

Response To RACGP Medicinal Cannabis Evaluation

**All Cannabinoids,
Multigenerational
Genomic and Epigenomic Toxicity,
Food Chain Contamination**



Preamble – Preliminary Questionnaire

What do the following issues all share in common:

1. Has no clinical trials to justify more than 80 alleged medical indications
2. Dramatically accelerates aging
3. Has been found in 80 / 80 recent mass murderers
4. Is a major driver of poor mental health in young adults (18-25 years)
5. Is a major driver of poor mental health in older adults (> 26 years)
6. Causes most major common mental disorders including anxiety, depression, PTSD, bipolar disorder, psychosis, schizophrenia
7. Is linked with rising suicide rates
8. Increases the rate of failed major adult relationships
9. Increases the unemployment rate
10. Causes poverty and homelessness
11. Drives drug overdoses from other drugs
12. Drives overdoses in children directly and as the sole exposure
13. Drove a doubling in the rate of serious mental illness in USA in recent decades
14. Drives the exponentiating autism epidemics
15. Drives the parabolically accelerating rate of USA congenital Atrial Septal Defects (secundum type)
16. Causes 12 congenital cardiac malformations in recent European epidemiological analysis
17. Drives Limbless birth defects rates elevated 60 times above background in France
18. Drives outbreaks of limblessness in Germany
19. Shares 12 of 13 teratogenic mechanisms of action with thalidomide
20. Shares 22 of 33 described birth defects with thalidomide
21. Concentrates certain environmental toxins in milk
22. Persistence of certain environmental toxins in milk for weeks
23. Grossly inadequate Government assays of environmental toxins
24. Disrupts the endocrine system particularly affecting the hypothalamic-pituitarygonadal axis
25. Is estrogenizing
26. A major driver of the commonest cancer in adults, breast cancer
27. A major driver of the cancer responsible for the most years of life lost in adults, testicular cancer

28. A major driver of the total childhood cancer
29. A major driver of the commonest cancer in children, acute lymphoid leukaemia
30. A major driver of inheritable cancer
31. A major driver of two of the most rapidly increasing adult cancers, liver and
32. pancreatic cancer
33. Is known to be toxic to the genome and linked with DNA breaks
34. All its congeners and chemical family members are similarly implicated
35. Is known to be toxic to the epigenome and destroys the epigenetic machinery
36. Damages the genes and epigenome for three to four generations
37. Is known to be toxic to the genome and linked with disruption of the mitotic machinery including kinetochores, centrosomes and mitotic spindles
38. Causes micronuclei
39. Damages sperm genetically 1
40. Damages sperm epigenetically 1
41. Damages sperm structurally and induces aging changes 1
42. Damages oocytes genetically 1
43. Damages oocytes epigenetically 1
44. Damages oocytes structurally and induces aging changes 1
45. Causes 20% loss of fertilized oocytes (zygotes) after only a single cell division 2
46. Poisons the soil
47. Poisons the aquatic environment
48. Contaminates the food chain
49. Is linked with wildlife poisonings of eagles, bears, cougars, owls, falcons and (badger-like) fishers
50. Precipitates allergies in the respiratory tract and skin
51. Collects and concentrates heavy metal toxins in roots, stems, leaves and flowers
52. Is often contaminated with fungi, bacteria and viruses
53. Inhibits mitochondrial function
54. Inhibits mitophagy 3,4
55. Increases the rates of mortality, premature mortality and years of life lost 5-15
56. And constitutes the modern “snake oil” of an almost universally unproven remedy
57. And is a fast growing major global industry...

Cannabis!

Community Leadership

Since much of the data about cannabis is at once massive, confused, conflicted and highly technical there is a clear need for professional bodies such as RACGP, AMA, ACOG (American College of Obstetricians and Gynaecologists)^{16,17}, AAP (American Association of Pediatrics)¹⁸⁻²¹ and NIDA / NIH^{22,23} to provide leadership and assistance to the community to navigate their way through this complex morass of information fraught with mixed motives and commercial actors whose interests are divergently and radically at variance with those of the general community. In places such as Amsterdam, Colorado, Oregon, Philadelphia, parts of Egypt, Morocco, Northern India and the northern rivers district of New South Wales where widespread cannabis use scenarios and commercial interests overwhelm those of the broader community the consequences are dire indeed by every metric²⁴. According to one list Australia has at least 143 cannabis companies including several legal firms A and 43 licenced medical cannabis companies^B.

Overall Comment

The Queensland Health discussion paper²⁵ correctly highlights the dearth of clinical evidence for the myriad of indications for which cannabis is marketed in Australia. Given that the gold standard for clinical trials is the prospective randomized clinical trial (RCT), with a single exception, such evidence is notably lacking for so-called “*medicinal cannabis*”. The single group of exceptions for which randomized trials have demonstrated some role for cannabis is refractory rare forms of paediatric epilepsy of Lennox-Gastaut Syndrome (LGS), Dravet syndrome (DS) and Tuberous Sclerosis complex (TSC)²⁶⁻³¹. In fact it would not be going too far to suggest that the nomenclature of “*medicinal cannabis*” is a radical misnomer as it implies that cannabis has been medically proven and its use is therefore sound – which in general terms it is a grossly misleading and egregiously false misapprehension.

Numerous bodies have confirmed that commercialization of cannabis has far outstripped the present state of cannabinoid therapeutic research. In such a context the solution recommended by the Discussion paper of shuffling the administrative burden from one Government department to another is clearly inappropriate and serves merely to perpetuate the present health and administrative confusion.

^A 135+ Australian Cannabis & Hemp Companies | Cannaus <https://www.cannaus.com.au/companies/>

^B [List of approved medicinal cannabis cultivators and producers in Australia | Office of Drug Control \(ODC\)](#)

Historical Context

It would appear the medical cannabis was legalized in Australia by a happy triple confluence of commercial interests, populist demand from its hallucinogenic, addictive and stuporific effects and a globalized movement sponsored by the mass media to this effect. A survey of 110 million patients in USA in 2022 showed that only 4,214 (0.0038%) were treated Epidiolex (cannabidiol) and in 40% none of the forms of paediatric epilepsy for which FDA had approved the medication were present ³². Such statistics confirm the view that the original trials claiming a role as **fourth line** medication in refractory LGS/DS were an **overstatement of its importance** in the therapeutic armamentarium. Assuming a similar incidence of refractory paediatric epilepsy in Queensland with a population of 5 million people one would expect only 114 such patients. Given that Australia has 143 cannabis companies and 43 licensed medical cannabis companies it would appear that the great majority of cannabis scripts in this country are written for other indications which have not been validated by robust clinical trial evidence.

Any medication is evaluated by a risk benefit consideration. It is appropriate therefore to embark upon such an enquiry in this case.

Benefits

The sole exception to this is refractory paediatric epilepsy, often associated with profound intellectual disability, chromosomal disorders, or severe genetic abnormalities. RCT exist for Lennox-Gastaut Syndrome (LGS), Dravet syndrome (DS) and Tuberous Sclerosis complex (TSC) where cannabidiol has been shown to result in some reduction of seizure frequency of 25-50% in about 25% of patients ²⁶⁻³¹. Side effects including sedation, diarrhoea and an elevation of liver enzymes are common and are seen in 50-90% of participants. However even in such disorders its take up is remarkably low. The remarkably low patient incidence of cannabidiol scripts was mentioned above, at 0.0038% ³². The experience described in a broader literature since the publication of these original clinical trials is broadly consistent with these results ³³⁻⁴⁵. It would be fair to comment though that for its relatively mild clinical effect cannabis has been overly hyped by the mass media and its usually **fourth (or greater) line place** in the therapeutic armamentarium in this group of disorders has been substantially overstated.

Outside of this single group of indications the clinical evidence for any of the alleged benefits of cannabis is weak or anecdotal. This position has been confirmed by reviews from numerous authorities including AMA, RACGP and the group of the Director of NIDA at NIH in Bethesda Maryland Dr Nora Volkow and colleagues ²².

