NUTRITION, CANNABIS AND CANCER

Case Presentations: Administering low-dose cannabis oil for the treatment of prostate cancer and brain cancer patients

Debra Kimless, M.D.
Medical Director, ForwardGro

The Verdes Foundation
New Mexico
2018

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ForwardGro

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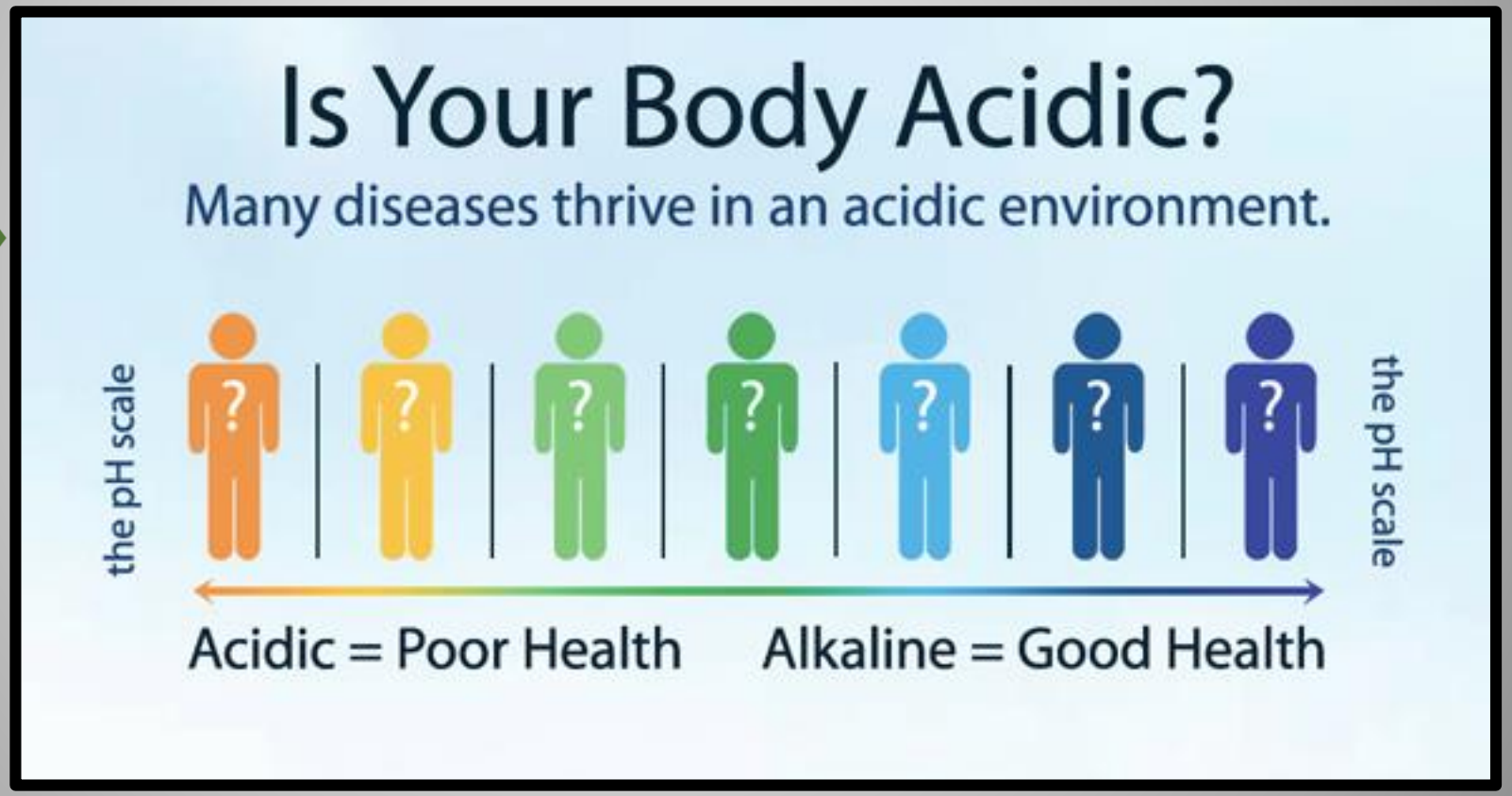
NUTRITION & pH



Morning urine pH

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April 2001 Journal of Leukocyte Biology
The effects of extracellular pH on immune function

- Evidence of impaired lymphocyte cytotoxicity and proliferation at acidic pH
- Acidic pH predominates at inflammatory loci
- Clinical acidosis are accompanied similarly by immunodeficiency

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VEGAN BLOOD KILLS CANCER??????

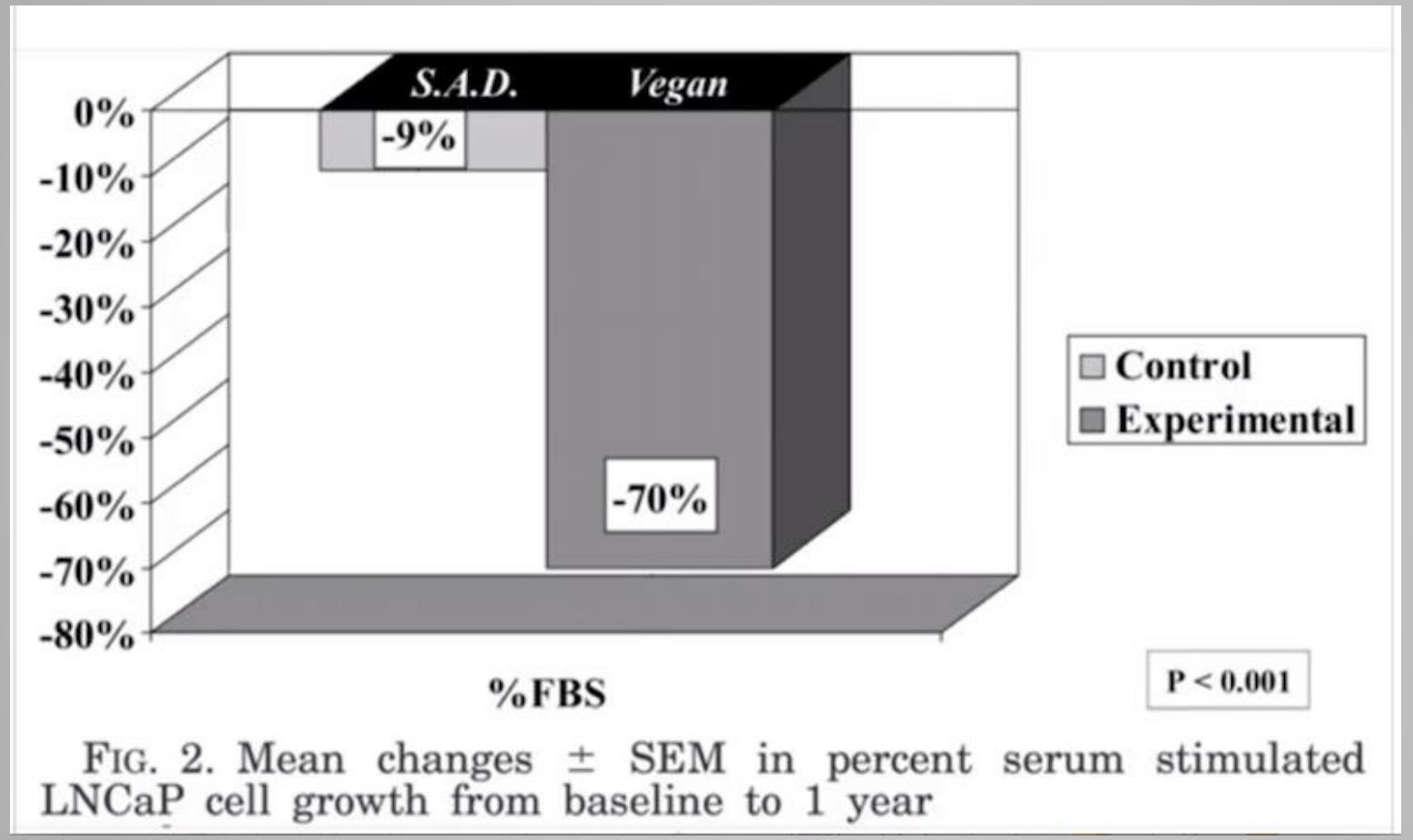

FIG. 2. Mean changes ± SEM in percent serum stimulated LNCaP cell growth from baseline to 1 year

Androgen Dependent Prostate Cancer Cells

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VEGAN BLOOD SLOWS GROWTH OF BREAST CANCER CELLS!!!!!

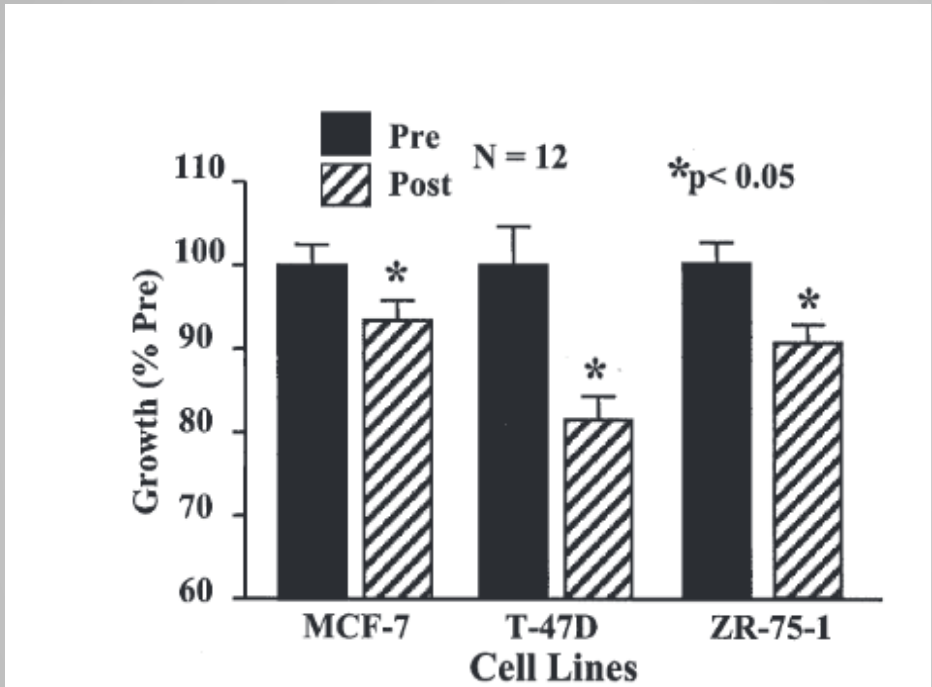

Figure 1. Effects of diet and exercise intervention on growth of breast cancer (BCa) cell lines. BCa cells were plated overnight in 10% fetal bovine serum, and the following day the media was removed and replaced with fresh media and 10% human serum pre- and postintervention. The cells were allowed to grow for 2 days, and growth was determined by the CellTiter Proliferation Assay (Promega, Madison, WI).

TWO WEEKS!!!

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VEGAN BLOOD KILLS BREAST CANCER!!!!

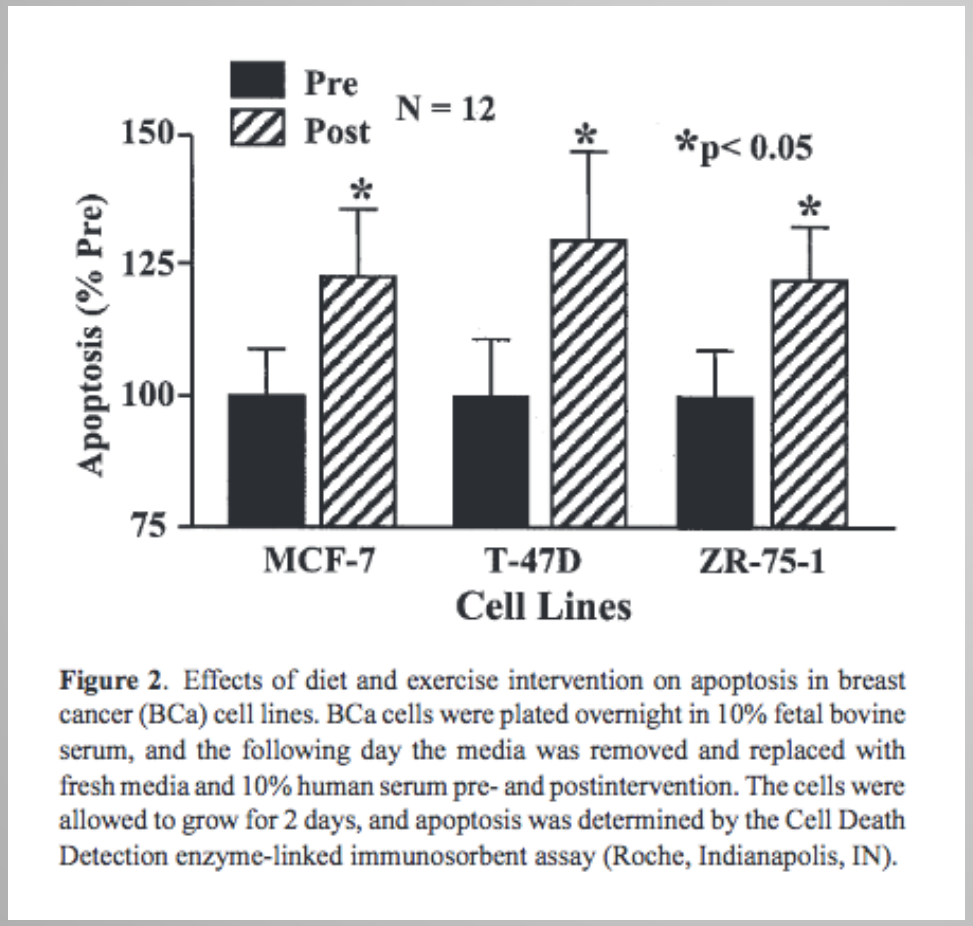

Figure 2. Effects of diet and exercise intervention on apoptosis in breast cancer (BCa) cell lines. BCa cells were plated overnight in 10% fetal bovine serum, and the following day the media was removed and replaced with fresh media and 10% human serum pre- and postintervention. The cells were allowed to grow for 2 days, and apoptosis was determined by the Cell Death Detection enzyme-linked immunosorbent assay (Roche, Indianapolis, IN).

