

Cannabis & Autism: Piecing it All Together

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Scope of the Problem

- Over the last 30 years, there has been a 3-fold increase in number children dx with ASD worldwide. **1 in 68** 8 year old children dx, 4:1 Male:Female, siblings 15-25% higher incidence
- No specific treatments are currently available
- Interventions Focus on:
 - Decreasing disruptive behaviors
 - Training and teaching self-help skills for greater independence
- Previous observations have shown that cannabidiol effects might include alleviation of psychosis, anxiety, facilitation of REM sleep and suppressing seizure activity

History of Cannabis Through the Ages

- Used as medicine for 5000 years all over the globe, its presence is documented ~10,000 years ago in Taiwan
- Referenced in the Old Testament
- Used as an anticonvulsant in Middle East and India for 4000 years
- Used heavily in women's health, for migraines, menstrual disorders, etc.
- Hemp required crop in 13 original colonies—Food, cloth, robe
- US Pharmacopeia 1850, Eli Lilly, Park Davis and others produced it
- Opium, cocaine in Coca-Cola, heroin developed, tablets (ASA and MSO4) made cannabis tinctures obsolete

POISON

No. 100 969

CHOCOLATE-COATED
TABLETS

CHLORODYNE

HALF STRENGTH

MORPH. HYDROCHL.

1-12 gr.

Ext. Cannabis 1-8 gr.

Nitroglycerin 1-600 gr.

Ext. Hyoscyam. 1-4 gr.

Oleores. Capsc. 1-20 gr.

Peppermint Oil q s.

Dose, 1 to 4 Tablets

872196A

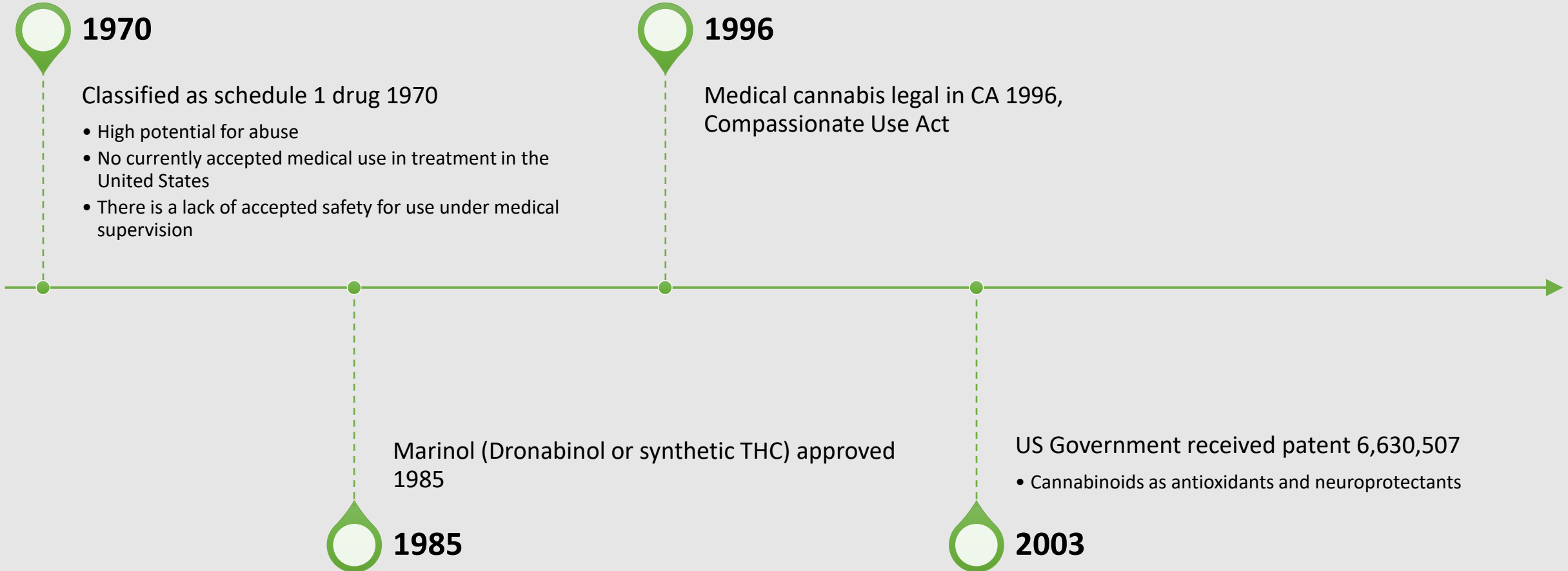
SHARP & DOHNE

BALTIMORE

History continued...