I run one of the largest private addiction medicine clinics in Queensland. The ONLY indication for which “medical” cannabis is prescribed in this large group of patients is to feed their long standing cannabis addiction without the interference of police. It is noted of course that in most cases patients have a “cover story” or excuse for their use which may be anxiety, depression, back pain, pain – or really virtually any real or imagined symptom – which – often enough are themselves symptoms of cannabis withdrawal or intoxication or brain or lung damage – but it only takes one or two questions to reveal the real nature of what is actually occurring.

That is to say that the effect of legalizing medical cannabis has just been to legitimate its long standing clandestine use albeit at a greatly inflated price and at a greatly elevated THC content. “*Medicinal cannabis*” far from being a misnomer, is actually just a legal fiction which effectively enables both the addiction in the patients and profiteering in the industry. As more and more classes of cannabis become subsidized by various public schemes this is actually a Government subsidized drug peddling Ponzi scheme for the primary benefit of organized business to the detriment of both the tax payer and the patients who are extorted for their generally exorbitant prices.

It should also be emphasized that the THC concentration of “*medicinal cannabis*” is much higher than the cannabis of former years. In the 1960’s 1-2% THC content by weight was common. Now it is exceptional to see cannabis products of less than 19% - 30% being logged on QScript.

It should also be noted that cannabis addiction can be treated relatively easily with just 10mg diazepam in 98% of cases. Thus cannabis use syndrome (formerly known as cannabis dependence or cannabis addiction) is NOT by itself a valid medical indication for the continued use of cannabis.

Risks

The risks and side effects of cannabis on many organ systems have been well described and well known for years ^{22,46,47}. They were highlighted by recent AMA and RACGP position papers on this subject. Key organ systems affected by cannabis include the central nervous system, upper and lower respiratory systems, endocrine system, bones, cardiovascular, immune and the reproductive systems and tracts ⁴⁷. It is worth noting here that all major psychiatric syndromes have now been shown to be linked with cannabis use including depression, anxiety, PTSD, cannabis induced psychosis, schizophrenia, bipolar disorder, suicidal thoughts and actions, and recently mass homicides. References have been presented elsewhere ^{48,49}.

A series of mass homicides have been presented from USA in ALL of which the offenders were found to have tested positive for cannabis ⁵⁰. Moreover there is also a substantial literature on cannabis and violence in several contexts ⁵¹⁻⁵⁹.

Autism

It should also be noted that there is an increasing and robust literature from Australia, Canada and USA showing that cannabis is also linked with autism and ADHD-like syndromes in children in a causal manner. This has been demonstrated in space-time geospatiotemporal studies, using the statistics of formal causal inference ⁶⁰⁻⁶⁴, by longitudinal prospective clinical cohort studies ⁶⁵⁻⁷⁵ and is supported by fMRI brain imaging studies ⁷⁶⁻⁷⁸. Many epigenetic changes have been described where prenatal cannabis exposure phenocopies autism-like epigenetic changes ⁷⁹⁻⁹¹. Autism-like synaptopathies have also been described from cannabis ^{83,92-104}. Cannabis has also been shown to alter neuroligins and neurexin epigenetically ⁸⁸ which are key synaptic structural morphogens and also strongly implicated in autism ^{102,105-109}. Cannabis has been shown to epigenetically ⁸⁸ perturb both the retinoid gradients ^{110,111} and both sides of the robo-slit ligand-receptor dyad which are some of the major factors controlling the massive forebrain outgrowth of the human rostral cerebrum ¹¹²⁻¹¹⁴. Robo-Slit is also a key dyadic pair controlling axonal (and also arterial) guidance within the brain and spinal cord ^{115,116}. Cannabis also disrupts signalling by stathmin which is a key guidance molecule also involved in axonal guidance and growth cone steering and transduction of directional pathfinding cues in outgrowing axonal projections ¹¹⁷. Cannabinoids also perturb both the neurogenesis and the differentiation of both inhibitory GABA-ergic and stimulatory glutamatergic cortical and hippocampal neurons of all types ^{1,48,64,118}. Cannabis disconnects key brain white matter tracts ¹¹⁹.

Therefore given the myriad of effects of cannabis on brain function and brain development in both the adult and developing organism, positive findings relating to severe neurodevelopmental outcomes in autism, ADHD and intellectual impairment generally must be considered expected and predictable and represent on-target neurotoxicity.



Overdose

An oft repeated but very misleading mantra is that “no one ever died from cannabis”. This is not true. There are numerous pathways from cannabis use to death including but not limited to:

- i. Mental illness – depression, anxiety, suicidal thoughts and actions, bipolar affective disorder, psychosis, schizophrenia can all lead to death
- ii. Gateway effects with death arising from drugs used secondarily for which cannabis was the gateway but not including cannabinoids at necropsy
- iii. Polydrug overdose including cannabis
- iv. Murder including mass murder – affects both perpetrator and victims
- v. Cardiac arrest from arrhythmia
- vi. Cardiac arrest from myocardial infarction
- vii. Road traffic accidents
- viii. Unemployment including homelessness
- ix. Poverty including homelessness
- x. Social isolation (exacerbated by failed relationships) including homelessness
- xi. Cancers – adult and child
- xii. Respiratory disease including chronic bronchitis, emphysema, lung cysts, asthmatic exacerbations
- xiii. Complications of congenital anomalies including chromosomal anomalies
- xiv. Accelerated aging syndromes
- xv. Acute paediatric poisonings and overdoses

Several of these merit further comment. The role of cannabis as a gateway drug to other drug use is now well established ¹²⁰⁻¹³². Cannabis is frequently found at coronial postmortem but is usually discounted. This is a major methodological error and reflects medical fashion and ignorance more than public health trends. Therefore in patients who die from heroin use, but they began their drug using career with cannabis but are negative for cannabinoids at autopsy, cannabis was a primary and earlier cause of that mortality. In decedents who die with cannabis in their system cannabis was a contributing cause of that statistic. Moreover Colorado data shows convincingly that overdoses from other drugs, like heroin, amphetamine, fentanyl and cocaine also become much more common as cannabis use becomes more widespread and is inevitably accompanied by increases in the use of other drugs.

Direct links between cannabis and deaths involving interpersonal violence were mentioned above.

Cannabis use is well known to be linked with sudden cardiac death by abrupt myocardial infarction and malignant arrhythmias. This has been documented in many reputable sources including the New England Journal of Medicine ^{46,133}.

Cancer

Our group and others have written extensively on the links shown by modern epidemiological studies between cannabis and many cancers ^{1,47,134-153}. In spatiotemporal and causal inferential analysis it was shown that cannabis was the primary driver of the 50% rise in total pediatric cancer ¹⁴⁵ which is a disorder whose prime genotoxic lesion is generally congenital or inherited ^{154,155}. It was shown that cannabis was the primary driver of the doubling in the rate of US testicular cancer which is the cause of the most years of life lost of any adult cancer ^{141,146}. We also showed that cannabis was the primary driver of recent surges in the rates of pancreatic and hepatic cancers in USA ^{89,136-138,147,156}. Cannabis was also shown to be a primary driver of rising breast cancer rates in USA which forms the commonest human cancer ¹³⁹. These findings in cancer epidemiology in USA were replicated in Europe ^{142,148,150}. We also showed in an analysis of European datasets that cannabis was a more powerful carcinogen than tobacco and alcohol, and in many analyses was more powerful than these two known carcinogens combined ¹⁴⁸.

