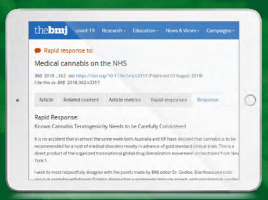
The Genotoxic Portfolio of Cannabis –The Growing Research

Coalition of Alcohol and Drug Educators
Dalgarno INSTITUTE

/DALGARNOSNB
NOBRAINER_DRUGS
DALGARNOINSTITUTE.ORG.AU

The genotoxicity of Cannabis has long been suspected, even acknowledged, be it only in part. Research over the last 5 to 10 years has confirmed the case. Much of this important research has been 'buried' in the deluge of 'hopeful' and even spectacular claims of the potential therapeutic capacity of cannabis. Claims and promises that have persisted for well over 20 years, yet with little to nothing to show for it. However, the harms associated with the use of this now heavily engineered plant/product are mounting, and the research is not only monitoring, but discovering these harms. If science and health matter, then all research must be thorough and properly vetted to ensure that health is advanced, not mere 'symptom abated' whilst disease, disorder or other harms grow.

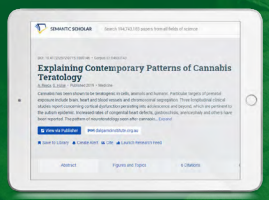
CHECK OUT... (CLICK TO VISIT)



1. "Known Cannabis Teratogenicity Should be Carefully Considered" BMJ Rapid Response. Accepted 06/08/2018.

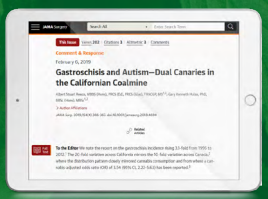
2. "Evolution of cortical neurogenesis in amniotes is controlled by robo signaling levels." Cell 174(3): 590-606. Published on Cell website.

3. A case-control genome wide association study of Substance Use Disorder (SUD) identifies novel variants on chromosome 7p14.1 in patients from the United Arab Emirates (UAE). American Journal of Medical Genetics Part B: Neuropsychiatric Genetics. Accepted 21st October 2018.

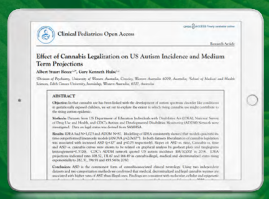


4. "Explaining Contemporary Patterns of Cannabis Teratology". Accepted in Clinical Pediatrics 18th January 2019.

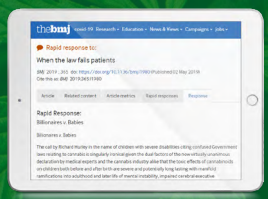
5. "Cannabis Problematics Include but are not Limited to Pain Management" JAMA. Published online 3rd February 2019.



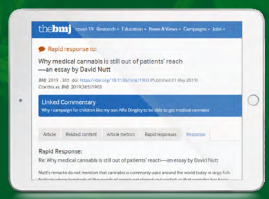
6. "Gastroschisis and Autism—Dual Canaries in the Californian Coalmine" Published online February 6th 2019. doi: 10.1001/jamasurg.2018.4694 PMID: 30725103 JAMA Surgery.



7. "Effect of Cannabis Legalization on US Autism Incidence and Medium Term Projections." Clinical Pediatrics: Open Access. Accepted 27th April 2019. 4(2): 1-17. ePublished 3rd May 2019. DOI: 10.24105/2572-0775.4.154 .

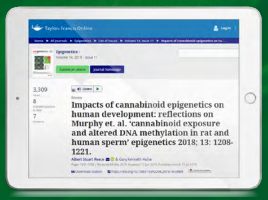


8. "When the Law Fails Patients." by Hurley R. in British Medical Journal. "Billionaires v Babies." Published 10th May 2019. 2019; 365:1980 doi: https://doi.org/10.1136/bmj.l1980



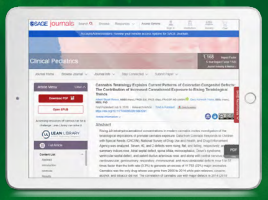
9. Rapid Response to "Why Medical Cannabis is still out of Patient's Reach." By Nutt D. BMJ 2019; 365:1903. doi: https://doi.org/10.1136/bmj.l1903. Published 10th May 2019.