TWO WEEKS!

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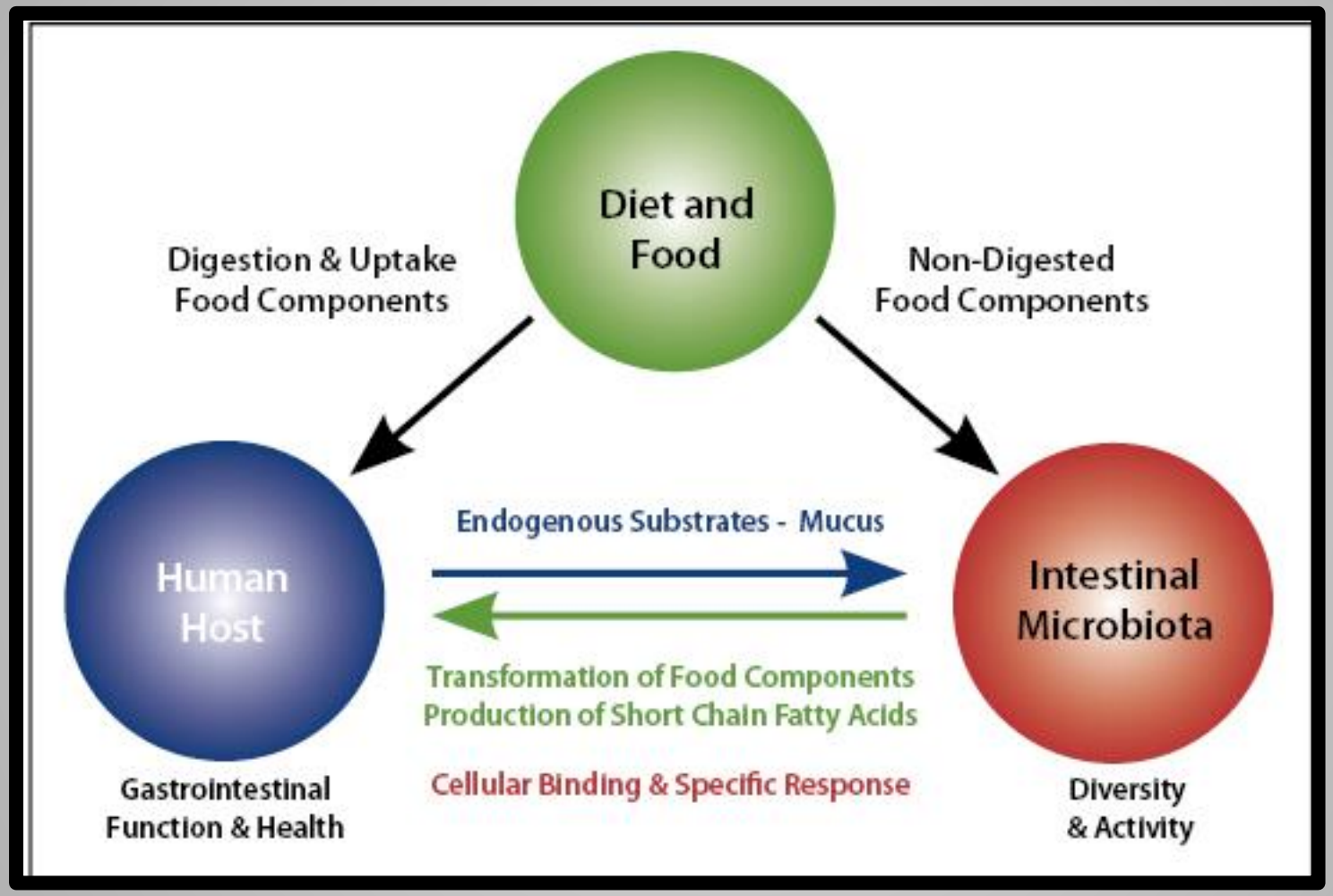

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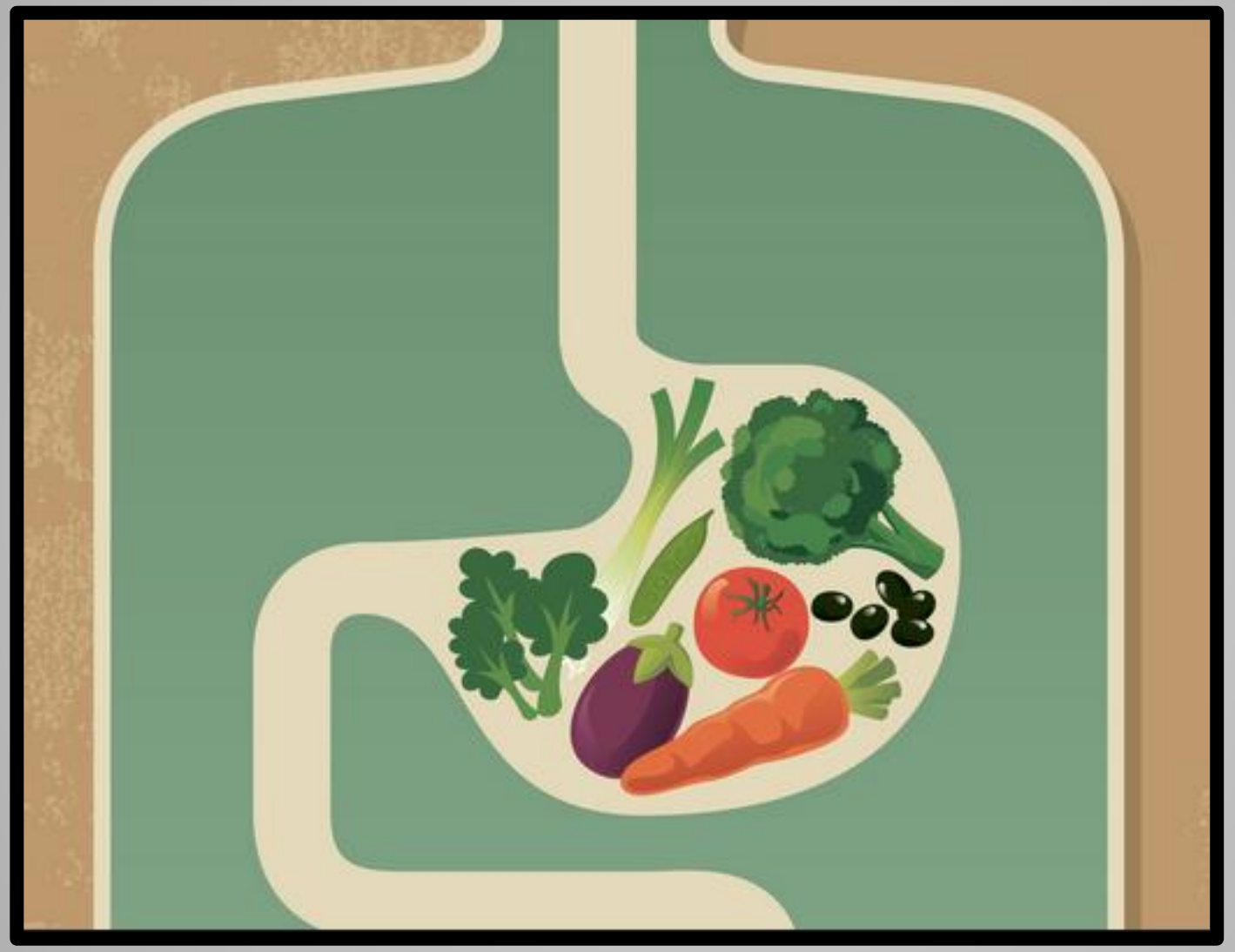

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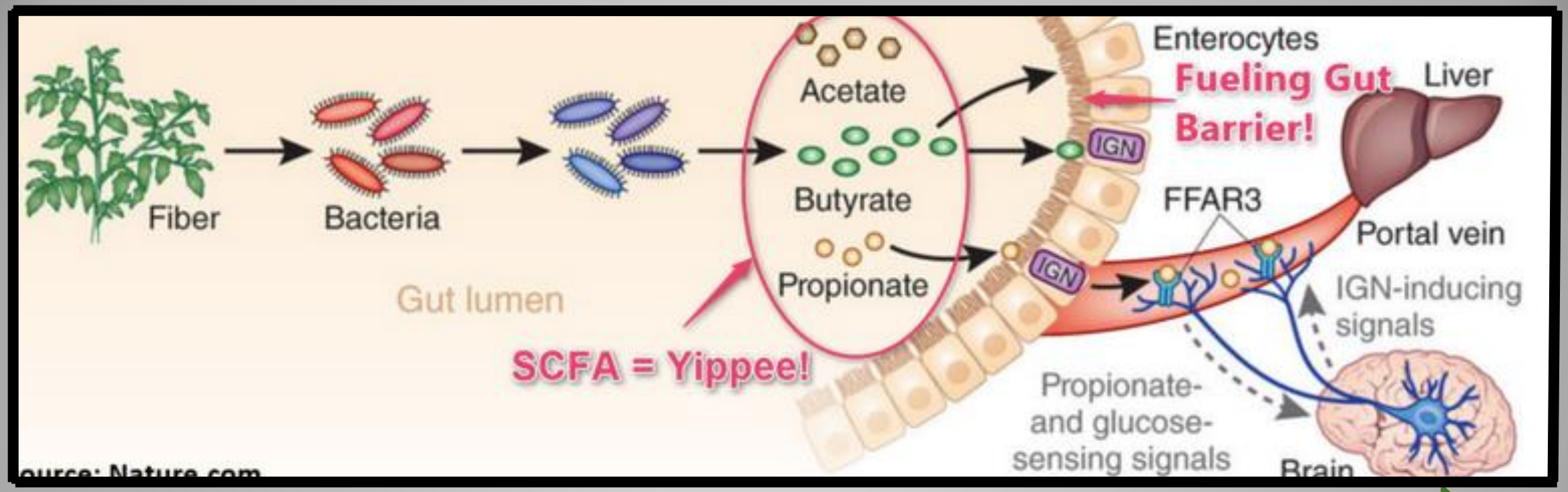