Aging

Cannabis has now been shown to be linked with accelerated aging at once by:

- i. Clinical syndromology ¹⁵⁷,
- ii. Direct biophysical measurement of increased arterial hardening ¹⁵⁸,
- iii. Elevated premature death rate ⁵⁻¹⁵,
- iv. Its induction of hepatic fibrosis and cirrhosis ¹⁵⁹
- v. Impaired mitochondrial function (referenced above)
- vi. Endocrine suppression especially affecting the hypothalamic – pituitary-gonadal axis ^{160,161}
- vii. Elevated rates of mental illness (referenced elsewhere ^{48,49})
- viii. Cellular changes in oocytes ¹⁶²
- ix. Cellular changes in sperm ¹⁶³⁻¹⁶⁸
- x. Growth inhibition ^{1,169}
- xi. DNA breakages (referenced elsewhere)
- xii. Elevated rates of congenital anomalies (referenced elsewhere)
- xiii. Elevated rates of cancer (referenced elsewhere)
- xiv. Epigenetic derangement generally ^{85-89,170,171}
- xv. Human cellular epigenetic age ¹⁷². Indeed this last is a dramatic effect with studies showing 29% advanced of biological epigenetic age by 30 years ¹⁷² and findings that this likely increases with time as a linear and quadratic function of age ¹⁵⁸.

Paediatric Overdose

Adults do not overdose on cannabis because there are no cannabis receptors in the brain stem which controls breathing. However this is not true for children and toddlers who do have cannabinoid receptors in their brain stem. Thus cannabis can directly cause very serious respiratory depression in infants

and toddlers who not infrequently require ventilation. Whilst statistics on this are difficult to locate they are kept in Colorado and Texas. Results there show uniformly that paediatric overdose deaths rise dramatically as cannabis use spreads. A 5-fold rise in paediatric (under five years) cannabis edible overdoses was reported in Texas 2017-2023¹⁷³. The overall overdose rate doubled in Texas 2012-2023 from 7.6 to 16.3 per 100,000 residents (114% rise C). In a USA national review of adolescent overdoses based on the CDC WONDER database after a decade of decreasing adolescent overdose rates 2010-2021 states with recreational programs saw overdose rates rise 88%, 479% and 115% in 2019, 2020 and 2021 respectively¹⁷⁴. In a USA national poisons database review 2017-2021 overdoses from paediatric edible cannabis products increased from 207 in 2017 to 3,054 in 2021 an increase of 1,375%¹⁷⁵. 98% of exposures occurred at home. Overdoses became more serious across this period with more patients requiring admission to hospital. Overdoses from both THC and cannabidiol are recognized as increasingly serious and constitute a subject of increasing interest and concern for pediatric physicians¹⁷⁶.

Colorado legalized cannabis on January 1st 2014^D. A study of the overdose rate in Colorado performed from the Colorado Children's hospital in Aurora and the Regional Poisons Centre showed that the rate of paediatric overdoses increased dramatically across this period (January 1 2009 to December 31 2015) in children younger than ten, with a median age of 2¹⁷⁷. The rate of pediatric admissions to hospital doubled from 1.2 to 2.3 / 100,000 population from the two years prior to legalization to the two years thereafter demonstrating a causal relationship to the cannabis legalization event. Cannabis edibles and edible infused products were involved in half the exposures (52% and 48% respectively). Poison centre notifications for these products increased from 9 in 2009 to 47 in 2015 an annual average rise of 34% which was almost twice the rate of rise of the remainder of the USA (19%)¹⁷⁷. Poor child supervision was implicated in more than half the cases (52%) presumably because the relevant adults were likely cannabis affected¹⁷⁷. This elevated trend has continued in Colorado. Whereas in 2017 56 children younger than 5 years were reported with cannabis overdoses by 2021 this number had jumped further to 151 (169%)^E.

^C [Texas Health Data - Drug-Related Deaths https://healthdata.dshs.texas.gov/dashboard/drugs-and-alcohol/drug-related-deaths](https://healthdata.dshs.texas.gov/dashboard/drugs-and-alcohol/drug-related-deaths)

^D [Cannabis in Colorado - Wikipedia https://en.wikipedia.org/wiki/Cannabis_in_Colorado#Results](https://en.wikipedia.org/wiki/Cannabis_in_Colorado#Results) ; [Colorado marijuana legalization timeline: 10 years of notable events https://www.denverpost.com/2023/12/31/colorado-marijuana-legalization-sales-timeline/](https://www.denverpost.com/2023/12/31/colorado-marijuana-legalization-sales-timeline/)

^E [Marijuana Exposures Among Colorado Children on the Rise | NarcononUS.org https://www.narcononus.org/articles/recent-news/marijuana-exposures-among-colorado-children-on-the-rise/](https://www.narcononus.org/articles/recent-news/marijuana-exposures-among-colorado-children-on-the-rise/)

Another Colorado study found that the age groups where cannabis use rose the most was 18- 25 years (from 19% to 34% 2003-04 to 2015-2016) and older than 26 years (5% to 15% 2003-04 to 2016-2017) ¹⁷⁸. Cannabis related hospitalizations rose from 575 /100,000 in 2000 to 2,413 in 2015 (319%). Adolescent emergency room visits rose from 172 to 780 (353%). The number of suicides with cannabis present rose from 40 to 158 2004-2015 (295%) and the percentage of suicides with cannabis present rose from 2.5% to 14.6% (484%) in the similar period ¹⁷⁸. Fatal drug overdoses in Colorado rose from 1999 to 2017 for prescription opioids from 73 to 372 (409%), for methamphetamine from 16 to 298 (1,652%), for heroin from 42 to 223 (420%) and for fentanyl from 0 to 81 (over 8,000%) ^F. Children's hospital visits for cannabis overdose rose from 1 in 2009 to 36 in 2017 (3,600%) and regional poisons centre notifications rose from 9 to 67 (644%) with a marked jump across the time of cannabis legalization (from 7 to 16 and 24 to 43, 128% and 79% 2013-2014) respectively ¹⁷⁸.

These data show unequivocally that wherever reliable data exists increased cannabis use including cannabis legalization is associated with severe impacts on the weakest and most vulnerable members of the community in this case children and toddlers.

Genotoxicity

The outcomes of genotoxicity are well established to be congenital anomalies (birth defects), cancer formation and aging. Moreover many lines of evidence indicate that such genotoxic damage can be transmitted intergenerationally for at least four generations i.e. the next 100 years! ¹⁷⁹ This is a major issue with cannabis and all cannabinoids albeit it is not widely understood, discussed or considered.

Cannabis and Δ^9 -THC has long been known to inhibit the synthesis of DNA, RNA and proteins ^{2,180-192} starting from 15 minutes after cannabis administration ^{189,193}. For the psychoactive metabolite 11-hydroxy- Δ^9 -THC (THC-COOH) this effect begins just five minutes after administration ^{189,193}.

Moreover many cannabinoids are known to induce single and double stranded DNA breaks directly ¹⁹⁴⁻¹⁹⁹. Indeed cannabis has long been known to test positive in the micronucleus assay which is a standard test for genotoxicity ^{152,198,200}. Micronucleus formation is a very serious genotoxic event with extremely serious downstream sequelae for cells, organs and organisms ²⁰¹⁻²¹⁰. A PubMed search reveals that cannabis is now linked with epigenomic disruption in over 200 studies (207 hits; PubMed Entrez search conducted January 26th 2025). This is most commonly studied by alteration in patterns of DNA methylation. Not only is the epigenome disrupted and disorganized but

^Fco_poisoning_deaths_1518prov_qtr.xls - Google Drive <https://drive.google.com/file/d/1vfi4kL9eD9rib7aEboteiGw67gOxXFpf/view>

so too are the critical readers, writers and erases of the epigenomic machinery including DNA methyltransferases 3 A and B, and TET1. The basic machinery of mitosis is grossly disrupted and disorganized by cannabis including proteins in the chromosomal centromeres, the kinetochores which bind the centrosomes to the mitotic spindle and even the tubulin which forms the microtubules of the mitotic spindle itself

¹⁶⁹. Thus cannabinoids disrupt all aspects of basic cell function.

