemporally and also at formal causal inference, with cannabis use [12]. Moreover we have also shown that this change is *heritable* with higher rates of autism-like disorders in children being tracked with cannabis [13-15] also across space and time and by formal causal inference [16]. We have also shown that this is explainable on the basis of the many neurotoxic features of cannabis including particularly its broad and heavy epigenomic footprint which implicates transgenerational transmissibility to multiple subsequent generations [17, 18].

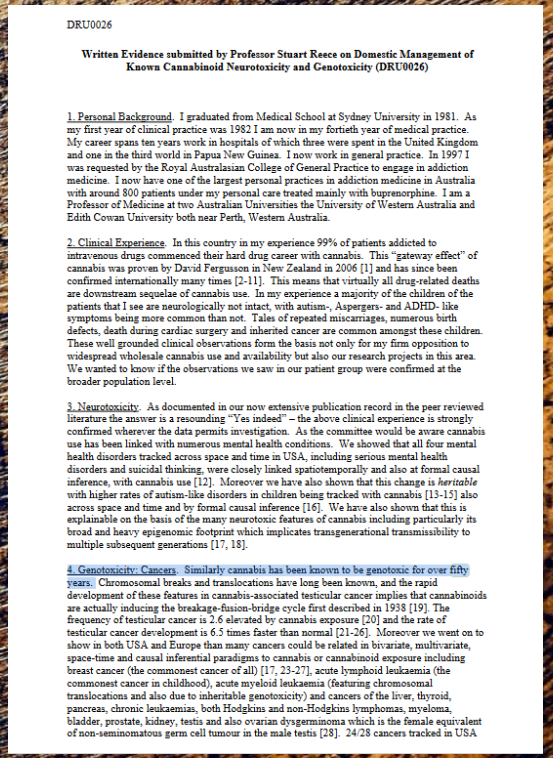
4. Genotoxicity: Cancers. Similarly cannabis has been known to be genotoxic for over fifty years. Chromosomal breaks and translocations have long been known, and the rapid development of these features in cannabis-associated testicular cancer implies that cannabinoids are actually inducing the breakage-fusion-bridge cycle first described in 1938 [19]. The frequency of testicular cancer is 2.6 elevated by cannabis exposure [20] and the rate of testicular cancer development is 6.5 times faster than normal [21-26]. Moreover we went on to show in both USA and Europe than many cancers could be related in bivariate, multivariate, space-time and causal inferential paradigms to cannabis or cannabinoid exposure including breast cancer (the commonest cancer of all) [17, 23-27], acute lymphoid leukaemia (the commonest cancer in childhood), acute myeloid leukaemia (featuring chromosomal translocations and also due to inheritable genotoxicity) and cancers of the liver, thyroid, pancreas, chronic leukaemias, both Hodgkins and non-Hodgkins lymphomas, myeloma, bladder, prostate, kidney, testis and also ovarian dysgerminoma which is the female equivalent of non-seminomatous germ cell tumour in the male testis [28]. 24/28 cancers tracked in USA

https://committees.parliament.uk/writtenevidence/107331/pdf/

Population studies

- From the latest medical/scientific journals
  - cannabis causal in:
    - 31 cancer types (tobacco is causal in 14)
    - 70% of pediatric cancer types
    - 89 of 95 birth defects tracked in Europe
    - neurotoxicity-related autism, psychosis and suicide
    - genotoxicity-related premature ageing (30% greater)

  - Because of the heavy epigenomic footprint of cannabis, it suggests “transgenerational transmissibility to multiple subsequent generations.”



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The mechanism

- 2016 – the mechanism of cannabis harm confirmed
  - cannabis literally shatters chromosomes
  - DNA repair mechanisms don't always reconstruct correctly

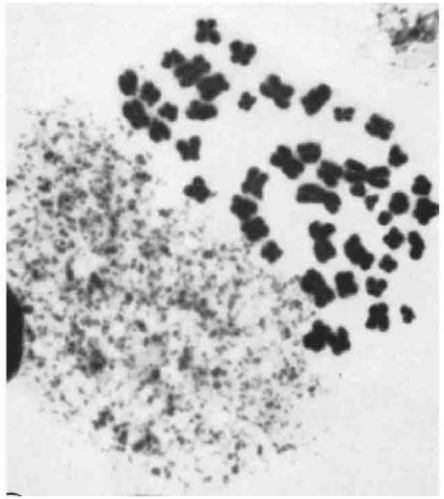

Fig. 1. Chromosomal Pulverization.
Original Report of Chromosomal Pulverization. Figure 7 , Kato H., Sandberg AA (1967). "Chromosome Pulverization in Human Binucleate Cells. Following Colcemid Treatment." J. Cell Biol. 34 (1): 35–45. Re-used by permission.

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Review

Chromothripsis and epigenomics complete causality criteria for cannabis- and addiction-connected carcinogenicity, congenital toxicity and heritable genotoxicity

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Interdisciplinary

ABSTRACT

The recent demonstration that massive scale chromosomal shattering or pulverization can occur abruptly due to errors induced by interference with the microtubule machinery of the mitotic spindle followed by haphazard chromosomal annealing, together with sophisticated insights from epigenetics, provide profound mechanistic insights into some of the most perplexing classical observations of addiction medicine, including cancerogenesis, the younger and aggressive onset of addiction-related carcinogenesis, the heritability of addictive neurocircuitry and cancers, and foetal malformations. Tetrahydrocannabinol (THC) and other addictive agents have been shown to inhibit tubulin polymerization which perturbs the formation and function of the microtubules of the mitotic spindle. This disruption of the mitotic machinery perturbs proper chromosomal segregation during anaphase and causes micronucleus formation which is the primary locus and cause of the chromosomal pulverization of chromothripsis and downstream genotoxic events including oncogene induction and tumour suppressor silencing. Moreover the complementation of multiple positive cannabis-cancer epidemiological studies, and replicated dose-response relationships with established mechanisms fulfils causal criteria. This information is also consistent with data showing acceleration of the aging process by drugs of addiction including alcohol, tobacco, cannabis, stimulants and opioids. THC shows a non-linear sigmoidal dose-response relationship in multiple pertinent *in vitro* and preclinical genotoxicity assays, and in this respect is similar to the serious major human mutagen thalidomide. Rising community exposure, tissue storage of cannabinoids, and increasingly potent phytocannabinoid sources, suggests that the threshold mutagenic dose for cancerogenesis will increasingly be crossed beyond the developing world, and raise transgenerational transmission of teratogenicity as an increasing concern.

Contents

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0027-5107/

https://www.sciencedirect.com/science/article/abs/pii/S0027510716300574

Cannabis harms series

- More detail in future episodes:
  - Cannabis and cancer
  - Cannabis and birth defects
  - Cannabidiol (CBD), cancer and birth defects
  - Cannabis and pain
  - Cannabis and driving
  - Hemp and psychoactive metabolites
  - Cannabis and psychosis
  - Cannabis and violence/homicide
  - Cannabis and suicide
  - Cannabis – its other harms

Next episode

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