

" This is the domain of addiction, where we constantly seek something outside ourselves to curb an insatiable yearning for relief or fulfillment. The aching emptiness is perpetual because the substances, objects, or pursuits we hope will soothe it are not what we really need.We haunt our lives without being fully present."

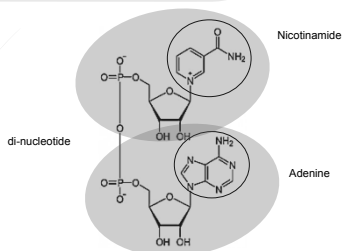
Gabor Mate, MD
In the Realm of Hungry Ghosts



NAD⁺ in Addiction Treatment

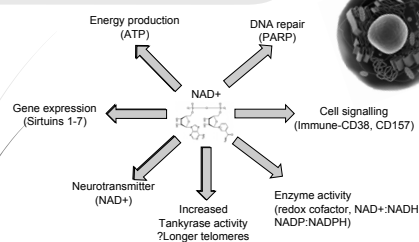
Ken Starr MD FACEM ABAM
Board Certified in Addiction Medicine
Arroyo Grande, CA

What is NAD⁺ (Nicotinamide Adenine Dinucleotide)

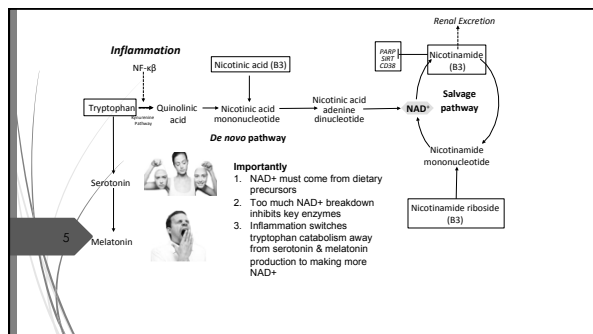


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What is NAD⁺ used for?



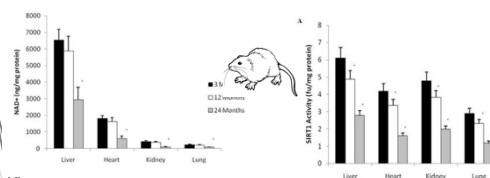
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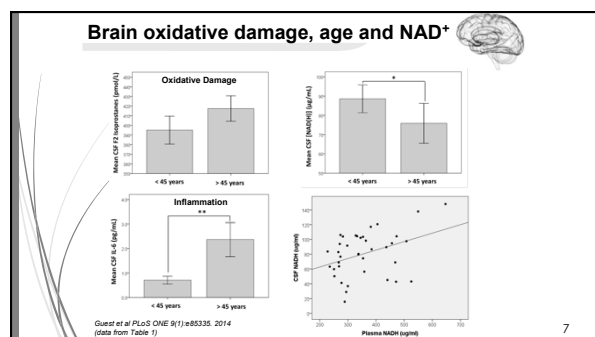
Conditions in which NAD⁺ can be depleted

↑ oxidative damage (with age)



Brady et al PLoS ONE 6(4):e19194 2011

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How do you raise NAD⁺ in the body?

Oral

- Nicotinamide riboside (NR)
- Nicotinamide mononucleotide (NMN)
- Nicotinic acid (Niacin)
- Nicotinamide (niacinamide)

Intravenous (IV)

NAD⁺

Maintain NAD⁺ by:

- 1) Reducing oxidative damage &
- 2) Inflammation (CD38)
- 3) Increasing synthesis

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NAD⁺ Sirtuin activity

- 1) Silent information regulators of gene transcription (SIRT6)
- 2) Wide range of functions
- 3) Regulate gene expression via histone deacetylation
- 4) Control gene expression
- 5) Cell cycle regulation
- 6) DNA repair and metabolic control

History of NAD⁺ Treatment in Addiction

- 1) NAD⁺ isolated By Von Euler in 1936
- 2) NAD⁺ used for alcohol treatment since 1939
- 3) Used extensively in South Africa since 1961
- 4) NAD⁺ used extensively for alcoholism & other chemical dependencies since 1974

An Article from the West. J. Surg., Obst. & Gynec. May-June 1961

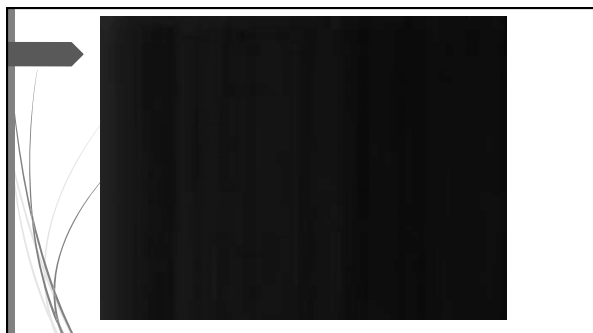
Diphosphopyridine Nucleotide in the Prevention, Diagnosis and Treatment of Drug Addiction

A Preliminary Report
Paul O'Hollaren, M.D.
Seattle, Washington
From the Research Department, Shadel Hospital

Results. Complete, immediate and permanent withdrawal of all addictive drugs has been achieved to date in this group of patients by means of this treatment. However, as in all therapies of addiction, several years' follow-up is necessary before final evaluation is possible.