10. "Epidemiological Associations of Various Substances and Multiple Cannabinoids with Autism in USA". Accepted 22nd May 2019. Clinical Pediatrics: Open Access. Published 31st May 2019. doi: 10.24105/2572-0775.4.155

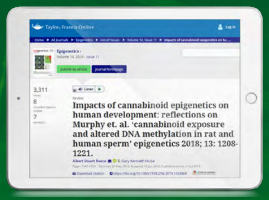


11. "Impacts of Cannabinoid Epigenetics on Human Development: Reflections on Murphy et. al. "Cannabinoid Exposure and Altered DNA Methylation in Rat and Human Sperm" Epigenetics 2018; 13: 1208-1221." Accepted Epigenetics 14th June 2019.

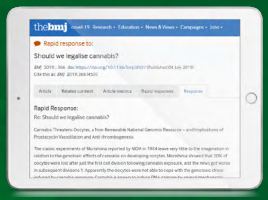
12. Should We Legalize Cannabis: "Cannabis Debates and Cannabis Debacles: Serious Downstream Implications of Cannabis Neurotoxicity and Genotoxicity" British Medical Journal, Rapid Responses, Published 7th July 2019



13. "Cannabis Teratology Explains Current Patterns of Coloradan Congenital Defects: The Contribution of Increased Cannabinoid Exposure to Rising Teratological Trends." Clinical Pediatrics. Published online 9th July 2019.



14. "Impacts of Cannabinoid Epigenetics on Human Development: Reflections on Murphy et. al. "Cannabinoid Exposure and Altered DNA Methylation in Rat and Human Sperm" Epigenetics 2018; 13: 1208-1221. 13th July 2019.

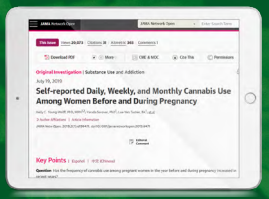


15. "Cannabis Threatens Oocytes, a Non-Renewable National Genomic Resource – and Implications of Prostacyclin Vasodilation and Anti-thrombogenesis" British Medical Journal Rapid Response. Accepted 19th July 2019.

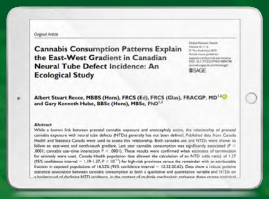
MORE OVER THE PAGE...

The Genotoxic Portfolio of Cannabis –The Growing Research

CHECK OUT... *(CLICK TO VISIT)*

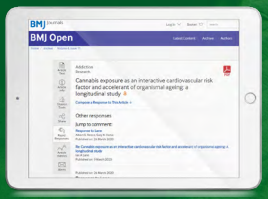


16. "Unrolling and Unravelling Far-Reaching Implications of Cannabis Use in Pregnancy Study." Comment in JAMA Network Online Accepted 31st July 2019. See Comments Tab.



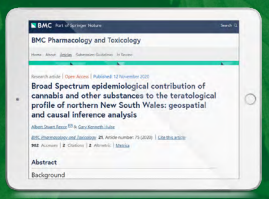
17. "Cannabis Consumption Patterns Parallel the East-West Gradient in Canadian Neural Tube Defect Incidence: An Ecological Study" Accepted for Global Pediatric Health 20th October 2019. Volume 6 (1): 1-12.

18. "Canadian Cannabis Consumption and Patterns of Congenital Anomalies: An Ecological Geospatial Analysis" Accepted in Journal of Addiction Medicine, 6th January 2020. MS No. JAM-D-00715R3. ePublished 13th March 2020.



19. "Response to Lane", Rapid Response to Ian A Lane. "Re: Cannabis exposure as an interactive cardiovascular risk factor and accelerant of organismal ageing: A longitudinal study" BMJ Open. ePublished 27th March 2020

20. "Cannabis in Pregnancy – Rejoinder, Exposition and Cautionary Tales." Accepted for Publication in Psychiatric Times, 18/07/2020. ePublished 10/10/2020.

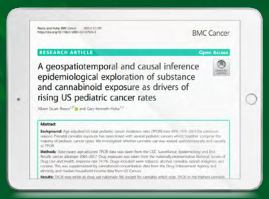


21. "Broad Spectrum Epidemiological Contribution of Cannabis and Other Substances to the Teratological Profile of Northern New South Wales: Geospatial and Causal Inference Analysis" Published in BMC Pharmacology and Toxicology 13/11//2020. (2020) 21:75 https://link.springer.com/article/10.1186/s40360-020-00450-1

22. "Response to Polocaro and Vettraino" Accepted in Missouri Medicine 04/10/2020.

