

CMCR hosts meeting on the future of MCR (Medical Cannabis Research)

By Dale Gieringer

"Cannabis and Health" was the stated theme of a conference held June 8 at the Center for Medicinal Cannabis Research on the UC San Diego campus. Benefit, not harm, is the new focus. \$10 million in tax revenue collected from cannabis consumers and providers will be allocated to researchers by the Bureau of Cannabis Control. The looming questions are: what research to fund, and which researchers.

The conference drew about a hundred attendees from every facet of the field.

Sherry Yafai, MD, represented the Society of Cannabis Clinicians. She was articulate, organized, on-target and passionate in defense of her practice. She only began practicing after Prop 64 on January 1, 2018, and only takes physician referrals. "I'm not a pot doc," she said.

Yafai described her patient population, which ranges from age 2 to 100 (!), and their various indications — mainly pain, cancer, and narcotics reduction. Most had tried marijuana in their youth and most don't want inhaled medicine.

Yafai emphasized how patients decrease use of other medications, including opiates, other controlled substances, and blood pressure drugs. She works with a "High Sobriety" group that uses non-smokable cannabis to treat drug addiction. Her patients — long-term addicts — are given maintenance doses of CBD-rich oils to get off drugs. She said she had successfully treated four long-term opiate addicts, helping them get entirely "clean" in 10 days using nothing more than cannabis oil.

Yafai noted that high-potency products are used in cancer treatment and formulations for epilepsy and drug abuse.

A French addiction specialist in the audience questioned her claim. Yafai said she would soon have data to present. (Earlier in the session she had taken the mike to respond to a presenter who questioned the medical need for high-potency products, noting that high doses were used in cancer treatment and formulations for epilepsy and drug abuse.)

The conference began with a lucid presentation by Dr. Piomelli about the history of medical cannabis, the cannabinoid receptor system, endocannabinoids, and the National Academy of Sciences, Engineering & Medicine (NASEM) report.

Piomelli said he wanted to work on specific chemical agonists, antagonists, and FAAH inhibitors. "I don't think cannabis is really a good drug," he said. "I think we can have better drugs." He remains concerned about prenatal exposure to cannabis, not because of the lower birth weight, which can be explained by smoking, but by possible effects on fetal stem cells, which haven't been investigated. (Overall though he is pro-cannabis and anti-prohibition.)

Ziva Cooper from Columbia University presented her research on pain treatment with cannabis and opioids. Subjects given sub-clinical doses of oxycodone and cannabis to treat cold-pressor-induced pain showed no response; but when the two drugs were combined, they were effective. Conclusion: cannabis increases analgesic but not intoxicating effects of opioids.

Marcel Bonn-Miller of University of Pennsylvania and Tilray discussed the lack of studies regarding cannabis and PTSD. Surveys of patients at SPARC et al show widespread use of cannabis amongst PTSD patients. They prefer high THC to CBD. Early results of an ongoing study of cannabis use by Bonn-Miller: only minor reductions in PTSD symptoms, but a high association with problematic use.

Doris Trauner of UCSF has received a grant from Insys and the Noorda Foundation to study cannabis in autism. She cited an Israeli study finding that 61% of parents reported behavioral improvements in autistic kids using CBD-rich cannabis.

Iain McGregor of University of Sydney, GW and Tilray, has received \$33 million from the Lambert family to study cannabis in Gervais syndrome. Australian GPs are more accepting of cannabis than specialists, he said. Quality control of CBD products a big problem. The placebo effect is strong. In a survey of epileptic children treated with cannabis, many samples deemed "effective" turned out to contain no CBD or CBDA. Surprisingly, driving performance tests found that patients given a mixture of 50-50 CBD/THC were no less impaired than those given pure THC.

Staci Gruber of McLean Hospital noted that studies on cannabis and cognition have focused mainly on young recreational users, not the older medical population. Those exposed to cannabis before age 16 tend to score significantly poorer on cognitive tests, but not those exposed later.

Rodent studies suggest that cannabis can help reverse age-related cognitive decline. Her studies of older medical users found reductions in opioid and drug use, reduction in depression, improvements in sleep, improvement in executive function, but the usual memory impairment.