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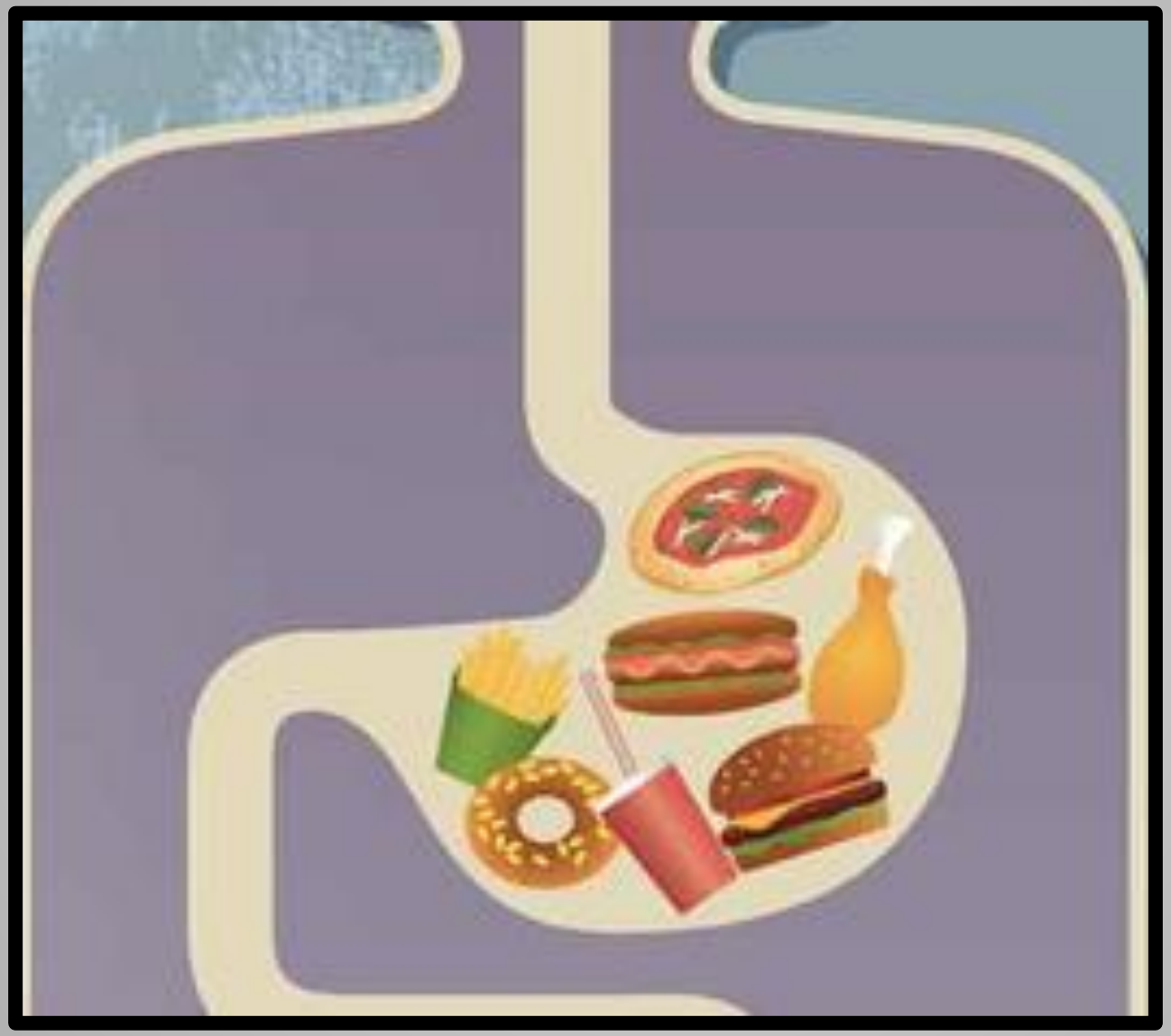

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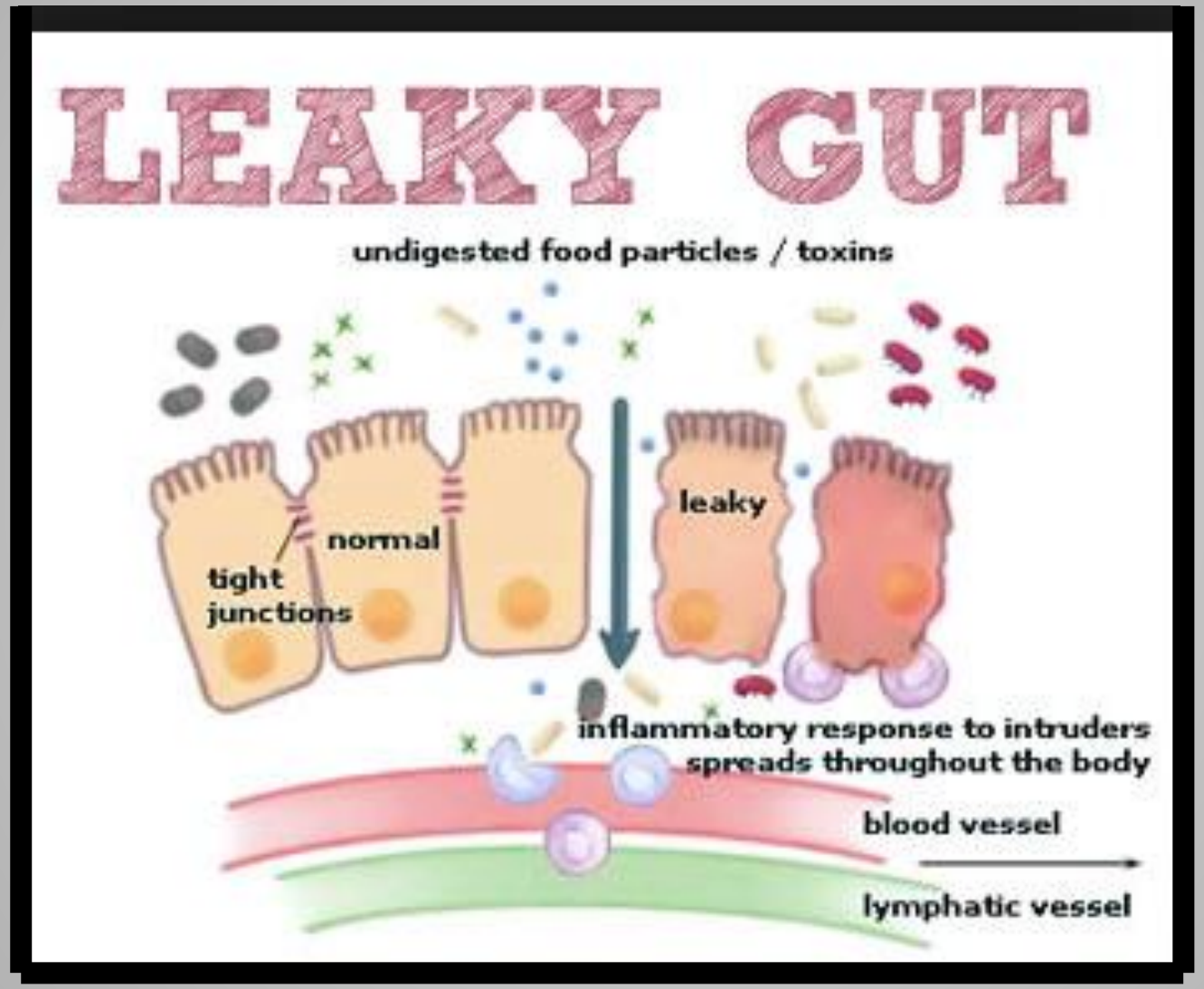

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Medical News & Perspectives

Starch-Based "Super Food" May Protect Against Variety of Diseases

Rita Rubin, MA

High-amylose maize starch is used to increase the fiber content in foods such as nutrition bars and improve the texture of gluten-free crackers and cookies, among other products.

And now, mouse studies suggest that modifying this starch by chemically linking acetate or butyrate to it might protect against autoimmune diseases such as type 1 diabetes and inflammatory bowel disease.

"I see this as the beginning of an era of the use of medicinal foods to treat human disease," said Charles Mackay, PhD, senior author of a recently published study in *Nature Immunology* that found that the acetylate- and butyrate-enhanced starch benefited the immune system in the gut, protecting against type 1 diabetes in a strain of mice bred to develop the disease.

Mackay, a professor of immunology at Monash University in Melbourne, Australia, fed nonobese diabetic (NOD) mice modified high-amylose maize starch. The modified starch, when fermented by gut bacteria in the animals' colons, produced higher levels of the short-chain fatty acids (SCFAs) acetate and butyrate than the nonmodified starch.

None of the mice fed a combination diet yielding high levels of both acetate and butyrate developed diabetes. The starches improved the integrity of the lining of the colon, reduced proinflammatory factors, and promoted immune tolerance. Type 1 diabetes in humans, like diabetes in the NOD mice, develops when T cells, a type of immune cells, mistake beta cells—the insulin-producing cells in the pancreas—as foreign invaders and attack and destroy them.

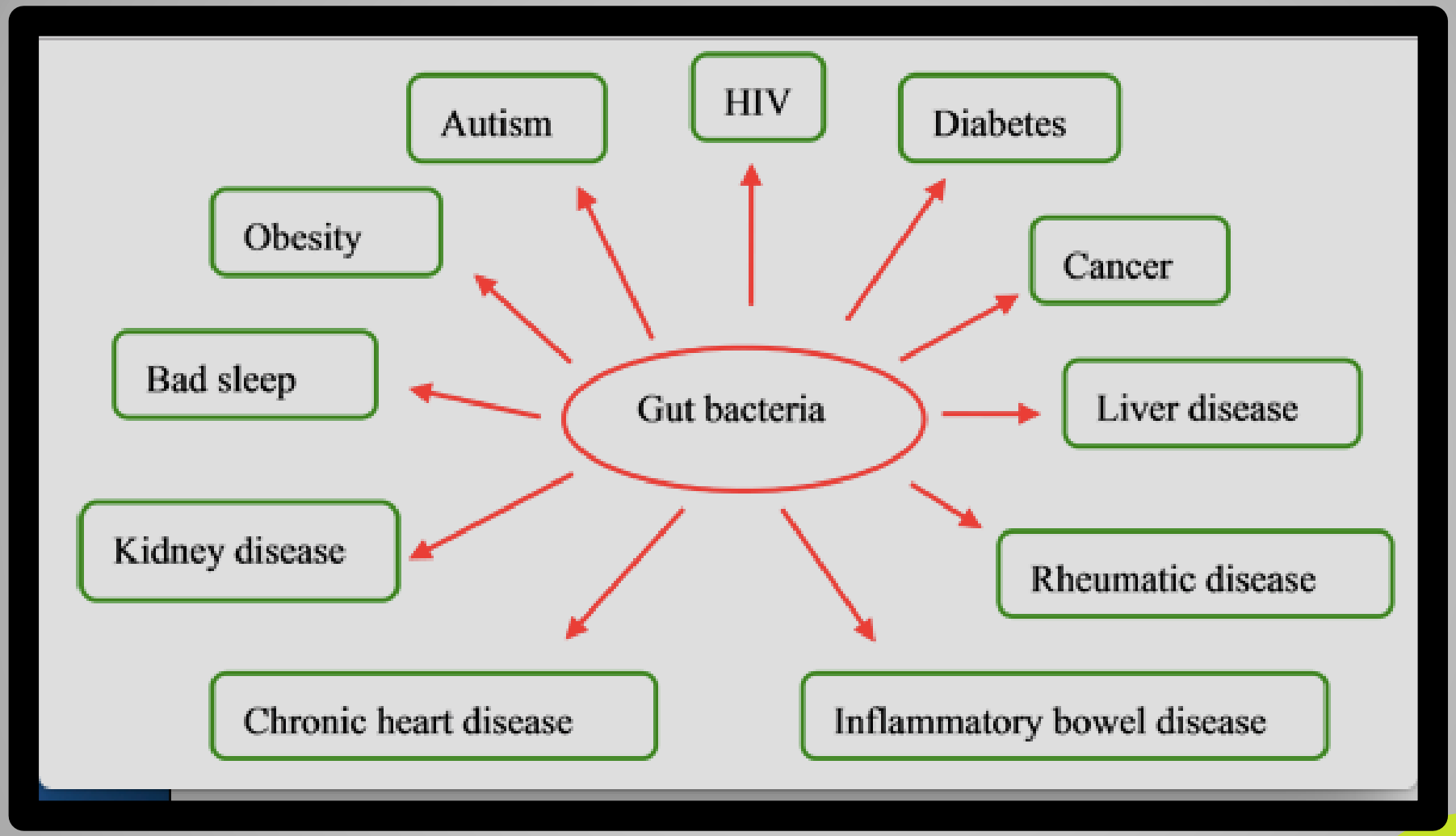
The findings suggest acetate and butyrate have different mechanisms of action. Acetate reduced the number of autoreactive T cells, key players in a variety of autoimmune diseases. Butyrate is the preferred energy source for the cells that line the colon, said Mackay's coauthor Julie Clarke, PhD, team leader for "Nutraceuticals for Gut Health" at the Commonwealth Scientific and Industrial Research Organisation (CSIRO) Health and Biosecurity in Adelaide, Australia. CSIRO is Australia's national science agency.

