Chapter I: Ocular Health and Ocular Disease

Learning Objectives

1. Discuss assessment protocols to determine level of endocannabinoid deficiencies of the ocular system.
2. Discuss therapeutic strategies to address endocannabinoid deficiencies of the ocular system.
3. Discuss patient care guidelines to implement cannabinoid therapy with standard of care pharmaceutical regimens pertaining to the ocular system.
4. Discuss educational guidelines for patients to monitor clinical outcomes when implementing cannabinoid protocols for ocular disorders.

The Endocannabinoid System and Cannabidiol (CBD) - Introduction

The endocannabinoid system (ECS) is a lipid-derived signaling system discovered within the past decade. Cannabinoids, which are homeostatic regulators, circulate throughout human and animal systems continuously, affecting all physiological processes. The endocannabinoid system is comprised of CB1 and CB2 receptors, which bind directly or indirectly to cannabinoids and phytocannabinoids. CB1 receptors are excitatory and are located in the central nervous system, lungs, liver, and kidney. CB2 receptors regulate immunological responses and are located in the immune and circulatory systems. Endogenous compounds, such as anandamide and arachidonylglerol (2-AG), are made by mammals from lipids and bind directly to the CB1 and CB2 receptors, serving as neurotransmitters for cannabinoids. Cannabidiol (CBD oil), a non-psychotropic cannabinoid naturally occurring in human and animal species, is also a phytocannabiniod, derived from the industrial hemp plant. While CBD does not bind directly with receptors, it does affect stress genes, such as Soat2 and Cyp27a1, which control sterol (i.e., cholesterol) metabolism. CBD increases the amount of anandamide and other vital lipids, thereby indirectly increasing the availability of circulating cannabinoids to bind with CB1 and CB2 receptors.

Research has shown that cannabidiol, in the form of CBD oil, has therapeutic benefits individually and adjunctively with other interventions. Cannabidiol (CBD) made from legal, industrial hemp contains less than .3% THC, rendering it non-psychoactive. CBD oil has antiemetic, anxiolytic, antitumoral, and immunologically inhibitory properties. Three categories differentiate the types of clinical endocannabinoid deficiency (CECD), which are associated with different disease processes and disorders: genetic, acquired, and idiopathic autoimmune. Many disorders have a combination of CECD origins, and supplementation with cannabidiol (CBD) requires ongoing assessment to facilitate optimal benefit for the individual.

The Human Endocannabinoid System

The human endocannabinoid system is responsible for memory networks in the brain, both excitatory and inhibitory, including the neurogenesis of hippocampal granule cells, which regulate the timing of the endocannabinoids in accordance with the brain's needs, pain perception, mood, appetite and taste regulation, and metabolic function, which regulates the storage of energy and transport of cellular nutrition. The endocannabinoid system affects the lipocytes and fat cells, collectively known as adipocytes, hepatocytes, the gastrointestinal tract, musculoskeletal system, and endocrine system. Cannabinoid receptors CB1 and CB2 facilitate the responses of the endocannabinoid system in the body, which are critical to maintaining

homeostasis. CB1 receptors are located in the central and peripheral nervous systems as well as the lungs, kidneys, and liver. CB2 receptors are predominantly expressed in the immune system and hematopoietic cells. The direct effect of the endocannabinoid deficiency (CECD) correlates with multisystemic clinical outcomes in such conditions as hyperinsulinemia, diabetes, atherosclerosis cardiovascular disease, and obesity. Three primary categories are herein defined to discuss endocannabinoid deficiency (CECD): genetic, acquired, and idiopathic autoimmune. Genetic endocannabinoid deficiency (CECD) relates to hereditary acquisition of a disorder; acquired refers to an infectious of traumatic origination, and idiopathic autoimmune refers to etiologies for endocannabinoid deficiencies (CECD) which do not have direct associations. Diseases and disorders are assigned to one or more of these categories because often secondary disorders arise with physiological changes associated with the primary diagnosis. For example, diabetes has been associated with endocannabinoid deficiency (CECD) and the disease is categorized as idiopathic autoimmune, with no distinct origin. Traumatic injury to the eye with retinal detachment adds the category of acquired endocannabinoid deficiency (CECD) as well to the assessment.

Cannabidiol (CBD), a non-psychotropic cannabinoid naturally occurring in human and animal species, occurs as a phytocannabinoid, CBD oil, which is derived from the industrial hemp plant. The restorative effects of cannabidiol (CBD oil), which increases anandamide and other lipid neurotransmitters, thereby restoring the endocannabinoid system, are of interest in the medical management of multiple disorders, including disorders of the ocular system, which is directly affected by the immunological and cardiovascular systems. Indeed, research supports that plant-derived cannabidiol (CBD) has neuroprotective and therapeutic ocular benefits.

Cannabidiol (CBD)

Cannabidiol (CBD) is a non-psychotropic and non-toxic compound which has been demonstrated to positively affect the human endocannabinoid system. Cannabidiol (CBD), derived from the hemp plant, demonstrates anti-inflammatory and immune-modulating properties. Cannabidiol (CBD) has a low affinity for CB1 and CB2 receptors in the human body, but acts as an indirect antagonist of their agonists. (Antagonists are defined as substances that stop or inhibit the effects of another substance on the cellular surface, producing the same effect as a substance which would normally bind to the receptor. Agonists are chemicals that bind to receptors and elicit a biological response). Therefore, cannabidiol (CBD) may enhance the therapeutic effects of THC, possibly by increasing the density of the CB1 receptors. Cannabidiol (CBD) has been demonstrated to cross the blood-brain barrier and exert antioxidant, antimicrobial, and neuroprotective properties, rendering it valuable in the prevention and treatment of oxidative ocular disorders and diseases.

Human Ocular System

The human eye is an asymmetrical globe, approximately one inch in diameter, comprised of five major components; the iris, cornea, pupil, sclera, and conjunctiva. The interpretation of vision is articulated as light projects through the pupil, a circular opening, and the lens, which allows the focus of light onto the rear (posterior) portion of the eye. The retina, which is a collection of light-sensing cells, converts light into electrical impulses which are signaled to the brain. Central vision is controlled by the macula, a small, highly sensitive area located inside the retina, and the fovea, a small depression within the macula, which provides the most acute vision. Genetic dominance influences the color of the eye, located within the iris, the pigmented area covered

by the clear dome called the cornea. The eye is protected by a fine layer of tissue which covers the anterior (front) of the organ, with the exception of the cornea.

Cannabidiol (CBD) and Ocular Disorders and Diseases

Diseases of the ocular system directly related to oxidative stress include retinal diseases such as glaucoma, uveitis, macular degeneration, and diabetic retinopathy. The human body evokes an active inflammatory response to mitigate damage from injury or infection via microglial cell and macrophage release. However, activation of microglial cells and macrophages is also associated with the release of glutamate, reactive oxidative species (ROS), nitric oxide (NO), and tumor necrosis factor (TNF), causing an escalation of inflammation, vascular deterioration, and neurodegradation. Cannabidiol (CBD), according to El-Ramessay and Tang (2008), blocks the oxidative stress response and activation of proteins such as p-38 MAPK and microglial cells, reducing damage associated with inflammatory responses.

Glaucoma

Glaucoma describes an array of ocular disorders associated with intraocular pressure imbalance, both elevated and normal to low, with associated loss of retinal ganglion cells, nerve damage, and visual loss, leading to possible blindness. Glaucoma is either categorized as open angle (slow onset and progression) or closed angle (painful and rapid progression) and pertains to the angle between the iris and the cornea through which fluid flows as a part of the trabecular network. There appears to be a hereditary predisposition to the development of glaucoma, suggesting a genetically associated endocannabinoid deficiency (CECD). Because the incidence of glaucoma increases exponentially with age, the neuroprotective benefits of cannabidiol (CBD) are of particular interest.

Research indicates that the release of excessive glutamate, a vital neurotransmitter normally present in retinal ganglion cells, induces ischemia-related neurotoxicity and cell death. Cannabidiol (CBD) has been demonstrated as a non-psychoactive antioxidant which reduces the production of reactive oxygen species (ROS). El-Remmessey demonstrated in 2003 that cannabidiol (CBD) is neuroprotective against glutamate-induced retinal injury, preventing formation of lipid peroxides, nitrite and nitrate compounds, and nitrotyrosine, the physiological basis for the development of glaucoma. Preventive use of cannabidiol (CBD) is therefore suggested in the prophylaxis of glaucoma.

Uveitis

Uveitis describes a collective group of inflammatory ocular diseases which produce edema and tissue destruction leading to vision loss or blindness. While the uvea of the eye is affected, other physiological components such as the lens, retina, optic nerve, and vitreous humor are likely targets. Anterior uveitis, (associated with rheumatologic and infectious diseases), intermediate, (associated with sarcoidosis and multiple sclerosis), posterior (associated with choroiditis and infectious diseases), and panuveitis (associated with Behcet's disease), respond to anti-inflammatory effects of cannabidiol (CBD) after the occurrence, according to Liu and Khalifa (2005). Endocannabinoid deficiency (CECD) is therefore relative to uveitis, and is acquired and idiopathic autoimmune relative to the aforementioned types of uveitis. Preventatively, cannabidiol (CBD) was found to exert neuroprotection against uveitis via the blockage of oxidative stress and damaging effects of endotoxins. In view of the research, the use of

cannabidiol (CBD) is suggested in the prevention of uveitis associated with autoimmune and infectious disease processes.

Macular Degeneration

The activation of microglial cells of the retina in dry macular degeneration enhances tissue damage caused by the underlying inflammatory disorder. Research indicates both genetic and acquired origins of endocannabinoid deficiency (CECD) disorder. CECD is associated with use of nicotine and macular degeneration is linked to tobacco use. Because macular degeneration affects millions of individuals over the age of seventy years, the research which indicates that cannabidiol (CBD) provides effective neuroprotective and anti-inflammatory properties suggests the preventive use of cannabidiol (CBD) throughout the life course.

Diabetic Retinopathy

Diabetic retinopathy is associated with the deterioration of the blood-retinal barrier and cell-death of the retinal ganglion cells, culminating in visual loss. The dysregulation of glucose metabolism which is characteristic of diabetes mellitus, enhances cell hyperpermeability in the retina, increasing the susceptibility of injury by reactive oxidative stress (ROS). Research indicates a significant hereditary factor in diabetes mellitus, but also suggests that endocannabinoid deficiency (CECD) is acquired and associated with an unhealthy diet and obesity which contribute to the development of the disease. Cannabidiol (CBD) has been demonstrated to reduce oxidative and nitrative stress in diabetic retinas by maintaining the integrity of the blood-retinal barrier through blockage of glutamate accumulation and neuronal cell death. Therefore, the use of cannabidiol (CBD) in diabetes is suggested to reduce inflammation and provide neuronal protection, essential to the prevention of diabetic retinopathy.

Endocannabinoid Deficiency (CECD) Classification: Ocular Disorders

Disorder	Origin of CECD
Glaucoma	Genetic
Uveitis	Acquired
Macular Degeneration	Genetic, Acquired
Diabetic Retinopathy	Genetic, Acquired

CEN Medical Cannabis Pharmacological Prescription and Coding System
Ocular Disorder Application

The CEN Medical Cannabis Pharmacological Prescription and Coding System (CEN/MCPPCS) provides language that enables the health care practitioner to communicate with the dispenser of medical cannabis. The first two letters of the system refer to the cannabis type: cannabis sativa, cannabis indica, or cannabis hybrida. The numerical value in percentage to the right of the colon refers to the recommended THC content in percentage, and the numerical value in sequence to the right of the THC percentage refers to the recommended CDB content.

(CEN/MCPPCS): Cannabis type (sativa, indica, hybrida; THC percentage or range/CBD percentage or range) or Hemp Cannabidiol (CBD)

Example: Cannabidiol (CBD oil) is recommended for the patient. The concentration of the CBD oil is 19.5% and the patient is to ingest 20 mg of CBD oil each day as adjunctive therapy in the treatment of chorioretinitis (ICD-9: 363.20). The prescription would therefore read:

Mary Jane Rider
Date of Birth: 03-09-1950
Diagnosis: Chorioretinitis, ICD-9 code: 363.20
CBD: 0.00%/ 19.5%. Take 20 mg. of CBD oil by mouth once daily. Use dropper as indicated.
Rich Jones, M.D.

The patient would then be able to purchase the CBD oil online or at a dispensary, offering the prescription to the pharmacist or technician.

Composition Assignments

1. Please suggest a plan of care based upon the following patient information. Discuss if CBD oil would be indicated with rationale and the type of endocannabinoid deficiency(s) (CECD) for the ocular disease process.
    a. A 48-year-old African American female with a history of diabetes mellitus schedules an appointment to discuss lifestyle and dietary management changes relevant to her disease. She is insulin dependent and has not experienced ocular problems associated with diabetes mellitus.
2. Please choose an article from the CEN library on an aspect of cannabidiol (CBD) and the ocular system. Write a two-hundred-word critical analysis paper on this research article and determine the following in your paper:
    a. Author and affiliation
    b. Study population
    c. Purpose
    d. Outcome of the study
    e. Importance of the research

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Chapter II: Neurological Health and Disease

Learning Objectives

1. Discuss assessment protocols to determine level of endocannabinoid deficiencies of the neurological system.
2. Discuss therapeutic strategies to address endocannabinoid deficiencies of the neurological system.
3. Discuss patient care guidelines to implement cannabinoid therapy with standard of care pharmaceutical regimens pertaining to the neurological system.
4. Discuss educational guidelines for patients to monitor clinical outcomes when implementing cannabinoid protocols for neurological disorders.

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The endocannabinoid system (ECS) is a lipid-derived signaling system discovered within the past decade. Cannabinoids, which are homeostatic regulators, circulate throughout human and animal systems continuously, affecting all physiological processes. The endocannabinoid system is comprised of CB1 and CB2 receptors, which bind directly or indirectly to cannabinoids and phytocannabinoids. CB1 receptors are excitatory and are located in the central nervous system, lungs, liver, and kidney. CB2 receptors regulate immunological responses and are located in the immune and circulatory systems. Endogenous compounds, such as anandamide and arachidonylglerol (2-AG), are made by mammals from lipids and bind directly to the CB1 and CB2 receptors, serving as neurotransmitters for cannabinoids. Cannabidiol (CBD oil), a non-psychotropic cannabinoid naturally occurring in human and animal species, is also a phytocannabiniod, derived from the industrial hemp plant. While CBD does not bind directly with receptors, it does affect stress genes, such as Soat2 and Cyp27a1, which control sterol (i.e., cholesterol) metabolism. CBD increases the amount of anandamide and other vital lipids, thereby indirectly increasing the availability of circulating cannabinoids to bind with CB1 and CB2 receptors.

Research has shown that cannabidiol, in the form of CBD oil, has therapeutic benefits individually and adjunctively with other interventions. Cannabidiol (CBD) made from legal, industrial hemp contains less than .3% THC, rendering it non-psychoactive. CBD oil has antiemetic, anxiolytic, antitumoral, and immunologically inhibitory properties. Three categories differentiate the types of clinical endocannabinoid deficiency (CECD), which are associated with different disease processes and disorders: genetic, acquired, and idiopathic autoimmune. Many disorders have a combination of CECD origins, and supplementation with cannabidiol (CBD) requires ongoing assessment to facilitate optimal benefit for the individual.

The Human Endocannabinoid System - Cerebral Endocannabinoid Network

The human endocannabinoid system is responsible for memory networks in the brain, both excitatory and inhibitory, including the neurogenesis of hippocampal granule cells, which regulate the timing of the endocannabinoids in accordance with the brain's needs, pain perception, mood, synaptic plasticity, motor learning, appetite and taste regulation, and metabolic function, which regulates the storage of energy and transport of cellular nutrition. Cannabinoid receptor binding sites are located in the forebrain areas associated with higher cognitive function, forebrain, midbrain, and hindbrain areas associated with movement control, and hindbrain areas associated with motor and sensory functions attributed to the autonomic nervous system. The endocannabinoid system affects the lipocytes and fat cells, collectively

known as adipocytes, hepatocytes, in the gastrointestinal tract, musculoskeletal system, and endocrine system. The endogenous arachidonate-based lipids, anandamide and 2-arachidonoylglycerol (2-AG) are physiological ligands for the cannabinoid receptors.

Cannabinoid receptors CB1 and CB2, two G-protein-coupled receptors, facilitate the responses of the endocannabinoid system in the body, which are critical to maintaining homeostasis. CB1 receptors are located in the central and peripheral nervous systems as well as the lungs, kidneys, and liver. CB2 receptors are predominantly expressed in the immune system and hematopoietic cells.