Epigenetic disruption also extends to the histone proteins which package DNA inside the cell nucleus. DNA inside chromosomes in cells is wound around a core octamer of nucleosomal proteins which control which genes are made available to the transcription machinery and so determine cell type, cellular (neural, immune and metabolic) memory and a myriad of other key cellular functions. Many workers have shown that cannabis disrupts histone formation necessarily disrupting the epigenome ^{189,211}. Indeed extensive disruptions of histones themselves, and therefore necessarily the histone code, was described in detail 30 years before the epigenome was even discovered ¹⁸⁹. In the case of sperm heads this disorganization is so massive as to be very obvious at electron microscopy ²¹². Obviously the implication of the sperm head in this issue raises the clear and present danger of transgenerational transmission of major indices of genotoxicity.

Olivetol - The Nucleus of All Cannabis

Importantly several studies now link this genotoxic effect with olivetol which is the C-ring nucleus structure common to all cannabinoids ^{2,213-219}. Thus all cannabinoids, including cannabidiol, cannabinol, cannabigerol, cannabichromene and all the congeners of Δ^1 -, Δ^6 -, Δ^7 -, Δ^8 -, Δ^9 -, Δ^{10} -, Δ^{11} -tetrahydrocannabinol are implicated. This becomes important from a regulatory point of view as it has been common practice around the world to legislate for control of Δ^9 -THC levels whilst leaving the concentration, dose and amount of other known genotoxic cannabinoids, unregulated. This is counterfactual and counter-evidentiary.

Mitochondria

It should also be understood that many cannabinoids have long been known to inhibit mitochondrial function ^{164,220-236}. Mitochondria possess all of the cannabinoid receptor and transduction machinery found in the plasma membrane of the cell ^{234,237-243}. Moreover they concentrate lipophilic cannabinoids in their convoluted internal membrane structure in a manner which increases at least three-fold over time ^{2,212,244-246}. Mitochondria cluster around the nucleus as many of the processes of genome maintenance and transcription require energy. Mitochondria communicate with the nucleus via energy supply (as ATP), the supply of epigenomic substrates and via mitonuclear stress signalling pathways ²⁴⁷. It is important to appreciate that

many of the epigenetic substrates and cofactors arise from mitochondrial intermediate metabolism. Thus inhibition of mitochondrial metabolism necessarily perturbs and disrupts genomic and epigenomic function mandatorily.

It is also important to observe that whereas mitochondria are gathered around the normal cell nucleus to supply it with energy and cofactors for maintenance of the genome and epigenome, this similar clustering behaviour around the micronuclei (generated by cannabinoid interference with the normal machinery of cell division and the consequent induction of chromosomal mis-segregation) generates oxygen free radicals which mediate the rupture of the micronuclear membrane and catastrophic shattering of the micronuclear chromatin ²⁰⁸⁻²¹⁰ inducing the genomic disaster of chromothripsis in the primary genome which is known to lead to major genotoxic outcomes including aging, the genesis of highly aggressive cancers, mental retardation



and congenital anomalies in offspring and frequently cell death²⁴⁸⁻²⁵¹. Far from being merely of theoretical interest, epidemiological evidence of chromosomal mis-segregation and deletion was found to be related primarily to cannabis exposure in human studies of both American and European paediatric populations^{135-138,252}.

Similarly the epigenome controls sites of DNA breakage due to genomic disruption and controls DNA repair and DNA availability for such key functions as DNA transcription and replication²⁵³⁻²⁶¹. In reciprocal manner the genome controls the epigenome as its genes provide the biological substrate from which the machinery of the epigenome is transcribed¹⁶⁹.

This leads to a key biological insight, namely that the genome-epigenome-mitochondrial mass are intimately, intricately and interdependently interrelated by myriad pathways and need to be considered and understood to function in a coordinated manner to control gene expression, cell phenotype, lineage commitment, aging and cell functions. Since the study of each of these layers of gene control necessarily requires different assays, tests and biometrics it is important always to appreciate that they are not separate but in fact different aspects of an intricately and intimately interconnected elegant and extremely sophisticated cellular regulatory network. This implies that to admit that cannabinoid mitochondriopathy is significant necessarily implies significant cannabinoid induced genotoxicity and cannabinoid induced epigenotoxicity. And by extension similar reciprocal concerns relate to cannabinoid genotoxicity and epigenotoxicity also.

Aging

Aging is widely understood to be the universal fate of all cells and all life forms. Radically transforming this general misperception is the recent demonstration of reversal of cellular and organismal aging by the use of stem cell factors by several leading research groups²⁶²⁻²⁶⁷. As noted above aging is one of the principal clinical stigmata of genotoxic lesions.

In a brilliant series of studies in a scientific *tour de force* the Sinclair laboratory from New York and their collaborators showed that the induction of just ten DNA breaks would cause the epigenome to rearrange itself to direct DNA repair at the breakage sites and that this epigenomic rearrangement then greatly accelerated the normal aging process²⁶⁸. Using stem cell reprogramming factors they were then able to reverse the epigenomic aging processes of cells including causing eye damage from optic nerve crush trauma, glaucoma and cataract to reverse and partially heal^{263,268}. They were also able to reverse female ovarian aging in a mouse model of chemotherapy

induced ovarian aging by dietary supplementation with nicotinamide mononucleotide to supplement cellular mitochondrial and nuclear levels of the critical metabolic co-factor nicotinamide adenine dinucleotide (NAD⁺)^{269,270}. Ataxia telangiectasia syndrome is a severe genetic disorder of deranged DNA repair characterized by increased DNA breaks and premature aging, senescence, many cancers and death. In mouse and worm models of this disorder they were able to show that nicotinamide supplementation improved mitochondrial function, mitophagy and DNA repair²⁷¹. The work elegantly demonstrated the mechanistic convergence of the interrelationships between genome and mitochondrial balance through the mitonuclear communication described above. This dual relationship was further confirmed by the use of nicotinamide supplements to support defective mitochondrial metabolism due to a failure to generate some of the mitochondrially encoded oxidative phosphorylation components in a sirtuin-1- and hypoxia inhibitory factor (HIF)-dependent manner thereby inducing a pseudohypoxic metabolic state which mimicked the warburg effect²⁷².

A clear conceptual understanding of this aging pathophysiology is of obvious relevance to the cellular and organismal pathophysiology induced by all common cannabinoids as they are concentrated in mitochondrial membranes and matrix and disrupt all three principal axes namely the genome, epigenome and mitochondrial compartments.

Given therefore that:

- i. All cannabinoids are implicated in these processes
- ii. Each layer is now very well documented
- iii. These effects may persist through genetic and epigenetic inheritance to multiple generations and
- iv. Cannabinoids typically persist in cell membranes for many months in chronic users
- v. Exacerbation of aging processes alone is common and ubiquitous and likely dose related
- vi. Bystander effects can occur through secondary and tertiary exposures

the conclusion becomes inescapable that the community has a major issue with cannabinoid related genotoxicity-epigenotoxicity-mitochondriopathy resulting from widespread cannabis usage, which can only be framed as a public health disaster.

Food Chain Contamination

International Experience

USA

California is said to have 6,881 registered cannabis farms ^G and likely more than ten times that number of unofficial illegal grow sites ^H. Local law enforcement is overwhelmed at the scale of the challenge ²⁷³. Much of this new industry is concentrated in the rural north of the states in counties such as Shasta, Humboldt, Siskiyou, Mendocino, Butte and Trinity. Much has been written about environmental contamination by the pesticides commonly used to protect these crops and the effects of downstream contamination on small rodents and the higher predators which eat them including owls, bald eagles, bears, cougars and fishers (like badgers) ²⁷⁴⁻²⁷⁸. Much has been written on the agricultural risks posed by cannabis farming including viral ²⁷⁹, bacterial ²⁸⁰⁻²⁸⁴ and fungal ²⁸⁴⁻³⁰¹ infections the accumulation by the plant of heavy metals ^{284,302-314} and the excessive use of precious water resources in a frequently dry climate endangering aquatic habitats and fisheries ³¹⁵⁻³¹⁹.