- Dupont (nylon), Mellon (financier), Hearst (journalism) and Harry Anslinger (Federal Bureau of Narcotics), alcohol prohibition ended in 1933 → criminalization of drugs (cannabis new target)
- 1944 La Guardia organized a study on cannabis. Interestingly, users were more often what would now be described as Asperger's. Cannabis is safe, low side effects, effective, does not lead to MSO4 or heroin addiction, does not contribute to crimes or juvenile delinquency
- Nixon's war on drugs. Ignoring new evidence that marijuana users were "timid, drowsy, and passive", pushed for criminalization

History



Perspective



CDC reports 6 million deaths annually from tobacco



480,000 tobacco deaths a year in the US

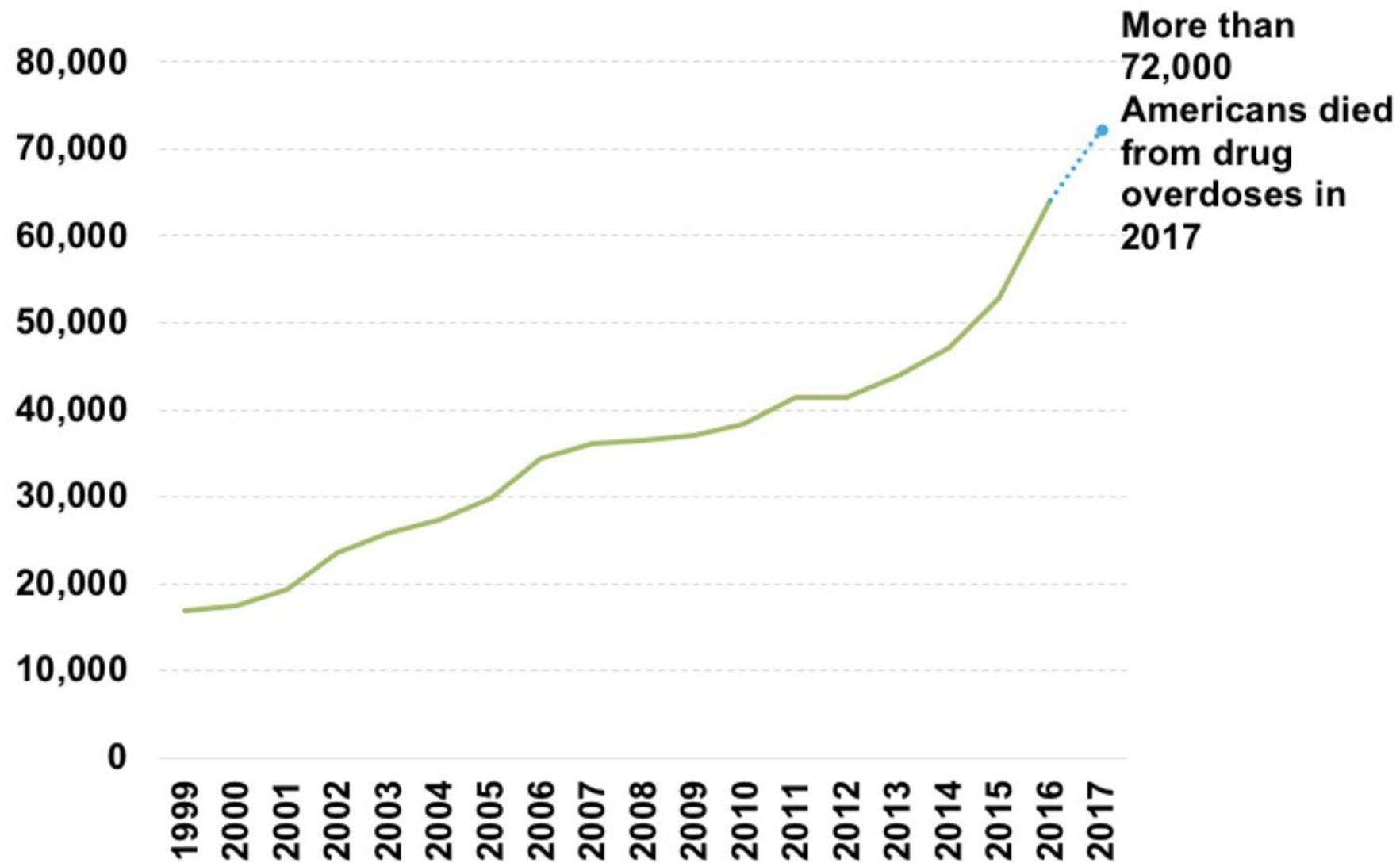


WHO reports 3.3 million deaths annually from alcohol



88,000 alcohol deaths a year in the US alone