The direct effect of endocannabinoid deficiency (CECD) correlates with multisystemic clinical outcomes in such conditions as hyperinsulinemia, diabetes, dementia, cardiovascular disease, multiple sclerosis, and obesity. Three primary categories are herein defined to discuss endocannabinoid deficiency (CECD): genetic, acquired, and idiopathic autoimmune. Genetic endocannabinoid deficiency (CECD) relates to hereditary acquisition of a disorder; acquired refers to an infectious of traumatic origination, and idiopathic autoimmune refers to etiologies for endocannabinoid deficiencies (CECD) which do not have direct associations. Diseases and disorders are assigned to one or more of these categories because often secondary disorders arise with physiological changes associated with the primary diagnosis. For example, HIV has been associated with endocannabinoid deficiency (CECD) and the disease is categorized as acquired, originating from an infectious source. The presentation of multiple sclerosis in HIV/AIDS, which affects the neurological system, supports adding the category of idiopathic autoimmune as well to the assessment. Because the endocannabinoid system facilitates communication and coordination between various cell types, deficiencies directly affect physiological homeostasis.

Cannabidiol (CBD), a non-psychotropic cannabinoid naturally occurring in human and animal species, occurs as a phytocannabinoid, CBD oil, which is derived from the industrial hemp plant. The restorative effects of cannabidiol (CBD oil), which increases anandamide and other lipid neurotransmitters, thereby restoring the endocannabinoid system, are of interest in the medical management of multiple disorders, including disorders of the neurological system, which is directly affected by the immunological. Indeed, research supports that plant-derived cannabidiol (CBD) has neuroprotective benefits.

Cannabidiol (CBD)

Cannabidiol (CBD) is a non-psychotropic and non-toxic compound which has been demonstrated to positively affect the human endocannabinoid system. Cannabidiol (CBD), derived from the hemp plant, demonstrates anti-inflammatory and immune-modulating properties. Cannabidiol (CBD) has a low affinity for CB1 and CB2 receptors in the human body, but acts as an indirect antagonist of their agonists. (Antagonists are defined as substances that stop or inhibit the effects of another substance on the cellular surface, producing the same effect as a substance which would normally bind to the receptor. Agonists are chemicals that bind to receptors and elicit a biological response.) Therefore, cannabidiol (CBD) may enhance the therapeutic effects of THC, possibly by increasing the density of the CB1 receptors. Cannabidiol (CBD) has been demonstrated to cross the blood-brain barrier and exert antioxidant, antimicrobial, and neuroprotective properties, rendering it valuable in the prevention and treatment of oxidative neurological disorders and diseases.

Human Brain
The brain is the core governing structure of the human body. At a weight of over three pounds, the human brain, comprised of eighty-six billion neurons and associated glial cells and blood vessels, is the largest and most complex of all mammalian brains. The human cerebral cortex, a thick layer of neural tissue, is divided into four lobes of the forebrain; the frontal, parietal, temporal and occipital lobes. Each lobe is comprised of cortical areas associated with particular executive functions, including self-control, planning, reasoning, abstract thought, motor control, language, and vision. The two hemispheres of the brain are defined by lateralization processes, such as language, which is associated with left-sided hemispheric dominance, and spatiotemporal reasoning, which is associated with right-sided dominance. The cerebellum, or hindbrain, located at the base of the brain above the brainstem, coordinates voluntary movements such as posture, balance, coordination, speech, and learned motor behaviors. Further, the brainstem, which includes the medulla oblongata pons, and the midbrain, regulates motor and sensory aspects of the central nervous system, as well as cardiac and respiratory functions. Finally, the endocannabinoid system, comprised of neuromodulatory lipids and receptors in the brain, regulates the vast array of physiological processes essential for human life.

Amyotrophic Lateral Sclerosis (**ALS**)
Amyotrophic lateral sclerosis (ALS), Lou Gehrig's Disease, is a neurodegenerative disorder characterized by muscle spasticity, rapid and progressive weakness, muscle wasting, dysphagia, expressive aphasia, and respiratory failure. Endocannabinoid deficiency (CECD), noted as genetic and acquired in ALS, has been documented, and is characterized by decreased cannabinoid availability and subsequent decline in the number of CB1 receptors. CB1 receptors are critical in the cerebral cortex and are responsible in reducing TAU protein proliferation. Further, CB2 receptors are also rendered dysfunctional in ALS, causing expedited inflammatory responses which correlate with the aggressive clinical neurological decline in affected individuals. Research supports the administration of cannabidiol (CBD) preventatively for neuroprotection in individuals with hereditary risk factors, and post-diagnosis, to decrease neuroinflammation, reduce neurodegeneration, and increase cerebral plasticity. Because cannabidiol (CBD) has an analgesic and antispasmodic effect, administration of cannabidiol (CBD) is supported by clinical research in the adjunctive management of spasm and associated pain in ALS.

Alzheimer’s Disease
Alzheimer’s disease is a progressive neurodegenerative disorder which affects the cerebral neurons causing loss of memory, language and cognitive abilities, and mood and behavioral changes. The death of neurons which normally produce acetylcholine, the neurotransmitter which facilitates communication within brain, characterizes a progressive neurological deterioration. Hippocampal nerve cells are initially affected causing short-term memory decline. With progression to the cerebral cortex, the decline of language skills and the impairment of judgment are clinically noted. The endocannabinoid deficiency (CECD) which characterizes Alzheimer’s is categorized as both genetic and idiopathic autoimmune. Aggregation of amyloid-beta tau proteins and profound neurodegeneration, neuroinflammation, and neurotoxicity which characterize Alzheimer’s, were induced in animal models. Reversal of social recognition dysfunction and anxiety was demonstrated after the administration of cannabidiol

(CBD), a non-psychoactive phytocannabinoid which exhibits neuroprotective, anti-inflammatory, and anti-oxidant properties, and which promotes neurogenesis in the brain. Further research supports using cannabidiol (CBD) as a preventive measure against Alzheimer's, noting the anti-inflammatory and neuroprotective properties of CBD. Thus, cannabidiol (CBD) can be useful after diagnosis, and proactively, in the management of Alzheimer's disease.

Parkinson's Disease

In Parkinson's disease, which affects the substantia nigra in the midbrain, the production of dopamine, and the basal ganglia, progressive symptoms including bradykinesia, muscle and joint stiffness, impaired balance, dysphasia, impaired reaction time, memory, sleep disturbances, depression, and anxiety, are associated with endocannabinoid deficiency (CECD) of genetic origin. Research indicates that the administration of cannabidiol (CBD) reduced dystonia, spasticity, and phytocannabinoid administration. Research indicates a positive human response to adjunctive use of cannabidiol (CBD) in the management of dystonia, tremor, psychosis, spasticity, and associated neuropathic pain. Because cannabidiol (CBD) exhibits neuroprotective and anti-inflammatory properties, administration is recommended prophylactically in individuals at genetic risk for disease development to preserve neuronal integrity and CB1 and CB2 receptor functionality in the cerebral cortex.

Huntington's Chorea

Huntington's chorea, a progressive neurodegenerative disorder, which affects motor coordination, causes involuntary movement patterns, cognitive and psychiatric decline, and behavioral abnormalities, is categorized as a disease associated with genetic endocannabinoid deficiency (CECD). In Huntington's chorea, CB1 receptors in the basal ganglia are significantly reduced, which affects the upregulatory responses of the CB2 receptors in lesioned areas. Cannabinoids, which normally provide neuroprotection, are progressively diminished in Huntington's chorea, which accounts for the neuronal destruction throughout the cerebral cortex and associated symptomatology, including painful dystonic movements, anxiety, and depression. Cannabidiol (CBD) has been demonstrated to slow progressive dystonic symptoms and associated pain, relieve anxiety, and enhance well-being in patients affected by the disease. In individuals at genetic predisposition for the development of Huntington's chorea, the neuroprotective effects of cannabidiol (CBD) may slow the onset and severity of symptoms associated with Huntington's chorea.

Cerebral Ischemia and Stroke

Cerebral ischemia refers to injury to the cerebral cortex as a result of an obstruction within the circulatory system of the brain. Factors which contribute to cerebral ischemia and stroke include atherosclerosis, hypertension, diabetes, and nicotine use. Cerebral thrombosis or cerebral embolism interrupts cerebral blood flow, resulting in paralysis, expressive and receptive aphasia, and/or death. The acquired endocannabinoid system deficiency (CECD), which precedes cerebral ischemia and cerebral stroke, reflects forebrain CB1 and CB2 receptor dysfunction and diminished circulating cannabinoids. Indeed, immediate administration of cannabidiol (CBD) up to four hours after a cerebral ischemic incident reduced inflammatory and residual motor deficits in human subjects. The antioxidant, anxiolytic, and neuroprotective properties of cannabidiol (CBD) were also found to be preventative in subjects predisposed to cerebral ischemia, enhancing cerebral function through restoration of circulating cannabinoids and functionality of CB1 and CB2 receptors.

Multiple Sclerosis
Multiple sclerosis is a neurodegenerative disorder characterized by the production of lesions in the cerebral cortex and spinal cord and diminished myelin cell production. Classified as remitting-relapsing, in which exacerbations with residual deficits and recovery spanning over years, or progressive, which alludes to a downward spiral of neurological deterioration following diagnosis, until death, multiple sclerosis affects such functions as motor coordination, cognition, and thermoregulation. The endocannabinoid system deficiency (CECD) in multiple sclerosis is idiopathic autoimmune, and sensory pathways are affected as myelin sheath destruction occurs. Pain and spasticity affect nearly all patients with multiple sclerosis. Cannabidiol (CBD), which has neuroprotective and analgesic affects, effectively reduces pain and spasticity associated with multiple sclerosis. Administration of cannabidiol (CBD) early in the diagnosis of multiple sclerosis is suggested to reduce the neuroinflammatory response within the cerebral cortex, and enhance cannabinoid binding to CB1 and CB2 receptors, and reduce potential myelin cell destruction.

Schizophrenia
Schizophrenia is a psychiatric disorder characterized by abnormal social behavior, inability to discern reality from fantasy, confused thought processes, hallucinations, limited social interactions and emotional expression, and inactivity. Research indicates that circulating cannabinoids in the forebrain are depleted and CB1 receptors become less dense, causing decrease receptivity. The endocannabinoid deficiency (CECD) in schizophrenia appears to be genetic and pharmacological approaches, which have focused upon the antagonism of dopamine receptors, has been of limited value. The administration of cannabidiol (CBD) has been shown to increase the density of CB1 receptors and increase available cannabinoids in the brain. Anxiety, hallucinations, and behavioral modification have been noted, warranting concurrent administration of cannabidiol (CBD) in the management of schizophrenia.

Epilepsy
Dravet syndrome or Severe Myoclonic Epilepsy of Infancy (SMEI), is form of irretractable epilepsy, which emerges in infancy with prolonged and frequent seizure activity. Behavioral and developmental delays, motor development and coordination, language and speech acquisition, growth and nutritional deficiencies, immunosuppression, sensory integration disorders, and autonomic nervous system dysregulation characterize this disorder. Sudden unexplained death in epilepsy is prevalent as well. Endocannabinoid deficiency (CECD) is categorized as idiopathic autoimmune, in light of the decrease in circulating cannabinoids and the reduced density of both CB1 and CB2 receptors. Research has conclusively demonstrated the benefit of the administration of cannabidiol (CBD) in Dravet syndrome, reducing persistent seizure activity in the majority of human subjects, reduction in associated symptoms, and improvement in cognitive function. Increased cannabinoid availability and increased density of CB1 and CB2 receptors correlates with neurological improvement in Dravet, supporting the possible concurrent and preventative use of cannabidiol (CBD) in other forms of epileptic disorders.

Migraine
Migraine is a chronic neurological disorder characterized by moderate to severe headaches accompanied by autonomic nervous symptoms including nausea and vomiting, light, sound, and smell sensitivities, and pain. Approximately one third of individuals present with an aura, or

transient visual, auditory, sensory, linguistic, or motor disturbance prior to migraine onset. Endocannabinoid deficiency (CECD) in migraine is categorized as genetic, with statistically significant hereditary prevalence. CB1 receptors in the cerebral cortex and trigeminal nucleus of the brainstem appear unable to process neurotransmitters, causing inflammatory responses which induce severe pain. Cannabidiol (CBD) is suggested to reduce neurovascular inflammation and provide analgesia in migraine and prophylaxis in chronic migraine.

Cancer of the Brain

Malignancy in the human brain can be the primary source of the respective cancer or secondary metastasis from a primary site. The anticarcinogenic effects of cannabidiol (CBD) in certain types of cancer are well documented. Gliomas and brain metastasis from breast and lung cancer are potential targets for cannabidiol (CBD) therapy. Cannabinoids produce antitumor effects through induction of cell death, cell growth inhibition, and inhibition of tumor angiogenesis. Endocannabinoid deficiency (CECD) in oncology is categorized as genetic and/or acquired and responds to administration of concentrated cannabidiol (CBD). Neuroprotection of non-transformed cells has also been demonstrated, suggesting adjunctive cannabidiol (CBD) therapy when chemotherapy and/or radiation are also recommended.

Depression & Anxiety

Major affective mood disorders, including depression and anxiety, are targets for cannabidiol (CBD) therapy. Depression, which is characterized by pervasive and persistent low mood, low self-esteem, and loss of interest in normally enjoyable activities, affects CB1 receptors in such areas as the anterior cingulate cortex and the subgenual cingulate. Neurodegeneration of the ventricles is also noted in chronic depression, highlighting CB2 receptor dysregulation as well. In anxiety disorders, CB1 receptors in the amygdala, which elicit the fight or flight response, and in the anterior cingulate cortex are affected. Excessive and persistent worry characterizes this disorder. Both depression and anxiety are categorized as either genetic or acquired endocannabinoid deficiencies (CECD), which respond to the administration of cannabidiol (CBD). The anxiolytic and antidepressant properties of cannabidiol (CBD) increase available circulating cannabinoids to affected cerebral areas in both disorders and enhance receptivity of dysfunctional CB1 and CB2 receptors.

Chronic Traumatic Encephalopathy (CTE)

Chronic traumatic encephalopathy (CTE) is associated with repetitive concussion to the brain, tau protein expression, neurodegeneration, mood disorders, including rage and depression, and dementia. CTE in football, basketball, boxing, and soccer, and among combat military personnel affects the endocannabinoid system as an acquired deficiency. Depending upon the area of traumatic injury, regional CB1 and CB2 receptors are affected. Available cannabinoids decline in CTE, affecting serotonin and dopamine responses, neurotransmitter communication, and the density of CB1 and CB2 receptors. Administration of cannabidiol (CBD) after the development of CTE has demonstrated a positive response, with reduction in symptomatology. Preventative cannabidiol (CBD) administration is recommended for individuals at risk for CTE because cannabidiol (CBD) reduces neuroinflammatory responses, acts as an anxiolytic - which reduces cell death - and restores the functionality of affected CB1 and CB2 receptors.

Endocannabinoid Deficiency (CECD) Classification: Neurological Disorders

Disorder	Origin of CECD
ALS	Genetic, Acquired
Alzheimer's	Genetic
Parkinson's	Genetic
Huntington's Chorea	Genetic
Cerebral Ischemia and Stroke	Genetic, Acquired
Multiple Sclerosis	Idiopathic Autoimmune
Epilepsy and Dravet's	Genetic
Migraine	Genetic, Acquired
Depression, Anxiety	Genetic, Acquired
CTE	Acquired

CEN Medical Cannabis Pharmacological Prescription and Coding System Neurological Disorder Application

The CEN Medical Cannabis Pharmacological Prescription and Coding System (CEN/MCPPCS) provides language that enables the health care practitioner to communicate with the dispenser of medical cannabis. The first two letters of the system refer to the cannabis type: cannabis sativa, cannabis indica, or cannabis hybrida. The numerical value in percentage to the right of the colon refers to the recommended THC content in percentage, and the numerical value in sequence to the right of the THC percentage refers to the recommended CDB content.

(CEN/MCPPCS): Cannabis type (sativa, indica, hybrida; THC percentage or range/CBD percentage or range) or Hemp Cannabidiol (CBD)

Example: Cannabidiol (CBD oil) is recommended for the patient. The concentration of the CBD oil is 19.5% and the patient is to ingest 25 mg. of CBD oil every six hours, 100 mg./day. Increase dose by 25 mg. every other day after one week to achieve a 200 mg./day daily or as tolerated for chronic traumatic encephalopathy (ICD-9: 348.30). The prescription would therefore read:

Marvin James Reynolds
Date of Birth: 09-01-1989
Diagnosis: Chronic traumatic encephalopathy (CTE), ICD-9 code: 348.30
CBD: 0.00%/ 19.5%. Take 25 mg. of CBD oil by mouth four times daily (q6h) daily. Increase dose by 25 mg after one week to achieve a daily dose of 200 mg./day in divided doses q 6h or as tolerated. Use dropper as indicated.
Margaret Henderson, M.D.

The patient would then be able to purchase the CBD oil online or at a dispensary, offering the prescription to the pharmacist or technician

Composition Assignments

Please suggest a plan of care based upon the following patient information.