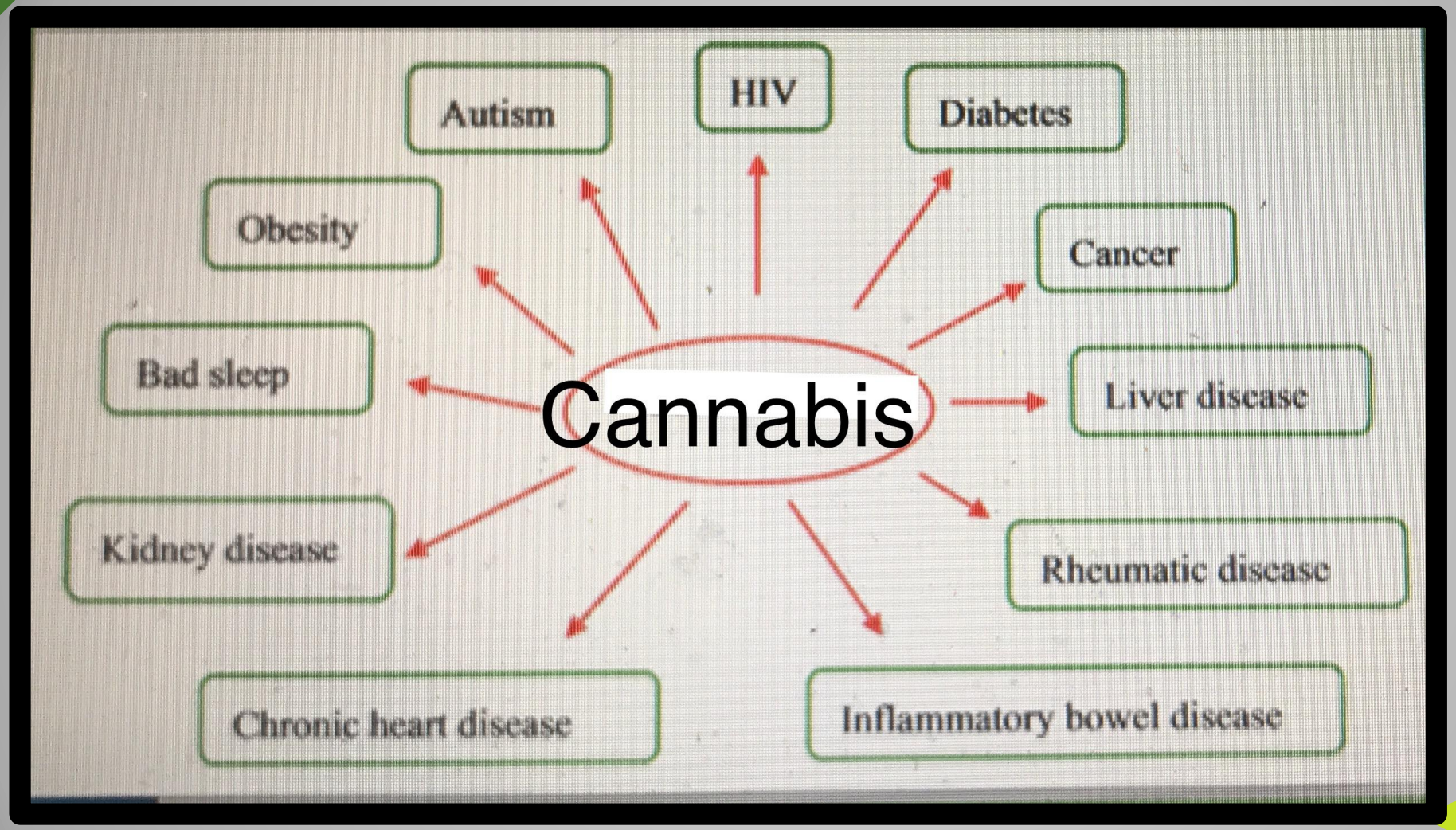
"Shaping of the gut microbiota to one with substantial production of SCFAs might be a strategy for preventing or treating many human diseases," Mackay, Clarke, and their coauthors concluded.

Will Humans Benefit?

If he can get funding, Mackay said, he would like to begin clinical trials within a year to test whether acetylated and butyrylated starch helps prevent development of type 1 diabetes in those at risk, namely relatives of people with the disease who have not been diagnosed with diabetes themselves but have an above-average risk of developing it. Those most at risk can be identified by screening for antibodies to the insulin-producing beta cells before symptoms appear.

But just because the acetate- and butyrate-enriched starch prevented diabetes in the NOD mice doesn't necessarily mean it will work in humans, noted Julia Greenstein, PhD, vice president of


Autism
HIV
Diabetes
Obesity
Cancer
Bad sleep
Gut bacteria
Liver disease
Kidney disease
Rheumatic disease
Chronic heart disease
Inflammatory bowel disease


Autism
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Liver disease
Kidney disease
Rheumatic disease
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Inflammatory bowel disease

What Constitutes a Low Dose or "MicroDose?

- 1 joint =1gram=1000mg
- 20% THC=200mg
- 30%-40%=60mg-80mg

- Micro-Dose ≤ 1mg-2mg
- Endocannabinoids-made on demand, used locally, broken down quickly, and not stored

LIGRESTI ET AL 2006

Effect of cannabinoids and *Cannabis* extracts on cancer cell growth

Various epithelial cell lines of various tumoral origin were treated with different concentrations of drugs, and after 4 days, the cell number was measured with Crystal Violet Vital staining (see *Materials and Methods*). Data are reported as mean ± S.E. of IC_{50} values (micromolar) calculated from three independent experiments. CBG, cannabigerol; CBC, cannabichromene; CBD-A, cannabidiol-acid; THC-A, THC-acid; CBD-rich, cannabidiol-enriched cannabis extract; THC-rich, THC-enriched cannabis extract.

	MCF-7	C_6	DU-145	KiMol	CaCo-2	MDA-MB-231	RBL-2H3	AGS
Δ^9-THC	14.2 ± 2.1	23.0 ± 4.2	>25	23.2 ± 1.5	16.5 ± 0.2	24.3 ± 4.2	15.8 ± 3.7	19.3 ± 1.5
THC-A	9.8 ± 0.4	18.0 ± 5.3	>25	21.0 ± 2.7	21.5 ± 1.4	18.2 ± 5.3	10.0 ± 3.4	>25
CBD	8.2 ± 0.3	8.5 ± 0.8	20.2 ± 1.8	6.0 ± 3.0	7.5 ± 0.5	10.6 ± 1.8	6.3 ± 1.5	7.5 ± 1.3
CBD-A	21.7 ± 3.2	18.0 ± 4.2	>25	12.7 ± 3.0	>25	>25	>25	>25
CBG	9.8 ± 3.4	13.0 ± 2.1	21.3 ± 1.7	8.2 ± 0.7	9.0 ± 1.4	16.2 ± 2.1	9.0 ± 0.7	8.2 ± 0.7
CBC	14.2 ± 1.4	13.0 ± 2.6	>25	7.3 ± 3.0	12.0 ± 2.4	20.4 ± 2.6	15.8 ± 4.2	18.3 ± 3.0
THC-rich	21.0 ± 0.5	18.5 ± 3.3	>25	23.0 ± 2.0	16.0 ± 0.5	25.2 ± 3.3	14.6 ± 3.1	22.0 ± 2.0
CBD-rich	6.0 ± 1.0	4.7 ± 0.6	20 ± 4.6	6.2 ± 2.9	12.3 ± 1.2	14.1 ± 1.6	7.0 ± 0.6	10.0 ± 1.9

TREATMENT

THCA 0.54mg

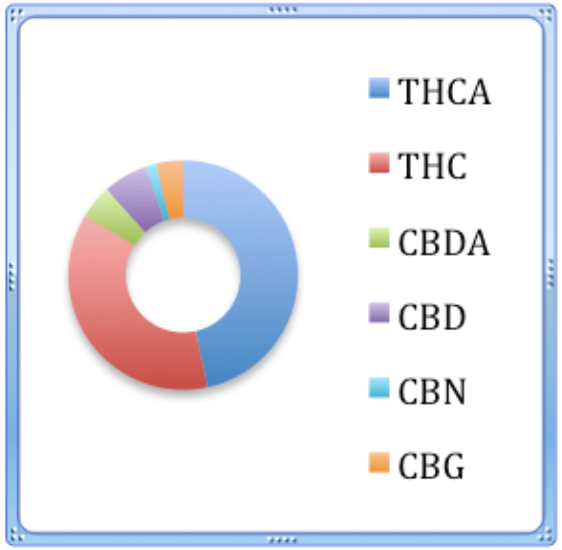
THC 0.43mg

CBDA 0.055mg

CBD 0.072mg

CBG 0.044mg

CBN 0.018mg



PROSTATE CANCER: Two Patients

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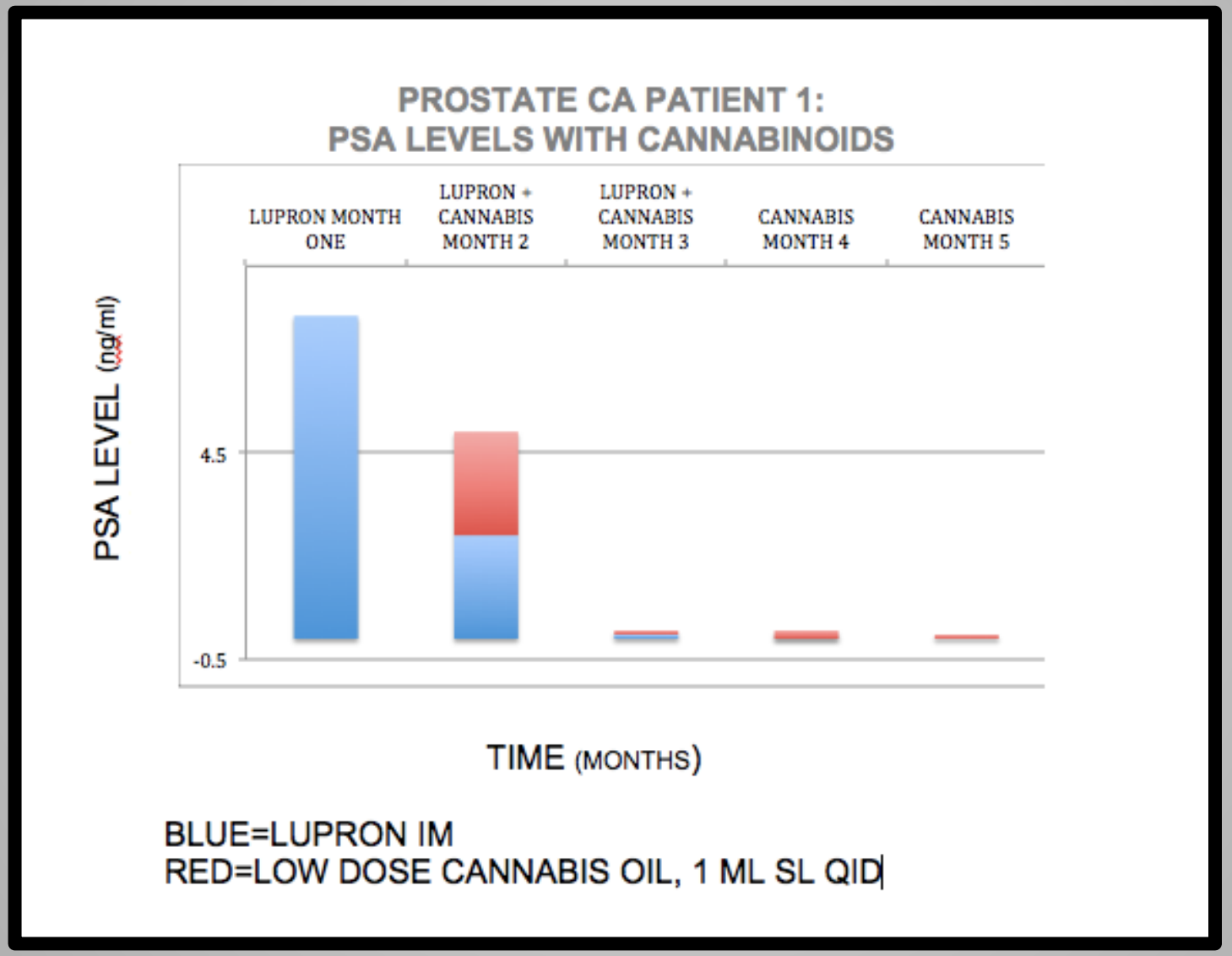
HISTORY

- 72 yar-old male with the recurrent prostate cancer.
- 2011 Diagnosed
- Gleason score 8, Clinical state T2b, and PSA 7.2.
- Treatment: hormone deprivation, seed implant and 25 sessions of IMRT.
- Result: PSA level dropped to 0.3 and remained stable from 7/2011-11/2015. 11/2015 -PSA level began to rise to 1.0
- 8/2016 PSA level 7.8, Biopsy revealed recurrent cancer of the prostate, CT scan and bone scans negative for metastasis