Conclusions

1. The author has successfully utilized diphosphopyridine nucleotide in the prevention, diagnosis and treatment of 104 cases of drug addiction.
2. Complete, immediate, total and permanent withdrawal can be achieved and maintained by proper administration and dosage of the medication.
3. Withdrawal is achieved with very few (and in some cases none) of the characteristic withdrawal symptoms, usually experienced with other treatments currently utilized.
4. Addictions treated in this series include: heroin, opium, morphine, meperidine, codeine, alcohol, methadone, cocaine, amphetamines, barbiturates and tranquilizers. Craving for the addictive drug, even heroin and opium, is completely removed.



Dr. Hitt in Tijuana Mexico

- ☐ Clinic in Mexico which offered NTR Therapy
- ☐ Patients from all over the world
- ☐ Claimed to cure addiction



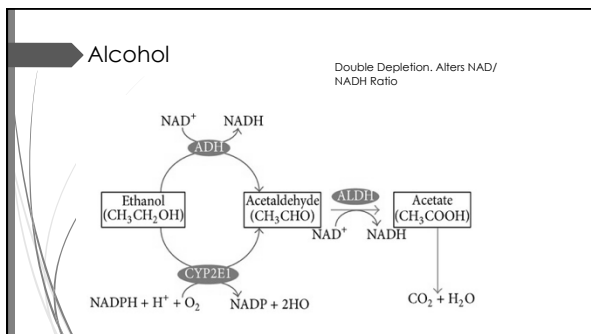
BR+TM
NAD
Brain Restoration Plus
 Nicotinamide Adenine Dinucleotide

Changes in Oxidative Damage, Inflammation and [NAD(H)] with Age in Cerebrospinal Fluid

Jade Guest^{1,2}, Ross Grant^{2,3*}, Trevor A. Mori⁴, Kevin D. Croft⁴

1 Australian Research Institute, Sydney Adventist Hospital, Sydney, New South Wales, Australia, 2 Department of Pharmacology, School of Medical Sciences, Faculty of Medicine, University of New South Wales, Sydney, New South Wales, Australia, 3 Sydney Medical School, University of Sydney, Sydney, New South Wales, Australia, 4 School of Medicine and Pharmacology, Royal Perth Hospital Unit, University of Western Australia, Perth, Western Australia, Australia

Age associated decrease in NAD levels
 Alcohol drinkers have lower levels of NAD+
 NAD levels decrease in response to alcohol stress.
 Increased neuro-inflammation and oxidative stress associated with lower NAD levels



Alcohol

- ☐ NAD alleviates Alcohol Withdrawal
- ☐ NAD reduces Cravings by modulating the neuroadaptive response involved with cravings "Sensitization"
- ☐ Reduces Negative Reinforcement
- ☐ Alters Stress Circuits

NAD+ Sirtuin activity

- 1 SIRT 1 activity is NAD+ dependent
- 2 SIRT activity increased in response to stress, fasting, exercise or low glucose availability. This in turn increases intracellular NAD levels
- 3 "turns off" the genes that help drive aging process

NAD+ levels

- 1 NAD+ helps with withdrawal, cravings and recidivism
- 2 NAD+ replaces the aldehyde/dopamine ligand in the NA= decreases withdrawal
- 3 Lower cravings mediated by the histone deacetylase function of SIRT1
- 4 In chronic alcohol abuse, histone proteins for genes become acetylated
- 5 SIRT1 (via NAD+) deacetylates these proteins reverses the epigenetic mediated mechanism for alcohol cravings
- 6 Alleviating withdrawal reduces the negative reinforcement stress circuit of alcoholism

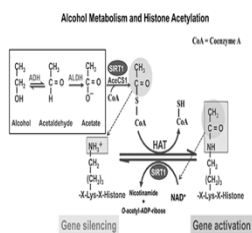
NAD+ in Alcohol Treatment

- 1 In chronic alcohol abuse, histone proteins for genes in the cortex and amygdala become acetylated at H3K9.
- 2 SIRT1 deacetylates Histones.
- 3 NAD+ reverses the epigenetic mechanism for alcohol cravings.
- 4 It's probably the histone deacetylase function of SIRT1 that reduces alcohol and drug cravings and recidivism.