1. Discuss if CBD oil would be indicated with rationale and the type of endocannabinoid deficiency (s) (CECD) for the neurological disease process.
    a. A 28-year-old African American male with a history of headaches schedules an appointment to discuss lifestyle and dietary management changes relevant to his disease. He is morbidly obese and has hypertension. He has just started an antihypertensive medication and was referred for nutritional counseling.
2. Please choose an article from the CEN library on an aspect of cannabidiol (CBD) and the neurological system. Write a two-hundred-word critical analysis paper on this research article and determine the following in your paper:
    a. Author and affiliation
    b. Study population
    c. Purpose
    d. Outcome of the study
    e. Importance of the research

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Chapter III: Gastrointestinal Health and Disease

Learning Objectives

1. Discuss assessment protocols to determine level of endocannabinoid deficiencies of the gastrointestinal system.
2. Discuss therapeutic strategies to address endocannabinoid deficiencies of the gastrointestinal system.
3. Discuss patient care guidelines to implement cannabinoid therapy with standard of care pharmaceutical regimens pertaining to the gastrointestinal system.
4. Discuss educational guidelines for patients to monitor clinical outcomes when implementing cannabinoid protocols for gastrointestinal disorders.

The Endocannabinoid System and Cannabidiol (CBD) - Introduction

The endocannabinoid system (ECS) is a lipid-derived signaling system discovered within the past decade. Cannabinoids, which are homeostatic regulators, circulate throughout human and animal systems continuously, affecting all physiological processes. The endocannabinoid system is comprised of CB1 and CB2 receptors, which bind directly or indirectly to cannabinoids and phytocannabinoids. CB1 receptors are excitatory and are located in the central nervous system, lungs, liver, and kidney. CB2 receptors regulate immunological responses and are located in the immune and circulatory systems. Endogenous compounds, such as anandamide and arachidonylglerol (2-AG), are made by mammals from lipids and bind directly to the CB1 and CB2 receptors, serving as neurotransmitters for cannabinoids. Cannabidiol (CBD oil), a non-psychotropic cannabinoid naturally occurring in human and animal species, is also a phytocannabiniod, derived from the industrial hemp plant. While CBD does not bind directly with receptors, it does affect stress genes, such as Soat2 and Cyp27a1, which control sterol (i.e., cholesterol) metabolism. CBD increases the amount of anandamide and other vital lipids, thereby indirectly increasing the availability of circulating cannabinoids to bind with CB1 and CB2 receptors.

Research has shown that cannabidiol, in the form of CBD oil, has therapeutic benefits individually and adjunctively with other interventions. Cannabidiol (CBD) made from legal, industrial hemp contains less than .3% THC, rendering it non-psychoactive. CBD oil has antiemetic, anxiolytic, antitumoral, and immunologically inhibitory properties. Three categories differentiate the types of clinical endocannabinoid deficiency (CECD), which are associated with different disease processes and disorders: genetic, acquired, and idiopathic autoimmune. Many disorders have a combination of CECD origins, and supplementation with cannabidiol (CBD) requires ongoing assessment to facilitate optimal benefit for the individual.

Human Endocannabinoid System

The human endocannabinoid system is responsible for memory networks in the brain, both excitatory and inhibitory, including the neurogenesis of hippocampal granule cells, which regulate the timing of the endocannabinoids in accordance with the brain's needs, pain perception, mood, synaptic plasticity, motor learning, appetite and taste regulation, and metabolic function, which regulates the storage of energy and transport of cellular nutrition. Cannabinoid receptor binding sites are located in the forebrain areas associated with higher cognitive function, forebrain, midbrain, and hindbrain areas associated with movement control, and hindbrain areas associated with motor and sensory functions attributed to the autonomic nervous system. The endocannabinoid system affects the lipocytes and fat cells, collectively

known as adipocytes, hepatocytes, in the gastrointestinal tract, musculoskeletal system, and endocrine system. The endogenous arachidonate-based lipids, anandamide and 2-arachidonoylglycerol (2-AG) are physiological ligands for the cannabinoid receptors. Cannabinoid receptors CB1 and CB2, two G-protein-coupled receptors, facilitate the responses of the endocannabinoid system in the body, which are critical to maintaining homeostasis. CB1 receptors are located in the central and peripheral nervous systems as well as the lungs, kidneys, and liver. CB2 receptors are predominantly expressed in the immune system and hematopoietic cells.

The direct effect of the endocannabinoid deficiency (CECD) correlates with multisystemic clinical outcomes in such conditions as hyperinsulinemia, diabetes, dementia, cardiovascular disease, multiple sclerosis, and obesity. Three primary categories are herein defined to discuss endocannabinoid deficiency (CECD): genetic, acquired, and idiopathic autoimmune. Genetic endocannabinoid deficiency (CECD) relates to hereditary acquisition of a disorder; acquired refers to an infectious of traumatic origination, and idiopathic autoimmune refers to etiologies for endocannabinoid deficiencies (CECD) which do not have direct associations. Diseases and disorders are assigned to one or more of these categories because often secondary disorders arise with physiological changes associated with the primary diagnosis. For example, colon cancer has been associated with endocannabinoid deficiency (CECD) and the disease is categorized as genetic, originating from a hereditary source. The presentation of primary multifocal leukoencephalopathy (PML), which affects the neurological system, supports adding the category of idiopathic autoimmune as well to the assessment. Because the endocannabinoid system facilitates communication and coordination between various cell types, deficiencies directly affect physiological homeostasis.

Cannabidiol (CBD), a non-psychotropic cannabinoid naturally occurring in human and animal species, occurs as a phytocannabinoid, CBD oil, which is derived from the industrial hemp plant. The restorative effects of cannabidiol (CBD oil), which increases anandamide and other lipid neurotransmitters, thereby restoring the endocannabinoid system, are of interest in the medical management of multiple disorders, including disorders of the gastrointestinal system, which is directly affected by the immunological and neurological systems. Indeed, research supports that plant-derived cannabidiol (CBD) has anti-inflammatory benefits.

Cannabidiol (CBD)

Cannabidiol (CBD) is a non-psychotropic and non-toxic compound, which has been demonstrated to positively affect the human endocannabinoid system. Cannabidiol (CBD), derived from the hemp plant, demonstrates anti-inflammatory and immune-modulating properties. Cannabidiol (CBD) has a low affinity for CB1 and CB2 receptors in the human body, but acts as an indirect antagonist of their agonists. (Antagonists are defined as substances that stop or inhibit the effects of another substance on the cellular surface, producing the same effect as a substance which would normally bind to the receptor. Agonists are chemicals that bind to receptors and elicit a biological response.) Therefore, cannabidiol (CBD) may enhance the therapeutic effects of THC, possibly by increasing the density of the CB1 receptors. Cannabidiol (CBD) has been demonstrated to cross the blood-brain barrier and exert antioxidant, antimicrobial, and neuroprotective properties, rendering it valuable in the prevention and treatment of gastrointestinal disorders and diseases.

Human Gastrointestinal System
The human gastrointestinal system is responsible for the digestion of food and assimilation into the body. Beginning in the oral cavity, saliva facilitates the production of a bolus of matter which is then swallowed, passing down the esophagus into the stomach. Amylase, which is contained in saliva, and gastric juices, breakdown food as peristalsis moves the matter to the small intestine. Chyme is dissolved in the small intestine and absorbed into the blood. Reabsorption of water and various minerals occurs in the colon of the large intestine and waste matter passes through the rectum to the anus for defecation.

The human gastrointestinal system is comprised of the upper and lower tracts. The upper gastrointestinal tract consists of the esophagus, stomach, and duodenum. The lower gastrointestinal tract consists of most of the small intestine and the large intestine. The accessory organs of the digestive system include the salivary glands, pancreas, liver, gallbladder, teeth, and tongue. These organs have a significant role in the digestive process including mastication and taste (salivary), synthesis of bile salts, lipid and plasma protein metabolism, and detoxification (liver), bile storage (gallbladder), and endocrine and exocrine functions (pancreas).

Gastrointestinal Health and Diseases
Diseases of the gastrointestinal system directly related to oxidative stress include disorders such as emesis, gastroesophageal reflux disease (GERD), gastric ulcer, irritable bowel syndrome, Crohn's Disease, colon cancer, and colorectal cancer. The human body evokes an active inflammatory response to mitigate damage from injury or infection via microglial cell and macrophage release. However, activation of microglial cells and macrophages is also associated with the release of glutamate, reactive oxidative species (ROS), nitric oxide (NO), and tumor necrosis factor (TNF), causing an escalation of inflammation, microvascular deterioration, and endocannabinoid degradation. Cannabidiol (CBD), according to El-Ramessay and Tang (2008), blocks the oxidative stress response and activation of proteins such as p-38 MAPK and microglial cells, reducing damage associated with inflammatory responses.

Nausea and Emesis
Endocannabinoid receptors, specifically CB1, located in the base of the fifth ventricle in the cerebral cortex are associated with nausea and emesis. Emesis is associated with acquired clinical endocannabinoid deficiency (CECD), induced by infectious processes such as staphylococcus enteritis and chemotherapy, such as Adriamycin. Chronic and severe, acute emesis is associated with electrolyte imbalance and dehydration which can be life-threatening. Research supports treatment with cannabidiol (CBD) to increase circulating cannabinoids, which are decreased in antigen and pharmacological blockade.

Gastroesophageal Reflux Disease (GERD)
Gastroesophageal reflux disease (GERD) is a chronic disorder caused by a failure of the lower esophageal sphincter, a valve which inhibits stomach acid, duodenal bile, and enzymes from returning to the esophagus. Failure of the esophageal sphincter causes chronic inflammation, pain, and mucosal damage in the esophagus. Clinical endocannabinoid deficiency (CECD) in GERD is defined as acquired or genetic and affects CB1 receptors in the gastrointestinal tract. Research indicates that administration of cannabidiol (CBD) increases circulating

endocannabinoids, reducing esophageal sphincter pressure, and directly protects the gastric mucosa, rendering CBD useful in both prevention and management of GERD.

Gastric Ulcer

Gastric ulceration refers to a localized area of erosion of the stomach lining. Abdominal pain and bleeding are associated with gastric ulceration. Often, Heliobacter pylori, a type of bacteria found in contaminated food and water, is present upon endoscopy. Triple antibiotic therapy is instituted to address Helicobacter pylori. Clinical endocannabinoid deficiency (CECD) in gastric ulceration is classified as acquired, affecting the CB1 receptors in the gastrointestinal tract, which are associated with motility and gastric emptying, as well as CB2 receptors, which modulate immune system response in the presence of infections. Research indicates that administration of cannabidiol (CBD) improves CB1 receptivity and increases cannabinoid availability, thereby improving reduced stasis associated with gastric erosion.

Irritable Bowel Syndrome

Irritable Bowel Syndrome (IBS) is a functional gastrointestinal disorder which affects the motility of the colon and associatively, the consistency of the fecal matter, without damaging the gastrointestinal mucosa. By definition, the symptoms of abdominal pain exceeding three times per month, relieved by a bowel movement, constitutes IBS. Subtyping of IBS is divided into four categories: IBS with constipation (IBS-C) in which fecal matter is hard > 25% of the time with watery fecal matter > 25% of the time; IBS with diarrhea (IBS-D) with watery fecal matter 25% of the time and hard fecal matter greater 25% of the time; Mixed IBS (IBS-M), with hard stools 25% of the time and watery stools 25% of the time, and Unsubtyped IBS (IBS-U) with hard stools and watery stools less than 25% of the time.

Clinical endocannabinoid deficiency (CECD) in IBS is considered idiopathic autoimmune and affects both cerebral and gastrointestinal CB1 and CB2 receptors. Glial cells actively mediate the inflammatory processes in the gastrointestinal system via CB2 receptors. Research has demonstrated that reactive inflammation in the bowel improves with the administration of Cannabidiol (CBD), which acts directly upon CB2 receptors in the bowel and CB1 receptors in the cerebral cortex, mediating the comorbidity factors of depression and anxiety which are integral in the manifestation of IBS.

Crohn's Disease

Crohn's disease, or regional enteritis, is an inflammatory bowel disease which can affect any part of the gastrointestinal tract and is associated with abdominal pain, diarrhea or occult positive stools, fever, and weight loss. Associated autoimmune symptoms external to the gastrointestinal tract include dermatitis, arthritis, fatigue, and ocular inflammation. Crohn's disease predisposes the individual to bowel obstruction and colon cancer. Clinical endocannabinoid deficiency (CECD) in Crohn's disease has both genetic and acquired classifications, since nicotine use increases the likelihood of developing this inflammatory bowel disease. Research indicates that cannabidiol (CBD) restores CB1 receptor capabilities, facilitating relaxation of the lower esophageal sphincter and modulation of colonic motility. Cannabidiol (CBD) administration also restores functionality of central and peripheral CB1 receptors, components of the endocannabinoid system that are imperative in the prevention and remediation of nausea and emesis.

Colon & Colorectal Cancer
Colon and colorectal cancers refer to the formation of malignancies in the tissues of the colon and rectum. Most of these malignancies are adenocarcinomas, which secrete mucus and other fluids. Clinical endocannabinoid deficiency (CECD) in colon and colorectal cancer is deemed genetic and acquired. CB1 and CB2 receptors in the gastrointestinal tract are targets for cannabidiol (CBD) therapy because CBD triggers cell death through an endoplasmic reticulum stress pathway, which activates autophagy and promotes apoptosis. Further, CBD upregulates the intracellular adhesion molecule, which decreases cancer cell invasiveness. Indeed, the use of cannabidiol (CBD) is suggested to prevent colon and colorectal cancer through preservation of the endocannabinoid system and receptor functionality.

Pancreatic Cancer
The development of malignancy in the pancreas, a glandular organ based behind the stomach, occurs primarily in the third decade of life. Pancreatic adenocarcinoma represents the majority of the cases and the malignancy is generally diagnosed in an advanced stage, rendering a poor prognosis. Symptoms include darkened urine, poor appetite, weight loss, lightened feces, abdominal and back pain, and jaundice. Clinical endocannabinoid deficiency (CECD) in pancreatic cancer is classified as genetic and acquired, with over twenty-five percent of cases being associated with nicotine use, obesity, and diabetes.

Cannabidiol (CBD) has been demonstrated to inhibit pancreatic cancer cell growth through the stimulation of CB1 receptors in the pancreas. Cannabinoids inhibit reactive oxidative stress (ROS) and inhibits the Krebs cycle, culminating in an anti-tumoral effect. Mediation of cancer cell metabolism by cannabidiol (CBD) induces autophagy, the catabolic mechanism, which involves the destruction of dysfunctional cellular components by liposomes, and malignant cell growth. Administration of cannabidiol (CBD) preventively in individuals at hereditary or acquired risk of pancreatic cancer is therefore warranted.

Hepatic Cancer
The liver filters the circulating blood continuously in the human body, converting substances absorbed from the gastrointestinal system into usable chemicals for absorption, and removing toxins and chemical byproducts which are then excreted. The likelihood of hepatocellular carcinoma increases because of the function of the liver. Predisposition to hepatic cancer arises directly from hepatitis, and secondarily from metastasis from a primary malignant site, such as the lung. Clinical endocannabinoid deficiency (CECD) in hepatocellular carcinoma is classified as acquired, and associated with infectious hepatitis B and C, and alcohol and nicotine use. Symptoms included jaundice, weight loss, nausea and emesis, and abdominal pain. Research noted anti-tumoral effect in hepatocellular carcinoma attributable to induction of cancer cell death, inhibition of cell proliferation, and inhibition of tumor angiogenesis. In hepatic malignancy, cannabinoids appear to kill tumor cells and protect non-transformed cells from malignancy, supporting use of cannabidiol (CBD) preventively in individuals at risk of developing hepatocellular carcinoma and among individuals diagnosed with metastasis to the liver from a primary source.

Cirrhosis
Cirrhosis of the liver refers to the development of fibrosis scarring of the liver and the formation of regenerative nodules which appear as the organ attempt to repair the damage. Cirrhosis is

most often associated with alcoholism, hepatitis B, hepatitis C, and fatty liver disease. Ascites and hepatic encephalopathy, portal hypertension and esophageal varices are life-threatening complications of cirrhosis. Liver transplantation has been poised as the only option in advanced cirrhosis.

Clinical endocannabinoid deficiency (CECD) is acquired in cirrhosis of the liver, attributable to the aforementioned risk factors. Research has shown that stimulation of CB2 receptors with cannabidiol (CBD) reduced portal hypertension, infiltration of inflammatory cells, and decreased fibrosis. In the management of cirrhosis of the liver, cannabidiol (CBD) is suggested for individuals in the early stages of cirrhosis and those at greatest risk for the development of the disease.

Endocannabinoid Deficiency (CECD) Classification: Gastrointestinal Disorders

Disorder	Origin of CECD
GERD	Acquired
Gastric ulcer	Acquired
IBS	Genetic
Crohn's disease	Genetic
Colon and Colorectal Cancer	Genetic
Pancreatic Cancer	Acquired
Cirrhosis of liver	Acquired

CEN Medical Cannabis Pharmacological Prescription and Coding System Gastrointestinal Disorder Application

The CEN Medical Cannabis Pharmacological Prescription and Coding System (CEN/MCPPCS) provides language that enables the health care practitioner to communicate with the dispenser of medical cannabis. The first two letters of the system refer to the cannabis type: cannabis sativa, cannabis indica, or cannabis hybrida. The numerical value in percentage to the right of the colon refers to the recommended THC content in percentage, and the numerical value in sequence to the right of the THC percentage refers to the recommended CDB content.