Total U.S. Drug Deaths





Cannabis deaths annually?

Zero

There are no receptors in the brainstem, therefore no overdose potential

You can take too much and feel like you are dying, but it is not terminal, and is self-limited.

Current Statistics

- 2014 JAMA states with legal cannabis have 24.8% decrease in opioid related overdoses
- Effect increases over time

Approved Conditions in Maryland

:

- Cachexia, anorexia, chronic pain, severe nausea, seizures, severe and persistent muscle spasms, glaucoma, PTSD and other condition that might benefit from cannabis
- Autism not specifically listed. It is an approved condition in Pennsylvania, Delaware, Georgia

Patient Statistics 04.21.2020

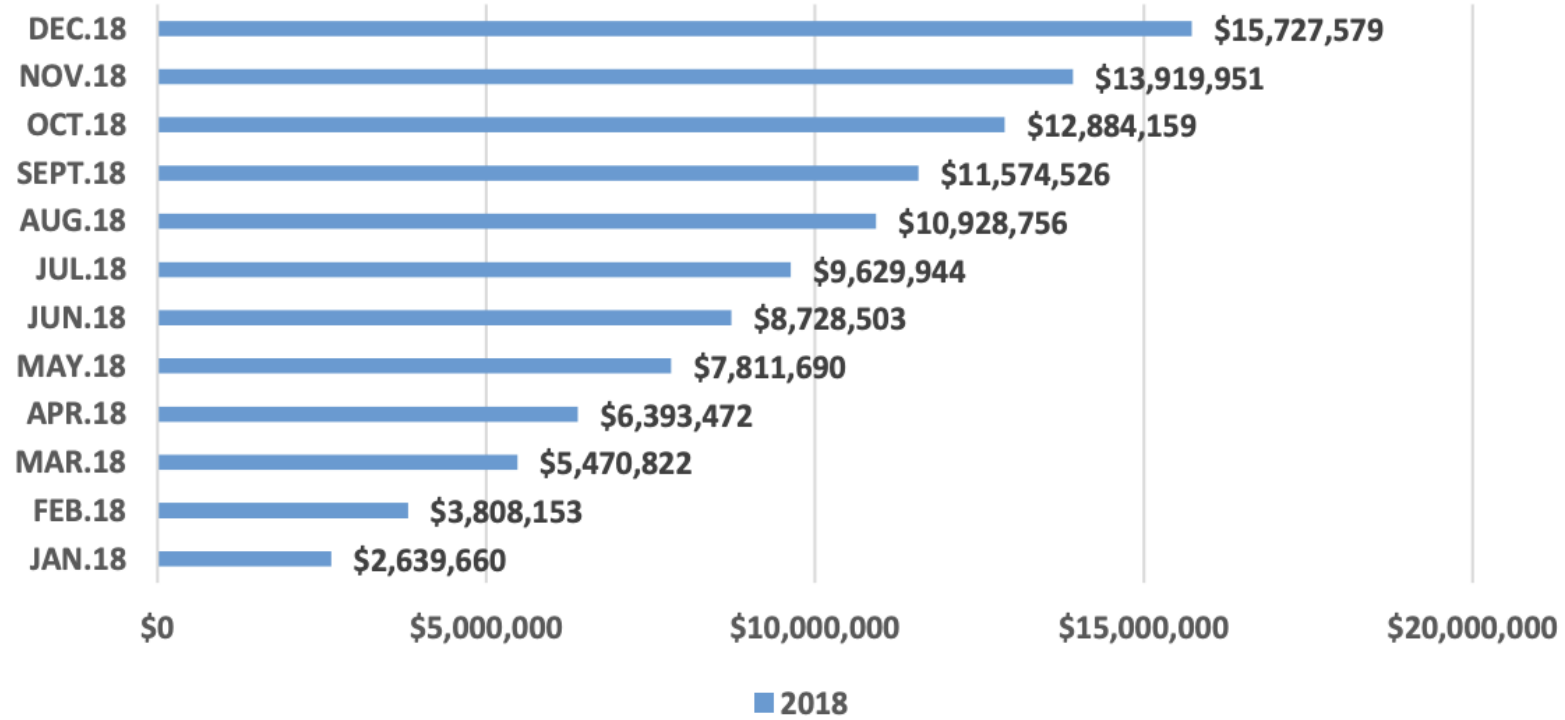
Number of Registered Providers by Board Type & Total Number of Providers:

Podiatry	21
Nursing	749
Physicians	927
Dental	121
Total Providers	1,818

Patient Information:

Certified Patients 98, 309

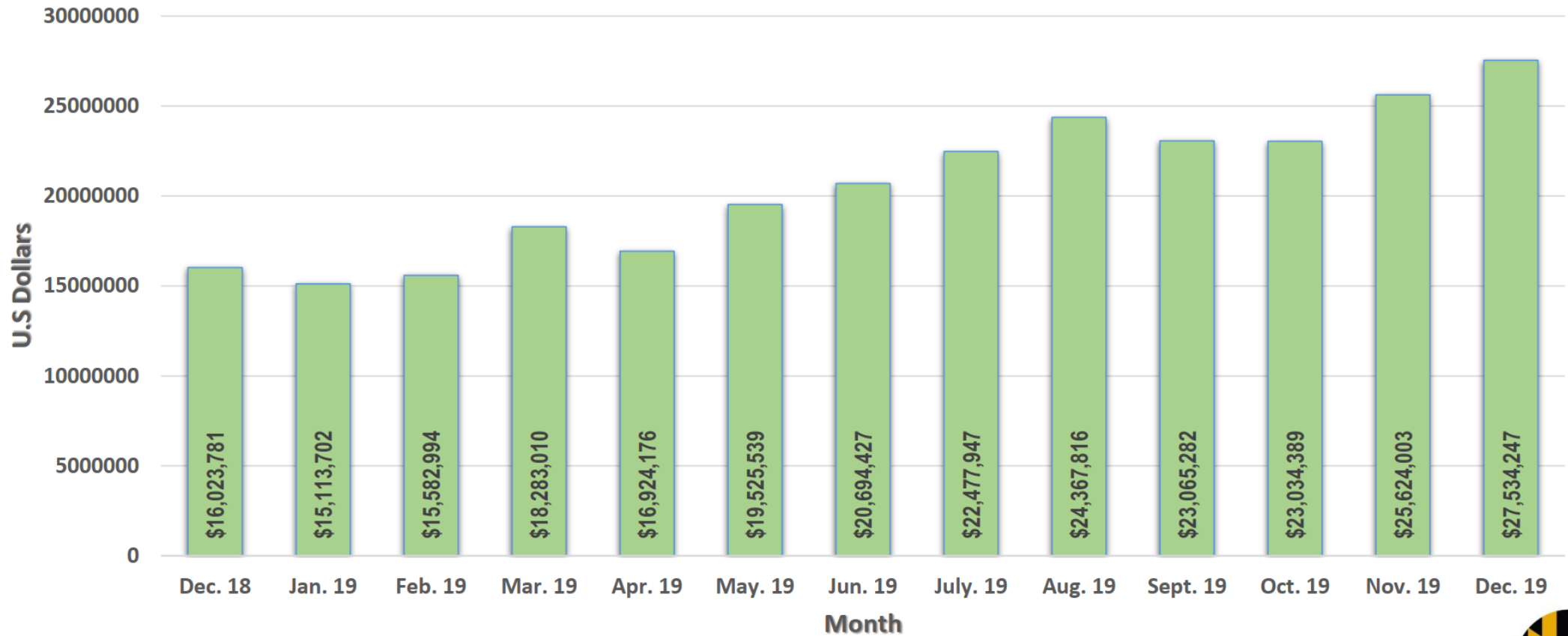
Maryland Medical Cannabis Sales 1st Calendar Year