Cannabis farms are known to use a lot of water for their rapidly growing crops which in large operations mature twice a week. It must therefore be considered that this water will run off from such plantations carrying in it concentrations of cannabinoids. Although these are known to be generally lipid soluble they will likely be carried on carrier molecules such as lipid droplets and organic debris which might be caught in such effluent in suspension.

Indeed this is such a problem that the Californian Water Resources Control Board has established rules and guidelines in an effort to control this issue and protect the natural water resources ³²⁰⁻³²². Indeed it has also been shown that the concentrations of cannabinoids which are measured in Californian waterways can be detected in offshore molluscs and have been shown to be genotoxic at these concentrations to multicellular model organisms ^{323,324}.

Quantities of cannabinoids have also been measured in the rivers of Canada ^{325,326} and in the Great Lakes region ³²⁷. THC is metabolized in the liver first to hydroxy-THC (THC-OH) which is still psychoactive ³²⁸ and then to the carboxy derivative 11-nor-9-carboxy- Δ^9 -tetrahydrocannabinol (THC-COOH). Concentrations of THC-COOH have been measured as high as 12.5 ng/L in the soluble phase of the influent going into sewerage treatment works.

^G [Cannabis cultivation licenses, by state U.S. 2022 | Statista https://www.statista.com/statistics/1108194/cannabis-cultivation-licenses-by-state-us/](https://www.statista.com/statistics/1108194/cannabis-cultivation-licenses-by-state-us/)

^H [Reality of legal weed in California: Illegal grows, deaths - Los Angeles Times https://www.latimes.com/california/story/2022-09-08/reality-of-legal-weed-in-california-illegal-grows-deaths](https://www.latimes.com/california/story/2022-09-08/reality-of-legal-weed-in-california-illegal-grows-deaths)

Importantly they calculated distribution coefficients of 1,052 ng/L with particulate matter and 35,000 ng/L with organic matter for THC ³²⁶. These authors detected THC-COOH at 1 ng/L in drinking water. From such data the authors were able to report average levels of cannabis use by residents of a small Canadian rural town of 53 mg/day/1,000 inhabitants respectively ³²⁶.

One review reported levels of THC-COOH as high as 2,590 ng/L in urban city wastewater effluent which fell to 169 (96.5%) in treated wastewater effluent ³²⁵. Chlorine used in waste water treatment plants and swimming pools was shown to generate chlorinated and oxygenated breakdown products of THC-COOH which are more toxic than THC, THC-COOH or even registered solvents and disinfectants ³²⁵. Thus swimming pools were described as being a likely source of transdermal exposure to cannabinoids. Levels of 79.9 ng/L THC-COOH were found in surface water and 1 ng/L in drinking water. The salient point is made that in 2017 that Colorado consumed 187 tons of cannabis and in 2018 Canada used 370 tons all of which is subsequently released into the environment ³²⁵.

A key question relates to the transferability of dietary cannabinoids into animal products. A very worrying paper was published on this point in Nature Food which demonstrated that 20% of dietary THC and 11% of dietary cannabidiol were bioavailable in the milk of dairy cows fed cannabis stalks ³²⁹. Worryingly this feed was derived from designate industrial *hemp* plants which were claimed to be low in THC content. The cannabinoid concentration of the silage feed was 1,254, 8,304, 39 and 450 mg/kg dry matter of Δ^9 -THC, cannabidiol, cannabinol and cannabidivarin respectively. Cows were fed 1mg/kg Δ^9 -THC during an initial one week adaptation period. Average ingested doses were 1.6 and 10.7 mg/kg and 3.1 and 20.4 mg/kg of Δ^9 -THC and cannabidiol in the low and high dose exposure groups respectively each for one week. Such doses resulted in steady state levels of Δ^9 -THC and cannabidiol after low- and high- dose exposures of 100 and 370, and 380 and 800 μ g/kilogram of milk respectively. It was further observed that cows given this feed would appear sedated, almost asleep on their feet, would freeze their motion in time, would stop chewing and would appear to have an unsteady gait and be apparently giddy and “stoned”. Treated cows fed less. Their milk yields dropped from 25 L/day to 19.8 L/day ³²⁹.

One week after hemp feeding Δ^9 -THC and cannabidiol were still detectable in the milk at 5 and 16 μ g/kg respectively in the high dose group ³²⁹. Both Δ^9 -THC and cannabidiol accumulated in the milk and were concentrated to levels 6-26 and 11-32 times those found in the plasma respectively.

For humans younger than 18 years it was found that consumption of milk from the low dose period would results in plasma levels exceeding the safe dose (known as the Average Reference Dose over 24 hours, ARfD) by a factor of 14 for average consumers but by 57-fold for high milk consumers ³²⁹. For all demographic and population groups it was found that consumption of milk from the period of high hemp exposure would results in levels exceeding the

ARfD by 120-fold. It was further shown that consumption of such cannabinoid contaminated milk could result in humans exceeding the ARfD in infants with high milk consumption even during the preliminary adaptation period ³²⁹.

It was also shown that the usual methods (gas chromatography with flame ionization detection, GC-FID) defined by official EU Government sources (Annex III Regulation EU Number 639/2014) for estimation of the cannabinoid content of the milk samples were incorrect in their readings as compared to state of the art techniques (high performance liquid chromatography coupled to tandem mass spectroscopy, HPLC/MS) by a factor of up to seven-fold ³²⁹. This becomes very important given that hemp is defined as having a THC content of 0.3% dry weight by the US Farm Act and 0.2% in the EU. If this level is in error by seven-fold then serious consequences may ensue, particularly given the build up of cannabinoids in milk and in human fatty tissues including brain and gonads.

Atrial Septal Defect in USA

We reported in 2016 about a curious phenomenon in USA in relation to atrial septal defect secundum type (ASD) which is its commonest form ³³⁰. At a time when the background rate of ASD in the was around 20 /10,000 births a group of states with a higher ASD rate appeared to be emerging. At the time this seemed troubling and concerning to us although the full explanation was not apparent at that time. Most concerning of all was the state with the highest ASD rate, namely Kentucky. We have since understood that Senator Mitch McConnell, in 2018 the Senate majority leader, was from that state and was a powerful champion of the USA Agricultural Improvement Act (commonly known as the “Farm bill”) at that time ³³¹. Whilst this bill was aimed to assist USA farmers Senator McConnell is said to have organized for the last minute insertion of clauses about cannabis and hemp which allowed and encouraged farmers exiting the tobacco industry to transfer to hemp cultivation. However these clauses are said to be so poorly written as to make their enforcement by the various Federal agencies almost impossible ³³¹. The massive USD\$867,000,000,000 budget of this bill provided powerful financial sponsorship to stimulate this transition into cannabis farming making cannabis cultivation a Federally sponsored industry ³³¹. This bill has been cited as the proximate cause of the flourishing USA cannabis farming industry and may have been a deliberate ploy by its sponsors ³. Kentucky was therefore

¹<https://www.degruyter.com/document/doi/10.1515/jdpa-2020-0006/html>

²Mitch McConnell's Cannabis Gambit: How The Farm Bill Unwittingly Fueled A THC Boom - Benzinga <https://www.benzinga.com/markets/cannabis/24/05/35598477/mitch-mcconnells-cannabis-gambit-how-the-farm-bill-unwittingly-fueled-a-thc-boom>

amongst the first to take advantage of these provisions and cannabis farming has since burgeoned in this state. Since then ASD became 15 times more common than elsewhere in the USA and the then reported rate across all races was 295.