TREATMENT

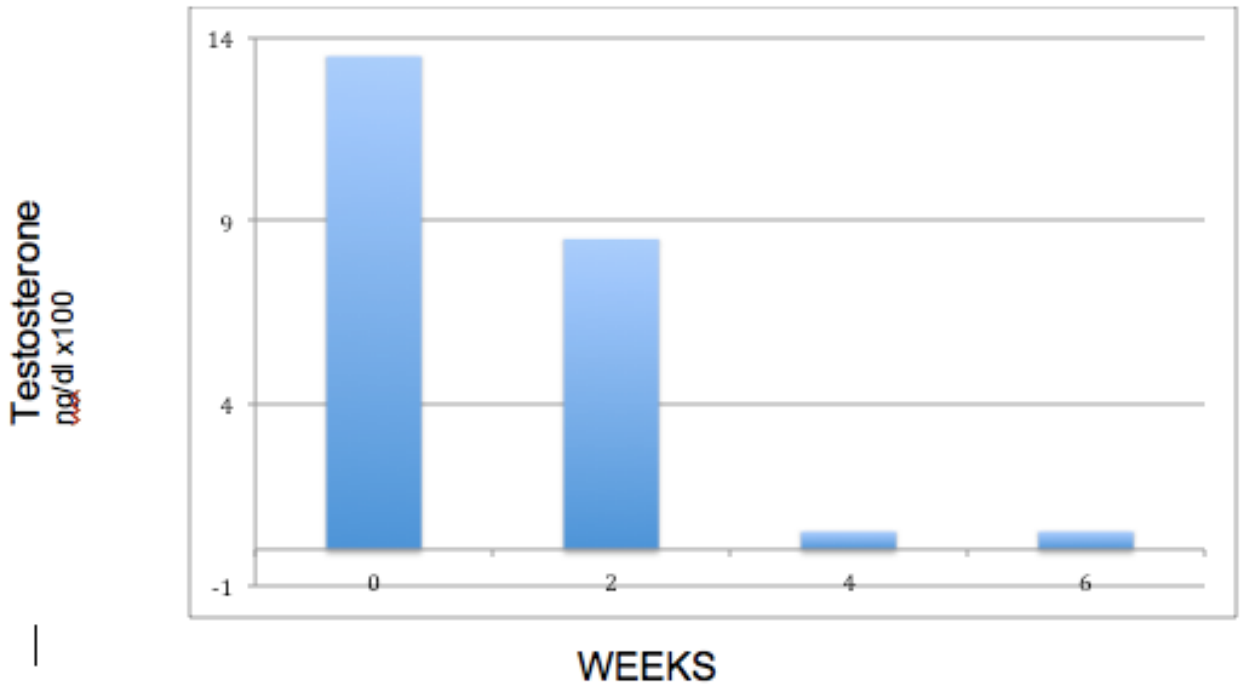
- BEGAN FIRST OF THREE LEUPROLIDE INJECTIONS
- PSA 7.8
- STARTED LOW DOSE CANNABIS OIL
- CHANGED DIET
- CONTINUED SECOND AND THIRD LEUPROLIDE INJECTION


PROSTATE CA PATIENT 1:
PSA LEVELS WITH CANNABINOIDS
LUPRON MONTH ONE
LUPRON + CANNABIS MONTH 2
LUPRON + CANNABIS MONTH 3
CANNABIS MONTH 4
CANNABIS MONTH 5
PSA LEVEL (ng/ml)
4.5
-0.5
TIME (MONTHS)
BLUE=LUPRON IM
RED=LOW DOSE CANNABIS OIL, 1 ML SL QID

HISTORY

- 81year-old otherwise healthy man with one year history of metastatic prostate cancer.
- Treatment with seed implants, radiation therapy and leuprolide injections.
- Escalating testosterone levels
- Surgery to remove the testicles (orchiectomy)

PROSTATE CA PATIENT 2:
TESTOSTERONE LEVELS WITH CANNABINOIDS



Blue= Low Dose Cannabis Oil 1ml SL 5 times a day

- Pacher, P. "Towards the Use of Non-Psychoactive Cannabinoids for Prostate Cancer". Brit. J. Pharmacology, 2013. 168(1):76-78.

Diaz-Laviada, et al. "The Endocannabinoid System in Prostate Cancer". Nat. Rev. Urol. 2011. 8:553-561.

Sreenvalsan, S. "Induction of Apoptosis by Cannabinoids in Prostate and Colon Cancer Cells is Phosphate Dependent". Anticancer Research, 2011 31(11) pp. 3799-3807.

BRAIN CANCER: Three Patients

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HISTORY:

- Otherwise healthy 69 year old
- Presents to ER post-ictal
- MRI reveals a tumor
- Biopsy diagnosed glioblastoma

CHIEF COMPLAINT:

- Lethargy
- Inability to perform ADL's without assistance
- Cognitive changes

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MEDICATIONS:

Carbamazepine (Tegretol®)

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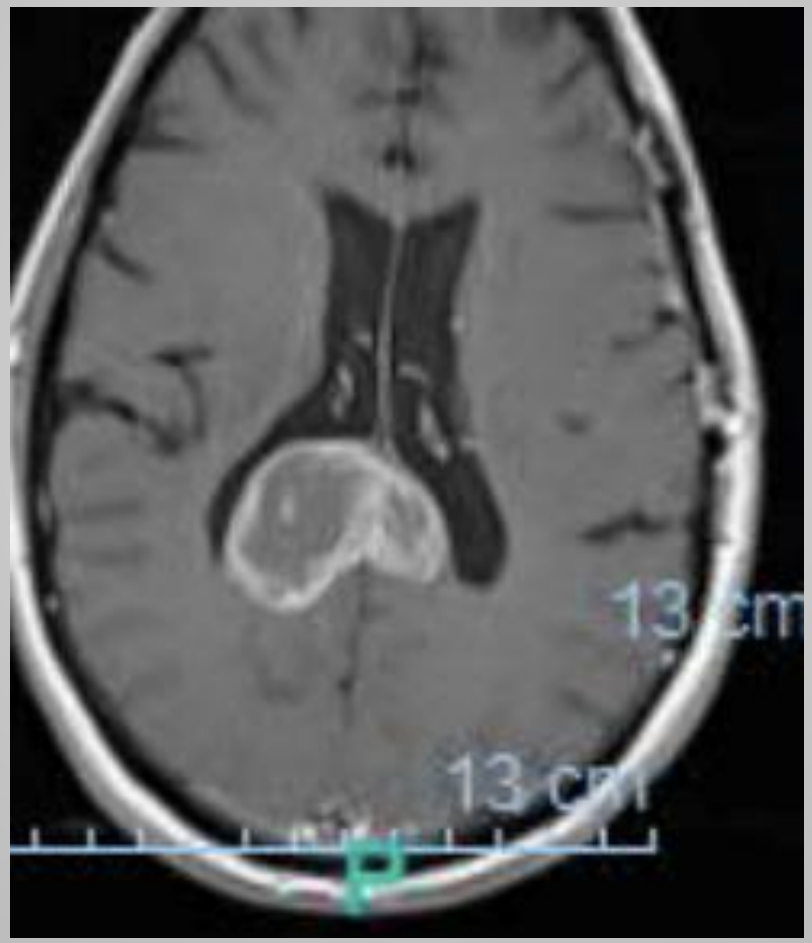
MRI PRE-TREATMENT



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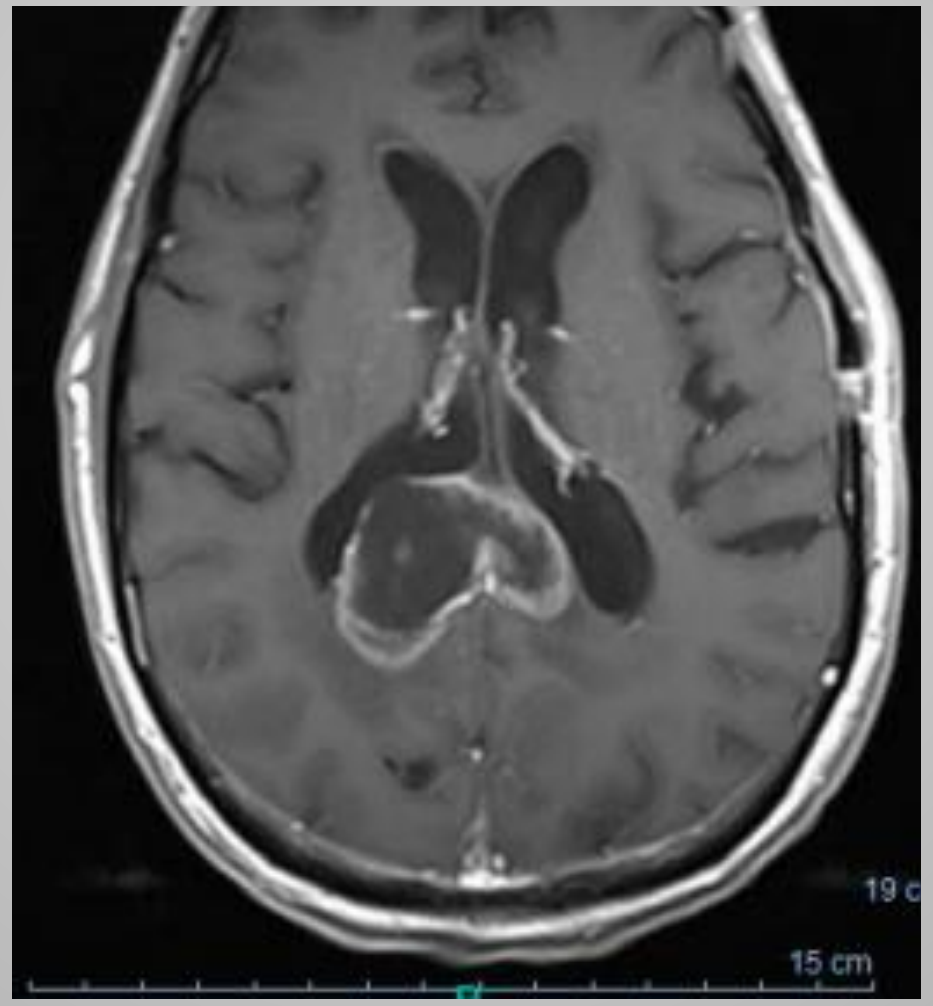
MRI TWO WEEKS LATER