Medical Cannabis Dispensary Sales (\$)

December 2018- December 2019

Total Retail Sales= \$ 268,251,313



Endocannabinoid System

ECS is a link between the mind and body

1940 Roger Adams extracted CBD from cannabis

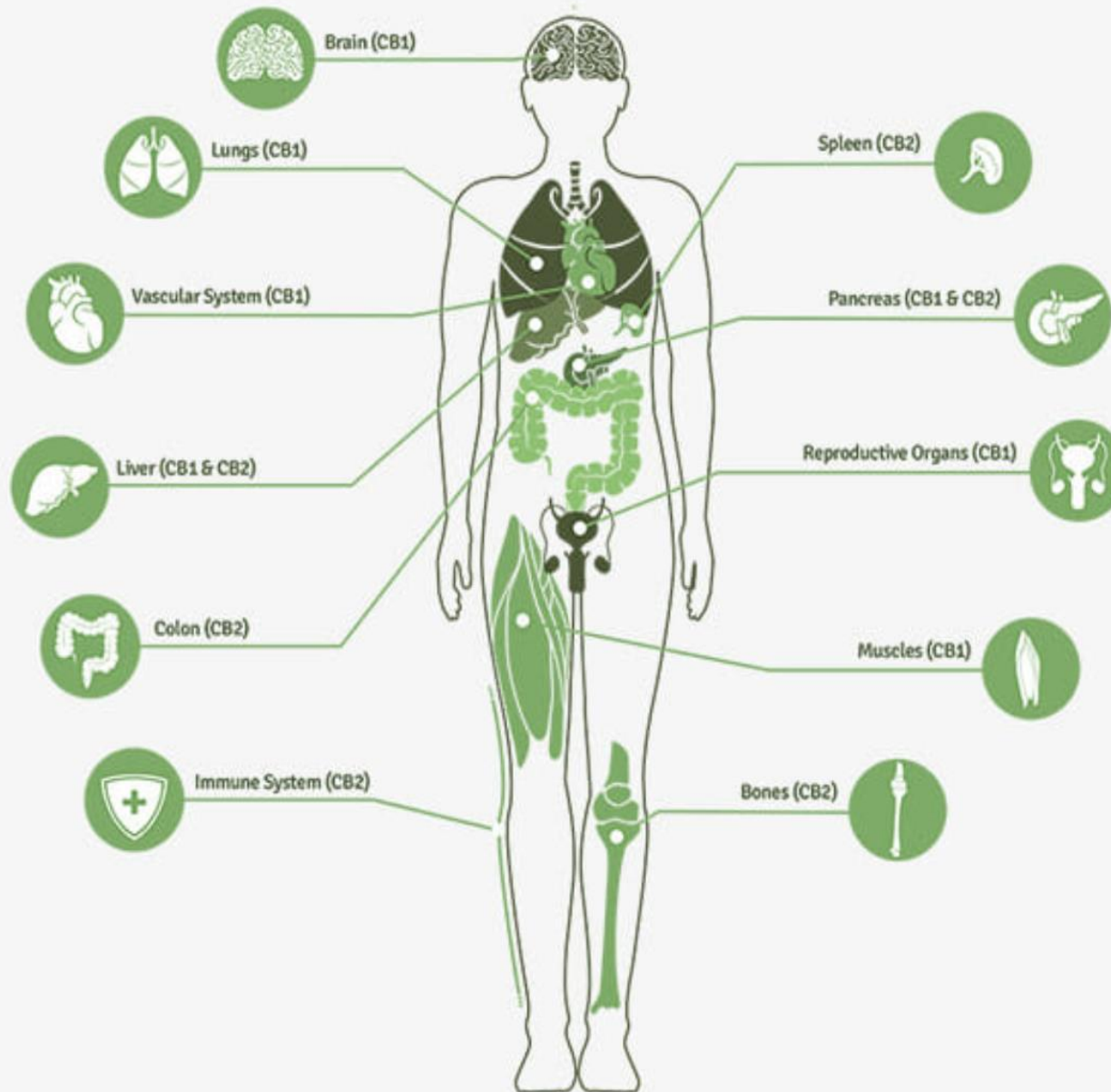
1988 Allyn Howlett and William Devane found CB1 in the brain of a rat, 1993 CB2 discovered