Four year time span (thus quadrennial) data has since been released from the US National Birth Defects and Prevention Network (NBDPN)³³². Nevada has since supplanted Kentucky as the leading state for ASD. The history of cannabis in Nevada is decriminalization in 2001 (Assembly Bill 453), medical cannabis allowed in 2013 (Senate Bill 374) and full legalization began January 1st 2017 following a state ballot^K. For the 2016-2020 quadrennium Nevada reported an ASD rate of 773 across all races and 850 amongst African Americans. Kentucky's rate in this later period was 333 in all races and 568 amongst African Americans. ASD rates amongst African Americans in Louisiana and Kentucky in the 2012-2015 period were 867 and 466 respectively. ASD rates amongst American Indians / Alaska Natives for Nevada, New Mexico, Alaska and Kentucky in 2016-2020 were 595, 349, 296, and 276 respectively. In the 2012-2015 quadrennium rates in Mississippi, Kentucky, Oregon, Ohio, Alaska and Nevada in all races were 739, 357, 316, 267, 252, and 190. Cannabis has been legalized in Oregon, Nevada, and Alaska^L.

This data may be compared with data from the USA National Survey of Drug Use and Health which showed that past month cannabis use in the over 26 years age group across the period from 2008-2009 to 2018-2019 rose from 4.42% to 9.39% nationwide ($P < 0.001$), from 4.63 to 9.78% in the northeast ($P < 0.001$), from 5.56% to 12.49% in the west ($P < 0.001$) and from 4.14% to 8.74% in the Midwest. In this period last month cannabis use tripled in Nevada from 7.74% to 22.04% ($P < 0.001$) and rose significantly in Colorado (7.31% to 15.62%, $P < 0.001$), Oregon (7.11% to 17.49%, $P < 0.001$), Mississippi (3.15% to 6.65%, $P = 0.003$), Alaska (9.3% to 16.25%, $P = 0.37$), Kentucky (3.40% to 6.42%, $P = 0.20$), Louisiana (3.27% to 8.71% ($P = 0.015$), New Mexico (4.49% to 10.99%, $P = 0.001$), Washington (5.53% to 16.54%, $P < 0.001$) and Vermont (7.75% to 17.11%, $P = 0.002$)^M.

The real significance of this ASD data is that early termination of pregnancy for anomaly (ETOPFA) is not practised for this congenital anomaly. The simple reality is that if serious anomalies were becoming more common across USA we would really not be aware of it since there are relatively limited longitudinal

^K <https://nevadastatecannabis.org/laws>

^L [Here's a Map of the U.S. States that Legalized Weed – HeyHelloHigh | Cannabis lifestyle for modern women https://heyhellohigh.com/2018/02/21/map-of-the-uss-states-that-legalized-weed-cannabis/](https://heyhellohigh.com/2018/02/21/map-of-the-uss-states-that-legalized-weed-cannabis/)

^M [Comparison of 2008-2009 and 2018-2019 Population Percentages \(50 States and the District of Columbia\) | CBHSQ Data https://www.samhsa.gov/data/report/comparison-2008-2009-and-2018-2019-nsduh-state-prevalence-estimates](https://www.samhsa.gov/data/report/comparison-2008-2009-and-2018-2019-nsduh-state-prevalence-estimates)

data relating to ETOPFA practices by congenital anomaly type. If the real situation is that many congenital anomalies are increasing in the trajectory followed by ASD then the real state of neonatal epidemiology must be very dire indeed.

This parabolic increase in ASD rates exceeds even the now well documented exponential rise in the cannabis – autism link which has been demonstrated at both the epidemiological and mechanistic epigenetic levels ^{60-62,64,80,85,86,90,333-346}.

Amelia in France and Germany

The major limb defects of amelia (no limbs) and phocomelia (flipper limbs) have been shown to be linked with cannabis use in both experimental animals ³⁴⁷⁻³⁴⁹ and in human epidemiological studies ^{142,350-357}. Detailed pathophysiological studies ^{88,116,358} provide possible and likely mechanistic bases for these observational findings ^{1,351-353,359,360}.

The case of a recent outbreak of major limb defects in the province of Ain on the eastern edge of France on the Swiss border, and also in the Normandy region of France is of particular interest ³⁶¹. It was reported that the epidemiologist Emmanuelle Amar notified seven cases of amelia (limblessness) and phocomelia (flipper limb) in Ain about October 22nd 2018 which took the standardized incidence of this major defect to 60 times background ³⁶¹. The parents were known to live on communes in fields of sunflowers and corn ³⁶¹. Environmental factors were suspected. On October 18th 2018 a major drug haul of 135kg of cannabis resin was made in the region of Ain ³⁶². The seizure of so massive a quantity of concentrated cannabis product in this region implies significant drug use or perhaps production in the area. Just a few months earlier in June 2018 it was reported that a mayor in the southwest of France made application to the President of France to grow crops of legal cannabis ³⁶³. This raises the very real possibility that the cases identified in France, which is reported to have amongst the highest rates of cannabis use in Europe ³⁶³ may have been associated with cannabis consumption, cannabis cultivation on the communes or potentially cannabinoid environmental contamination. In response to this report the French Government launched an enquiry - and terminated Dr Amar's employment ³⁶⁴. More recently (2023) it is possible to find advice online about the best strains of cannabis to grow in the region of Ain ³⁶⁴.

A midwife in a hospital in Germany reported three cases of major limb defect in her institution ³⁶⁵. As a result enquiry was made and over 30 more cases were identified. However as Germany has no national register of birth defects both the regional rate and the time trend of such major anomalies cannot be determined. It is known that cannabis use is becoming much more common in Germany and medical use was allowed from April 1st 2024³⁶⁶.

Australia.

A significant cannabis operation is located at Caboolture north of Brisbane. At present it has 2,950 square meters under cultivation, harvests biweekly and produces 10,000 kg of cannabis annually. Plans are to double this in 2025 ^N. Another large grow site which is described as a \$400 million venture, is being built in Toowoomba by Asterion Cannabis including a 40 hectare glass house aiming to produce 500,000kg annually with a value on the export market exceeding \$1billion annually ^O. The hemp building company based in Victoria builds houses from hemp, advises that its products are non-toxic, and markets “hempcrete” a mixture of hemp fibre and lime used like concrete for walls and similar structures ^P.

Toowoomba is located close to the headwaters of the Condamine river which flows into the Murray-Darling Basin. The Murray is Australia’s largest waterway. Both the Murray and the Murrumbidgee river are heavily used for irrigation. In Australia’s dry climate it often does not flow in its lower reaches but is reduced to a series of water holes. This implies that any cannabinoids emanating from Australia’s enormous grow sites would become more concentrated as the amount of available water declines.

In 2014 Australia’s richest person Gina Rinehart bought Bannister Downs Dairy in Northcliffe Western Australia. A state of the art creamery was built there in 2018 ^Q. The northern rivers area of New South Wales is a well known centre for alternate culture and cannabis cultivation. Gina Rinehart bought the 1918 hectare dairy farm there in 2023 called Split Rock Dairy. It was converted to Wagyu beef production which is a high end beef product commanding high prices on the international market ^R. In 2019 Ms. Rinehart invested \$15 million

^N <https://www.cannaus.com.au/companies/spring-sciences/>

^O [Australia's biggest medicinal marijuana farm to be built in Queensland's conservative garden city - ABC News https://www.abc.net.au/news/rural/2021-04-15/australias-biggest-medicinal-cannabis-farm-toowoomba/100070770](https://www.abc.net.au/news/rural/2021-04-15/australias-biggest-medicinal-cannabis-farm-toowoomba/100070770)

^P [The Leaders In Hemp & Lime Construction https://www.thehempbuildingcompany.com.au/](https://www.thehempbuildingcompany.com.au/) Viewed 02.02.2025.