(CEN/MCPPCS): Cannabis type (sativa, indica, hybrida; THC percentage or range/CBD percentage or range) or Hemp Cannabidiol (CBD)

Example: Cannabidiol (CBD oil) is recommended for the patient. The concentration of the CBD oil is 19.5% and the patient is to ingest 50 mg. of CBD oil four times each day every six hours, as adjunctive therapy in the treatment of colon cancer, (ICD-9: 363.20). The prescription would therefore read:

Charles Gary Reynolds
Date of Birth: 09-01-1939
Diagnosis: Adenocarcinoma of the colon, ICD-9 code: 153.9
CBD: 0.00%/ 19.5%. Take 50 mg. of CBD oil by mouth four times daily, every 6 hours. Use dropper as indicated.
Zakra Kahn, M.D.

The patient would then be able to purchase the CBD oil online or at a dispensary, offering the prescription to the pharmacist or technician.

Composition Assignments:

1. Please suggest a plan of care based upon the following patient information. Discuss if CBD oil would be indicated, with rationale and the type of endocannabinoid deficiency(s) (CECD) for the gastrointestinal disease process.
    a. A 71-year-old African American male with a history of tobacco and alcohol use schedules an appointment because he has experienced intermittent episodes of abdominal pain. He has yellowed sclera of his eyes and a distended abdomen.
2. Please choose an article from the CEN library on an aspect of cannabidiol (CBD) and the gastrointestinal system. Write a two-hundred-word critical analysis paper on this research article and determine the following in your paper:
    a. Author and affiliation
    b. Study population
    c. Purpose
    d. Outcome of the study
    e. Importance of the research

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Chapter IV: Musculoskeletal Health and Disease

Learning Objectives

1. Discuss assessment protocols to determine level of endocannabinoid deficiencies of the musculoskeletal system.
2. Discuss therapeutic strategies to address endocannabinoid deficiencies of the musculoskeletal system.
3. Discuss patient care guidelines to implement cannabinoid therapy with standard of care pharmaceutical regimens pertaining to the musculoskeletal system.
4. Discuss educational guidelines for patients to monitor clinical outcomes when implementing cannabinoid protocols for musculoskeletal disorders.

The Endocannabinoid System and Cannabidiol (CBD) - Introduction

The endocannabinoid system (ECS) is a lipid-derived signaling system discovered within the past decade. Cannabinoids, which are homeostatic regulators, circulate throughout human and animal systems continuously, affecting all physiological processes. The endocannabinoid system is comprised of CB1 and CB2 receptors, which bind directly or indirectly to cannabinoids and phytocannabinoids. CB1 receptors are excitatory and are located in the central nervous system, lungs, liver, and kidney. CB2 receptors regulate immunological responses and are located in the immune and circulatory systems. Endogenous compounds, such as anandamide and arachidonylglerol (2-AG), are made by mammals from lipids and bind directly to the CB1 and CB2 receptors, serving as neurotransmitters for cannabinoids. Cannabidiol (CBD oil), a non-psychotropic cannabinoid naturally occurring in human and animal species, is also a phytocannabiniod, derived from the industrial hemp plant. While CBD does not bind directly with receptors, it does affect stress genes, such as Soat2 and Cyp27a1, which control sterol (i.e., cholesterol) metabolism. CBD increases the amount of anandamide and other vital lipids, thereby indirectly increasing the availability of circulating cannabinoids to bind with CB1 and CB2 receptors.

Research has shown that cannabidiol, in the form of CBD oil, has therapeutic benefits individually and adjunctively with other interventions. Cannabidiol (CBD) made from legal, industrial hemp contains less than .3% THC, rendering it non-psychoactive. CBD oil has antiemetic, anxiolytic, antitumoral, and immunologically inhibitory properties. Three categories differentiate the types of clinical endocannabinoid deficiency (CECD), which are associated with different disease processes and disorders: genetic, acquired, and idiopathic autoimmune. Many disorders have a combination of CECD origins, and supplementation with cannabidiol (CBD) requires ongoing assessment to facilitate optimal benefit for the individual.

Human Endocannabinoid System

The human endocannabinoid system is responsible for memory networks in the brain, both excitatory and inhibitory, including the neurogenesis of hippocampal granule cells, which regulate the timing of the endocannabinoids in accordance with the brain's needs, pain perception, mood, synaptic plasticity, motor learning, appetite and taste regulation, and metabolic function, which regulates the storage of energy and transport of cellular nutrition. Cannabinoid receptor binding sites are located in the forebrain areas associated with higher cognitive function, forebrain, midbrain, and hindbrain areas associated with movement control, and hindbrain areas associated with motor and sensory functions attributed to the autonomic

nervous system. The endocannabinoid system affects the lipocytes and fat cells, collectively known as adipocytes, hepatocytes, in the gastrointestinal tract, musculoskeletal system, and endocrine system. The endogenous arachidonate-based lipids, anandamide and 2-arachidonoylglycerol (2-AG) are physiological ligands for the cannabinoid receptors. Cannabinoid receptors CB1 and CB2, two G-protein-coupled receptors, facilitate the responses of the endocannabinoid system in the body, which are critical to maintaining homeostasis. CB1 receptors are located in the central and peripheral nervous systems, as well as the lungs, kidneys, and liver. CB2 receptors are predominantly expressed in the immune system and hematopoietic cells.

The direct effect of the endocannabinoid deficiency (CECD) correlates with multisystemic clinical outcomes in such conditions as hyperinsulinemia, osteoporosis, diabetes, dementia, cardiovascular disease, multiple sclerosis, and obesity. Three primary categories are herein defined to discuss endocannabinoid deficiency (CECD): genetic, acquired, and idiopathic autoimmune. Genetic endocannabinoid deficiency (CECD) relates to hereditary acquisition of a disorder; acquired refers to an infectious of traumatic origination, and idiopathic autoimmune refers to etiologies for endocannabinoid deficiencies (CECD) which do not have direct associations. Diseases and disorders are assigned to one or more of these categories because often secondary disorders arise with physiological changes associated with the primary diagnosis. For example, diabetes has been associated with endocannabinoid deficiency (CECD) and the disease is categorized as genetic, originating from a hereditary source. The presentation of rheumatoid arthritis, which affects the musculoskeletal and immune systems, supports adding the category of idiopathic autoimmune as well to the assessment. Because the endocannabinoid system facilitates communication and coordination between various cell types, deficiencies directly affect physiological homeostasis.

Cannabidiol (CBD), a non-psychotropic cannabinoid naturally occurring in human and animal species, occurs as a phytocannabinoid, CBD oil, which is derived from the industrial hemp plant. The restorative effects of cannabidiol (CBD oil), which increases anandamide and other lipid neurotransmitters, thereby restoring the endocannabinoid system, are of interest in the medical management of multiple disorders, including disorders of the musculoskeletal system, which is directly affected by the immunological and neurological systems. Indeed, research supports that plant-derived cannabidiol (CBD) has neuroprotective and anti-inflammatory benefits.

Cannabidiol (CBD)

Cannabidiol (CBD) is a non-psychotropic and non-toxic compound, which has been demonstrated to positively affect the human endocannabinoid system. Cannabidiol (CBD), derived from the hemp plant, demonstrates anti-inflammatory and immune-modulating properties. Cannabidiol (CBD) has a low affinity for CB1 and CB2 receptors in the human body, but acts as an indirect antagonist of their agonists. (Antagonists are defined as substances that stop or inhibit the effects of another substance on the cellular surface, producing the same effect as a substance which would normally bind to the receptor. Agonists are chemicals that bind to receptors and elicit a biological response.) Therefore, cannabidiol (CBD) may enhance the therapeutic effects of THC, possibly by increasing the density of the CB1 receptors. Cannabidiol (CBD) has been demonstrated to cross the blood-brain barrier and exert antioxidant, antimicrobial, and neuroprotective properties, rendering it valuable in the prevention and treatment of musculoskeletal disorders and diseases.

Human Musculoskeletal System
The human musculoskeletal system is a complex organ system which provides the structure and support for the function of movement. Comprised of skeleton, muscle, cartilage, tendons, ligaments, joints, and connective tissue, the musculoskeletal system supports and protects the internal organs, and provides form to the human body. Calcium and phosphorus are stored in the human skeleton and hematopoietic components arise from the bone marrow. Muscle fibers and connective tissues adhere to the skeletal system, providing form, and bones are bound to each through joints, with cartilage protecting the ends of bone as they interact with one another. The contraction of muscles enables movement of the bone attached to a respective joint.

The endocannabinoid system affects the function and integrity of the musculoskeletal system. CB1 and CB2 receptors are located throughout the musculoskeletal system and are targets for the treatment of disorders of movement, and diseases of bone and muscle that are related to clinical endocannabinoid deficiencies (CECD).

Musculoskeletal Health and Diseases
Diseases of the musculoskeletal system directly related to clinical endocannabinoid deficiency (CECD) and associated reactive oxidative stress include disorders such as osteoarthritis, rheumatoid arthritis, osteoporosis, bone cancer, bone fracture, and muscle spasm. The human body evokes an active inflammatory response to mitigate damage from injury or malignancy via microglial cell and macrophage release. However, activation of microglial cells and macrophages is also associated with the release of glutamate, reactive oxidative species (ROS), nitric oxide (NO), and tumor necrosis factor (TNF), causing an escalation of inflammation, microvascular and osteoblast and osteoclast deterioration, and endocannabinoid degradation. Cannabidiol (CBD), according to El-Ramessay and Tang (2008), blocks the oxidative stress response and activation of proteins such as p-38 MAPK and microglial cells, reducing damage associated with inflammatory responses.

Osteoarthritis
The most common form of arthritis, osteoarthritis, causes an inflammatory response which affects the musculoskeletal system, including joint, bone, and cartilage. Symptoms include pain, limited range of motion, and swelling of the affected area. As osteoarthritis degrades cartilage over time, direct contact between bones increases symptoms. A disorder of the skeletal system, which affects joints and cartilage as well and bone, osteoarthritis most commonly occurs in the spine, knees, hips, and hands.

Clinical endocannabinoid deficiency (CECD) associated with osteoarthritis is both genetic and acquired, affecting CB2 receptors in the musculoskeletal system. Risk factors associated with acquired CECD related to osteoarthritis include obesity, sedentary lifestyle, smoking, and traumatic injury. Administration of cannabidiol (CBD) preventatively and post-diagnosis of osteoarthritis is suggested to reduce the inflammatory response throughout the musculoskeletal system, and increase anandamide production, which enhances cannabinoid binding to CB2 receptors, thereby reducing cartilage destruction.

Rheumatoid Arthritis
Rheumatoid arthritis is a multisystemic idiopathic autoimmune disorder that affects the musculoskeletal system and manifests as a progressive deterioration of the joints, primarily. As a secondary manifestation, rheumatoid arthritis affects the cardiac, pulmonary, and ocular systems. Pain and debilitation reduce mobility and function over time. CB2 receptors are affected in the idiopathic autoimmune clinical endocannabinoid deficiency (CECD) associated with rheumatoid arthritis, causing an abnormal inflammatory response. Research indicates that prophylactic administration of cannabidiol (CBD) reduces inflammatory responses by enhancing receptivity to binding via lipid neurotransmitters bolstered by CBD administration. CBD is recommended after diagnosis as well, as adjunctive therapy with medications and physical therapy to manage symptoms and enhance mobility in rheumatoid arthritis.

Bone Cancer
Malignancy of the bone can be either primary or secondary. Bone-derived malignancies arise from cells and tissues of the skeletal system. Secondary bone cancers metastasize from primary cancer sites, including carcinomas of the prostate, breast, thyroid, lungs, and kidneys. Clinical endocannabinoid deficiency (CECD) associated with bone cancers are idiopathic autoimmune and reflect abnormality in CB2 receptor function. Research supports using cannabidiol (CBD) to prevent metastasis from primary cancer sites as well as prophylactic use in adult populations.

Osteoclast Formation
Osteoclast formation involves the re-absorption of bone tissue, which is critical for the maintenance, repair, and restructuring of the skeletal system. The osteoclast disassembles and reabsorbs bone and osteoblasts form new bone. The endocannabinoid system controls the immune function via the CB2 receptors in the skeletal system, regulating cellular production. Clinical endocannabinoid deficiency (CECD), associated with osteoclast impairment is defined as idiopathic autoimmune. Reduction in osteoclast formation affects the stability and strength of the skeletal system. Research indicates that increasing levels of lipid neurotransmitters, such as anandamide, using cannabidiol (CBD) increases production of viable osteoclasts, thereby reducing and/or ceasing osteoclast deterioration and associated skeletal manifestations.

Osteoporosis
Osteoporosis is a disorder of the skeletal system which causes progressive reduction in bone mass and density, altering the proteins within the bones. As microstructural changes occur in osteoporosis, the likelihood of fracture and pain occurs with alterations in posture. Considered genetic and acquired relative to clinical endocannabinoid deficiency (CECD), osteoporosis affects primarily perimenopausal women and the elderly and is associated with morbidity and mortality related to hip and spinal fractures. Administration of cannabidiol (CBD) is highly recommended for at-risk populations, because CB2 receptors are critical in the regulation of bone cell homeostasis.

Bone fracture
Traumatic injury to the bone is associated with pain, reduced mobility, and reduced range of motion. The endocannabinoid system regulates osteoblast and osteoclast formation via CB2 receptors. In acquired CECD, administration of cannabidiol (CBD) reduces abnormal inflammatory responses, increases the production of viable osteoblast and osteoclasts, and

provides analgesic benefit. Cannabidiol (CBD) is recommended for adults throughout the lifespan to reduce the severity of bone fracture in the event of trauma, and enhance the recovery in the event of a traumatic injury.

Muscle Spasm

The contraction of involuntary muscles, which produces a hypertonic response and associated pain, defines spasm. The incident and force of muscle spasm is associated with the excitatory CB1 receptor, a component of the endocannabinoid system. In clinical endocannabinoid deficiency (CECD), which affects the musculoskeletal system, anandamide levels decrease, causing hyperactivity of misdirected nerve impulses. An acquired CECD, spasm of the muscle causes debilitating pain and immobility. Restoration of the CB1 receptor uptake via cannabidiol (CBD) administration produces analgesia. Similarly, increased CB2 function reduces abnormal immunological responses, thereby reducing inflammation around the affected area. Cannabidiol (CBD) is recommended preventatively for athletes and active adults to prevent sudden onset of muscle spasms and post-incident with analgesics and physical therapy to reduce symptoms.

Sarcoma of the Muscle

Malignancy of the muscle, defined as sarcoma of the muscle, is associated with tumor production. Clinical endocannabinoid deficiency (CECD), considered idiopathic in sarcoma of the muscle, can be restored with cannabidiol (CBD) and used as adjunctive treatment with chemotherapy and genetic augmentation to treat sarcoma of the muscle. Because metastasis is common with this malignancy, early intervention with cannabidiol (CBD) is warranted to reduce the incidence of malignant cell proliferation.

Endocannabinoid Deficiency (CECD) Classification: Neurological Disorders

Disorder	Origin of CECD
Osteoarthritis	Idiopathic Autoimmune, Acquired
Rheumatoid Arthritis	Idiopathic Autoimmune
Bone Cancer	Idiopathic Autoimmune
Bone Fracture	Acquired
Muscle Spasm	Acquired
Osteoclast Formation	Idiopathic Autoimmune
Osteoporosis	Genetic, Acquired
Sarcoma of the Muscle	Idiopathic Autoimmune

CEN Medical Cannabis Pharmacological Prescription and Coding System Musculoskeletal Disorder Application

The CEN Medical Cannabis Pharmacological Prescription and Coding System (CEN/MCPPCS) provides language that enables the health care practitioner to communicate with the dispenser of medical cannabis. The first two letters of the system refer to the cannabis type: cannabis sativa, cannabis indica, or cannabis hybrida. The numerical value in percentage to the right of the colon refers to the recommended THC content in percentage, and the numerical value in sequence to the right of the THC percentage refers to the recommended CDB content.

(CEN/MCPPCS): Cannabis type (sativa, indica, hybrida; THC percentage or range/CBD percentage or range) or Hemp Cannabidiol (CBD)

Example: Cannabidiol (CBD oil) is recommended for the patient. The concentration of the CBD oil is 19.5% and the patient is to ingest 50 mg. of CBD oil four times each day every six hours, as adjunctive therapy in the treatment of sarcoma of the muscle, (ICD-9: 171.9). The prescription would therefore read:

Frank K. Lippy
Date of Birth: 09-01-1959
Diagnosis: Sarcoma of the muscle, ICD-9 code: 171.9
CBD: 0.00%/ 19.5%. Take 50 mg. of CBD oil by mouth four times daily, every 6 hours. Use dropper as indicated.
Bret Moorse, M.D.

The patient would then be able to purchase the CBD oil online or at a dispensary, offering the prescription to the pharmacist or technician.