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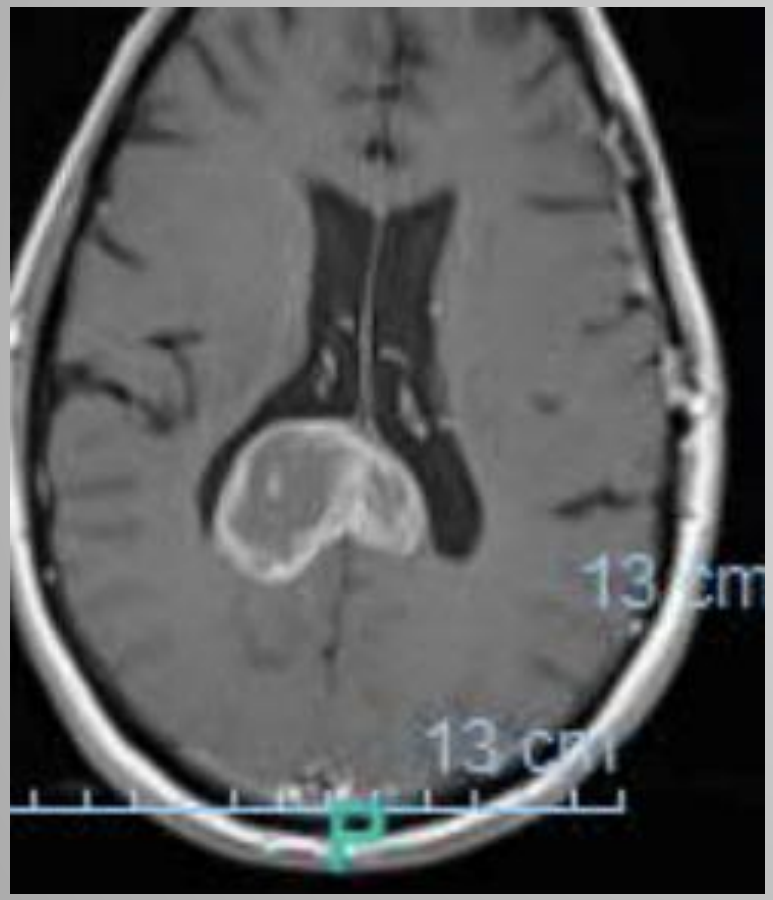
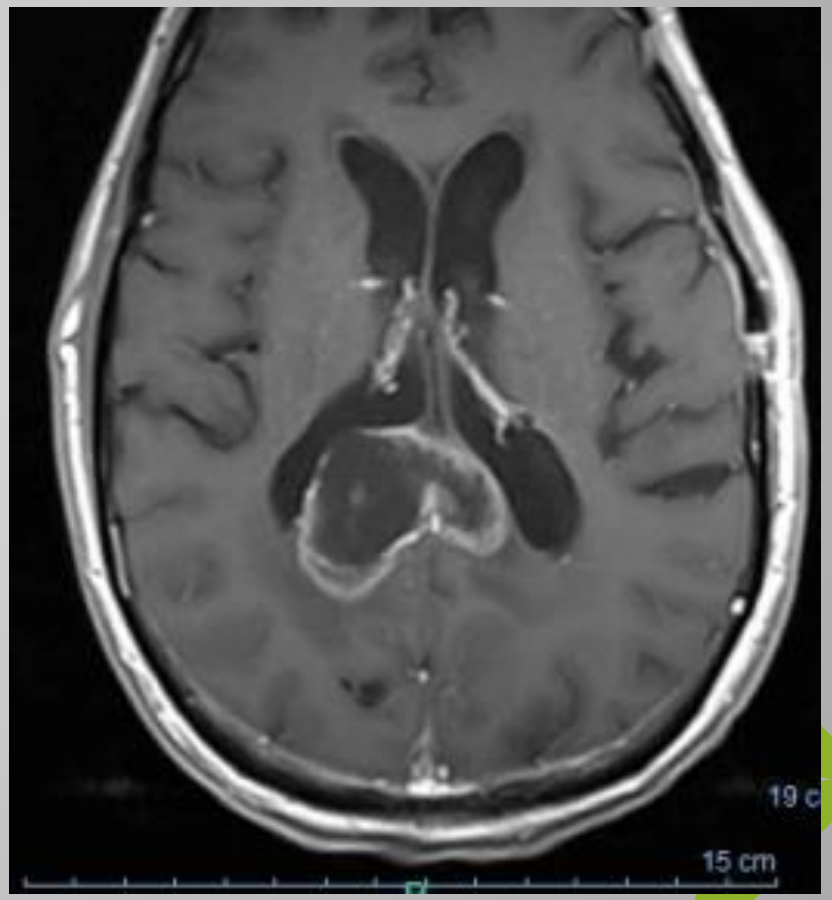
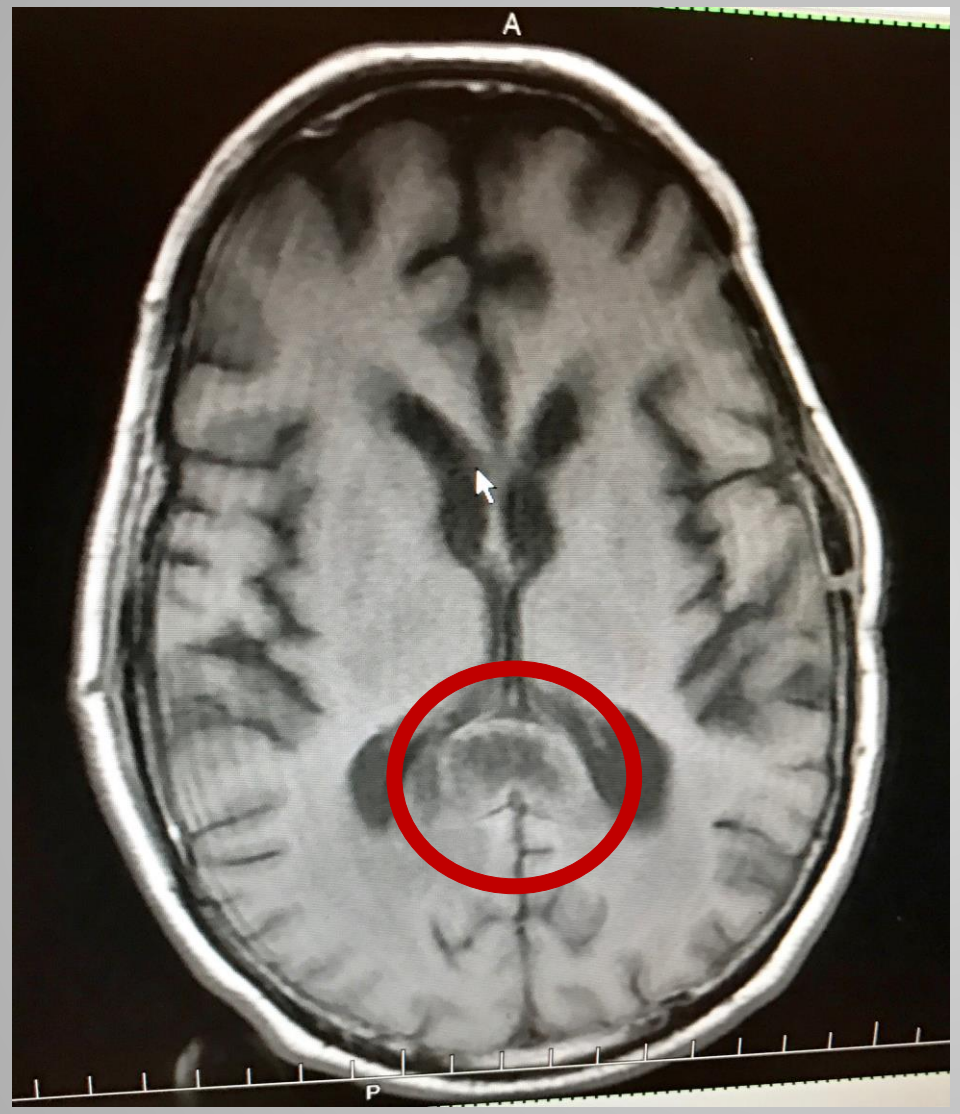
COMPARISON:







9 MONTHS LATER…

HISTORY:

- 78 yr old male with a diagnosis of anaplastic astrocytoma grade 3.
- Treated with temozolomide for six months after initial diagnosis.
- Repeat MRI revealed a larger tumor. The chemotherapy was changed to Lomustine

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Treatment with the cannabis oil commenced two weeks after initiation of Lomustine.

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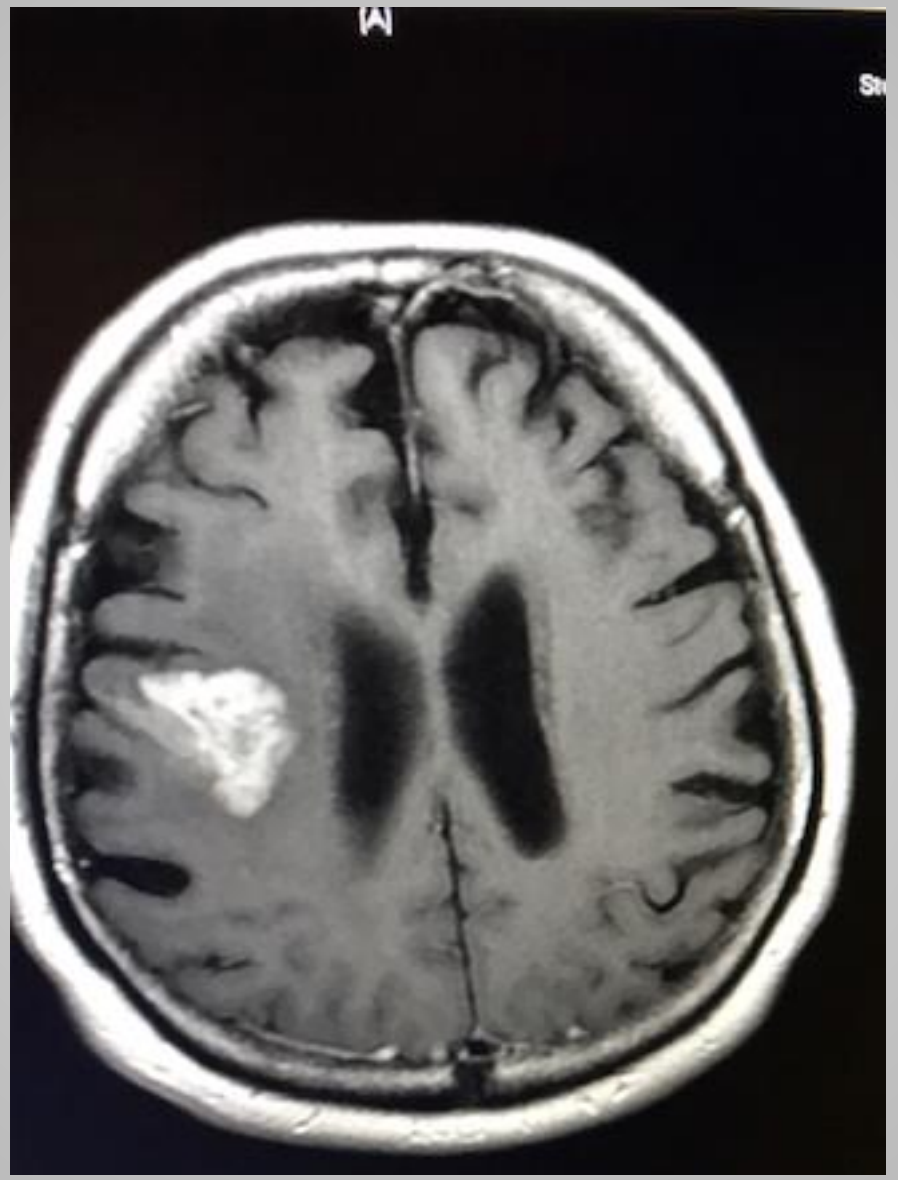

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After six weeks of combination Lomustine and cannabis oil treatment an MRI revealed tumor size reduction.

Also, during the combination treatment the patient reports improvement of sensorium, activity, and speech.

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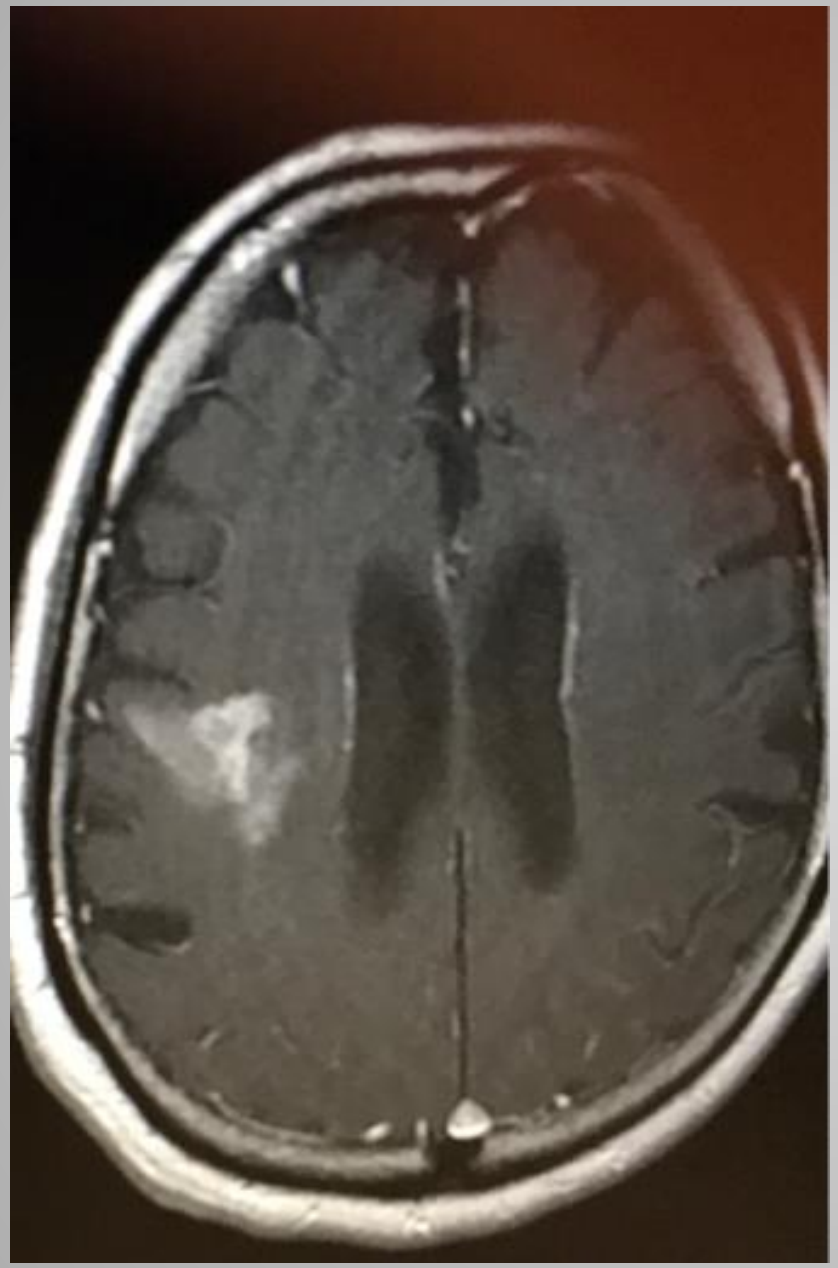
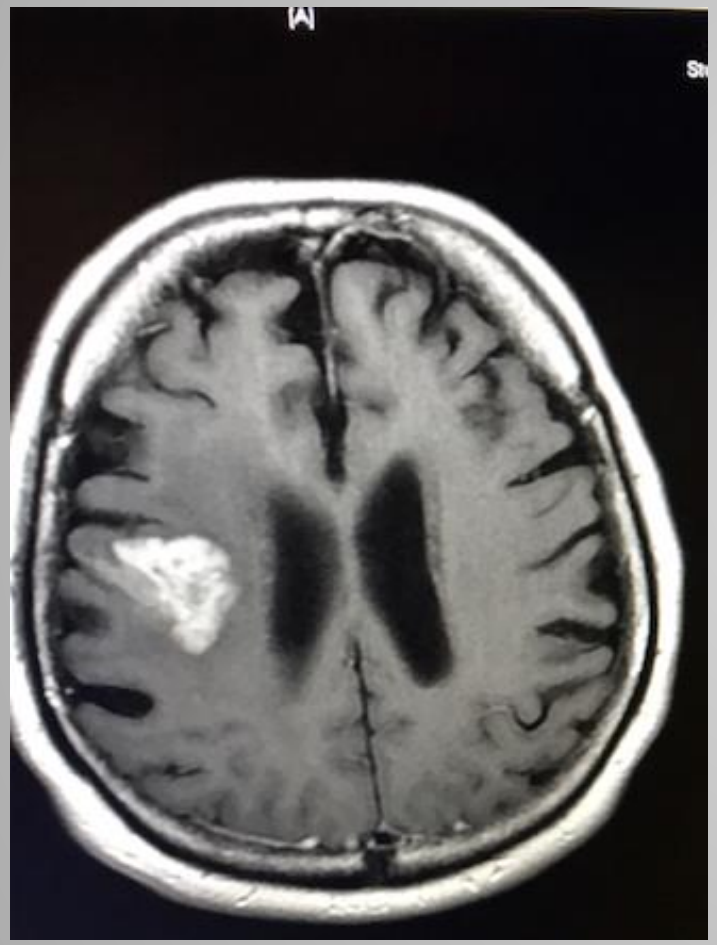


