THE ENDOCANNABINOID SYSTEM AND YOUR PATIENTS

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► A scientific discovery that is not yet taught in medical or nursing schools.
► Most practicing healthcare professionals know little or nothing about the ECS.
► The ECS plays a vital role in the comfort and quality of life for hospice patients.

This presentation will cover the basic physiology and function of the ECS and the potential role of cannabis and the cannabinoids.

New Discovery!
The Endogenous Cannabinoid System

The Endocannabinoid System (ECS)

► Emerging science on a newly discovered molecular signaling system in the human body and all animals except insects.
► Function: Maintain balance or homeostasis
**ENDOCANNABINOID SYSTEM**

- **1988:** Cannabinoid receptors discovered in the brain – CB<sub>1</sub>
- **1992:** Endogenous cannabinoid discovered – Anandamide
- **1993:** Cannabinoid receptors discovered in the immune system – CB<sub>2</sub>
- **1995:** 2<sup>nd</sup> endocannabinoid discovered – 2-arachidonyl glycerol or 2-AG

**2000: more discoveries...**
- Cannabinoid receptors found in the spinal cord
- Endocannabinoids trigger feeding in newborn mice
- Cannabinoid receptor found in lungs

**BASIC COMPONENTS OF THE ECS**

The basic components of the ECS include:

- Cannabinoid Receptors (CB<sub>1</sub> and CB<sub>2</sub>)
- Endocannabinoids (Anandamide, 2-AG)
- Enzymes involved in the synthesis and degradation of cannabinoids
Basic Components of the ECS

The endocannabinoid system is a group of neuromodulatory lipids and their receptors in the brain are involved in a variety of physiological processes with the primary purpose to -

FUNCTION OF THE ECS

► The total effect of the ECS is to regulate homeostasis and prevent disease and slow aging. The ECS is a control system which involves tissue receptor proteins, cellular communication and control, molecular anatomy and the scavenging of oxygen free radicals.

► Its antioxidant and anti-inflammatory effects are applicable to most disease processes and that is why it is vital to good health.
PRIMARY FUNCTION OF THE ECS

- Basal Ganglia
  Movement - motor skills, learning

- Cerebellum
  Movement - coordination, muscles

- Medulla
  Nausea / Vomiting (CTZ)

- Cerebral Cortex
  Higher cognitive functioning

- Hypothalamus
  Appetite / metabolic process

- Hippocampus
  Learning, memory, stress

- Spinal Cord
  Peripheral sensation including pain

THE ECS IS IN ANIMALS AS WELL

- All mammals and other vertebrates have an ECS. You have to have a spine to have an ESC. So birth with a spine, is birth with an endocannabinoid system.
The ECS helps us:
► EAT...
► SLEEP...
► RELAX...
► PROTECT...
► FORGET...

Vincenzo Di Marzo, PhD, 1998

Runner’s high thought to be from the release of endorphins.
► But it is more likely that “runner's joy” is from the release of anandamide in the brain.

Greg Gerdeman, PhD

Phytocannabinoids: A group of C₂₁ terpenophenolic compounds uniquely produced by cannabis; e.g. THC, CBD, CBG

Endogenous cannabinoids: produced within our body; e.g. anandamide and 2-AG

Synthetic cannabinoids: man-made cannabinoids as medicine and for research; e.g. dronabinol is synthetic THC in sesame oil, nabilone
Different types of cannabinoids elicit different responses within the receptors. Two notable types are **Receptor Antagonists** and **Receptor Agonists** (not complicated)

- **Receptor Agonists** – TURN ON or activate the receptor
- **Receptor Antagonist** – TURN OFF or block the receptor

**CANNABINOIDS AND THE ECS**

The Human Endocannabinoid System

- CB1 receptors are transmembrane
- CB2 receptors are transmembrane

CB receptors are found on cell surfaces and help with body functions.

