**MARIJUANA – THE CHANGING LANDSCAPE**

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Public attitude towards marijuana and the pertaining laws in United States are undergoing historical shift. The pediatric healthcare providers should be prepared to address the anticipated consequences for the mother-fetus dyad, the neonate, and the growing child. Political climates rather than scientific evidence of benefit or harm are at the crux of state regulations for access to marijuana. Since 2005, the perceived risk of regular marijuana use has declined from 40% to 20% which is reflected in the sharp rise in the acceptance and use of marijuana products by not only adults but also adolescents. In this article we review the legal perspective and the effects of marijuana use on the pediatric population.

**LEGALIZATION:** In 1996 California became the first state to approve medical marijuana. In 2012, Colorado and Washington were the first to legalize recreational marijuana above 21 years of age. To date, 31 states and the District of Colombia have legalized medical marijuana and 8 of these states including District of Colombia have also legalized recreational use. (Fig 1) As a result, a niche market for cannabis products was created with gradual increase in the potency, including variety of oral preparations. Ingestion is associated with increased frequency of overdosing, evidenced by the

**FIG. 1 - MARIJUANA REGULATIONS BY STATE**

**MARIJUANA & TEXAS:** The Texas Compassionate Use Act (Senate Bill 339) was enacted by the Texas Legislature in 2015 (84th Legislative Session). The only medical condition covered is intractable epilepsy. Only low-THC Cannabis / CBD oil can be dispensed by registered dispensing organization (3 in state now), which came into existence recently from September to December 2017. It was this year (2018) that the 1st patient in Texas received medical marijuana. Only Texas residents can avail, after prescription from a limited 20 registered physicians under Compassionate Use Program (CUP). We have no registered physician in El Paso, the closest place is Amarillo, TX. For more updated information, providers can visit https://www.dps.texas.gov/rsd/CUP/index.htm.

**MARIJUANA & THE BODY:** The endogenous endocannabinoids: anandamide and 2-arachidonoylglycerol play a role in maintaining homeostasis through their ubiquitous receptors in the CNS, connective tissues, gonads, endocrine glands, and organs (CB1) and immune system and associated structures (CB2). The cannabinoid receptors were not discovered until 1990.

There are over 60 cannabinoids in marijuana with delta-9-tetrahydrocannabinol (THC), the primary psychoactive constituent and agonist to CB1, followed by cannabidiol (CBD), an antagonist to CB1 and CB2. The evidence of medical benefit of marijuana is very limited. Marijuana may be useful in glaucoma, nausea, AIDS-associated anorexia/wasting, chronic pain, inflammation, multiple sclerosis and epilepsy. Evidence of the adverse effects, in both short term (impaired memory, impaired coordination during driving, impaired judgement and paranoia/psychosis at high doses) and long term (addiction, cognitive impairment, diminished life satisfaction/achievement, chronic bronchitis, and exacerbation of psychosis in schizophrenia) is increasing. Recently, marijuana has been shown to permanently alter brain development in adolescent heavy users.

**MARIJUANA DURING PERINATAL PERIOD:** The mechanisms of cannabinoids effects on fetal development are multitude from pre-conception to fetal effects (Fig 2). The self-reported prevalence of marijuana use in pregnancy is from 2% to 5%. The half-life of marijuana in fat tissue is long (~8 days). In pregnant chronic users it can be detected in the blood for up to 30 days. THC crosses the placenta, which in conjunction with the slow fetal clearance, results in prolonged fetal exposure, even after consumption is discontinued. Data on the effects of other byproducts during marijuana smoking including carcinogens and the effects of passive smoking are lacking. A long-term follow-up study of neonates exposed to marijuana in utero showed multiple adverse effects including MRI evidence of altered neural activity during visuospatial working and memory processing at age 18-22 years.