1992 Raphael Mechoulam et al. discovered **anandamide**, having discovered THC in 1964

ECS found all across the body in tissues, organs, cells, glands

Promotes homeostasis and health, “**Relax, Eat, Sleep, Forget & Protect**”

THE BODY'S ENDOCANNABINOID SYSTEM



Cannabinoids. What are they?

Therapeutic compounds and the active ingredients found in cannabis.

- **Phytocannabinoids** plant based cannabinoids, produced by cannabis
- **Endogenous Cannabinoids** Produced in humans and other animals
- **Synthetic Cannabinoids** Produced in the lab
 - **Marinol, Nabilone, Sativex**

CBD (Cannabidiol)

CBD has been used to treat pain (chronic and neuropathic), diabetes, cancer, and neurodegenerative diseases, such as Huntington's disease. Animal studies indicate that a high dose of CBD inhibits the effects of lower doses of THC. Some studies suggest that oral or oromucosal CBD may prolong and/or intensify the effects of THC, though this has been disputed.

Data to suggest that high-dose oral CBD (150–600 mg per day) may exert a therapeutic effect for **epilepsy**, **insomnia**, and **social anxiety disorder**.

- Cannabidiol in humans-the quest for therapeutic targets. *Zhornitsky S, Potvin S*
- *Pharmaceuticals (Basel)*. 2012 May 21; 5(5):529-52.

THC

THC is the major psychoactive (intoxicating) component of cannabis and acts on CB₁ receptors in the central nervous system. Stimulates serotonin synthesis, inhibits its reuptake and promotes its release. May also modulate dopamine imbalances in headaches (Russo)

THC and cannabinoids inhibit prostaglandin E2 synthesis

THC oral potency as anti-inflammatory is 20x ASA and 2x HC (inhibits cyclooxygenase and lipoxygenase)

Opioids, cannabinoids & eicosanoids signal through common NO gap coupling

THC promotes downregulation of inflammation

CBD & THC



THC and CBD are neuroprotective antioxidants that exceed the potency of Vit C & E.



CBD is non-intoxicating and does not act directly on CB1 and CB2 receptors. It is thought to be a negative allosteric modulator at CB1.



CBD in combination with THC has received regulatory approvals in several European countries and is under study in registered trials with the FDA.



Epidiolex 25mg/kg showed a 50% reduction in sz, SEs somnolence and decreased appetite

What is the Entourage Effect?

- Mother nature does it best
- Why the “one note” of synthetic THC doesn’t work all that well
- Cannabinoids (108 or more) in cannabis and **terpenes** (over 100) work synergistically to give a variety of effects. The terpenes appear to modulate the cannabinoids’ effects.



