Weeding out the Evidence
Marijuana in Paediatric Epilepsy

Dr Michelle Lorentzos, Neurology Fellow
Annual Neurology Update
19th November, 2014
Issues for discussion today

• What is currently happening with paediatric epilepsy and marijuana?

• What is the evidence?

• Where to from here?
Case 1

A 16yo boy with Lennox Gastaut phenotype
daily seizures
barely verbal
behavioural comorbidities
refractory to medications

“Doctor, I want to try marijuana for my son.”
Taking a cannabis ‘tincture’ 5 times daily and has left school.
Case 2

A 2yo boy multiple seizure types and encephalopathy
hundreds of seizures daily
family sceptical of conservative medication
refractory to medications

“Doctor, I want to try marijuana for my child.”
Some opening remarks

- The vast majority of parents want the best for their children

- The vast majority of clinicians want the best for their patients

- Most children with epilepsy respond to current anti-epileptic medication

- Anti-epileptic medications are not perfect – however we know what to look for in the vast majority of cases

- The debate about medical cannabis is NOT the same debate as recreational marijuana use
What is all the fuss about?
Charlotte Figi (pictured since her treatment), six, has Dravet syndrome - a rare and severe form of epilepsy. She was having a thousand seizures a week and her parents were told to prepare for the worst.

And incredibly, after just a few months, Charlotte has finally begun to walk and talk for the first time - to the amazement of doctors - and her seizures have almost completely stopped.

Mrs Figi said: 'We tried everything possible, and doctors kept telling us she was going to die. When Matt first told me about the treatment I was horrified - I didn't want my daughter to get high.'
What do we know about cannabis and the brain?
Cannabis and the brain

• Cannabinoid receptors are found in brainstem, neocortical and limbic areas
• They are thought to influence levels of catecholaminergic neurotransmitters
• They are also thought to influence thalamo-cortical projections and improve synchronicity
Cannabis in Epilepsy

- In humans, cannabis has been reported to be associated with improved and worsened seizure control.

- A case-control study comparing 308 patients with first seizures and 294 patients with surgical emergencies showed cannabis was associated with reduced seizure incidence. For men with unprovoked seizure, the OR was 0.36 (95% CI 0.18-0.74) for marijuana use within 90 days of hospitalisation.

- There have been no RCTs. Worsening seizure control with cannabis may be in part due to lifestyle factors that accompany the use of the substance.
2 studies suggested seizure reduction

Cunha 1980
• 15 patients
• CBD n=7 versus placebo n=8
• Follow up for 4 ½ months
• 4/7 CBD and 1/8 placebo patients were seizure free

Mechoulam 1978
• 9 patients
• CBD n=4 versus placebo n=5
• Follow up for 3 months
• 2/4 CBD and no placebo patients were seizure free
2 studies with no clear difference

Ames 1985
• 12 patients with intellectual disability and seizures
• Randomised to sunflower oil or placebo
• Follow up for 4 weeks
• No statistically significant reduction in seizures

Trembly 1990
• 12 patients with epilepsy in cross over trial
• Follow up 18 months
• No statistically significant difference
How are parents accessing medication?
New Hampshire House Committee Advances Proposal to Legalize Recreational Cannabis

The New Hampshire House Ways and Means Committee has advanced House Bill 492, a proposal to legalize recreational cannabis, to the full House. The proposed law – which passed the House in January but was sent back to committee to rework the bill’s tax system – would legalize possession of up to an ounce of cannabis, and would legalize state-licensed cannabis retail outlets to distribute cannabis to those 21 and

Georgia Senate Unanimously Approves Bill to Legalize Medical Cannabis Oil

Georgia’s Senate has given unanimous approval to House Bill 885, a proposal to legalize cannabis oil for medical purposes. The measure passed the state’s House of Representatives earlier this month with an 117 to 0 vote. Under the bill, academic medical centers in the state would be permitted to produce low-THC cannabis oil, which they would be authorized to distribute to those with cancer, glaucoma and seizures. The measure would also provide protection from arrest for anyone in possession of cannabis oil that was obtained from another state, as long as they have

Alabama Legislature Passes Bill to Establish Million Dollar Medical Cannabis Study, Goes to Governor

Alabama’s full Legislature has passed Senate Bill 174, a proposal to establish a study on the use of cannabis extract in treating seizure disorders. Cannabis extract. The measure passed the Senate unanimously today, approving minor changes made by the House of Representatives (which also passed the bill unanimously), the measure now heads to Governor Robert Bentley, who can either sign

Utah Governor Signs Medical Cannabis Bill Into Law

Utah Governor Gary Herbert has signed House Bill 105, a measure to legalize medical cannabis extracts. “Cannabis oils show promise of offering some relief to Utahns suffering from seizures and epilepsy and we should do all we can to help them,” the governor said in a statement released yesterday. Once the proposal takes effect (July 1st), House Bill 105 will allow those in the state who receive a recommendation from a neurologist to legally possess and use cannabis extract that’s low in THC (tetrahydrocannabinol) and high in CBD (cannabidiol). First they must receive a waiver from Utah’s