Tom Marcotte of UCSF gave a good presentation on cannabis and driving ability. Some signs of impairment observed in driving studies, but may be offset by subjects' awareness of their condition. No apparent increase in accidents in Colorado post-legalization; more drivers are being screened for drugs than before. THC less impairing than anti-depressants, hypnotics, alcohol. Need to look at effects of oral dosing.

Alan Budney of Dartmouth apologized for being the one addiction specialist at the forum. His presentation was disorganized, informal and lacking in data. His bogeyman: the "popular myth that cannabis is good for everything."

Yafai was part of the "Real World Cannabis Use" panel. Ryan Vandrey of John Hopkins and Insys spoke on "What's in real-world cannabis?" He was the first speaker to bring up terpenes and flavonoids, which remain totally unstudied. He complained about the general lack of standardization in current products, poor testing quality control, inadequate labeling, questionable contaminants, etc.

Mahmoud ElSohly spoke about his drug development at the University of Mississippi. He showed pictures of the Ol' Miss farm, which features both indoor and outdoor gardens. El Sohly's surveys show a substantial increase over the last 10 years in THC/CBD ratio of cannabis grown in the US — despite the popularization of CBD. This could be because El Sohly tests samples confiscated by law enforcement, not legal products from medical states.

He is working on suppositories. He said that THC by itself is useless in suppositories and tampons, it needs to be in modified form of THC-hemisuccinate in order to penetrate. He is also working on glaucoma formulations with longer activity than inhaled/ingested THC, which wear off too quickly. He has a promising formulation that is active for four hours and is seeking to extend it to eight hours.

El Sohly is also doing research on CBD and opioids. He has found that CBD combined with a sub-active dose of oxycodone produces analgesic effects. I asked him about the many cannabis topicals, creams,

lotions, etc., on the market. He wasn't sure about CBD, but THC can't penetrate the skin, he said. Topicals and suppositories claiming to provide THC are "fakes."

(A representative from Mary's Medicinals told me they sell epidermal patches that use a patented carrier to help THC penetrate the skin.)

Tilray has applied to FDA to do clinical trials.

Three manufacturing companies were invited to discuss their activities. Tiffany Devitt of Cannacraft, Lynn Honderd of Mary's Medicinals, which specializes in transdermal patches, and Catherine Jacobson of Tilray, which is working on childhood epilepsy and has applied to FDA to do clinical trials. Jacobson previously worked with GW on Epidiolex, which should be approved by FDA in the next month or so. After that the DEA must still grant it a special schedule.

The last session featured government officials speaking on regulations and barriers to research. Dominic Chiapperino of the FDA Controlled Substances Office described the agency's role in cannabis regulation. The FDA oversees the "8-factor analysis" that is required for rescheduling. Chiapperino pointed to the need for larger clinical trials, alternatives to smoked marijuana (e.g., vaporizing), and evaluation of longer-term chronic use. He mentioned that his agency sent 20 warning letters to CBD manufacturers who had nationally marketed products and were making egregious health claims.

Lori Ajax of California's Bureau of Cannabis Control outlined her agency's ongoing efforts to implement state regulations. The emergency regulations have been extended to Dec 31, but can't be extended again; they will shortly be issuing their permanent regulations for comment. Addressing the many concerns expressed at the forum about the quality of existing products, Ajax said that state-regulated products are thoroughly tested and labeled so as to meet requisite standards for product control. There is still a shortage of licensed labs: just 31 out of a statewide goal of 100.

Despite promise to add sources:

Ol' Miss still lone supplier of cannabis for research

In August 2016 — towards the end of the Obama era — the Drug Enforcement Administration said it would license more cultivators of cannabis for research purposes. Two years later, after accepting 26 applications from would-be suppliers, DEA has licensed none and has stopped taking applications. Mahmoud ElSohly, PhD, at the University of Mississippi, retains his monopoly status.

Supervising the stall is the Dixie Pixie, US Attorney General Jeff Sessions. "It'd be healthy to have some more competition in the supply, but I'm sure we don't need 26 new suppliers," he twinkled.

Lyle Craker, a professor at the University of Massachusetts at Amherst, has been applying for a DEA license to cultivate cannabis for research since 1999! Craker is among the 26 who haven't heard back as we go to press in September 2018.



MAHMOUD ELSOHLY (RIGHT) SHOWS SANJAY GUPTA the walk-in safe where cannabis grown on the Ol' Miss campus under contract with NIDA is stored. GRAPHIC FROM CNN.