Terpenes

A-PINENE

ANTI-INFLAMMATORY
BRONCHODILATOR
AIDS MEMORY
ANTI-BACTERIAL

also found in
pine needles



LINALOOL

ANESTHETIC
ANTI-CONVULSANT
ANALGESIC
ANTI-ANXIETY

also found in
lavender



BETA

CARYOPHYLLENE

ANTI-INFLAMMATORY
ANALGESIC
PROTECTS CELLS LINING THE
DIGESTIVE TRACT

also found in
black pepper



MYRCENE

CONTRIBUTES TO
SEDATIVE EFFECT OF
STRONG INDICAS
SLEEP AID
MUSCLE RELAXANT

also found in
hops



LIMONENE

TREATS ACID REFLUX
ANTI-ANXIETY
ANTIDEPRESSANT

also found in
citrus



Ingestion Options

Vaporization

- Flower
- Concentrates

Sublingual

- Tinctures
- Tablets

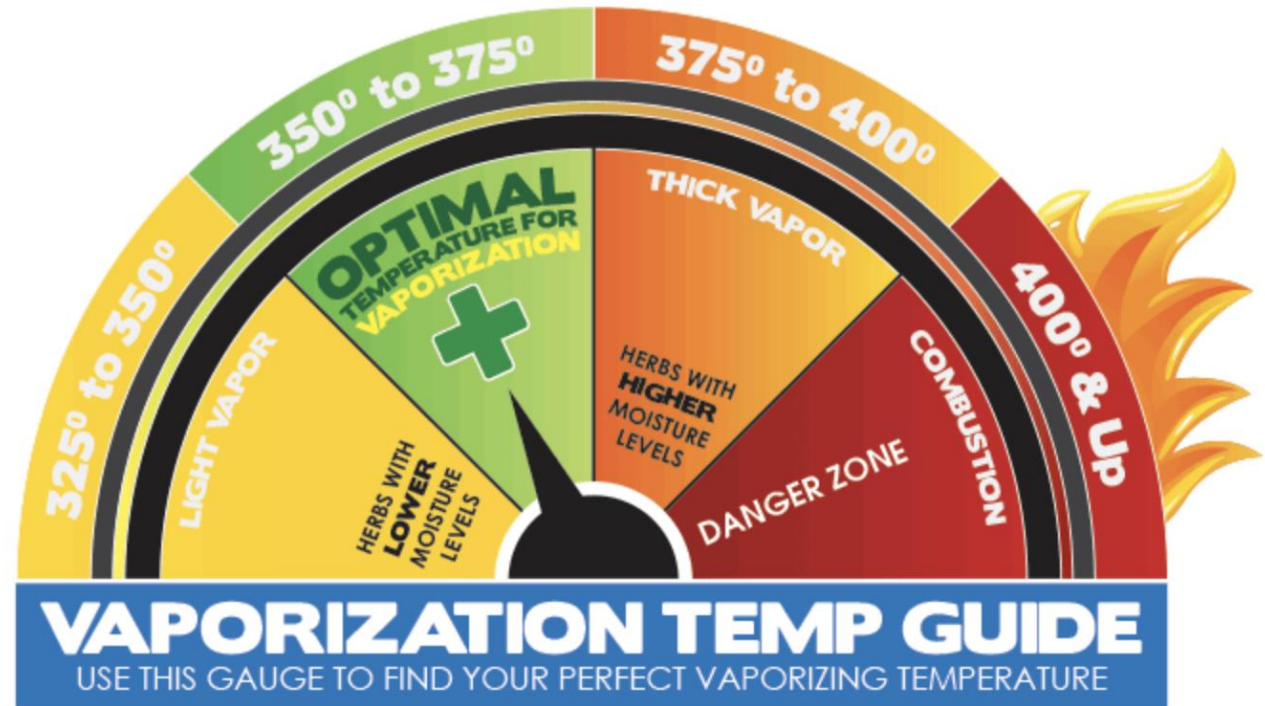
Oral

- Elixirs
- Edibles

Topical

- Balms/Lotions
- Patches
- Bath Soaks

VAPORIZATION



SMOKING OR COMBUSTION





TINCTURES AND TABLETS

ELIXIRS AND EDIBLES



TOPICALS



Drug Interactions



- Approximately 60% of clinically Rx drugs are metabolized by CYP3A4
- Hepatic cytochrome 450 (CYP450) isoenzymes 2C9 and 3A4 play a significant role in the primary metabolism of THC and CBN, whereas 2C19 and 3A4 may be responsible for metabolism of CBD
- Separate cannabis doses by at least 2 hours from other Rx