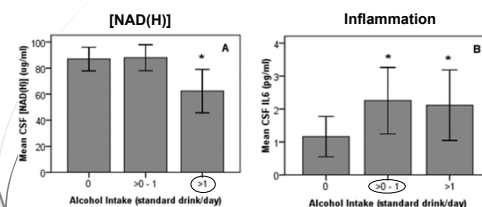
NAD+ in Alcohol Treatment

- 1 NAD+ replaces the aldehyde/ dopamine ligand at the opioid receptor in NA, preventing withdrawal.
- 2 NAD+ binding at the opioid receptor, may be the mechanism for alleviating opioid withdrawal.

Histone Deacetylase silences the reward mechanism of cocaine and morphine in reward center

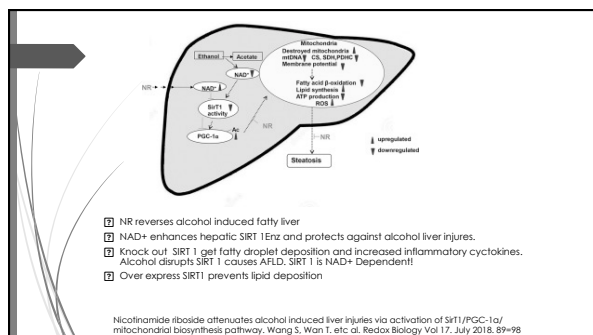


Alcohol ↓ brain NAD+ & ↑ inflam.



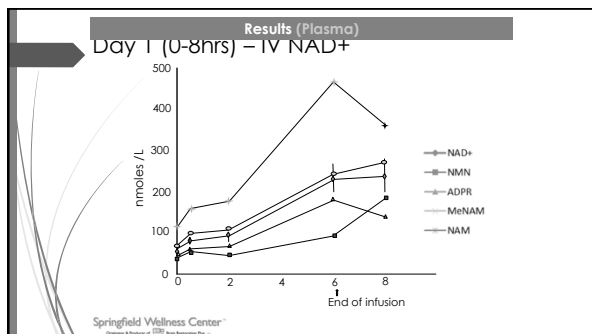
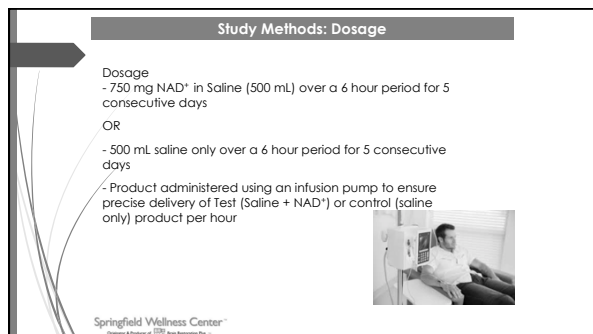
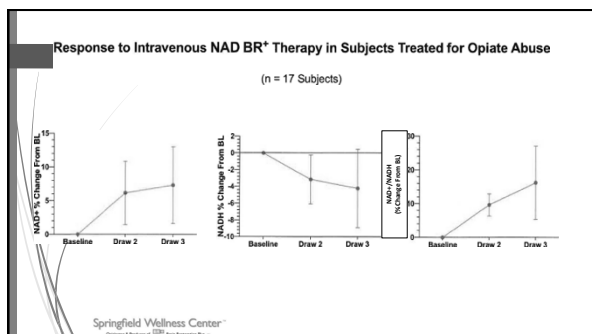
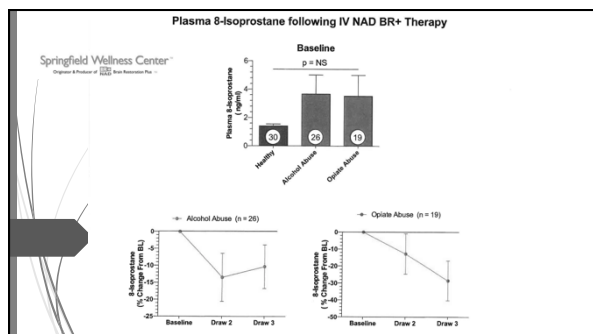
Guest et al PLoS ONE 9(1):e85335. 2014

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Opiates

- [1] NAD+ alleviates opiate withdrawal and cravings
- [2] Some evidence NAD+ binds directly to opiate receptors
- [3] NAD+ activates SIRT1 in reward center (NA)
 - [4] Drug induced expression of transcription factors enhance reward effects
 - [5] NAD Therapy reverses this "reward effect" of drugs on epigenetic level.
 - [6] Histone deacetylation silences the reward mechanism.
 - [7] This has both short term and long term benefits



Results Update



Key observations:

- [NAD⁺] increased by >400% of 6 hrs in plasma
- [NAD⁺] increased by ~35% at 8hrs in **RBC's**
- No significant increase in **RBC** NAM
- The rise in NAD⁺ in plasma throughout the 6hr infusion was paralleled by a rise in all metabolites:
 - NAM ~410%
 - MeNAM ~350%
 - ADPR ~390%
 - NMN ~410%
- NAM/MeNAM appear to be significant contributors to an apparent rapid metabolism of infused NAD⁺

Springfield Wellness Center

Springfield, MA 01104 | 413.246.2222

Response to Intravenous NAD⁺ Therapy
in Subjects Treated for Opiate Abuse

(n = 10 Subjects)

8-isoprostane
(% Change From BL)

Baseline Draw 2 Draw 3

Time Point	8-isoprostane (% Change From BL)
Baseline	0
Draw 2	-22
Draw 3	-22

Springfield Wellness Center[®]

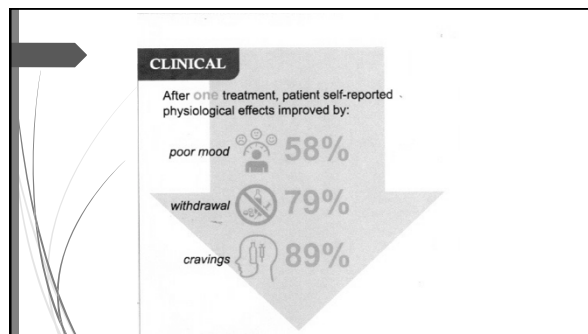
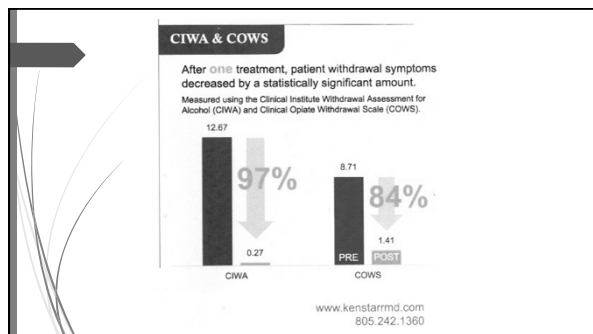
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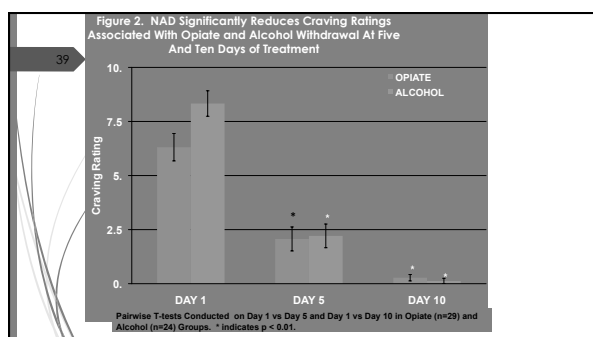
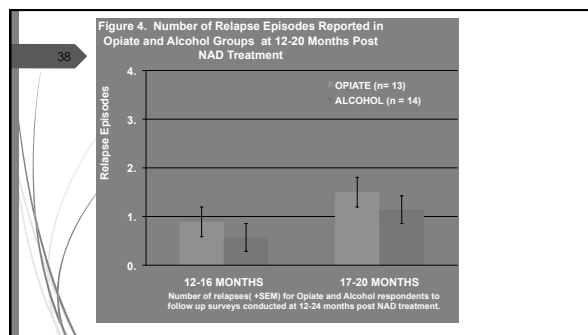
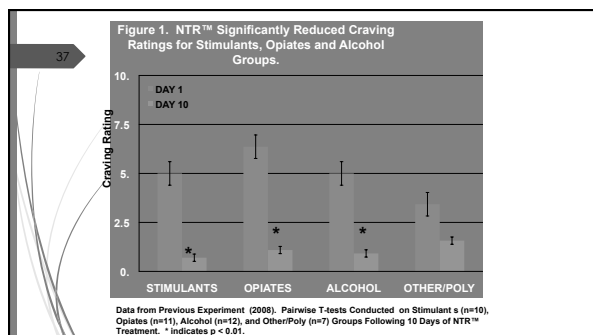
FIRST DAY QUESTIONNAIRE

Please fill out completely, and as accurately as possible. There is no wrong answer, and no answer will have a effect on your treatment.

PATIENT NAME _____ DATE _____

DAY # _____ **ROTATION DAY I** _____ **STAFFS INITIALS** _____





Drug & alcohol Detox

- ☐ 4-10 days
- ☐ Alleviates detox symptoms first few days
- ☐ Second part appears to be a restoration of Neurotransmitters
- ☐ Long acting opiates/benzos will need longer duration treatment
- ☐ Higher doses initially: 1500mg/day- 500mg/day