Companies Plan Study on Aquatic Hemp

By Press Release
New Growth Opportunities
Emerging to Leverage Underwater Timber Operations & Enhance Models for Project Sustainability
BLAINE, WA – (Marketwired – Mar. 18, 2014) – Hollund Industrial Marine, Inc. (“Hollund”), an underwater forest management company, announced today that it will participate in a Hemp study with North Cal Wood Products, Inc. (“North Cal”). North Cal is conducting a market research study on Hemp, with a goal of launching a pilot project to cultivate organic hemp in aquaponic systems applying new aquaculture and biodynamic farming principles. Hollund’s interest in North Cal’s

New Poll: 74% of Registered Voters in Florida Support Initiative to Legalize Medical Cannabis

A new University of North Florida poll released yesterday asked registered voters whether they would vote in favor of Proposion 2, Florida’s initiative to legalize medical cannabis which is on the November’s ballot. 74% said “Yes”, with just 22% responding “No.” Specifically, the question was: “Proposition 2 on the statewide ballot in the fall of 2014 is called ‘Use of Marijuana for Certain Medical Conditions.’ This
Zero Tolerance of Pain & Suffering

Scientific matters can only be clarified by prolonged, faithful bona fide observations in friendly exchange of opinion, never by imprisonment. A person’s right to know, to learn, to inquire, to make bona fide errors, to investigate must, by all means, be safe, if the word FREEDOM should ever be more than an empty political slogan.

2013 NSW Government Inquiry into the use of cannabis for medical purposes.

Use of cannabis for medical purposes (Inquiry)

The Inquiry will examine the efficacy and safety of using cannabis for medical purposes; and how cannabis should be supplied for medical use; the legal implications and issues concerning the use of cannabis for medical purposes and any other related matters. The Inquiry will examine a range of modes by which the chemical properties of cannabis may be accessed for therapeutic purposes, from smoking of the plant to the manufacturing of pharmaceutical products consumed in nasal sprays, tablet or other forms.

- Submissions to the Inquiry
- Submission from Mullaways
- Submission from Dr Ian Webster AO
- Cannabis and chronic pain: the poor man’s analgesic
- Public Hearing 1 Transcript 11 March 2013
- Mullaways on Pages 31 to 39 of Transcript
- Public Hearing 2 Transcript 18 March 2013
- Executive Summary & Recommendations
Concerns

• Does it work?
• If it works, at what dosage and in what form? (5 x daily?)
• What are the adverse effects? Short and long term?
• Who is prescribing the product and what are their qualifications?
• Who is making the product and what are their qualifications?
• How much should people be paying?
• How do we handle the legal repercussions?
• What about schooling?
What are parents saying?


Porter BE¹, Jacobson C.
A Facebook survey

• Nineteen responses were received
• Thirteen children had Dravet syndrome, four had Doose syndrome, and one each had Lennox-Gastaut syndrome and idiopathic epilepsy.
• The average number of antiepileptic drugs (AEDs) tried before using cannabidiol-enriched cannabis was 12.
Results of the survey

16 (84%) of the 19 parents reported a reduction in their child's seizure frequency while taking cannabidiol-enriched cannabis.

- 2 (11%) reported complete seizure freedom
- 8 (42%) reported a greater than 80% reduction in seizure frequency
- 6 (32%) reported a 25-60% seizure reduction.

Other beneficial effects included increased alertness, better mood, and improved sleep. Side effects included drowsiness and fatigue.
Why not have a trial?
The Trial

GWPharm — Epidiolex

Epidiolex® is an investigational drug and has not been approved for use by the FDA or any other national regulatory agency.

- Orphan drug designation granted for Epidiolex in Dravet & Lennox-Gastaut syndromes by FDA
- There are now 21 active expanded access (EA) INDs covering age range 1 month to 40 years
- Approximately 300 total patients are authorized to be treated under these EA INDs
- The large majority of these INDs (estimated at 95%) are for patients > 1 year and < 17 years

Click here to read Dravet syndrome press release
Click here to read Lennox-Gastaut syndrome press release
The Epidiolex Trial

- FDA approved study, led by Dr Orlin Devinsky
- Trial of cannabidiol without THC
- Assess dose tolerability in an open-label design
- Monitoring with bloods counts, liver function tests, attentiveness
- Measuring outcome with video monitoring
- Initially 5 sites with 25 patients at each site – now 21 sites with 300 patients
- Dravet and Lennox Gastaut
Where to from here?

- Opportunities for collegial discussion
- Safeguards for patients on medical cannabis
  - Open disclosure
  - Monitoring for interactions, side effects
- Appraising the new evidence
- Understand that commencing and ceasing a medication always has risks/benefits
References

- Gordon, E. and Devinsky, O. Alcohol and Marijuana: Effects on Epilepsy and Use by Patients with Epilepsy. Epilepsia,2001; 42 (10)1266-1272
- Porter J.E, Jacobson, C., Report of parent survey of cannabidiol-enriched cannabis in paediatric treatment-resistant epilepsy. Epilepsy Behaviour, 20103; Dec 29 (3), 574-7