Composition Assignments:

1. Please suggest a plan of care based upon the following patient information. Discuss if CBD oil would be indicated with rationale and the type of endocannabinoid deficiency (s) (CECD) for the musculoskeletal disease process.
    a. A 77-year-old women presents with severe pain and swelling of her left knee. She denies any trauma but states that her bone density score is well below the average for her age group and that her doctor wants her to start physical therapy.
2. Please choose an article from the CEN library on an aspect of cannabidiol (CBD) and the musculoskeletal system. Write a two-hundred-word critical analysis paper on this research article and determine the following in your paper:
    a. Author and affiliation
    b. Study population
    c. Purpose
    d. Outcome of the study
    e. Importance of the research

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Chapter V: Cardiovascular Health and Cardiovascular Disease

Learning Objectives

1. Discuss assessment protocols to determine level of endocannabinoid deficiencies of the cardiovascular system.
2. Discuss therapeutic strategies to address endocannabinoid deficiencies of the cardiovascular system.
3. Discuss patient care guidelines to implement cannabinoid therapy with standard of care pharmaceutical regimens pertaining to the cardiovascular system.
4. Discuss educational guidelines for patients to monitor clinical outcomes when implementing cannabinoid protocols for cardiovascular disorders.

The Endocannabinoid System and Cannabidiol (CBD) - Introduction

The endocannabinoid system (ECS) is a lipid-derived signaling system discovered within the past decade. Cannabinoids, which are homeostatic regulators, circulate throughout human and animal systems continuously, affecting all physiological processes. The endocannabinoid system is comprised of CB1 and CB2 receptors, which bind directly or indirectly to cannabinoids and phytocannabinoids. CB1 receptors are excitatory and are located in the central nervous system, lungs, liver, and kidney. CB2 receptors regulate immunological responses and are located in the immune and circulatory systems. Endogenous compounds, such as anandamide and arachidonylglerol (2-AG), are made by mammals from lipids and bind directly to the CB1 and CB2 receptors, serving as neurotransmitters for cannabinoids. Cannabidiol (CBD oil), a non-psychotropic cannabinoid naturally occurring in human and animal species, is also a phytocannabiniod, derived from the industrial hemp plant. While CBD does not bind directly with receptors, it does affect stress genes, such as Soat2 and Cyp27a1, which control sterol (i.e., cholesterol) metabolism. CBD increases the amount of anandamide and other vital lipids, thereby indirectly increasing the availability of circulating cannabinoids to bind with CB1 and CB2 receptors.

Research has shown that cannabidiol, in the form of CBD oil, has therapeutic benefits individually and adjunctively with other interventions. Cannabidiol (CBD) made from legal, industrial hemp contains less than .3% THC, rendering it non-psychoactive. CBD oil has antiemetic, anxiolytic, antitumoral, and immunologically inhibitory properties. Three categories differentiate the types of clinical endocannabinoid deficiency (CECD), which are associated with different disease processes and disorders: genetic, acquired, and idiopathic autoimmune. Many disorders have a combination of CECD origins, and supplementation with cannabidiol (CBD) requires ongoing assessment to facilitate optimal benefit for the individual.

The Human Endocannabinoid System

The human endocannabinoid system is responsible for memory networks in the brain, both excitatory and inhibitory, including the neurogenesis of hippocampal granule cells, which regulate the timing of the endocannabinoids in accordance with the brain's needs, pain perception, mood, synaptic plasticity, motor learning, appetite and taste regulation, and metabolic function, which regulates the storage of energy and transport of cellular nutrition. Cannabinoid receptor binding sites are located in the forebrain areas associated with higher cognitive function, forebrain, midbrain, and hindbrain areas associated with movement control, and hindbrain areas associated with motor and sensory functions attributed to the autonomic

nervous system. The endocannabinoid system affects the lipocytes and fat cells, collectively known as adipocytes, hepatocytes, in the gastrointestinal tract, musculoskeletal system, and endocrine system. The endogenous arachidonate-based lipids, anandamide and 2-arachidonoylglycerol (2-AG) are physiological ligands for the cannabinoid receptors. Cannabinoid receptors CB1 and CB2, two G-protein-coupled receptors, facilitate the responses of the endocannabinoid system in the body, which are critical to maintaining homeostasis. CB1 receptors are located in the central and peripheral nervous systems as well as the lungs, heart, kidneys, and liver. CB2 receptors are predominantly expressed in the immune system and hematopoietic cells.

The direct effect of the endocannabinoid deficiency (CECD) correlates with multisystemic clinical outcomes in such conditions as hyperinsulinemia, osteoporosis, diabetes, dementia, cardiovascular disease, multiple sclerosis, and obesity. Three primary categories are herein defined to discuss endocannabinoid deficiency (CECD): genetic, acquired, and idiopathic autoimmune. Genetic endocannabinoid deficiency (CECD) relates to hereditary acquisition of a disorder, acquired refers to an infectious of traumatic origination, and idiopathic autoimmune refers to etiologies for endocannabinoid deficiencies (CECD) which do not have direct associations. Diseases and disorders are assigned to one or more of these categories because often secondary disorders arise with physiological changes associated with the primary diagnosis. For example, diabetes has been associated with endocannabinoid deficiency (CECD) and the disease is categorized as genetic, originating from a hereditary source. The presentation of atherosclerosis, which affects the vascular system, supports adding the category of acquired as well to the assessment. Because the endocannabinoid system facilitates communication and coordination between various cell types, deficiencies directly affect physiological homeostasis.

Cannabidiol (CBD), a non-psychotropic cannabinoid naturally occurring in human and animal species, occurs as a phytocannabinoid, CBD oil, which is derived from the industrial hemp plant. The restorative effects of cannabidiol (CBD oil), which increases anandamide and other lipid neurotransmitters, thereby restoring the endocannabinoid system, are of interest in the medical management of multiple disorders, including disorders of the cardiovascular system, which is directly affected by the immunological and neurological systems. Indeed, research supports that plant-derived cannabidiol (CBD) has anxiolytic and anti-inflammatory benefits.

Cannabidiol (CBD)

Cannabidiol (CBD) is a non-psychotropic and non-toxic compound which has been demonstrated to positively affect the human endocannabinoid system. Cannabidiol (CBD), derived from the hemp plant, demonstrates anti-inflammatory and immune-modulating properties. Cannabidiol (CBD) has a low affinity for CB1 and CB2 receptors in the human body, but acts as an indirect antagonist of their agonists. (Antagonists are defined as substances that stop or inhibit the effects of another substance on the cellular surface, producing the same effect as a substance which would normally bind to the receptor. Agonists are chemicals that bind to receptors and elicit a biological response.) Therefore, cannabidiol (CBD) may enhance the therapeutic effects of THC, possibly by increasing the density of the CB1 receptors. Cannabidiol (CBD) has been demonstrated to cross the blood-brain barrier and exert antioxidant, antimicrobial, and neuroprotective properties, rendering it valuable in the prevention and treatment of oxidative ocular disorders and diseases.

Human Cardiovascular System
The cardiovascular system is comprised of the heart and circulatory system. The endocannabinoid system interfaces with the cardiovascular system, mainly via CB1 receptors. Perfusion, cardiac output, blood pressure, and vessel patency are all influenced by the endocannabinoid system within the cardiovascular system. The intrinsic relationship between the two becomes evident in the development of abnormalities of the cardiovascular and circulatory systems, including cardiac arrhythmias, atherosclerosis, and myocardial ischemia. Clinical endocannabinoid deficiency (CECD) affects the function of the heart and cannabidiol (CBD) is currently being evaluated as a pharmaceutical in certain cardiac disorders.

Cardiovascular Disorders and Diseases - Atherosclerosis
Atherosclerosis, which reduces increases the risk of stroke, myocardial infarction, and hypertension, is directly related to the clinical endocannabinoid deficiency (CECD) and dysfunctional response of the immune system to the presence of endothelial adhesion molecules. The CB2 receptors located through the circulatory system regulate immune responses. Research indicates that phytocannabinoids, such as cannabidiol (CBD), reduce inflammatory responses to the presence of abnormal endothelial molecules and also reduce reactive oxidative stress (ROS), which is associated with cell death. CBD, therefore, as a potent anxiolytic, is suggested for the prevention of atherosclerosis, a disorder with basis in genetic and acquired Clinical Endocannabinoid Deficiency (CECD).

Cardiomyopathy
Cardiomyopathy is characterized by decreased diastolic and systolic myocardial performance and is associated with increased oxidative stress and expression of adhesion molecules. Vascular adhesion molecules increase fibrosis and connective tissue proliferation, ultimately culminating in cell death. Cardiomyopathy is considered an acquired clinical endocannabinoid deficiency (CECD) and is often associated with diabetes mellitus and metabolic syndrome. Research supports that CB1 and CB2 receptors respond to cannabidiol (CBD) in cardiomyopathy, improving cardiac dysfunction, reducing oxidative stress and associated cell death, and reducing inflammatory response by improving CB2 receptivity via increased anandamide levels. Reduction in fibrosis was likewise associated with cannabidiol (CBD) administration, supporting the importance of improved cellular glucose usage in such conditions as diabetes and hyperinsulinemia, which thereby improves cardiomyopathy associated with these disorders. In primary cardiomyopathy, benefits are likewise reflected, warranting consideration of cannabidiol (CBD) supplementation.

Hypertension
Hypertension, in which circulating blood pressure exceeds human physiological normatives, is associated with cerebral vascular incident, dementia, myocardial infarction, and peripheral vascular disease. As both acquired and genetic clinical endocannabinoid deficiency (CECD), affecting CB1 and CB2 receptors throughout the body, hypertension is affected by reduced circulating cannabinoids. Administration of cannabidiol (CBD) increases anandamide levels, a lipid neurotransmitter that binds with CB1 and CB2 receptors directly, which correlates with relaxation of blood vessels and corresponding reduction in systemic blood pressure. Cannabidiol (CBD) supplementation is therefore supported for individuals at risk for malignant hypertension

and adjunctively for individuals diagnosed and treated with hypertension, as deemed appropriate by the attending physician.

Myocardial Ischemia

Myocardial ischemia refers to the restriction of blood supply to the heart, reducing the oxygen and glucose required for cellular function. As a result of myocardial ischemic incidences, damage to the tissue of the myocardium occurs and is demonstrable through electrocardiogram and echocardiogram. Associated with acquired clinical endocannabinoid deficiency (CECD), myocardial ischemia is associated with decreased available cannabinoids to both CB1 and CB2 receptors located in the cardiac muscle. Research indicates that administration of cannabidiol (CBD) improves outcome in myocardial ischemia, reducing residual damage, and may be indicated preventatively in individuals with diabetes, hypertension, and atherosclerosis to prevent or reduce the severity of myocardial ischemic episodes.

Myocardial Infarction

Myocardial infarction refers to the cessation of blood flow to a portion of the cardiac muscle, with associated oxygen reduction, and damage to the myocardial tissue. Blockage of a coronary artery is commonly associated with myocardial infarction which may or may not proceed to cardiac arrest and possible death. The accumulation of blood cells and cholesterol, and subsequent immune response, which adds further blockage within a coronary artery, contributes to the likelihood of myocardial infarction. Endocannabinoid receptors in the myocardial tissue, both CB1 and CB2, are affected by clinical endocannabinoid deficiency. Research indicates that the administration of cannabidiol, (CBD), improved outcome in myocardial infarction and in prevention of atherosclerosis, which is associated with myocardial infarction. Cannabidiol (CBD) reduced inflammation and abnormal immunological response within the coronary arteries, reducing the likelihood of endothelial wall plaque formation. Adjunctive administration of cannabidiol is warranted for consideration in the management and prevention of myocardial infarction and associated cell death.

Endocannabinoid Deficiency (CECD) Classification: Cardiovascular Disorders

Disorder	Origin of CECD
Atherosclerosis	Acquired
Cardiomyopathy	Acquired
Hypertension	Genetic, Acquired
Myocardial Ischemia	Acquired
Myocardial Infarction	Acquired

CEN Medical Cannabis Pharmacological Prescription and Coding System Cardiovascular Disorder Application

The CEN Medical Cannabis Pharmacological Prescription and Coding System (CEN/MCPPCS) provides language that enables the health care practitioner to communicate with the dispenser of medical cannabis. The first two letters of the system refer to the cannabis type: cannabis sativa, cannabis indica, or cannabis hybrida. The numerical value in percentage to the right of the colon refers to the recommended THC content in percentage, and the numerical value in sequence to the right of the THC percentage refers to the recommended CDB content.

(CEN/MCPPCS): Cannabis type (sativa, indica, hybrida; THC percentage or range/CBD percentage or range) or Hemp Cannabidiol (CBD)

Example: Cannabidiol (CBD oil) is recommended for the patient. The concentration of the CBD oil is 19.5% and the patient is to ingest 50 mg. of CBD oil four times each day every six hours, as adjunctive therapy in the treatment of atherosclerosis, (ICD-9: 440.9). The prescription would therefore read:

Cynthia Small
Date of Birth: 06-01-1949.
Diagnosis: Atherosclerosis, ICD-9 code: 440.9
CBD: 0.00%/ 19.5%. Take 50 mg. of CBD oil by mouth four times daily, every 6 hours. Use dropper as indicated.
Michael Roberts, M.D.

The patient would then be able to purchase the CBD oil online or at a dispensary, offering the prescription to the pharmacist or technician.

Composition Assignments

1. Please suggest a plan of care based upon the following patient information. Discuss if CBD oil would be indicated with rationale and the type of endocannabinoid deficiency (s)(CECD) for the cardiovascular disease process.
    a. A 54-year-old male with hypertension and a history of alcohol use presents with intermittent chest pain and shortness of breath. He states that he has been given nitroglycerine by his doctor to relieve angina, which sometimes occurs with climbing stairs.
2. Please choose an article from the CEN library on an aspect of cannabidiol (CBD) and the cardiovascular system. Write a two-hundred-word critical analysis paper on this research article and determine the following in your paper:
    a. Author and affiliation
    b. Study population
    c. Purpose
    d. Outcome of the study
    e. Importance of the research

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Chapter VI: Pulmonary Health and Pulmonary Disease

Learning Objectives

1. Discuss assessment protocols to determine level of endocannabinoid deficiencies of the pulmonary system.
2. Discuss therapeutic strategies to address endocannabinoid deficiencies of the pulmonary system.
3. Discuss patient care guidelines to implement cannabinoid therapy with standard of care pharmaceutical regimens pertaining to the pulmonary system.
4. Discuss educational guidelines for patients to monitor clinical outcomes when implementing cannabinoid protocols for pulmonary disorders.

The Endocannabinoid System and Cannabidiol (CBD) - Introduction

The endocannabinoid system (ECS) is a lipid-derived signaling system discovered within the past decade. Cannabinoids, which are homeostatic regulators, circulate throughout human and animal systems continuously, affecting all physiological processes. The endocannabinoid system is comprised of CB1 and CB2 receptors, which bind directly or indirectly to cannabinoids and phytocannabinoids. CB1 receptors are excitatory and are located in the central nervous system, lungs, liver, and kidney. CB2 receptors regulate immunological responses and are located in the immune and circulatory systems. Endogenous compounds, such as anandamide and arachidonylglerol (2-AG), are made by mammals from lipids and bind directly to the CB1 and CB2 receptors, serving as neurotransmitters for cannabinoids. Cannabidiol (CBD oil), a non-psychotropic cannabinoid naturally occurring in human and animal species, is also a phytocannabiniod, derived from the industrial hemp plant. While CBD does not bind directly with receptors, it does affect stress genes, such as Soat2 and Cyp27a1, which control sterol (i.e., cholesterol) metabolism. CBD increases the amount of anandamide and other vital lipids, thereby indirectly increasing the availability of circulating cannabinoids to bind with CB1 and CB2 receptors.

Research has shown that cannabidiol, in the form of CBD oil, has therapeutic benefits individually and adjunctively with other interventions. Cannabidiol (CBD) made from legal, industrial hemp contains less than .3% THC, rendering it non-psychoactive. CBD oil has antiemetic, anxiolytic, antitumoral, and immunologically inhibitory properties. Three categories differentiate the types of clinical endocannabinoid deficiency (CECD), which are associated with different disease processes and disorders: genetic, acquired, and idiopathic autoimmune. Many disorders have a combination of CECD origins, and supplementation with cannabidiol (CBD) requires ongoing assessment to facilitate optimal benefit for the individual.

The Human Endocannabinoid System

The human endocannabinoid system is responsible for memory networks in the brain, both excitatory and inhibitory, including the neurogenesis of hippocampal granule cells, which regulate the timing of the endocannabinoids in accordance with the brain's needs, pain perception, mood, synaptic plasticity, motor learning, appetite and taste regulation, and metabolic function, which regulates the storage of energy and transport of cellular nutrition. Cannabinoid receptor binding sites are located in the forebrain areas associated with higher cognitive function, forebrain, midbrain, and hindbrain areas associated with movement control, and hindbrain areas associated with motor and sensory functions attributed to the autonomic nervous system. The endocannabinoid system affects the lipocytes and fat cells, collectively

known as adipocytes, hepatocytes, in the gastrointestinal tract, musculoskeletal system, and endocrine system. The endogenous arachidonate-based lipids, anandamide and 2-arachidonoylglycerol (2-AG) are physiological ligands for the cannabinoid receptors. Cannabinoid receptors CB1 and CB2, two G-protein-coupled receptors, facilitate the responses of the endocannabinoid system in the body, which are critical to maintaining homeostasis. CB1 receptors are located in the central and peripheral nervous systems as well as the lungs, kidneys, and liver. CB2 receptors are predominantly expressed in the immune system and hematopoietic cells.