Cannabidiol Based Medical Cannabis in Children with Autism—A Retrospective Feasibility Study

(2018 *Neurology* Aran et al)

- Retrospective study on 60 children
- CBD enriched cannabis oil
- Behavior outbreaks improved in 61%
- Communication improved in 47%
- Anxiety improved in 39%
- Stress in 33%
- Disruptive behavior in 33%

Real life Experience of Medical Cannabis Treatment in Autism: Analysis of Safety and Efficacy.

Lihi Bar-Lev Schleider, Raphael Mechoulam, Naama Saban, Gal Meiri & Victor Novack (2019) Scientific Reports

Reports

- 188 ASD patients treated with medical cannabis 2015-2017
- 30% CBD, 1.5% THC oil (20:1)
- Symptoms inventory, global assessment, side effects at 6 months
- After 6 months, 82.4% in active treatment, 60% assessed:
 - 30.1% significant improvement
 - 53.7% moderate improvement
 - 6.4% slight improvement
 - 8.6% no change
 - 25.2% experienced at least one SE, most common was restlessness (6.6%)

Patient Population

- Mean age 12.9 yrs, 7.4% less than 5, 37.2% 6-10, 38.2% 11-18
- 81.9% male
- 14.4% suffered from epilepsy
- 3.7% ADHD

Quality of Life

- Quality of Life, mood, ability to perform ADLs assessed before treatment at 6 months
 - Good quality of life reported by 31.3% prior to treatment, 66.8% at 6 months
 - Ability to dress and shower independently 26.4% to 42.9%
 - Good sleep (3.3%) and good concentration (0%) increased to 24.7% & 14%
- Seizures
 - 84.6% reported disappearance of sx, 2 patients reported improvement
 - Restlessness and rage attacks improved in 91% and 90.3% respectively

Key to Success

- Slow titration of dose—up to 2 months.
- Wide dosage range from one to 20 drops TID
- Every patient is different, so don't compare your results to others

Why does it work?

- ASD may result from a dysregulation of endocannabinoid system
Krueger, et al. “Evidence for a Common Endocannabinoid-Related Pathomechanism in Autism Spectrum Disorders” *Neuron* 78, May 8, 2013
- CBD enhances oxytocin and vasopressin release, important in bonding and social interaction
- Anandamide levels lower in ASD Karhson et al “Plasma anandamide concentrations are lower in children with autism spectrum disorder” *Molecular Autism*, (2018) 9:18
- ASD 3-9 year olds have high levels of CB2 receptors Sinascalco “Cannabinoid receptor type 2, but not type 1, is up-regulated in peripheral blood mononuclear cells of children affected by autistic disorders” *J Autism Dev Disord* 2013

Endocannabinoid System

Chakrabarti et al
“Endocannabinoid Signaling in Autism” *Neurotherapeutics* (2015)

- Controls emotional responses
- Behavioral reactivity to context
- Social interaction, social reward responsiveness
- Densely wired throughout our bodies
- Altered in several neurodegenerative diseases and inflammatory states
- Influences circadian rhythms
- Mediates anxiety
- Involved with seizure activity including epilepsy

Importance of SAFE Medication



- Not all CBD is safe
- Insist on seeing COAs, buy from someone reputable
- Not regulated (yet) so amount listed may not be accurate, it may or may not contain THC
- I like Social brand out of Oregon. Biggest CBD company in US.
- Hemp vs. Cannabis. By definition, hemp must contain $< 0.3\%$ THC
- MMCC.Maryland.gov for more information