**THE CANNABIS PLANT**

- Annual
- Dioecious plant; Sinsemilla (without seeds) is the unfertilized female
- Family Cannabaceae (with hops)
THE CANNABIS PLANT

► **Hemp**
  + Low THC, high CBD

► **Marijuana or marihuana**
  + Mexican name for the plant
  + Used to create "reefer madness" about a new and dangerous drug that threatens our youth.
  + Known today as a "drug of abuse"
  + HCPs should avoid this racist and derogatory name for the plant

THE CANNABIS PLANT

**Hemp:**

► Cannabis plant with a THC content less than 0.3%, grown for its seed and fiber

► Has been used commercially in thousands of products for more than 12,000 years

► Can describe any industrial or nutritional product from cannabis that is not used as a drug

► Since hemp is generally rich in CBD it is currently used as a source of "CBD only" cannabis products

THE CANNABIS PLANT

► **Cannabis sativa**
  + Tall with long slender leaves, mind active

► **Cannabis indica**
  + Wider leaves, stocky plant, body active

► **Cannabis ruderalis**
  + Less studied

► **Cannabis Americana**
  + Pre-prohibition cannabis pharmaceuticals
THE CANNABIS PLANT

- Phyto-cannabinoid "Indica" comes from a plant whose leaves look like this:

- Phyto-cannabinoid "Sativa" comes from a plant whose leaves look like this:

THERAPEUTIC EFFECTS OF CANNABINOIDS
- Analgesic
- Anti-emetic
- Antioxidant
- Relaxant
- Anxiolytic
- Antipsychotic
- Antimicrobial
- Sedative
- Anti-inflammatory
- Appetite stimulant
- Neuroprotective
- Anti-depressant
- Anti-neoplastic
- Bone stimulant
- \( \downarrow \) intraocular pressure
- Anti-seizure
**PHYTO-CANNABINOIDs**

- **Delta-9-tetrahydrocannabinol (Δ-9-THC or THC)**
  - Primary psychoactive cannabinoid – produces the “high” or euphoria
  - anti-emetic
  - Analgesic
  - anti-inflammatory
  - antioxidant

**PHYTO CANNABINOIDs**

- **Cannabidiol (CBD)**
  - Non-psychoactive cannabinoid
  - Modulates the psychoactive effects of THC while improving the therapeutic effects of THC
  - Anxiolytic
  - Analgesic
  - Antipsychotic
  - Anti-inflammatory
  - Antioxidant
  - Antispasmodic

**PHYTO CANNABINOIDs**

- **Cannabinol (CBN)**
  - Oxidation breakdown product of THC
  - Sedative
  - Antibiotic

- **Delta-8-tetrahydrocannabinol (Δ-8-THC)**
  - Resembles Δ-9-THC, but little psychoactive effects
  - Anti-emetic

**PHYTO-CANNABINOIDS**

- **THCa** – *(raw form does not cause euphoria)*
  - Tetrahydrocannabinolic Acid is a biosynthetic precursor of tetrahydrocannabinol, the active component of Cannabis. When purified, it forms a powder which is unstable in the presence of acids, heat, oxygen, and/or light. Known for its anti-inflammatory, anti-spasmodic, anti-cancer effects.

- **CBDa** – *(raw form)* Cannabidiolic Acid
  - Is one of the four possible outcomes of Cannabigerolic acid (CBBga) being processed into cannabigerol (CBG), Cannabichromic acid (CBCa), Tetrahydrocannabinolic acid (THCa), and CBDa. Known for its anti-cancer and anti-inflammatory properties.

**JUICING RAW CANNABIS**
**THE “GRANDFATHER OF MEDICAL CANNABIS**

- Raphael Mechoulam, PhD
- Isolated THC in 1964
- Lab based in Israel
- Key in the discovery of the ECS
- Described the “Entourage effect” of whole cannabis
- “The Scientist” – new documentary on Mechoulam by Zach Klein

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**CANNABIS SYNERGISM**

- **THE ENTOURAGE EFFECT!**
  - The whole plant works best like an orchestra rather than its individual components as solo pieces.
  - “This type of synergism may play a role in the widely held (but not experimentally based) view that in some cases plants are better drugs than the natural products isolated from them.” (Mechoulam & Ben-Shabat 1999)
  - “The whole is greater than the sum of its parts.” (McPartland)

1 + 1 = 3

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**Food For Thought**

- What happens when exogenous cannabinoids are brought into the body?
- Is there such a thing as an Endocannabinoid Deficiency?