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FIG. 2 - CANNABINOIDS ENDANGER FETAL/NEONATAL DEVELOPMENT THROUGH MULTIPLE MECHANISMS

Intake of Cannabis, leads to prolonged elevation of serum cannabinoid levels

Resulting in (pre- or post implantation)

Embryological/ Fetal exposure

Leads to pre- implantation

Barriers to successful implantation

END RESULT

- VEGF
- Folic acid
- PCNA
- MAPK
- Cellular migration
- CB1/CB2 activation
- BDNF pathway

Disrupting

- Angiogenesis
- Neurogenesis
- Replication
- Cellular development
- Tissue differentiation
- Cellular processes
- Cognitive development

MISCARRIAGE LOW BIRTH WEIGHT DEVELOPMENT DELAY MAPK BIRTH DEFECTS OTHER COMPLICATIONS

- Impairment of fallopian motility
- Ectopic pregnancy
- Non-hatched or non-viable embryo
- Decreased uterine receptivity
- Spontaneous Abortion


MARIJUANA & BREAST FEEDING: THC the main compound in marijuana, is present in human milk 8-times then maternal plasma levels4. Its metabolites are found in infant feces, indicating that THC is absorbed and metabolized by the infant6. Rapidly distributed and stored in the brain and adipose tissue, has long t1/2 (25–57 hours) and stays positive in the urine of neonates for 2–3 weeks (varies depending on occasional vs chronic use). Evidence of THC exposure on infant development via breastfeeding alone is sparse and conflicting. American Breastfeeding medicine, in a recent update (clinical protocol #21, 2015) states that — “although the data are not strong enough to recommend not breastfeeding with any marijuana use, we urge caution”6. As per last committee opinion by ACOG on July, 2015 - “there is insufficient data to evaluate the effects of marijuana use on infants during lactation and breastfeeding, and in the absence of such data, they discourage marijuana use”.

MARIJUANA IN PEDIATRIC POPULATION: Marijuana products have a diverse lingo for the adolescent population, like naturally derived products called Shatters, Budders, Waxes, while synthetic products popular by name of spice and K2. With the new popularity, the mode of abuse has also changed from just smoking to now more popular vaping, ingestion (candies, cookies etc.) and topical application. Although it is still illegal for any one less than 21 to use marijuana (if not medically prescribed) there are no guidelines or restrictions on advertisement of marijuana products to this population. The rise of edible marijuana products has also led to easier access of highly concentrated products, leading to more cases of marijuana toxicity. The proportion of unintentional marijuana ingestions in patients younger then 12 years of age has also increased significantly in medical marijuana states12. As per our local poison control data, marijuana seems to be a common culprit in pediatric population for calls to poison control.

MARIJUANA & THE AMERICAN ACADEMY OF PEDIATRICANS: In March, 2015 AAP published a 10-point recommendation for marijuana supporting decriminalization, but opposing legalization12. AAP supports strict enforcement of all regulations limiting access, marketing and advertising to youth in states with legalized recreational use. Further, AAP states that the development of pharmaceutical cannabinoids should be promoted along with the development of policies promoting research on the medical use. Finally, AAP recommends changing marijuana from a DEA schedule I to II to facilitate research13.

CONCLUSION: Marijuana is one of the earliest cultivated plants used over millennia in daily life. The waxing and waning use in USA has been affected by the changing economic and political climates. Its categorization in Schedule I and the war on drugs have restricted research and limited our understanding of its beneficial and harmful effects. The resultant backlash movement, which ushered the rapidly spreading legalization of both medicinal and recreational marijuana, is causing societal acceptance and increased use in populations particularly vulnerable to its harmful effects. Is marijuana going to be a public health issue like tobacco or alcohol is yet to be seen. The healthcare providers must follow the rapidly changing federal and state laws pertaining to marijuana, advocate for more research and strive to increase their knowledge to support their patients in the quest to improve health.

(References available on request)
OSTEOSARCOMA: BORDERLAND EXPERIENCE

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OSTEOSARCOMA

Osteosarcoma is the most common malignant bone tumor in children and adolescents. There is a much higher incidence in adolescence thought to be associated with accelerated growth. There are approximately 450 children in the United States diagnosed annually. The most common primary sites are the long bones, the distal femur and proximal tibia. It can develop, however, in virtually any bone.