SIX WEEKS LATER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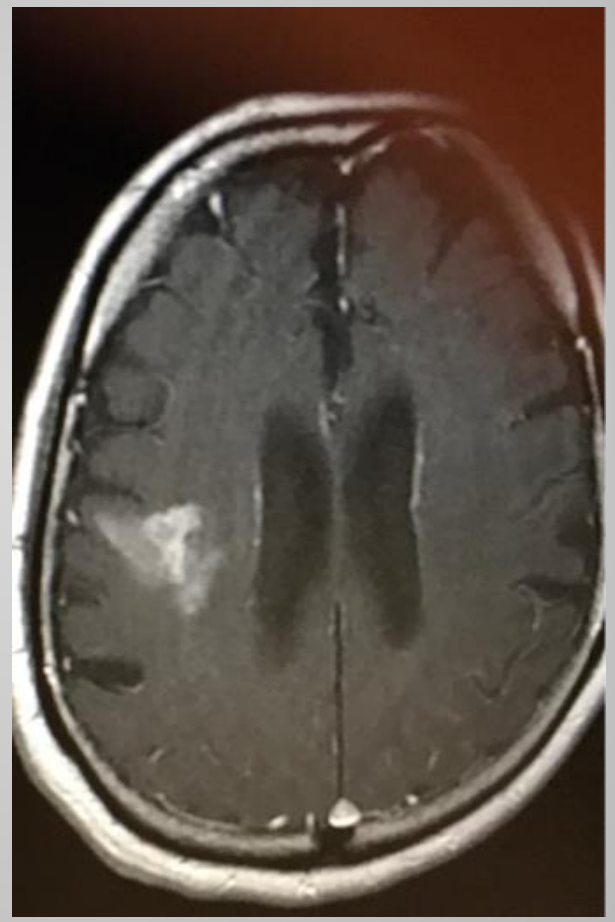

STUDIES:

Marcu JP et al: “Cannabidiol enhances the inhibitory effects of Δ9-tetrahydrocannabinol on human glioblastoma cell proliferation and survival”. Mol Cancer Ther *9*: 180-189, 2010.

María Salazar, et al. “Cannabinoid action induces autophagy-mediated cell death through stimulation of ER stress in human glioma cells”. J. Clinical Investigation 2009.

Blazquez et.al. “Cannabinoids inhibit glioma cell invasion by down-regulating matrix metalloproteinase-2 expression”. 68.6 (2008) 1945-52.

Blazquez et.al. “Cannabinoids inhibit the vascular endothelial growth factor pathway in gliomas” Cancer Research 64.16 (2004) ; 5617-23.

Massi et.al. “Antitumor effects of cannabidiol, a nonpsychoactive cannabinoid, on human glioma cell lines”. The Journal of Pharmacology and Experimental Therapeutics 308.3 (2004) 838-845.

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ADDITIONAL STUDIES:

Solinas et.al. “Cannabidiol, a nonpsychoactive cannabinoid compound, inhibits proliferation and invasion in U87-MG and T98G glioma cells through a multitarget effect”. PLoS One 8.10 (2013): e76918.

Vaccani et.al. “Cannabidiol inhibits human glioma cell migration through a cannabinoid receptor-independent mechanism” British Journal of Pharmacology 144.8 (2005): 1032-1036.

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HISTORY:

- 8 yo with Acute Lymphocytic Leukemia
- Failed MULTIPLE CHEMOTHERAPY AND RADIATION TRIALS
- Failed BONE MARROW TRANSPLANT
- HOSPICE

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CHIEF COMPLAINTS:

- CHRONIC NAUSEA
- LACK OF APPETITE
- HEADACHE
- LACK OF ENERGY

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EVALUATION:

- LETHARGIC
- NON-COMMUNICATIVE
- SWOLLEN

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MEDICATIONS:

METHADONE 10 mg/day
MORPHINE 13.5 mg/day

BOTH IN DIVIDED DOSES

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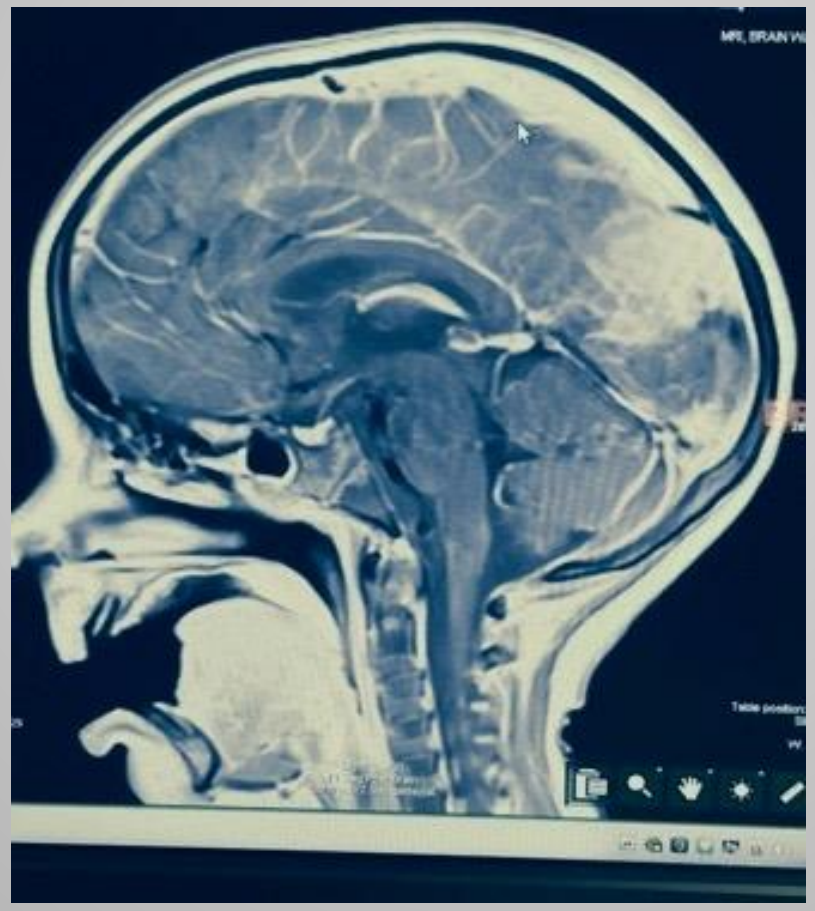
MRI FEBRUARY 2015



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GOALS:

- IMPROVE QUALITY OF LIFE
- IMPROVE PAIN
- TRANSITION OFF OPIOIDS

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TREATMENT

- 1 ml oil SL four times a day

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RESPONSE:

- INITIAL REDUCTION AND THEN REPLACEMENT OF ALL OPIOIDS
- MORE ACTIVE
- “APPROPRIATE” DEMEANOR

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MRI APRIL 2015

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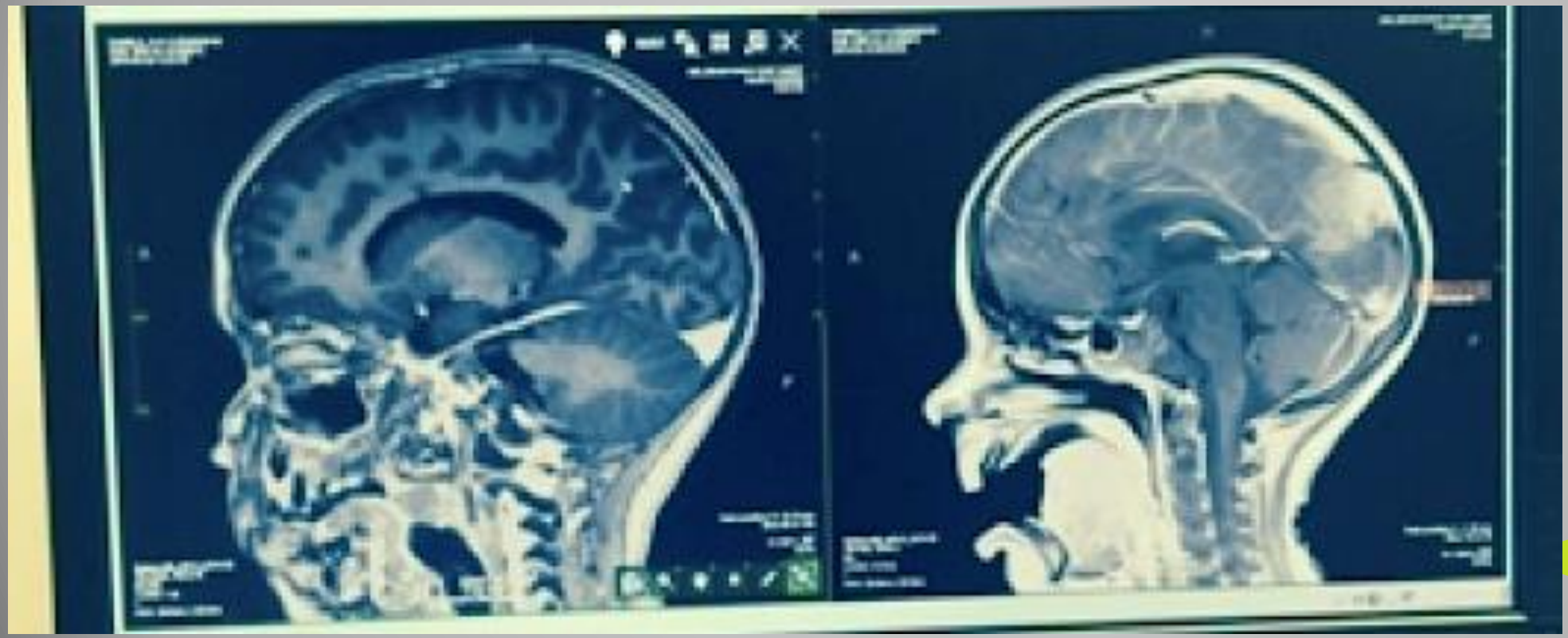
COMPARISON



STUDIES:

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Powles, T. et.al. " Cannabis Induced Cytotoxicity in Leukemic Cell Lines; The Role of the Cannabinoid Receptors and the MAPK Pathway". Blood 105 (2005): 1214-1221.

Herrera, R. et.al. "The CB2 Cannabinoid Receptor Signals Apoptosis via Ceramide-Dependent Activation of the Mitochondrial Intrinsic Pathway" Experimental Cell Research 312.11 (2006): 2121-2131.

Jia, W. et.al. "Delta-9-Tetrahydrocannabinol Apoptosis in Jurkat Leukemia T Cells is Regulated by Translocation of Bad to Mitochondria" Molecular Cancer Research 4.8 (2006): 549-562.

McKallip, R. et.al. "Cannabidiol- Induced Apoptosis in Human leukemia Cells: A Novel Role of CBD in the Regulation of p22 phox and Nox4 Expression" J. Molecular Pharmacology 70(3) (2006): 897-908.

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ADDITIONAL STUDIES:

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Liu, W. "Enhancing the in-vitro Cytotoxic Activity of Delta-9-Tetrahydrocannabinol in Leukemic Cells Through a Combinatorial Approach" Leukemia and Lymphoma 49(9) (2008): 1800-1809.

Scott, Katherine Ann et al. "Enhancing the Activity of Cannabidiol and other Cannabinoids In Vitro Through Modifications to Drug Combinations and Treatment Schedules" ANTICANCER RESEARCH *33*: 4373-4380 (2013)

Singh, Y. et.al. "Cannabis Extract Treatment for Acute Lymphoblastic Leukemia with a Philadelphia Chromosome Mutation" Case Reports in Oncology 6.3 (2013): 585-592.