^Q [Our Partner | Bannister Downs Dairy https://bannisterdowns.com.au/about-us/partnerships?utm_source=chatgpt.com](https://bannisterdowns.com.au/about-us/partnerships?utm_source=chatgpt.com)

^R https://www.weeklytimesnow.com.au/subscribe/news/1/?sourceCode=WTWEB_WRE170_a&dest=https%3A%2F%2Fwww.weeklytimesnow.com.au%2Fproperty%2Fgina-rineharts-hancock-agriculture-purchases-split-rock-dairy%2Fnews-story%2F13713d5bbe523932aae0adf88fbcbee2&memtype=anonymous&mode=premium

in Little Green Pharma, an Australian medical cannabis company, for a capital raise aiming at penetrating the emerging cannabis market in Denmark and the EU [§]. The site included 21,500m² for cultivation and 4,000m² for post-harvest manufacturing aiming to produce 12,000kg cannabis flower annually and comprised Europe's largest cannabis production facility. Little Green pharma also has a large cannabis production facility in the Margaret river area of Western Australia [†]. Margaret river is a major centre for alternative lifestyle and hosts large cannabis farms [‡]. Margaret River is 164 km from Northcliffe where the beef cattle are raised. In both regions there may be concerns that the feed of the cattle may be contaminated from cannabis grown in the nearby vicinity.

Two major papers were released in 2011 from the International Birth Defects Surveillance Research and Clearing House, which is the major international collaboration of the birth defects registries relating to major limb defects of phocomelia (flipper limbs) and amelia (no limbs ^{367,368}. The only city in the world which was at the top of both incidence tables was Melbourne, Victoria. This is intriguing as Melbourne has a large immigrant population from many nations in Europe and Asia, none of which report high incidences of major limb defects. A simple google search reveals that the city is surrounded by cannabis farms. One Victorian cannabis farm is a \$160million dollar project and another is a \$184million dollar project [¶]. Australian Primary Hemp based in Geelong grows and markets cannabis for food products ^{¶¶}.

The most famous Victorian amelic patient is Nick Vujicic who is tetra-amelic and is an internationally renowned motivational speaker [×]. At the time of his birth (December 1st 1982) no one in his family had this problem [¶]. His parents were very conservative and were church pastors. It is therefore unlikely that any known drug exposure occurred gestationally. Nick is now married and has four children. His children have all 16 limbs. Nick's parents were advised at the time of his birth that no genetic factor was implicated in the

[§] <https://investlittlegreenpharma.com/site/about/company-overview>

[†] <https://www.abc.net.au/news/rural/2020-08-01/buy-local-trend-during-coronavirus-medicinal-cannabis-demand/1251533>

[‡] [How To Grow Hemp In Australia - Growing Hemp In Our Great Country | Margaret River Hemp Co](#)

[¶] [Revealing where cannabis is growing in Australia | Cannaus](#) <https://www.cannaus.com.au/national/where-cannabis-is-growing-in-australia/>

^{¶¶} [Australian Primary Hemp | ASX-Listed, Hemp Retail | Cannaus](#) <https://www.cannaus.com.au/companies/australian-primary-hemp/>

[×] [Home - Nick Vujicic](#) <https://nickvujicic.com/>

[¶] [Nick Vujicic - Wikipedia](#) https://en.wikipedia.org/wiki/Nick_Vujicic

aetiopathogenesis of his condition ^z. Together these factors point towards some environmental factor operating around the time of his conception or gestation which may have interfered with limb development.

Cannabis disrupts many major morphogens which together orchestrate and control body patterning and limb development ³⁵¹⁻³⁵³. The arm buds form at days ²²⁻²⁴, and leg buds form at days ²⁴⁻²⁶ of gestation ¹¹⁶. It is therefore possible that some external teratogen may have been introduced at this period to interrupt and truncate limb development. Cannabis has been linked with amelia both by animal studies ³⁴⁷⁻³⁴⁹ and several epidemiological studies in humans ³⁵⁰⁻³⁵³. In particular Δ^9 -THC and cannabidiol have been shown to directly interrupt sonic hedgehog which is one of the major body morphogens and is critically involved in limb formation ³⁵⁸. Cannabis has also been shown to interfere with sonic hedgehog expression epigenetically ^{169,351-353}. Cannabis has also been shown to disrupt many morphogen gradients including bone morphogenetic proteins ³⁶⁹⁻³⁷¹, retinoic acid ³⁷²⁻³⁷⁴, Wnt signalling ³⁷⁵⁻³⁸⁰, fibroblast growth factor ^{381,382}, and sonic hedgehog ³⁵⁸. It therefore becomes easy to see how gradient disruption at critical periods might interfere with this delicately balanced and finely choreographed sequential and orchestrated process.

Thalidomide

Although this is only one case it is interesting to recall that awareness of the thalidomide birth defect disaster was triggered by just three cases of the gestational use of thalidomide by nursing Sister Pat Sparrow who alerted the Dr William McBride to the effect ^{AA}. An early report to Lancet in 1962 referenced just five similar cases ³⁸³. That was the starting point from which the modern drug regulatory regime emerged with a remarkably uniform emphasis on safety and genotoxicity testing trans-jurisdictionally and internationally ^{384,385}.

Relevantly it has recently been shown that in fact cannabis shares 12 of the 13 described cellular mechanisms with thalidomide and 22 of its 33 described congenital anomalies ³⁵⁶.

^z Vujcic N. "Life without Limits: Inspiration for a Ridiculously Good Life." DoubleDay Press 2010.

^{AA}

https://www.bing.com/images/search?view=detailV2&ccid=dmXSxVXP&id=10B730540B48C3CB8455CCA9_F20BC893F7BDE0A5&thid=OIP.dmXSxVXPCAV3X4mUEslgHaEK&mediaurl=https%3a%2f%2fi.ytimg.c om%2fvi%2fUeglNxQ5gwg%2fmaxresdefault.jpg&exph=720&expw=1280&q=Thalidomide+scandal&simid=

Indeed in its context, given this well defined literature it must be surmized that the advocates and commercial entrepreneurs driving the present cannabis tsunami are well aware that cannabinoids are profoundly problematical in terms of genotoxicity and epigenotoxicity assays which is why they need cannabis legalization laws as a workaround to circumvent the global safeguards and systems which have been set in place to prevent a recurrence of exactly this nightmare of the widespread popularization of a hazardous known genotoxin.

Conclusion

It goes without saying that such food chain contamination occurs without population knowledge or consent. This removes the free choice from any supposed "*right to use drugs*" since the right not to be exposed to cannabinoids is removed from the target population. This includes such vulnerable populations as pregnant women, nursing mothers, the very old, the very young, the mentally ill, those allergic to cannabinoids or those suffering from virtually any chronic disease. Moreover given that cannabinoids and their congeners are known genotoxins and epigenotoxins with effects active for at least four generations not only is the target population's health degraded but so too is that of several subsequent generations yet to arrive.

In such a situation it becomes impossible to avoid the conclusion that cannabis is an unequivocal public health disaster and environmental catastrophe of the highest magnitude with multigenerational impacts.

Given the very limited number of clinical trials for various rare forms of pediatric epilepsy, and very low rate at which such prescriptions are issued in USA it becomes impossible not to conclude that cannabis is the completely unjustified modern "*snake oil*" of today. What is different about this is that its genotoxic risks have been known since at least 1969. Its epigenotoxic risks to histones have been known since 1976 which is well before the mechanics of the epigenome were themselves explicated.

It becomes impossible therefore not to conclude that the society broadly has succumbed to the seduction of the sedative - euphoric activities of this hallucinogen. The above review has been limited by time and space as I was only allowed ten days for its preparation. However it has been sufficient to document that the risk: benefit equation for cannabis is very different to its popularly understood air brushed public image as a "*soft drug*". "*Soft*" is not an appropriate appellation to summarize the trail of destruction and woe outlined in the above commentary and the pages of references which follow.