The direct effect of the endocannabinoid deficiency (CECD) correlates with multisystemic clinical outcomes in such conditions as hyperinsulinemia, osteoporosis, diabetes, dementia, cardiovascular disease, multiple sclerosis, and obesity. Three primary categories are herein defined to discuss endocannabinoid deficiency (CECD): genetic, acquired, and idiopathic autoimmune. Genetic endocannabinoid deficiency (CECD) relates to hereditary acquisition of a disorder; acquired refers to an infectious of traumatic origination, and idiopathic autoimmune refers to etiologies for endocannabinoid deficiencies (CECD) which do not have direct associations. Diseases and disorders are assigned to one or more of these categories because often secondary disorders arise with physiological changes associated with the primary diagnosis. For example, asthma has been associated with endocannabinoid deficiency (CECD) and the disease is categorized as genetic, originating from a hereditary source. The presentation of neoplastic disease of the lung supports adding the category of idiopathic autoimmune as well to the assessment. Because the endocannabinoid system facilitates communication and coordination between various cell types, deficiencies directly affect physiological homeostasis.

Cannabidiol (CBD), a non-psychotropic cannabinoid naturally occurring in human and animal species, occurs as a phytocannabinoid, CBD oil, which is derived from the industrial hemp plant. The restorative effects of cannabidiol (CBD oil), which increases anandamide and other lipid neurotransmitters, thereby restoring the endocannabinoid system, are of interest in the medical management of multiple disorders, including disorders of the pulmonary system, which is directly affected by the immunological, cardiovascular, and neurological systems. Indeed, research supports that plant-derived cannabidiol (CBD) has anti-tumoral and anti-inflammatory benefits.

Cannabidiol (CBD)
Cannabidiol (CBD) is a non-psychotropic and non-toxic compound, which has been demonstrated to positively affect the human endocannabinoid system. Cannabidiol (CBD), derived from the hemp plant, demonstrates anti-inflammatory and immune-modulating properties. Cannabidiol (CBD) has a low affinity for CB1 and CB2 receptors in the human body, but acts as an indirect antagonist of their agonists. (Antagonists are defined as substances that stop or inhibit the effects of another substance on the cellular surface, producing the same effect as a substance which would normally bind to the receptor. Agonists are chemicals that bind to receptors and elicit a biological response.) Therefore, cannabidiol may enhance the therapeutic effects of THC, possibly by increasing the density of the CB1 receptors. Cannabidiol (CBD) has been demonstrated to cross the blood-brain barrier and exert antioxidant, antimicrobial, and neuroprotective properties, rendering it valuable in the prevention and treatment of oxidative ocular disorders and diseases.

Human Pulmonary System
The pulmonary, or respiratory, system of specific organs executes the process by which oxygen and carbon dioxide are exchanged with external air. The lungs, trachea, bronchi, and diaphragm facilitate respiration and gaseous exchange, which facilitates oxygenation of the blood through diffusion.

The endocannabinoid system is critical in facilitating the ability of the lungs to execute respiration. CB1 and CB2 receptors are dispersed throughput the respiratory system and research indicates that clinical endocannabinoid deficiencies contribute to the development of chronic and malignant pulmonary diseases.

Cannabidiol (CBD) and Pulmonary Disorders and Diseases: **Asthma**
Asthma is an inflammatory disease of the respiratory system that causes shortness of breath and reduced tidal volumes of the lungs. Reactive airway disease accompanies asthma, which is chronic but can rapidly become fatal without intervention. The endocannabinoid system is critical in managing the inflammatory response in asthma via CB1 and CB2 receptors. CB1 receptors activate bronchodilator effects by relaxing smooth muscle, thereby easing respiratory distress. CB2 receptors control immunological response in the lungs and the endocannabinoid system modulates the potential hyperactive response to an antigen. Clinical endocannabinoid deficiency (CECD) associated with asthma is both genetic and idiopathic autoimmune. Research indicates that elevating anandamide levels in the pulmonary system via the intake of cannabidiol, reduced morbidity associated asthma by modulating the inflammatory response in asthma.

Emphysema
Emphysema, or Chronic Obstructive Pulmonary Disease (COPD), is a progressive disease of the lungs, which restricts oxygenation and perfusion, thereby affecting not only the respiratory system, but also the cardiovascular and neurological systems. Clinical Endocannabinoid Deficiency (CECD) associated with emphysema is acquired, reflecting the increased incidence secondary to cigarette smoking. CB1 and CB2 receptors in the respiratory tract respond favorably to cannabidiol in clinical research, reducing chronic inflammation of the lungs and inducing bronchodilation, which increases oxygenation. Cannabidiol (CBD) possesses anxiolytic and anti-inflammatory properties, and is warranted in emphysema to increase tidal volume and reduce inflammatory processes of the lung.

Lung Cancer
Lung cancer is an acquired malignancy that is most commonly associated with cigarette smoking. Genetic malformations occur early on in the use of tobacco and the development of malignancy may not occur until decades later. The endocannabinoid system is critical in maintaining homeostasis of the immunological system and both CB1 and CB2 receptors are affected by tobacco use. The acquired clinical endocannabinoid deficiency (CECD) associated with lung cancer, nonsmile cell and small cell alike, responds to the administration of cannabidiol (CBD) in clinical research. CBD oil also inhibits metastasis of lung cancer, which commonly spreads to the brain and spine. Preventively, cannabidiol (CBD) is recommended in individuals who may be at risk for lung cancer, including those who have been exposed to

second-hand smoking. In treatment, adjunctive therapy with cannabidiol (CBD) may inhibit metastasis from primary lung tumors.

Pneumonia (Interstitial)
Pneumonia, associated with bacteria or viral infections, causes respiratory dysfunction and often distress in individuals with underlying autoimmune diseases, such as multiple sclerosis. Clinical endocannabinoid deficiency (CECD) associated with pneumonia affects CB2 receptors, which regulate immunological responses. Indeed, CECD deficiency may cause hyperactivity of certain white cells, which then further inhibit respiratory function. Cannabidiol (CBD) possesses antibacterial and anti-inflammatory properties, which may augment the benefit of antibiotic and steroidal therapies in the management of pneumonia. In individuals at increased risk for pneumonia, supplementation with cannabidiol routinely increases circulating anandamide, which then binds directly to CB2 receptors. In combination with preventative health practices, the addition of cannabidiol (CBD) may reduce the incidence or severity of the occurrence of bacterial and/or viral infections associated with pneumonia.

Pulmonary Hypertension
Pulmonary hypertension is a chronic and potentially life-threatening disorder, which increases the pulmonary artery pressure, increasing the likelihood of vessel rupture and mortality. Cannabidiol (CBD) induces relaxation of vessel walls, lowering systemic blood pressure. Research indicates administration of cannabidiol (CBD) in pulmonary hypertension significantly reduced pulmonary artery pressure by affecting CB1 binding abilities. In combination with treatment, supplementation with cannabidiol (CBD) is suggested in individuals at-risk or diagnosed with pulmonary hypertension.

Endocannabinoid Deficiency (CECD) Classification: Pulmonary Disorders

Disorder	Origin of CECD
Asthma	Genetic
Emphysema	Acquired
Lung Cancer	Acquired
Pneumonia	Acquired
Pulmonary Hypertension	Idiopathic Autoimmune

CEN Medical Cannabis Pharmacological Prescription and Coding System Pulmonary Disorder Application
The CEN Medical Cannabis Pharmacological Prescription and Coding System (CEN/MCPPCS) provides language that enables the health care practitioner to communicate with the dispenser of medical cannabis. The first two letters of the system refer to the cannabis type: cannabis sativa, cannabis indica, or cannabis hybrida. The numerical value in percentage to the right of the colon refers to the recommended THC content in percentage, and the numerical value in sequence to the right of the THC percentage refers to the recommended CDB content.

(CEN/MCPPCS): Cannabis type (sativa, indica, hybrida; THC percentage or range/CBD percentage or range) or Hemp Cannabidiol (CBD)

Example: Cannabidiol (CBD oil) is recommended for the patient. The concentration of the CBD oil is 19.5% and the patient is to ingest 50 mg. of CBD oil four times each day every six hours, as adjunctive therapy in the treatment of lung cancer, (ICD-9: 162.9). The prescription would therefore read:

Samuel Ruthersberg
Date of Birth: 10-01-1949.
Diagnosis: Small cell carcinoma of the lung, ICD-9 code: 162.9
CBD: 0.00%/ 19.5%. Take 50 mg. of CBD oil by mouth four times daily, every 6 hours. Use dropper as indicated.
Victor Hahn, M.D.

The patient would then be able to purchase the CBD oil online or at a dispensary, offering the prescription to the pharmacist or technician.

Composition Assignments

1. Please suggest a plan of care based upon the following patient information. Discuss if CBD oil would be indicated with rationale and the type of endocannabinoid deficiency (s)(CECD) for the pulmonary disease process.
    a. A 53-year-old male with a history of smoking for greater than 20 years complains of weight loss, shortness of breath and fatigue. A chest x-ray shows a left mediastinal mass.
2. Please choose an article from the CEN library on an aspect of cannabidiol (CBD) and the pulmonary system. Write a two-hundred-word critical analysis paper on this research article and determine the following in your paper:
    a. Author and affiliation
    b. Study population
    c. Purpose
    d. Outcome of the study
    e. Importance of the research

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Chapter VII: Dermatological Health and Dermatological Disease

Learning Objectives

1. Discuss assessment protocols to determine level of endocannabinoid deficiencies of the dermatological system.
2. Discuss therapeutic strategies to address endocannabinoid deficiencies of the dermatological system.
3. Discuss patient care guidelines to implement cannabinoid therapy with standard of care pharmaceutical regimens pertaining to the dermatological system.
4. Discuss educational guidelines for patients to monitor clinical outcomes when implementing cannabinoid protocols for dermatological disorders.

The Endocannabinoid System and Cannabidiol (CBD) - Introduction

The endocannabinoid system (ECS) is a lipid-derived signaling system discovered within the past decade. Cannabinoids, which are homeostatic regulators, circulate throughout human and animal systems continuously, affecting all physiological processes. The endocannabinoid system is comprised of CB1 and CB2 receptors, which bind directly or indirectly to cannabinoids and phytocannabinoids. CB1 receptors are excitatory and are located in the central nervous system, lungs, liver, and kidney. CB2 receptors regulate immunological responses and are located in the immune and circulatory systems. Endogenous compounds, such as anandamide and arachidonylglerol (2-AG), are made by mammals from lipids and bind directly to the CB1 and CB2 receptors, serving as neurotransmitters for cannabinoids. Cannabidiol (CBD oil), a non-psychotropic cannabinoid naturally occurring in human and animal species, is also a phytocannabiniod, derived from the industrial hemp plant. While CBD does not bind directly with receptors, it does affect stress genes, such as Soat2 and Cyp27a1, which control sterol (i.e., cholesterol) metabolism. CBD increases the amount of anandamide and other vital lipids, thereby indirectly increasing the availability of circulating cannabinoids to bind with CB1 and CB2 receptors.

Research has shown that cannabidiol, in the form of CBD oil, has therapeutic benefits individually and adjunctively with other interventions. Cannabidiol (CBD) made from legal, industrial hemp contains less than .3% THC, rendering it non-psychoactive. CBD oil has antiemetic, anxiolytic, antitumoral, and immunologically inhibitory properties. Three categories differentiate the types of clinical endocannabinoid deficiency (CECD), which are associated with different disease processes and disorders: genetic, acquired, and idiopathic autoimmune. Many disorders have a combination of CECD origins, and supplementation with cannabidiol (CBD) requires ongoing assessment to facilitate optimal benefit for the individual.

The Human Endocannabinoid System

The human endocannabinoid system is responsible for memory networks in the brain, both excitatory and inhibitory, including the neurogenesis of hippocampal granule cells, which regulate the timing of the endocannabinoids in accordance with the brain's needs, pain perception, mood, synaptic plasticity, motor learning, appetite and taste regulation, and metabolic function, which regulates the storage of energy and transport of cellular nutrition. Cannabinoid receptor binding sites are located in the forebrain areas associated with higher cognitive function, forebrain, midbrain, and hindbrain areas associated with movement control, and hindbrain areas associated with motor and sensory functions attributed to the autonomic nervous system. The endocannabinoid system affects the lipocytes and fat cells, collectively

known as adipocytes, hepatocytes, in the gastrointestinal tract, musculoskeletal system, and endocrine system. The endogenous arachidonate-based lipids, anandamide and 2-arachidonoylglycerol (2-AG) are physiological ligands for the cannabinoid receptors. Cannabinoid receptors CB1 and CB2, two G-protein-coupled receptors, facilitate the responses of the endocannabinoid system in the body, which are critical to maintaining homeostasis. CB1 receptors are located in the central and peripheral nervous systems as well as the lungs, kidneys, and liver. CB2 receptors are predominantly expressed in the immune system and hematopoietic cells.

The direct effect of the endocannabinoid deficiency (CECD) correlates with multisystemic clinical outcomes in such conditions as hyperinsulinemia, osteoporosis, diabetes, dementia, cardiovascular disease, multiple sclerosis, and obesity. Three primary categories are herein defined to discuss endocannabinoid deficiency (CECD): genetic, acquired, and idiopathic autoimmune. Genetic endocannabinoid deficiency relates to hereditary acquisition of a disorder; acquired refers to an infectious of traumatic origination, and idiopathic autoimmune refers to etiologies for endocannabinoid deficiencies (CECD) which do not have direct associations. Diseases and disorders are assigned to one or more of these categories because often secondary disorders arise with physiological changes associated with the primary diagnosis. For example, dermatitis has been associated with endocannabinoid deficiency (CECD) and the disease is often categorized as acquired, originating from an extrinsic source. The presentation of scleroderma, which is multisystemic, supports adding the category of idiopathic autoimmune as well to the assessment. Because the endocannabinoid system facilitates communication and coordination between various cell types, deficiencies directly affect physiological homeostasis.

Cannabidiol (CBD), a non-psychotropic cannabinoid naturally occurring in human and animal species, occurs as a phytocannabinoid, CBD oil, which is derived from the industrial hemp plant. The restorative effects of cannabidiol (CBD oil), which increases anandamide and other lipid neurotransmitters, thereby restoring the endocannabinoid system, are of interest in the medical management of multiple disorders, including disorders of the dermatological system, which is directly affected by the immunological and neurological systems. Indeed, research supports that plant-derived cannabidiol (CBD) has analgesic, anti-tumoral, and anti-inflammatory benefits.

Cannabidiol (CBD)

Cannabidiol (CBD) is a non-psychotropic and non-toxic compound, which has been demonstrated to positively affect the human endocannabinoid system. Cannabidiol (CBD), derived from the hemp plant, demonstrates anti-inflammatory and immune-modulating properties. Cannabidiol (CBD) has a low affinity for CB1 and CB2 receptors in the human body, but acts as an indirect antagonist of their agonists. (Antagonists are defined as substances that stop or inhibit the effects of another substance on the cellular surface, producing the same effect as a substance which would normally bind to the receptor. Agonists are chemicals that bind to receptors and elicit a biological response.) Therefore, cannabidiol (CBD) may enhance the therapeutic effects of THC, possibly by increasing the density of the CB1 receptors. Cannabidiol (CBD) has been demonstrated to cross the blood-brain barrier and exert antioxidant, antimicrobial, and antitumoral properties, rendering it valuable in the prevention and treatment of oxidative dermatologic disorders and diseases.

Human Dermatological System
The largest organ of the human body is the skin, which protects and armors the underlying adipose tissue, muscle, ligaments, viscera, and skeletal system. Multiple layers of ectodermal tissue facilitate insulation, temperature regulation, sensation and synthesis of vitamin D and B for the human body. As the initial line of defense, the skin protects the body from pathogens and minimizes dehydration, managing water loss. Pigmentation of the skin varies in the world and originated from geographical location and climate category.

The endocannabinoid system facilitates immunological and nervous system responses throughout the dermatological system via CB1, autonomically through CB1 receptors, and immunologically through CB2 receptors. Various manifestations of endocannabinoid deficiency affect the dermatological structures, increasing the incidence of diseases which affect the skin and underlying tissues.

Cannabidiol (CBD) and Dermatological Disorders and Diseases: **Dermatitis**
Chronic dermatological conditions, such as psoriasis, and acute conditions, such as contact dermatitis, cause rash, pruritus, increased risk of infection, and psychological stress. The immunological response often increases symptoms associated with dermatitis. CB1 and CB2 receptors in genetic and acquired clinical endocannabinoid deficiency (CECD) in dermatitis respond to the administration of cannabidiol (CBD). Research indicates that cannabidiol (CBD) possesses anti-inflammatory and analgesic properties, which reduce symptoms. Further, the increased uptake of administered cannabidiol (CBD) has been found to regulate the immunological responses to dermatitis, thereby improving symptoms and reducing anxiety and depression associated with dermatitis. Cannabidiol (CBD) is suggested as adjunctive therapy in the management of both chronic and acute dermatitis.