BALM
SPRAY
CREAM
MUD
SOAK

CIPN

1. Over 1 million people have been treated with Taxol who are alive today
2. CIPN has no FDA approved treatment
3. Extremely debilitating

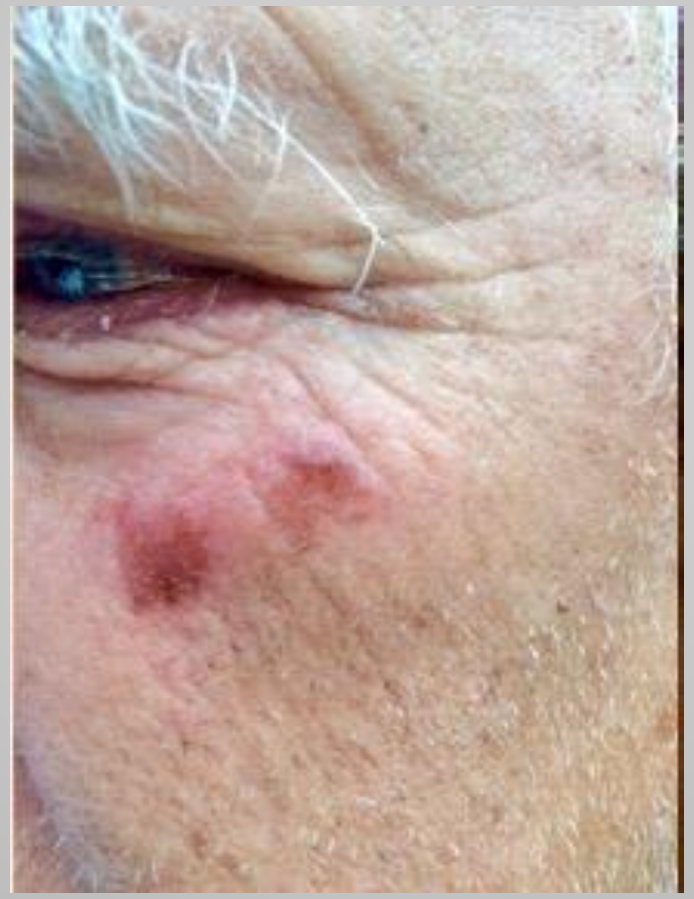
Case: 68 yo female s/p ovarian cancer treatment, unable to wear shoes/socks because of painful feet.

Was prescribed Lyrica, anti-depressants, anti-seizure medicines and opioids.

She did poorly with all attempts at treatment and didn't want to try opioids for fear of addiction.

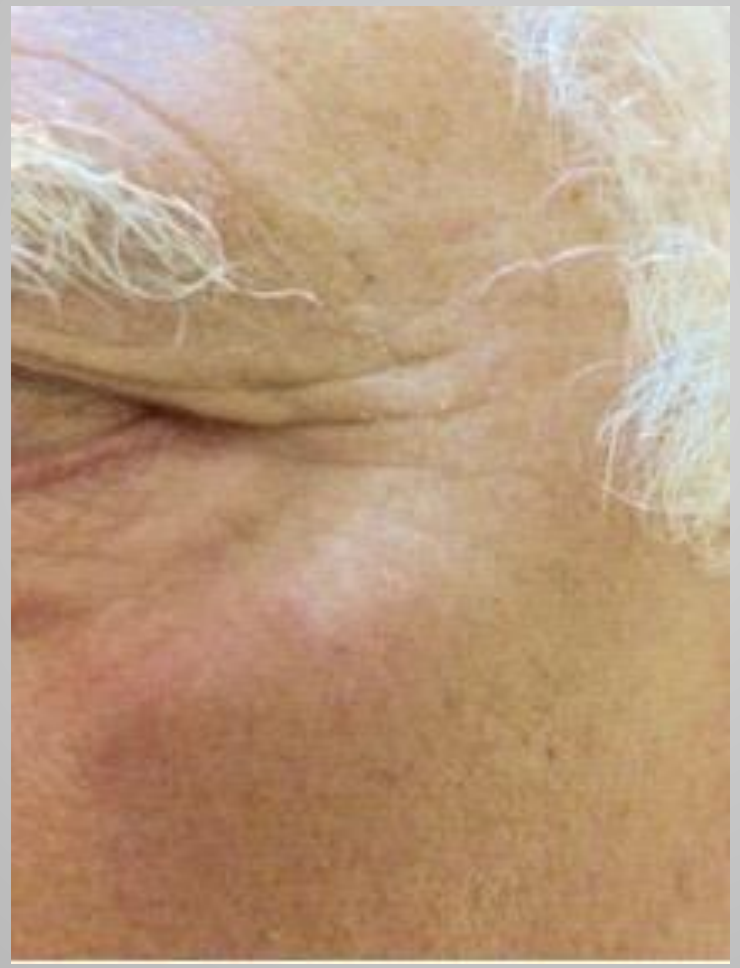
Successfully treated with topical cannabis cream three times/day.

Actinic Keratosis



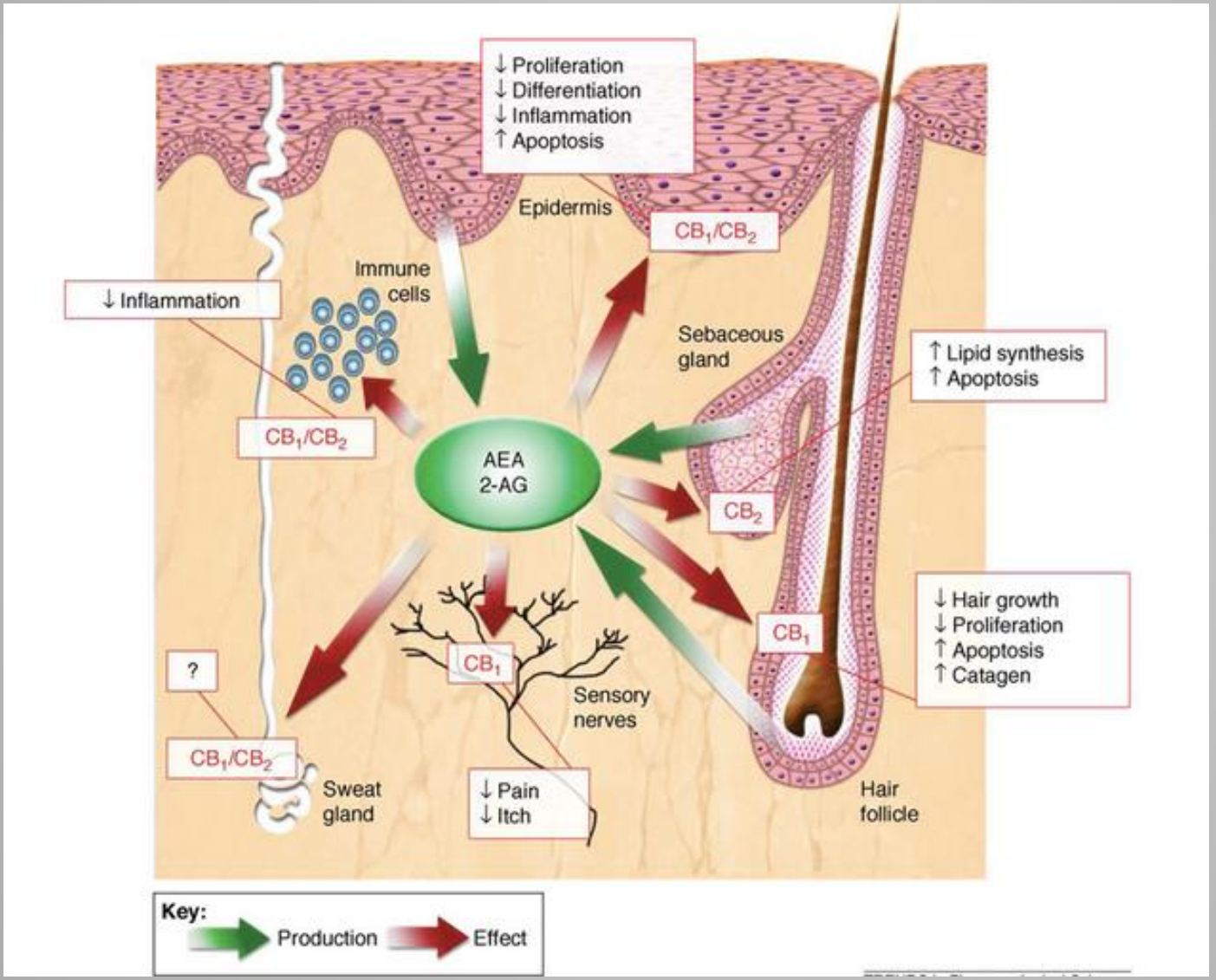
NEWMEXICO MEDICAL CANNABIS CONFERENCE

Six Weeks Later…

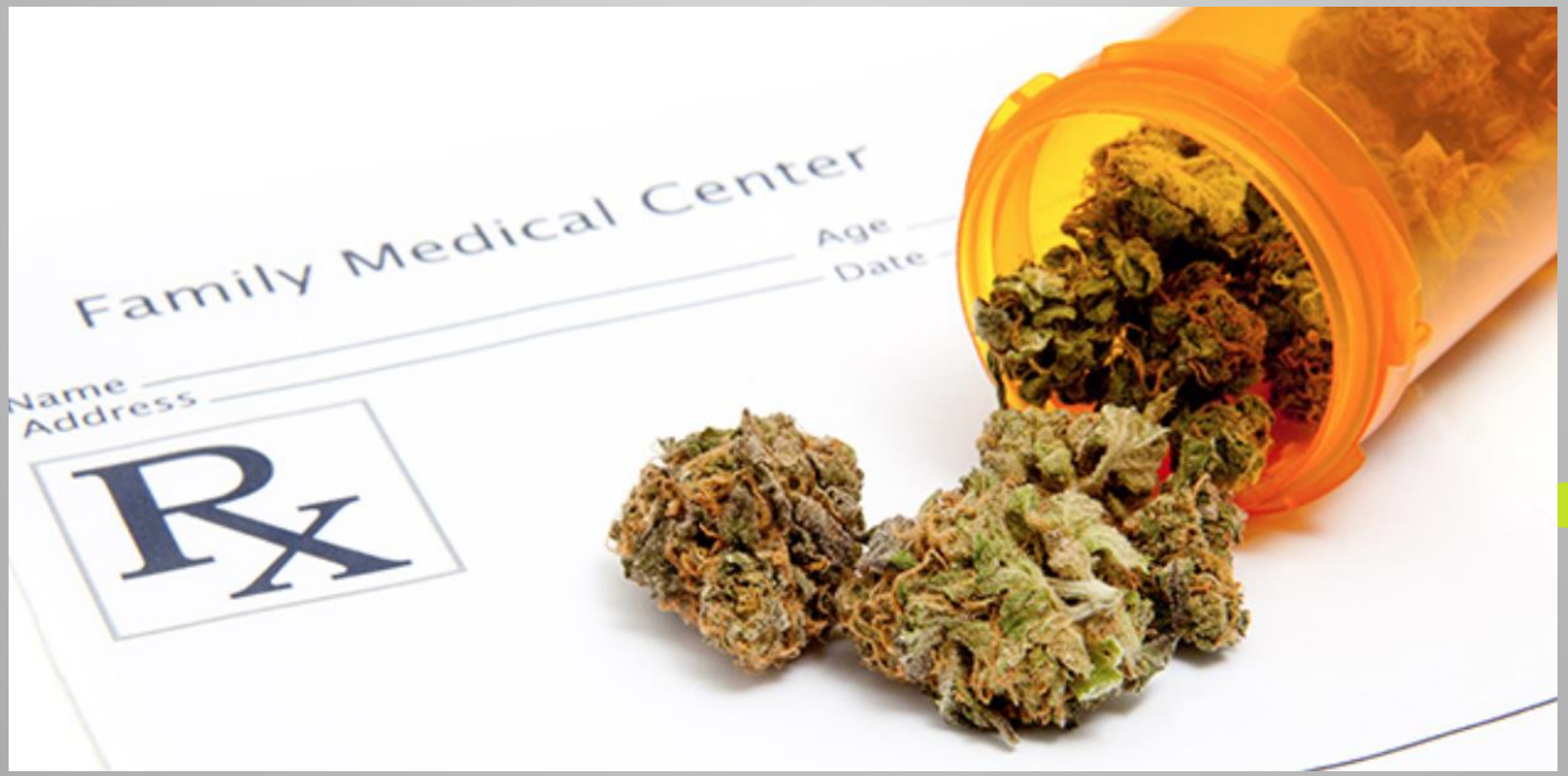


NEWMEXICO MEDICAL CANNABIS CONFERENCE

ECS and SKIN


↓ Proliferation
↓ Differentiation
↓ Inflammation
↑ Apoptosis
Epidermis
CB1/CB2
Immune cells
↓ Inflammation
Sebaceous gland
↑ Lipid synthesis
↑ Apoptosis
CB1/CB2
AEA
2-AG
CB2
CB1
↓ Hair growth
↓ Proliferation
↑ Apoptosis
↑ Catagen
?
CB1
Sensory nerves
CB1/CB2
Sweat gland
↓ Pain
↓ Itch
Hair follicle
Key:
Production
Effect


Fruits & Vegetables
Choose a variety of colors and kinds. You should consume and servings of fruits and vegetables per day.


Family Medical Center
Age
Date
Name
Address
Rx

Email me: DrDeb@ForwardGro.com