The cause or etiology is unclear. Most cases appear to be sporadic as opposed to a genetic condition. There are, however, inherited or genetic conditions that do increase risk, notably Hereditary Retinoblastoma, Bloom Syndrome, Li Fraumeni Syndrome, Diamond Blackfan Anemia, Paget’s Disease, Werner Syndrome and Rothmund Thomson Syndrome.

Pain in the affected limb is the most frequent complaint. There may also be swelling and limitation of movement. Often times a child will have a “pathological fracture” following an otherwise minor activity while participating in a sport. A simple X-ray can usually identify a tumor. The patient, at that time, should be referred to Southwest University Pediatric Blood and Cancer Center at EPCH for further evaluation and treatment. A further staging work up includes a MRI of the affected limb, CT of the chest, Bone Scan, along with a biopsy of the lesion.

Overall prognosis is greatly influenced as to whether the disease or tumor is localized or metastatic, (disease outside of the primary site). The most common site of spread is to the lungs as disease is spread hematogenously. Approximately 15-20% of patients will present with metastatic disease at the time of diagnosis. Five year overall survival is upwards of 80-85% for localized disease as opposed to 25-30% for upfront metastatic disease.

Treatment includes upfront chemotherapy, (neoadjuvant), and surgery with subsequent adjuvant chemo-therapy. Length of treatment is close to one year. Complete surgical resection of the primary tumor with clean margins is paramount for survival. A good indication of chemotherapy sensitivity, thus prognosis, is the percent of necrosis of the tumor at the time of resection. Most patients are eligible for a limb sparing surgery, where the tumor or affected bone is removed and the limb is spared. A bone graft or type of prosthesis is used to replace that which is resected. Although the limb is spared, there can be restricted movement to various degrees in the affected limb. An amputation of the limb, although less common today, is unavoidable if the tumor has invaded the joint capsule or is affecting surrounding blood vessels or nerves. With newer and better developments of prosthetic replacements, function can be restored to allow children to engage in most activities including sports.

To date, EPCH, has cared for 23 children diagnosed with osteosarcoma, seventeen of which were adolescents, ranging in age from 13-18 years. Four patients did not survive their disease. Five patients lost a limb. Three out of the five adolescents who lost a limb were diagnosed this year and are still receiving chemotherapy. Two patients are currently receiving experimental therapy for refractory disease. Treatment of osteosarcoma is associated with both short and long term toxicities from chemotherapy, as well as, functional disability as a consequence of skeletal reconstruction after resection of the primary tumor or the loss of a limb. These patients need on going follow up care for years to come.

It is only by participation in National Clinical trials that we further cure rates for childhood cancer. We are proud to be a center of excellence and an accredited member of Children’s Oncology group, (COG).

The Children’s Oncology Group is the largest pediatric clinical trials group in the world and has treated more children with cancer than any other organization. There are over 200 hospitals that are COG members. Every trial or treatment plan is reviewed by experts who come from COG as well as other agencies such as the National Cancer Institute, and Internal Review Boards, along with Safety Monitoring Boards. New clinical trials are taking the best known treatment plan and seeing what might make it better, whether that is adding a new drug, shortening the interval of giving the drug(s) or adding a specific targeted agent. Physicians can only have access to state of the art treatment protocols by being a COG member. We are the only children’s Hospital with COG membership within a 500 mile radius.

September is recognized as Childhood Cancer Awareness month. This September we wish to thank these children and teens for their bravery and optimistic perseverance. They have been supporters and motivators to each other and, undoubtedly, an inspiration to us all.
## 2018 PEDIATRIC GRAND ROUNDS

The First & Third Wednesday of Every Month

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**Save the Date**

2nd Annual West Texas Down Syndrome Health Symposium

**Presented by:**

Gigi’s Playhouse

November 17th, 2018

7:30 a.m. - 3:30 p.m.

www.gigisplayhouse.org/elpaso

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