You’ll be glad you did...!
ENHANCING THE ECS

Several ways to strengthen the endocannabinoid system

- Good nutrition, avoid foods like refined grains, sugar and trans fats.
- Consume healthy, non-inflammatory choices such as; fruits, vegetables, nuts, seeds, and healthy fat sources like hemp seed oil, olive oil, fish, and eggs.

ENHANCING THE ECS

Several ways to strengthen the endocannabinoid system

- Acupuncture
- Yoga
- Massage
- Exercise

ENHANCING THE ECS

Another path to enhance or support the ECS is to consume exogenous cannabinoids.

- Cannabis offers a natural exogenous source of essential fatty acids and cannabinoids
- Hemp seeds and hemp seed oil
- Raw cannabis leaves and flowers – juiced
- Cannabis-based medicines (vaporized, tinctures, oil concentrates, edibles, topicals)
Clinical Endocannabinoid Deficiency

- Concept introduced by Ethan Russo, MD

- Some conditions such as migraines, fibromyalgia, and idiopathic bowel syndrome may be the result of a clinical endocannabinoid deficiency.


Clinical Endocannabinoid Deficiency

- **Hypothesis**: All humans have an underlying "endocannabinoid tone" that is a reflection of levels of AEA and 2-AG, their production, metabolism, and the relative abundance and state of cannabinoid receptors.

- **Theory**: In certain conditions, whether congenital or acquired, endocannabinoid tone becomes deficient and productive of pathophysiological syndromes.

Cannabis and the Endocannabinoid System

- Cannabis extracts are proving to be remarkably effective against a wide range of diseases for thousands of people. Numerous factors influence an individual’s unique response to cannabis medicine, including genetics. Some people may never be able to benefit due to rare genetic mutations. However, more and more studies are proving to be beneficial for the majority of people.
**CANNABIS & HOSPICE PATIENTS**

- Management of chronic pain without mental clouding
- Natural Sleep aid without “hangover” effects
- Anti-inflammatory effects
- Appetite stimulant and anti-emetic
- Antidepressant
- Replaces many pharmaceuticals that have unwanted side effects
- Spiritual effects r/t facing end of life...

**CANNABIS AND THE LAW**

**CANNABIS: PRE-PROHIBITION**

- History of medicinal use since recorded history
- Popular in the U.S. prior to the Marihuana Tax Act of 1937

Due to the high taxes imposed on cannabis it fell out of favor and was removed from the US Pharmacopeia in 1940.
THE CONTROLLED SUBSTANCES ACT OF 1970

► Schedule I – Forbidden – heroin, LSD, MDMA, marijuana
► Schedule II – highly addictive: cocaine, morphine, dilaudid, oxycodone, methadone, PCP, methamphetamine
► Schedule III – anabolic steroids, codeine or hydrocodone with aspirin or acetaminophen, and dronabinol
► Schedule IV – Benzodiazepines, Darvon, tramadol
► Schedule V – lomotil, cough suppressants with codeine

CANNABIS NOW IN SCHEDULE I (FEDERAL LAW)

► Not safe for medical use
► No therapeutic value
   "No currently accepted medical use in treatment in the United States"
► Highly Addictive

Legal States of Medical Cannabis in the United States
WHY CBD RICH ONLY LAWS?