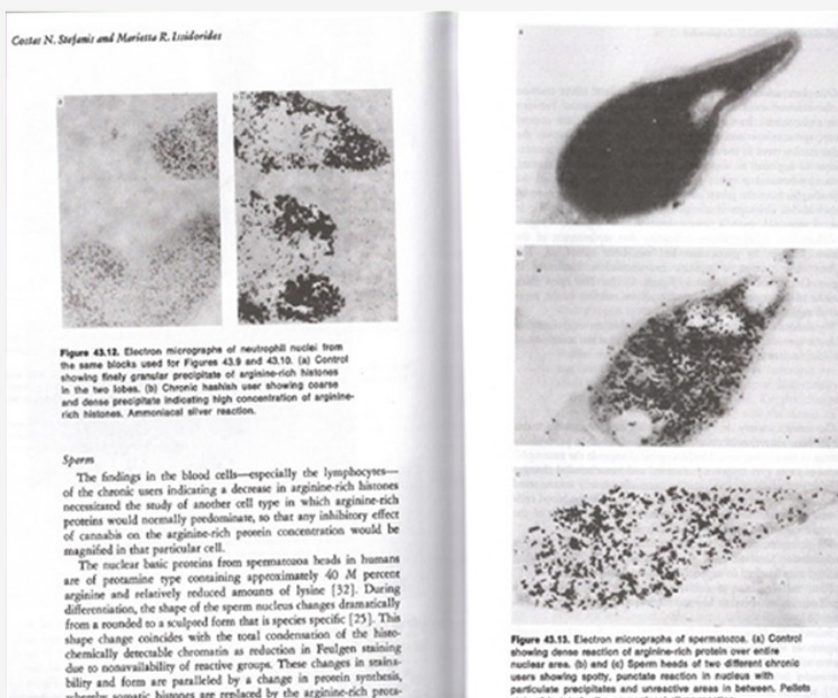
What is urgently needed is for the medical profession to sound the alarm bells of the culture much better than we have done hitherto. Our professional organs such as RACGP and AMA provide excellent routes for just this complete with wide open exposure in the mass media. Should we instead succumb to either the siren voices of chemical seduction and enslavement or commercial or community pressure we will have failed in our professional and fiduciary duty to the communities we serve and to their offspring to come for several generations; and makes us complicit in their egregious wholesale betrayal. To allow the continued desecration and denudation of our human, genetic, epigenetic, psychological, reproductive, social and natural environments is a great professional and moral crime against all seven.

This we must not do.

We were told.

Our Duty now and the higher call of Honour is to tell all; community education as a matter of the highest urgency is now our imperative and emergent priority.

Human Sperm Head Histone Assay, 1976



Human Neutrophils

Human Sperm Heads

Stefanis C.N. & Issidorides M.R. (1976) "Cellular Effects of Chronic Cannabis Use in Man"
 In Marihunana: Chemistry, Biochemistry and Cellular Effects Vol. 1
 (eds Nahas G.G., Paton W.D.M., & Idanpaan-Heikkla J.E.) Chapter. 43, 533-550 (Springer-Verlag).

Human Sperm Head Assay, 1999

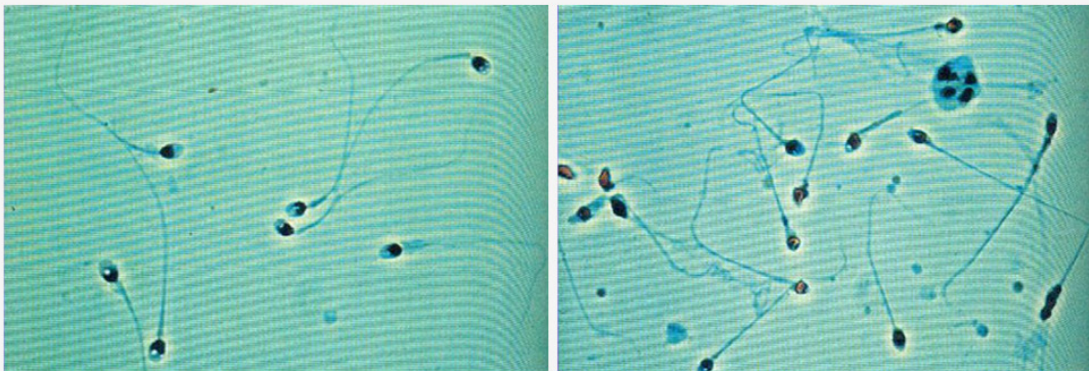


Fig. 8. Top: Normal ovoid shape human spermatazoa sampled from tobacco smoker and moderate alcohol drinker. Bottom: Nonovoid and immature form present among ovoid shape human spermatazoa sampled from daily marijuana smoker.

Hembree W.C. Nahas G.G., Zeidenberg P., Huang H.F.S. Changes in Human Spermatozoa Associated with High Dose Marijuana Smoking.
In: Nahas G.G. SKM, Harvey D.J., Agurell S., ed. Marijuana and Medicine.
Totowa, New Jersey: Humana Press; 1999:367-78

Oocyte - Chromosomal Damage, 1984

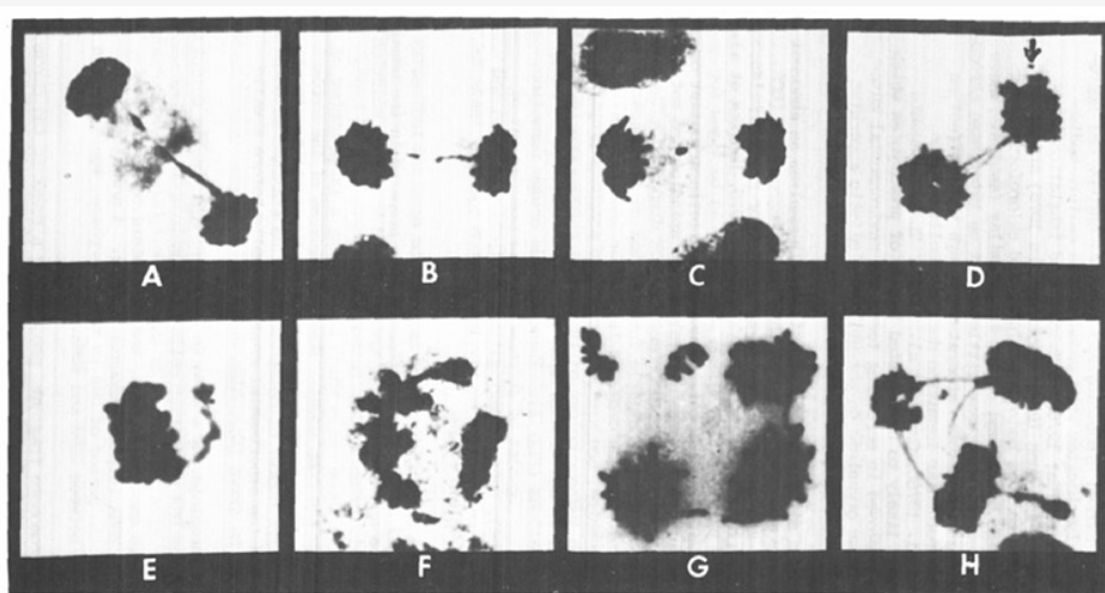


Figure 1. Errors of chromosome segregation (ECS). From Henrich et al. (1980). (A) Anaphase bridge. (B) Severed bridge. (C) Anaphase lag. (D) Micronucleus (arrow) and multiple bridges. (E) Chromosome out of phase with others in metaphase. (F) Unequal segregation in bipolar division. (G) Multipolar division. (H) Multipolar division and bridges.

Effects of cannabis and natural cannabinoids on chromosomes and ova

A Morishima

NIDA Res Monogr. 1984;44:25-45.

In vitro induction of segregational errors of chromosomes by natural cannabinoids in normal human lymphocytes

Environ Mutagen. 1980;2(2):139-47. doi: 10.1002/em.2860020206.
R T Henrich, T Nogawa, A Morishima

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