23. "Co-Occurrence Across Time and Space of Drug- and Cannabinoid- Exposure and Adverse Mental Health Outcomes in the National Survey of Drug Use and Health: Combined Geotemporospatial and Causal Inference Analysis" Accepted in BMC Public Health 22nd October 2020. Published 04/11/2020. 20:1655 https://doi.org/10.1186/s12889-020-09748-5 .

24. "Contemporary epidemiology of rising atrial septal defect trends across USA 1991–2016: a combined ecological geospatiotemporal and causal inferential study." BMC Pediatrics 2020; 20:539-550.



25. "A geospatiotemporal and causal inference epidemiological exploration of substance and cannabinoid exposure as drivers of rising US pediatric cancer rates." BMC Cancer. 2021; 21: (1) 197- 230.

Whilst it is obvious that low birth weight has been noted by many papers looking at the effects of cannabis in pregnancy a much more serious pattern is also emerging which has been replicated now in five jurisdictions namely Hawaii [1], Colorado [2], Canada [3], Australia [4]and USA [5-7]. In fact in 6 it was shown that cannabinoids are genotoxic for at least 20% of the human genome by way of chromosomal toxicity. Moreover cannabis has been shown to inhibit sonic hedgehog signalling by several mechanisms [8] which has profound implications for foetal development as sonic hedgehog is one of the most important human embryonic morphogens of all [9]. Sonic hedgehog inhibition alone both implies and accounts for elevated rates of the numerous birth defects in which prenatal cannabis exposure is now implicated.

Cannabinoids also have a heavy epigenetic footprint. This has serious and multi-generational impacts. Moreover, cannabinoids have also been shown to inhibit mitochondrial metabolism by many means including direct inhibition through a full complement of endocannabinoid signalling machinery held on their inner and outer mitochondrial membranes and in the intermembrane space.

Both the epigenomic and metabolic effects of cannabinoids are critical and are also closely related as metabolic state controls epigenetic state both directly through substrate supply and indirectly through small molecular signalling shuttles which have the effect of coordinating nuclear and mitochondrial genomic expression and signalling mitonuclear stress[10]. That is to say that metabolic state and epigenomic state – and hence multigenerational inheritance – are closely and intimately related.

1. Forrester MB, Merz RD. Risk of selected birth defects with prenatal illicit drug use, Hawaii, 1986-2002. Journal of toxicology and environmental health 2007;70:7-18.
2. Reece AS, Hulse GK. Cannabis Teratology Explains Current Patterns of Coloradan Congenital Defects: The Contribution of Increased Cannabinoid Exposure to Rising Teratological Trends. Clin Pediatr (Phila) 2019;58:1085-123.
3. Reece AS, Hulse GK. Canadian Cannabis Consumption and Patterns of Congenital Anomalies: An Ecological Geospatial Analysis. J Addict Med 2020;14:e195-e210.
4. Reece AS, Hulse GK. Broad Spectrum epidemiological contribution of cannabis and other substances to the teratological profile of northern New South Wales: geospatial and causal inference analysis. BMC Pharmacol Toxicol 2020;21:75.
5. Reece A.S., Hulse G.K. Cannabis in Pregnancy – Rejoinder, Exposition and Cautionary Tales. Psychiatric Times 2020;October 10, 2020:https://www.bing.com/h?q=Cannabis+in+Pregnancy+%E2%80%93+Rejoinder%2C+Exposition+and+Cautionary+Tales&cvid=22538e0124c04711b92017489c63214a&aqs=edge..69i57.439j0j1&pglt=43&FORM=ANSPA1&PC=U531.
6. Reece A.S., Hulse G.K. Epidemiological Overview of Multidimensional Chromosomal and Genome Toxicity of Cannabis Exposure in Congenital Anomalies and Cancer Development Scienitifc Reports 2021.
7. Reece AS, Hulse GK. Cannabis and Pregnancy Don't Mix. Mo Med 2020;117:530-1.
8. Fish EW, Murdaugh LB, Zhang C, et al. Cannabinoids Exacerbate Alcohol Teratogenesis by a CB1-Hedgehog Interaction. Sci Rep 2019;9:16057.
9. Carlson BM. Human Embryology and Developmental Biology. 6 ed. Philadelphia: Elsevier; 2019.
10. Canto C, Menzies KJ, Auwerx J. NAD(+) Metabolism and the Control of Energy Homeostasis: A Balancing Act between Mitochondria and the Nucleus. Cell Metab 2015;22:31-53.