A Discovery By Inference

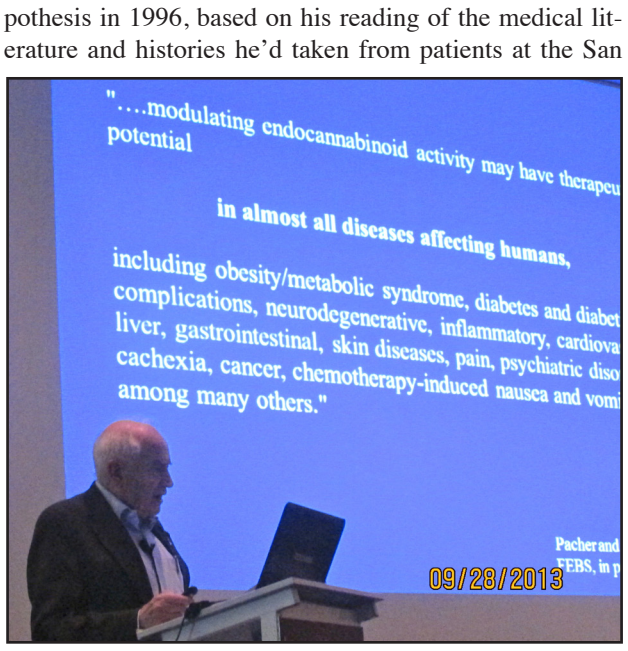
By Fred Gardner

While studies reported in journals help keep scientists and doctors abreast of recent developments, conferences offer a preview of ongoing research and a chance to question and network with the investigators. Scientists who attend meetings of researchers in other fields remark the unusually non-competitive, collegial openness at get-togethers of cannabinoid researchers.

The International Association for Cannabinoid Medicines grew out of a group founded in 1997 by a German physician, Franjo Grotenhermen, the "Association for Cannabis as Medicine." (Similarly, the C-word in the International Cannabinoid Research Society's name has been changed from "Cannabis.")

At the September 2013 IACM meeting in Cologne, Raphael Mechoulam recounted a hypothesis published by Pal Pacher and George Kunos in *FEBS (The Journal of the Federation of European Biochemical Societies)*: "modulating endocannabinoid activity may have therapeutic potential in almost all diseases affecting humans."

Tod Mikuriya, MD, had posited essentially the same hypothesis in 1996, based on his reading of the medical literature and histories he'd taken from patients at the San Francisco Cannabis Buyers Club.

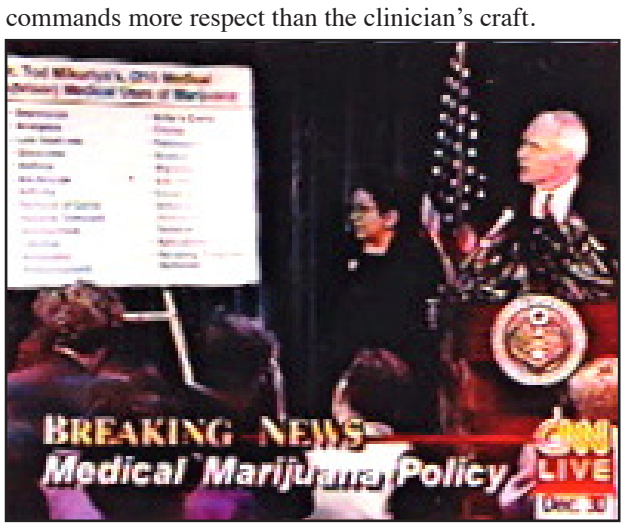


Professor Raphael Mechoulam, at the 2013 meeting of the IACM, admiringly quoted a statement by Pacher and Kunos, "modulating endocannabinoid activity may have therapeutic potential in almost all diseases affecting humans." A slide provided a partial list of conditions involving the endocannabinoid system.

Mikuriya, who died in 2007, was a psychiatrist with a practice in the East Bay, and a scholar who had compiled an anthology of the pre-prohibition medical literature devoted to cannabis. It was he, with the support of organizer Dennis Peron, who insisted that California's medical marijuana initiative legalize its use in treating not just a short list of grave illnesses, but also "any other condition for which marijuana provides relief.

Mikuriya's finding that cannabis alleviates a very wide range of symptoms —and his inference that compounds in the plant act on many physiological systems— were met with contempt by federal officials. At a press conference in December 1996, Drug Czar Barry McCaffrey scoffed that Mikuriya practiced "Cheech and Chong medicine," and Attorney General Janet Reno threatened to revoke the licenses of physicians who approved marijuana use by patients.

Hearing Mechoulam refer matter-of-factly in 2013 to "endocannabinoid involvement in a myriad of bodily processes," I couldn't help thinking that Tod (co-founder of *O'Shaughnessy's*) had reached the same conclusion from a different direction. An insightful doctor can discern things about a drug's mechanism of action. Pharmacology is not the only route to the truth, although as "hard science," it commands more respect than the clinician's craft.



Drug Czar Barry McCaffrey, at a press conference in December 1996, ridiculed Dr. Tod Mikuriya's finding that marijuana provides relief for a very wide range of conditions. A partial list of treatable conditions, culled from a website and attributed to Mikuriya, was blown up for display on an easel.

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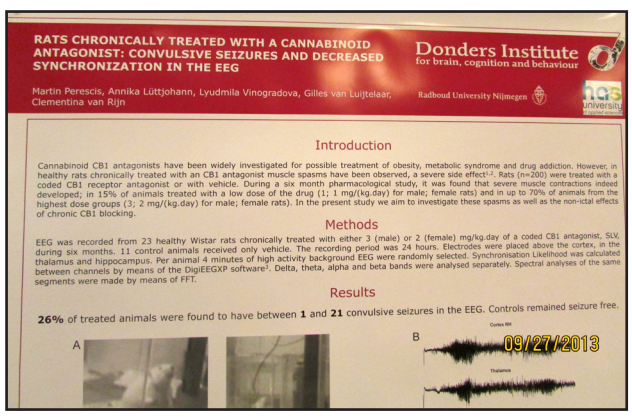
Another IACM presentation that Tod anticipated, in a sense, linked Rimonabant to epileptic seizures. Rimonabant is a cannabinoid-antagonist drug that Sanofi-Aventis marketed for treating metabolic syndrome. It was approved by European regulatory authorities in 2006 but had to be withdrawn when it led to a spate of suicides.

Tod had written a letter to the U.S. Food and Drug Administration urging that Rimonabant be rejected because any drug blocking the CB1 receptor would very likely cause a wide range of adverse effects —not just mood-related ones. This is an important point because drug manufacturers still dream of marketing synthetic cannabinoid antagonist drugs, and some would have us believe that suicidality was the one and only problem with Rimonabant.

An IACM poster by Dutch researcher Martin Perescis described a study in which he and his team treated 200 rats with either an antagonist drug or placebo for six months. "Severe muscle contractions developed in 15% of animals treated with a low dose of the drug... and in up to 70% of animals from the highest dose groups." Video recordings showed that over the course of 24 hours, "26% of animals treated with this CB1 antagonist were found to have between 1 and 21 convulsive seizures in the EEG, whereas controls remain seizure free."



Cannabinoid antagonist drugs can induce seizures in rats, according to an IACM poster by Martin Perescis and colleagues in the Netherlands. Their findings put the lie to the oft-repeated assertion that the only adverse effect of the antagonist drug Rimonabant was suicidal ideation.