► Sanjay Gupta documentary ("Weed" on CNN)
► Charlotte’s Web for Dravet’s syndrome (rare seizure d/o in children)
► Legislators (not health care professionals) are making decisions based on reefer madness myths about whole cannabis (with THC)
► From March 2014 to June 2015, 15 state legislatures passed CBD only bills

CANNABIS LAW IN THE CAROLINAS: LEGAL CBD ACCESS STATUES

North Carolina Epilepsy Alternative Treatment Act of 2015
HB 766
Patients who have been diagnosed with intractable epilepsy by a board certified neurologist that is affiliated with a hospital licensed in the State may possess hemp extract that is:

► Composed of < 0.9% THC and at least 5% CBD by weight.
► Contains no other psychoactive substance.
► Possesses in close proximity to the hemp extract, a certificate of analysis that indicates the hemp extract’s ingredients, including the percentage of THC and CBD by weight.

North Carolina Epilepsy Alternative Treatment Act of 2015
HB 766
The caregiver of the pediatric patient must be at least 18 years of age, a resident of North Carolina and must register with the Department of Health and Human Services and possess a statement written and dated by a neurologist that states that the patient:

► Has been examined and is under the care of the neurologist.
► Suffers from intractable epilepsy.
► May benefit from treatment with “hemp extract.”
CANNABIS LAW IN THE CAROLINAS: LEGAL CBD ACCESS STATUES

South Carolina Industrial Hemp Act of 2014
Act No. 216

An individual may legally cultivate, produce, or otherwise grow industrial hemp that is to be used for any lawful purpose. This includes the manufacture of industrial hemp products and scientific, agricultural, or other research related to other lawful applications for industrial hemp.

► Excludes industrial hemp from the definition of marijuana.
► Includes consumable products in the definition of hemp products.
► Consumable products must have < 0.3% THC by weight or volume.

CANNABIS LAW IN THE CAROLINAS: LEGAL CBD ACCESS STATUES

SC medical cannabis therapeutic treatment research Act of 2014 - Act No. 221

For patients and their parents, legal guardians, and other care givers who possess a written certification from a physician licensed in the state in which a person has been diagnosed with a severe form of epilepsy not adequately treated by traditional medical therapies, any form of any plant of the genus Cannabis that contains <0.9% THC > 15% CBD has been removed from the definition of marijuana.

Cannabis Laws in the Carolinas: Research Studies and Trials Legalized

North Carolina
• Hope 4 Haley and Friends- bill signed July 3, 2014.
• Amended by HB 766 July, 2015.

South Carolina
• Medical Cannabis Therapeutic Treatment Research Act- bill signed June 2, 2014.
• Created Julian’s Law, which allows for FDA approved clinical trials to treat patients who have certain forms of epilepsy with CBD.
• To date, no clinical trials have begun.
### Cannabis Laws in the Carolinas: Requirements for Studies/Trials

#### North Carolina
- Only a neurologist can diagnose a pt with intractable epilepsy.
- Neurologists must be board certified and affiliated with the neurology department of at least one hospital licensed in the state.

#### South Carolina
- Any physician who is board certified and practicing in an academic medical center in this state and treating patients with severe forms of epilepsy may serve as the principal investigator.

Only patients with epilepsy able to participate in these studies.

### Cannabis Law in the Carolinas: 2015-2016 Legislative Session - 1st Half

#### North Carolina
- Enact Medical Cannabis Act (House Bill 78), introduced in February 2015, received an unfavorable committee report on March 25, 2015, stopping any further action on the bill.

#### South Carolina
- Medical Marijuana Program Act (House Bill 4037 and Senate Bill 672), introduced in April 2015 as companion bills, received a hearing in separate House and Senate committees prior to the General Assembly’s recess.

### Cannabis Law in the Carolinas: 2015-2016 Legislative Session - 2nd Half

#### North Carolina
- The North Carolina General Assembly is not expecting to consider any cannabis-related legislation in the next half of its session.

#### South Carolina
- The Medical Marijuana Program Act remains intact in two committees during the General Assembly’s recess. The debate resumes in January 2016.
"We should be thinking of cannabis as a medicine first that happens to have some psychoactive properties, as many medicines do, rather than as an intoxicant that happens to have a few therapeutic properties on the side."

– Dr. Tod Mikuriya

REFERENCES

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- www.themedicalcannabisinstitute.org