Diabetic Ulcer
Diabetic ulceration occurs when decreased circulatory perfusion accompanies diabetes. Reduced blood flow to the periphery, including legs and feet, causes chronic ulceration, cellulitis and recurring infection. Clinical endocannabinoid deficiency (CECD) in diabetes mellitus responds to adjunctive administration of CBD oil with oral hypoglycemic agents and insulin. CB1 and CB2 receptors are restored with cannabidiol (CBD) administration, reducing sensory and dysfunctional immunological responses, respectively. Cannabidiol (CBD) possesses anti-inflammatory and anti-bacterial properties, which potentiate therapeutic healing options, such as hyperbaric oxygen therapy, in the management of diabetic ulcerations.

Scleroderma
Scleroderma, a systemic autoimmune disorder manifesting initially and most frequently as a dermatologic exacerbation, causes hardening of the skin and tissues. Alterations in oxygen perfusion and aberrant immunological responses contribute to symptoms of pain and fatigue. Clinical endocannabinoid deficiency (CECD) in scleroderma is considered idiopathic autoimmune, affecting CB1 and CB2 receptors throughout the human body. Administration of cannabidiol (CBD) has been shown to improve skin elasticity, reduce dermatological exacerbations, and relieve discomfort associated with this chronic disorder.

Skin Cancer
Malignancy of the skin includes such malignancies as squamous cell carcinoma and malignant melanoma. Tumoral growth and visceral dissemination of malignancy characterizes carcinoma of the skin, categorized as acquired and idiopathic autoimmune clinical endocannabinoid deficiency (CECD). Administration of cannabidiol (CBD) triggers malignant cell death, inhibiting tumor growth, and metastasis to viscera. Further, autophagy, which removes cellular waste, is enhanced by cannabidiol (CBD), expediting malignant cell death. Administration of cannabidiol (CBD) is warranted given conclusive research which supports anti-tumoral, anti-bacterial, and analgesic effects of CBD oil.

Endocannabinoid Deficiency (CECD) Classification: Dermatological Disorders

Disorder	**Origin of CECD**
Dermatitis	Genetic, Acquired
Diabetic Ulcer	Acquired
Scleroderma	Idiopathic Autoimmune
Skin Cancer	Idiopathic Autoimmune

CEN Medical Cannabis Pharmacological Prescription and Coding System:
Dermatological Disorder Application
The CEN Medical Cannabis Pharmacological Prescription and Coding System (CEN/MCPPCS) provides language that enables the health care practitioner to communicate with the dispenser of medical cannabis. The first two letters of the system refer to the cannabis type: cannabis sativa, cannabis indica, or cannabis hybrida. The numerical value in percentage to the right of the colon refers to the recommended THC content in percentage, and the numerical value in sequence to the right of the THC percentage refers to the recommended CDB content.

(CEN/MCPPCS): Cannabis type (sativa, indica, hybrida; THC percentage or range/CBD percentage or range) or Hemp Cannabidiol (CBD)

Example: Cannabidiol (CBD oil) is recommended for the patient. The concentration of the CBD oil is 19.5% and the patient is to ingest 50 mg. of CBD oil four times each day every six hours, as adjunctive therapy in the treatment of dermatitis, (ICD-9:690.1). The prescription would therefore read:

Triana Bartholomew
Date of Birth: 09-01-1939.
Diagnosis: Seborrheic dermatitis, ICD-9 code: 690.1
CBD: 0.00%/ 19.5%. Take 50 mg. of CBD oil by mouth four times daily, every 6 hours. Use dropper as indicated.
David Posner, M.D.

The patient would then be able to purchase the CBD oil online or at a dispensary, offering the prescription to the pharmacist or technician.

Composition Assignments:

1. Please suggest a plan of care based upon the following patient information. Discuss if CBD oil would be indicated with rationale and the type of endocannabinoid deficiency (s)(CECD) for the dermatological disease process.
    a. A 65-year-old male complains of localized itching of the left leg. Upon examination, skin appears reddened and cellulites is evident. The patient states he was recently prescribed an oral hypoglycemic agent by his physician.
2. Please choose an article from the CEN library on an aspect of cannabidiol (CBD) and the dermatological system. Write a two-hundred-word critical analysis paper on this research article and determine the following in your paper
    a. Author and affiliation
    b. Study population
    c. Purpose
    d. Outcome of the study
    e. Importance of the research

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Chapter VIII: Endocrine Health and Endocrine Disease

Learning Objectives

1. Discuss assessment protocols to determine level of endocannabinoid deficiencies of the endocrine system.
2. Discuss therapeutic strategies to address endocannabinoid deficiencies of the endocrine system.
3. Discuss patient care guidelines to implement cannabinoid therapy with standard of care pharmaceutical regimens pertaining to the endocrine system.
4. Discuss educational guidelines for patients to monitor clinical outcomes when implementing cannabinoid protocols for endocrine disorders.

The Endocannabinoid System and Cannabidiol (CBD) - Introduction

The endocannabinoid system (ECS) is a lipid-derived signaling system discovered within the past decade. Cannabinoids, which are homeostatic regulators, circulate throughout human and animal systems continuously, affecting all physiological processes. The endocannabinoid system is comprised of CB1 and CB2 receptors, which bind directly or indirectly to cannabinoids and phytocannabinoids. CB1 receptors are excitatory and are located in the central nervous system, lungs, liver, and kidney. CB2 receptors regulate immunological responses and are located in the immune and circulatory systems. Endogenous compounds, such as anandamide and arachidonylglerol (2-AG), are made by mammals from lipids and bind directly to the CB1 and CB2 receptors, serving as neurotransmitters for cannabinoids. Cannabidiol (CBD oil), a non-psychotropic cannabinoid naturally occurring in human and animal species, is also a phytocannabiniod, derived from the industrial hemp plant. While CBD does not bind directly with receptors, it does affect stress genes, such as Soat2 and Cyp27a1, which control sterol (i.e., cholesterol) metabolism. CBD increases the amount of anandamide and other vital lipids, thereby indirectly increasing the availability of circulating cannabinoids to bind with CB1 and CB2 receptors.

Research has shown that cannabidiol, in the form of CBD oil, has therapeutic benefits individually and adjunctively with other interventions. Cannabidiol (CBD) made from legal, industrial hemp contains less than .3% THC, rendering it non-psychoactive. CBD oil has antiemetic, anxiolytic, antitumoral, and immunologically inhibitory properties. Three categories differentiate the types of clinical endocannabinoid deficiency (CECD), which are associated with different disease processes and disorders: genetic, acquired, and idiopathic autoimmune. Many disorders have a combination of CECD origins, and supplementation with cannabidiol (CBD) requires ongoing assessment to facilitate optimal benefit for the individual.

The Human Endocannabinoid System

The human endocannabinoid system is responsible for memory networks in the brain, both excitatory and inhibitory, including the neurogenesis of hippocampal granule cells, which regulate the timing of the endocannabinoids in accordance with the brain's needs, pain perception, mood, synaptic plasticity, motor learning, appetite and taste regulation, and metabolic function, which regulates the storage of energy and transport of cellular nutrition. Cannabinoid receptor binding sites are located in the forebrain areas associated with higher cognitive function, forebrain, midbrain, and hindbrain areas associated with movement control, and hindbrain areas associated with motor and sensory functions attributed to the autonomic nervous system. The endocannabinoid system affects the lipocytes and fat cells, collectively

known as adipocytes, hepatocytes, in the gastrointestinal tract, musculoskeletal system, and endocrine system. The endogenous arachidonate-based lipids, anandamide and 2-arachidonoylglycerol (2-AG) are physiological ligands for the cannabinoid receptors. Cannabinoid receptors CB1 and CB2, two G-protein-coupled receptors, facilitate the responses of the endocannabinoid system in the body, which are critical to maintaining homeostasis. CB1 receptors are located in the central and peripheral nervous systems as well as the lungs, kidneys, and liver. CB2 receptors are predominantly expressed in the immune system and hematopoietic cells.

The direct effect of the endocannabinoid deficiency (CECD) correlates with multisystemic clinical outcomes in such conditions as hyperinsulinemia, osteoporosis, diabetes, dementia, cardiovascular disease, multiple sclerosis, and obesity. Three primary categories are herein defined to discuss endocannabinoid deficiency (CECD): genetic, acquired, and idiopathic autoimmune. Genetic endocannabinoid deficiency relates to hereditary acquisition of a disorder, acquired refers to an infectious of traumatic origination, and idiopathic autoimmune refers to etiologies for endocannabinoid deficiencies (CECD) which do not have direct associations.

Diseases and disorders are assigned to one or more of these categories because often secondary disorders arise with physiological changes associated with the primary diagnosis. For example, endocrine disease has been associated with endocannabinoid deficiency (CECD) and the disease is categorized as genetic, originating from a hereditary source. The presentation of primary multifocal leukoencephalopathy (PML), which affects the neurological system, supports adding the category of idiopathic autoimmune as well to the assessment. Because the endocannabinoid system facilitates communication and coordination between various cell types, deficiencies directly affect physiological homeostasis.

Cannabidiol (CBD), a non-psychotropic cannabinoid naturally occurring in human and animal species, occurs as a phytocannabinoid, CBD oil, which is derived from the industrial hemp plant. The restorative effects of cannabidiol (CBD oil), which increases anandamide and other lipid neurotransmitters, thereby restoring the endocannabinoid system, are of interest in the medical management of multiple disorders, including disorders of the endocrine system, which is directly affected by the immunological and neurological systems. Indeed, research supports that plant-derived cannabidiol (CBD) has neuroprotective and anti-inflammatory benefits.

Cannabidiol (CBD)

Cannabidiol (CBD) is a non-psychotropic and non-toxic compound that has been demonstrated to positively affect the human endocannabinoid system. Cannabidiol (CBD), derived from the hemp plant, demonstrates anti-inflammatory and immune-modulating properties. Cannabidiol (CBD) has a low affinity for CB1 and CB2 receptors in the human body, but acts as an indirect antagonist of their agonists. (Antagonists are defined as substances that stop or inhibit the effects of another substance on the cellular surface, producing the same effect as a substance which would normally bind to the receptor. Agonists are chemicals that bind to receptors and elicit a biological response.) Therefore, cannabidiol (CBD) may enhance the therapeutic effects of THC, possibly by increasing the density of the CB1 receptors. Cannabidiol (CBD) has been demonstrated to cross the blood-brain barrier and exert antioxidant, antimicrobial, and neuroprotective properties, rendering it valuable in the prevention and treatment of oxidative endocrine disorders and diseases.

Human Endocrine System
The endocrine system refers to the collection of glands of an organism that secrete hormones directly into the circulatory system to be carried towards a distant target organ. The major endocrine glands include the pineal gland, pituitary gland, pancreas, ovaries, testes, thyroid gland, parathyroid gland, hypothalamus, gastrointestinal tract and adrenal glands. The endocrine system is in contrast to the exocrine system, which secretes its hormones using ducts. The endocrine system is an information signal system like the nervous system, yet its effects and mechanism are classifiably different. The endocrine system's effects are slow to initiate, and prolonged in their response, lasting from a few hours up to weeks. The nervous system sends information very quickly, and responses are generally short lived. In vertebrates, the hypothalamus is the neural control center for all endocrine systems. The field of study dealing with the endocrine system and its disorders is endocrinology, a branch of internal medicine.

Special features of endocrine glands are, in general, their ductless nature, their vascularity, and commonly the presence of intracellular vacuoles or granules that store their hormones. In contrast, exocrine glands, such as salivary glands, sweat glands, and glands within the gastrointestinal tract, tend to be much less vascular and have ducts or a hollow lumen.

In addition to the specialized endocrine organs mentioned above, many other organs that are part of other body systems, such as bone, kidney, liver, heart and gonads, have secondary endocrine functions. For example the kidney secretes endocrine hormones such as erythropoietin and renin. A number of glands that signal each other in sequence are usually referred to as an axis, for example, the hypothalamic-pituitary-adrenal axis.

As opposed to endocrine factors that travel considerably longer distances via the circulatory system, other signaling molecules, such as paracrine factors involved in paracrine signaling diffuse over a relatively short distance.

Cannabidiol (CBD) and Endocrine Disorders and Diseases: Diabetes
Diabetes is an endocrine disorder with a strong hereditary component, affecting children and adults throughout the lifespan. The development of insulin resistance and glucose dysregulation characterizes diabetes mellitus, affecting the cardiovascular, immunological, and neurological systems as well as the endocrine system. Clinical endocannabinoid deficiency (CECD), characterized as genetic and acquired, affects excitatory CB1 receptors and immune-responsive CB2 receptors in the endocrine system. Research supports the benefit of cannabidiol (CBD) in reducing insulin resistance and as a hypoglycemic agent. Preventatively in individuals at risk for diabetes mellitus, and as adjunctive therapy under physician supervision in management of serum glucose, cannabidiol is suggested to improve disease management and prevent secondary manifestations of the disease, such as diabetic neuropathy.

Hypothyroidism
Hypothyroidism is a disease which affects the thyroid glands ability to secrete associated hormones, leading to weight gain, fatigue, immune dysfunction, and internal temperature regulation dysfunction. Medical management includes hormonal supplementation, and cannabidiol (CBD) has been shown to improve symptoms of hypothyroidism as adjunctive therapy. CB1 receptors are directly affected in hypothyroidism, which is considered idiopathic autoimmune and genetic

in relation to clinical endocannabinoid deficiency (CECD). In individuals at risk for the development of hypothyroidism, preventative administration is warranted to improve the function and receptivity of CB1 receptors to anandamide, the lipid neurotransmitter which is increased by CBD oil.

Thyroid cancer

Malignant tumors of the thyroid affect hormonal function, rendering the individual with profound symptoms of fatigue and depression. Clinical endocannabinoid deficiency (CECD) in thyroid cancer affects CB2 receptors, reducing the ability of the immune system to eradicate malignancy. The anti-tumoral benefits of cannabidiol (CBD) are well documented and administration is suggested as adjunctive therapy in the management of thyroid cancer. In patients at risk for developing thyroid cancer associated with hypothyroidism, prophylactic use of cannabidiol may be considered to prevent thyroid dysfunction. Metastatic disease associated with cancer has been inhibited by the use of cannabidiol in human studies, suggesting beneficial use in diagnosed metastatic disease.

Endocannabinoid Deficiency (CECD) Classification: Endocrine Disorders

Disorder	Origin of CECD
Diabetes	Genetic
Hypothyroidism	Genetic
Thyroid cancer	Idiopathic Autoimmune

CEN Medical Cannabis Pharmacological Prescription and Coding System Endocrine Disorder Application

The CEN Medical Cannabis Pharmacological Prescription and Coding System (CEN/MCPPCS) provides language that enables the health care practitioner to communicate with the dispenser of medical cannabis. The first two letters of the system refer to the cannabis type: cannabis sativa, cannabis indica, or cannabis hybrida. The numerical value in percentage to the right of the colon refers to the recommended THC content in percentage, and the numerical value in sequence to the right of the THC percentage refers to the recommended CDB content.

(CEN/MCPPCS): Cannabis type (sativa, indica, hybrida; THC percentage or range/CBD percentage or range) or Hemp Cannabidiol (CBD)

Example: Cannabidiol (CBD oil) is recommended for the patient. The concentration of the CBD oil is 19.5% and the patient is to ingest 50 mg. of CBD oil four times each day every six hours, as adjunctive therapy in the treatment of thyroid cancer, (ICD-9: 193). The prescription would therefore read:

Nancy Hershel
Date of Birth: 11-01-1979.
Diagnosis: Thyroid cancer, ICD-9 code: 193
CBD: 0.00%/ 19.5%. Take 50 mg. of CBD oil by mouth four times daily, every 6 hours. Use dropper as indicated.
Eli Oster, M.D.

The patient would then be able to purchase the CBD oil online or at a dispensary, offering the prescription to the pharmacist or technician.

Composition Assignments:

1. Please suggest a plan of care based upon the following patient information. Discuss if CBD oil would be indicated with rationale and the type of endocannabinoid deficiency (s)(CECD) for the endocrine disease process.
    a. A 40-year-old African American female complains of fatigue, weight gain, and difficulty concentrating. Recent lab studies indicate hypothyroidism.
2. Please choose an article from the CEN library on an aspect of cannabidiol (CBD) and the reproductive system. Write a two-hundred-word critical analysis paper on this research article and determine the following in your paper:
    a. Author and affiliation
    b. Study population
    c. Purpose
    d. Outcome of the study
    e. Importance of the research

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Chapter IX: Reproductive Health and Gynecological Disease

Learning Objectives

1. Discuss assessment protocols to determine level of endocannabinoid deficiencies of the reproductive system.
2. Discuss therapeutic strategies to address endocannabinoid deficiencies of the reproductive system.
3. Discuss patient care guidelines to implement cannabinoid therapy with standard of care pharmaceutical regimens pertaining to the reproductive system.
4. Discuss educational guidelines for patients to monitor clinical outcomes when implementing cannabinoid protocols for reproductive disorders.

The Endocannabinoid System and Cannabidiol (CBD) - Introduction

The endocannabinoid system (ECS) is a lipid-derived signaling system discovered within the past decade. Cannabinoids, which are homeostatic regulators, circulate throughout human and animal systems continuously, affecting all physiological processes. The endocannabinoid system is comprised of CB1 and CB2 receptors, which bind directly or indirectly to cannabinoids and phytocannabinoids. CB1 receptors are excitatory and are located in the central nervous system, lungs, liver, and kidney. CB2 receptors regulate immunological responses and are located in the immune and circulatory systems. Endogenous compounds, such as anandamide and arachidonylglerol (2-AG), are made by mammals from lipids and bind directly to the CB1 and CB2 receptors, serving as neurotransmitters for cannabinoids. Cannabidiol (CBD oil), a non-psychotropic cannabinoid naturally occurring in human and animal species, is also a phytocannabiniod, derived from the industrial hemp plant. While CBD does not bind directly with receptors, it does affect stress genes, such as Soat2 and Cyp27a1, which control sterol (i.e., cholesterol) metabolism. CBD increases the amount of anandamide and other vital lipids, thereby indirectly increasing the availability of circulating cannabinoids to bind with CB1 and CB2 receptors.

Research has shown that cannabidiol, in the form of CBD oil, has therapeutic benefits individually and adjunctively with other interventions. Cannabidiol (CBD) made from legal, industrial hemp contains less than .3% THC, rendering it non-psychoactive. CBD oil has antiemetic, anxiolytic, antitumoral, and immunologically inhibitory properties. Three categories differentiate the types of clinical endocannabinoid deficiency (CECD), which are associated with different disease processes and disorders: genetic, acquired, and idiopathic autoimmune. Many disorders have a combination of CECD origins, and supplementation with cannabidiol (CBD) requires ongoing assessment to facilitate optimal benefit for the individual.

The Human Endocannabinoid System

The human endocannabinoid system is responsible for memory networks in the brain, both excitatory and inhibitory, including the neurogenesis of hippocampal granule cells, which regulate the timing of the endocannabinoids in accordance with the brain's needs, pain perception, mood, synaptic plasticity, motor learning, appetite and taste regulation, and metabolic function, which regulates the storage of energy and transport of cellular nutrition. Cannabinoid receptor binding sites are located in the forebrain areas associated with higher cognitive function, forebrain, midbrain, and hindbrain areas associated with movement control, and hindbrain areas associated with motor and sensory functions attributed to the autonomic nervous system. The endocannabinoid system affects the lipocytes and fat cells, collectively

known as adipocytes, hepatocytes, in the gastrointestinal tract, musculoskeletal system, and endocrine system. The endogenous arachidonate-based lipids, anandamide and 2-arachidonoylglycerol (2-AG) are physiological ligands for the cannabinoid receptors. Cannabinoid receptors CB1 and CB2, two G-protein-coupled receptors, facilitate the responses of the endocannabinoid system in the body, which are critical to maintaining homeostasis. CB1 receptors are located in the central and peripheral nervous systems as well as the lungs, kidneys, and liver. CB2 receptors are predominantly expressed in the immune system and hematopoietic cells.

The direct effect of the endocannabinoid deficiency (CECD) correlates with multisystemic clinical outcomes in such conditions as hyperinsulinemia, osteoporosis, diabetes, dementia, cardiovascular disease, multiple sclerosis, and obesity. Three primary categories are herein defined to discuss endocannabinoid deficiency (CECD): genetic, acquired, and idiopathic autoimmune. Genetic endocannabinoid deficiency (CECD) relates to hereditary acquisition of a disorder; acquired refers to an infectious of traumatic origination, and idiopathic autoimmune refers to etiologies for endocannabinoid deficiencies (CECD) which do not have direct associations. Diseases and disorders are assigned to one or more of these categories because often secondary disorders arise with physiological changes associated with the primary diagnosis. For example, endometriosis has been associated with endocannabinoid deficiency (CECD) and the disease is categorized as genetic, originating from a hereditary source. The presentation of breast cancer as well to the assessment adds the categorization of idiopathic autoimmune to the diagnosis. Because the endocannabinoid system facilitates communication and coordination between various cell types, deficiencies directly affect physiological homeostasis.

Cannabidiol (CBD), a non-psychotropic cannabinoid naturally occurring in human and animal species, occurs as a phytocannabinoid, CBD oil, which is derived from the industrial hemp plant. The restorative effects of cannabidiol (CBD oil), which increases anandamide and other lipid neurotransmitters, thereby restoring the endocannabinoid system, are of interest in the medical management of multiple disorders, including disorders of the reproductive system, which is directly affected by the immunological and neurological systems. Indeed, research supports that plant-derived cannabidiol (CBD) has analgesic and anti-inflammatory benefits.

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Cannabidiol (CBD) is a non-psychotropic and non-toxic compound which has been demonstrated to positively affect the human endocannabinoid system. Cannabidiol (CBD), derived from the hemp plant, demonstrates anti-inflammatory and immune-modulating properties. Cannabidiol (CBD) has a low affinity for CB1 and CB2 receptors in the human body, but acts as an indirect antagonist of their agonists. (Antagonists are defined as substances that stop or inhibit the effects of another substance on the cellular surface, producing the same effect as a substance which would normally bind to the receptor. Agonists are chemicals that bind to receptors and elicit a biological response.) Therefore, cannabidiol (CBD) may enhance the therapeutic effects of THC, possibly by increasing the density of the CB1 receptors. Cannabidiol (CBD) has been demonstrated to cross the blood-brain barrier and exert antioxidant, antimicrobial, and anti-tumoral properties, rendering it valuable in the prevention and treatment of reproductive disorders and diseases.

Human Reproductive System
The reproductive system is comprised of sexual organs that define the gender of the species. Reproductive organs facilitate procreation and sexual pleasure in human beings. Stressful lifestyles, environmental factors, and genetic influences affect sexual behavior and health in males and females. For example, sexually transmitted diseases, such as HIV, affect the immune system and inhibit the ability of the individual to fight opportunistic infections. The influence of the endocannabinoid system, with excitatory CB1 receptors and immunological CB2 receptors located throughout the reproductive system, is essential in understanding disorders that affect reproductive health.

Cannabidiol (CBD) and Reproductive Disorders and Diseases: **Endometriosis**
Endometriosis is a painful, inflammatory disease in which endometrial tissue resides in the abdominal cavity. Affected by monthly hormonal changes, endometriosis proliferates, causing intraabdominal bleeding and adhesions. Infrequently, endometriosis can progress to other organs, including the lungs. Even with hormonal and surgical intervention, endometriosis causes chronic pain and disability for millions of women.

The endocannabinoid system regulates hormonal imbalance in the reproductive system. CB2 receptors are affected by clinical endocannabinoid deficiency in endometriosis and phytocannabinoid replacement increases anandamide binding to the CB2 receptors. The anti-inflammatory and analgesic properties of cannabidiol (CBD) are effective adjunctively in the management of inflammatory conditions such as endometriosis and may be considered in individual plans of care.

Endometrial Cancer
Endometrial adenocarcinoma causes intraabdominal masses in women. Early detection is associated with improved prognosis, but treatment is radiation and chemotherapy. Clinical endocannabinoid deficiency (CECD) associated with endometrial adenocarcinoma is idiopathic autoimmune, with deficits affecting CB2 receptors. Cannabidiol (CBD) has been shown to reduce tumor growth and inhibit metastasis and is therefore warranted as adjunctive therapy in malignancy. Additionally, symptom relief with cannabidiol includes analgesia and reduced anxiety associated with the diagnosis.

Prostate Cancer
Prostate cancer affects millions of men and is associated with an excellent prognosis in early detection. Because many men do not receive prostate examinations and PSH screenings, later detection is associated with poor prognosis secondary to metastasis. Clinical endocannabinoid deficiency (CECD) in prostate cancer affects primarily the CB2 receptors and is considered idiopathic autoimmune. Preventatively, in early detection, and adjunctively with radiation or surgical intervention, cannabidiol (CBD) is suggested to maintain prostate health and inhibit metastasis of malignant cells in confirmed disease.

Testicular Cancer
Testicular cancer is a life-threatening malignancy which affects men across the life-span. Because of the proximity to the lymph system, testicular cancer is difficult to manage unless detected early in the disease. Categorized as an idiopathic autoimmune clinical cannabinoid deficiency (CECD), testicular cancer responds to adjunctive use of cannabidiol. CBD has been demonstrated to reduce malignant cell metastasis and is therefore recommended adjunctively in management of this disease process.

Endocannabinoid Deficiency (CECD) Classification: Reproductive Disorders

Disorder	Origin of CECD
Endometrial Cancer	Idiopathic Autoimmune
Endometriosis	Idiopathic Autoimmune
Prostate Cancer	Idiopathic Autoimmune
Testicular Cancer	Idiopathic Autoimmune

CEN Medical Cannabis Pharmacological Prescription and Coding System Reproductive Disorder Application
The CEN Medical Cannabis Pharmacological Prescription and Coding System (CEN/MCPPCS) provides language that enables the health care practitioner to communicate with the dispenser of medical cannabis. The first two letters of the system refer to the cannabis type: cannabis sativa, cannabis indica, or cannabis hybrida. The numerical value in percentage to the right of the colon refers to the recommended THC content in percentage, and the numerical value in sequence to the right of the THC percentage refers to the recommended CDB content.

(CEN/MCPPCS): Cannabis type (sativa, indica, hybrida; THC percentage or range/CBD percentage or range) or Hemp Cannabidiol (CBD)

Example: Cannabidiol (CBD oil) is recommended for the patient. The concentration of the CBD oil is 19.5% and the patient is to ingest 50 mg. of CBD oil four times each day every six hours, as adjunctive therapy in the treatment of prostate cancer, (ICD-9: 185). The prescription would therefore read:

Ralph Kerns
Date of Birth: 01-21-1959.
Diagnosis: Prostate cancer, ICD-9 code: 185
CBD: 0.00%/ 19.5%. Take 50 mg. of CBD oil by mouth four times daily, every 6 hours. Use dropper as indicated.
Kenneth Richardson, M.D.

The patient would then be able to purchase the CBD oil online or at a dispensary, offering the prescription to the pharmacist or technician.

Composition Assignments

1. Please suggest a plan of care based upon the following patient information. Discuss if CBD oil would be indicated with rationale and the type of endocannabinoid deficiency (s)(CECD) for the reproductive disease process.
    a. A 36-year-old female complains of abdominal pain with menses and has a family history of endometriosis. Patient states severe depression and anxiety bi-monthly. Patient is scheduled for laparoscopy for suspected endometriosis.
2. Please choose an article from the CEN library on an aspect of cannabidiol (CBD) and the reproductive system. Write a two-hundred-word critical analysis paper on this research article and determine the following in your paper:
    a. Author and affiliation
    b. Study population
    c. Purpose
    d. Outcome of the study
    e. Importance of the research

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Chapter X: Dental Health and Dental Disease

Learning Objectives

1. Discuss assessment protocols to determine level of endocannabinoid deficiencies of the dental system.
2. Discuss therapeutic strategies to address endocannabinoid deficiencies of the dental system.
3. Discuss patient care guidelines to implement cannabinoid therapy with standard of care pharmaceutical regimens pertaining to the dental system.
4. Discuss educational guidelines for patients to monitor clinical outcomes when implementing cannabinoid protocols for dental disorders.

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nervous system. The endocannabinoid system affects the lipocytes and fat cells, collectively known as adipocytes, hepatocytes, in the gastrointestinal tract, musculoskeletal system, and endocrine system. The endogenous arachidonate-based lipids, anandamide and 2-arachidonoylglycerol (2-AG) are physiological ligands for the cannabinoid receptors. Cannabinoid receptors CB1 and CB2, two G-protein-coupled receptors, facilitate the responses of the endocannabinoid system in the body, which are critical to maintaining homeostasis. CB1 receptors are located in the central and peripheral nervous systems as well as the lungs, kidneys, and liver. CB2 receptors are predominantly expressed in the immune system and hematopoietic cells.

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Cannabidiol (CBD), a non-psychotropic cannabinoid naturally occurring in human and animal species, occurs as a phytocannabinoid, CBD oil, which is derived from the industrial hemp plant. The restorative effects of cannabidiol (CBD oil), which increases anandamide and other lipid neurotransmitters, thereby restoring the endocannabinoid system, are of interest in the medical management of multiple disorders, including disorders of the dental system, which is directly affected by the immunological system. Indeed, research supports that plant-derived cannabidiol (CBD) has analgesic and anti-inflammatory benefits.

Cannabidiol (CBD)
Cannabidiol (CBD) is a non-psychotropic and non-toxic compound which has been demonstrated to positively affect the human endocannabinoid system. Cannabidiol (CBD), derived from the hemp plant, demonstrates anti-inflammatory and immune-modulating properties. Cannabidiol (CBD) has a low affinity for CB1 and CB2 receptors in the human body, but acts as an indirect antagonist of their agonists. (Antagonists are defined as substances that stop or inhibit the effects of another substance on the cellular surface, producing the same effect as a substance which would normally bind to the receptor. Agonists are chemicals that bind to receptors and elicit a biological response.) Therefore, cannabidiol may enhance the therapeutic effects of THC, possibly by increasing the density of the CB1 receptors. Cannabidiol (CBD) has been demonstrated to cross the blood-brain barrier and exert antioxidant, antimicrobial, and analgesic properties, rendering it valuable in the prevention and treatment of dental disorders and diseases.

Human Dental System
The human dental system includes teeth, gum, and oral cavity structures. Twenty primary and twenty-eight to thirty-two permanent teeth are included in the taxonomical naming of tooth structures. Endocannabinoid receptors, both CB1 and CB2, are disseminated throughout the gums, tongue, salivary glands, maxillary and mandibular structures and glands, and oral cavity. Clinical endocannabinoid deficiency (CECD) in dental disease increases the incidence of infections and systemic disorders, including dissemination to the brain and heart.

Cannabidiol (CBD) and Dental Disorders and Diseases: **Periodontal Disease**
Periodontal disease is generally considered an acquired Clinical Endocannabinoid Deficiency (CECD), secondary to behaviors which increase the incidence of disease: poor oral hygiene, cigarette smoking, and oral tobacco use. As adjunctive treatment with oral rinses and improved dental hygiene, cannabidiol (CBD) is recommended to alleviate the discomfort associated with the disease and also reduce the inflammatory processes. Research indicates improvement with administration of cannabidiol (CBD) and reduction in painful tissues within the oral cavity.

Submandibular Gland Inflammation
Submandibular gland inflammation is an acquired clinical endocannabinoid deficiency (CECD) associated with dehydration, poor oral hygiene, and chronic inflammatory disorders. Painful and swollen submandibular glands characterize this disorder, which responds to the analgesic and anti-inflammatory effects of cannabidiol (CBD), Consideration of adjunctive CBD oil with standard of care is warranted given research outcomes.

Endocannabinoid Deficiency (CECD) Classification: Dental Disorders

Disorder	**Origin of CECD**
Periodontal Disease	Acquired
Submandibular Gland Inflammation	Acquired, Idiopathic Autoimmune

CEN Medical Cannabis Pharmacological Prescription and Coding System
Dental Disorder Application
The CEN Medical Cannabis Pharmacological Prescription and Coding System (CEN/MCPPCS) provides language that enables the health care practitioner to communicate with the dispenser of medical cannabis. The first two letters of the system refer to the cannabis type: cannabis sativa, cannabis indica, or cannabis hybrida. The numerical value in percentage to the right of the colon refers to the recommended THC content in percentage, and the numerical value in sequence to the right of the THC percentage refers to the recommended CDB content.

(CEN/MCPPCS): Cannabis type (sativa, indica, hybrida; THC percentage or range/CBD percentage or range) or Hemp Cannabidiol (CBD)

Example: Cannabidiol (CBD oil) is recommended for the patient. The concentration of the CBD oil is 19.5% and the patient is to ingest 50 mg. of CBD oil four times each day every six hours, as adjunctive therapy in the treatment of periodontal disease, (ICD-9: 523.9). The prescription would therefore read:

Helen James
Date of Birth: 02-06-1940.
Diagnosis: Periodontal Disease, ICD-9 code: 523.9
CBD: 0.00%/ 19.5%. Take 50 mg. of CBD oil by mouth four times daily, every 6 hours. Use dropper as indicated.
Francis Grother, D.D.S.

The patient would then be able to purchase the CBD oil online or at a dispensary, offering the prescription to the pharmacist or technician.

Composition Assignments:

1. Please suggest a plan of care based upon the following patient information. Discuss if CBD oil would be indicated with rationale and the type of endocannabinoid deficiency (CECD) for the dental disease process.
    a. A 55-year-old male with a history of cigarette use presents with reddened and swollen gums, and generalized discomfort. Patient denies alcohol use and any other allergic reactions. Patient has recently undergone a tooth extraction.
2. Please choose an article from the CEN library on an aspect of cannabidiol (CBD) and the dental system. Write a two-hundred-word critical analysis paper on this research article and determine the following in your paper:
    a. Author and affiliation
    b. Study population
    c. Purpose
    d. Outcome of the study
    e. Importance of the research

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