

The Art of Treatment: Clinical Applications and Challenges

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What we are up against!



Cigarettes and Tobacco Dependence

- Cigarette smoke – complex mixture of 7,000 chemicals with over 60 known carcinogens
- Most efficient delivery device for nicotine that exists- better than intravenous
- Cigarette manufacturers have modified cigarettes over the past decades to maximize nicotine delivery to the brain
- High doses of arterial nicotine cause upregulation of the nicotinic acetylcholine receptors
- Genetic factors influence tobacco dependence
- Left untreated 60% of smokers die from a tobacco-caused disease

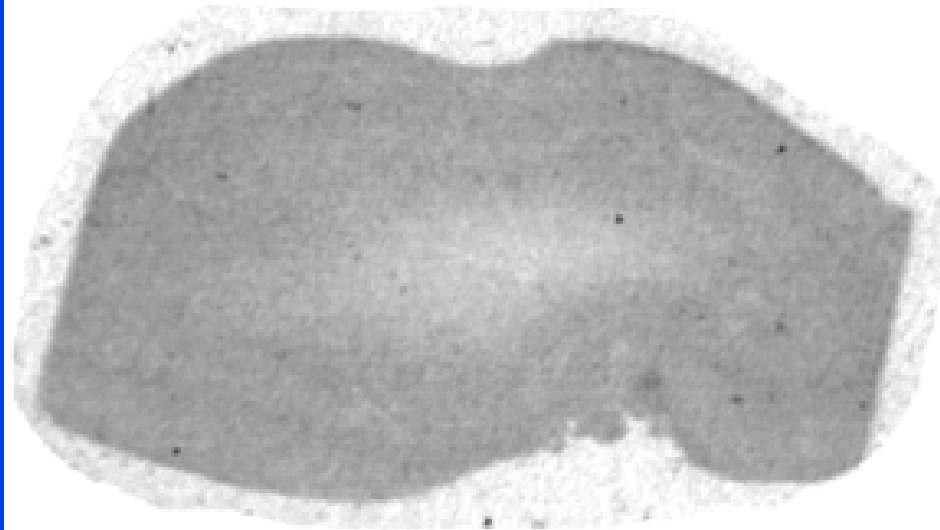
Hurt RD, Robertson CR JAMA 280:1173, 1998

- **Why would anyone smoke with this hanging over their head?**
- **It is in the brain!**



Temporal Cortex

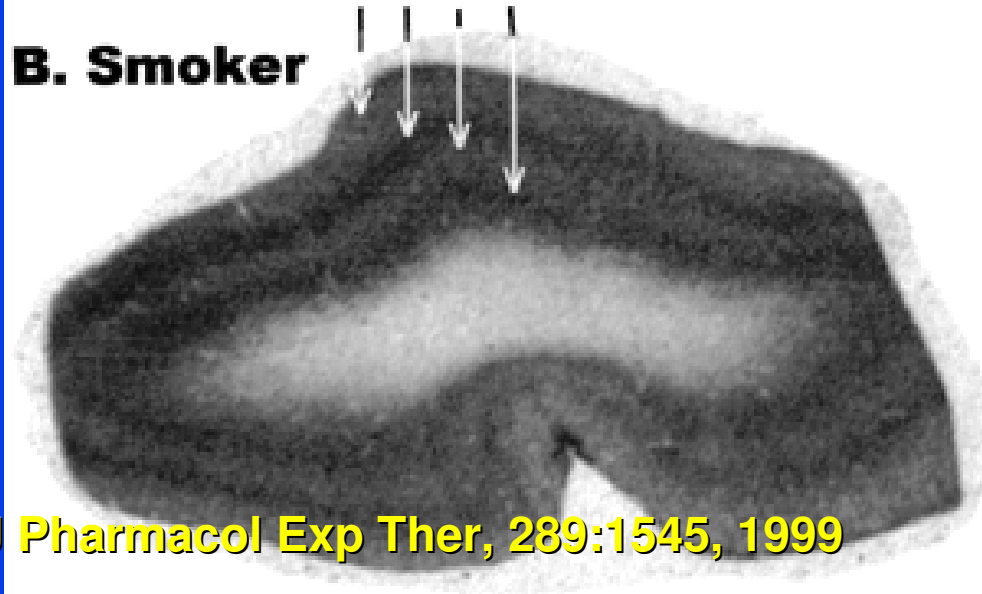
A. Nonsmoker



Cortical Layers

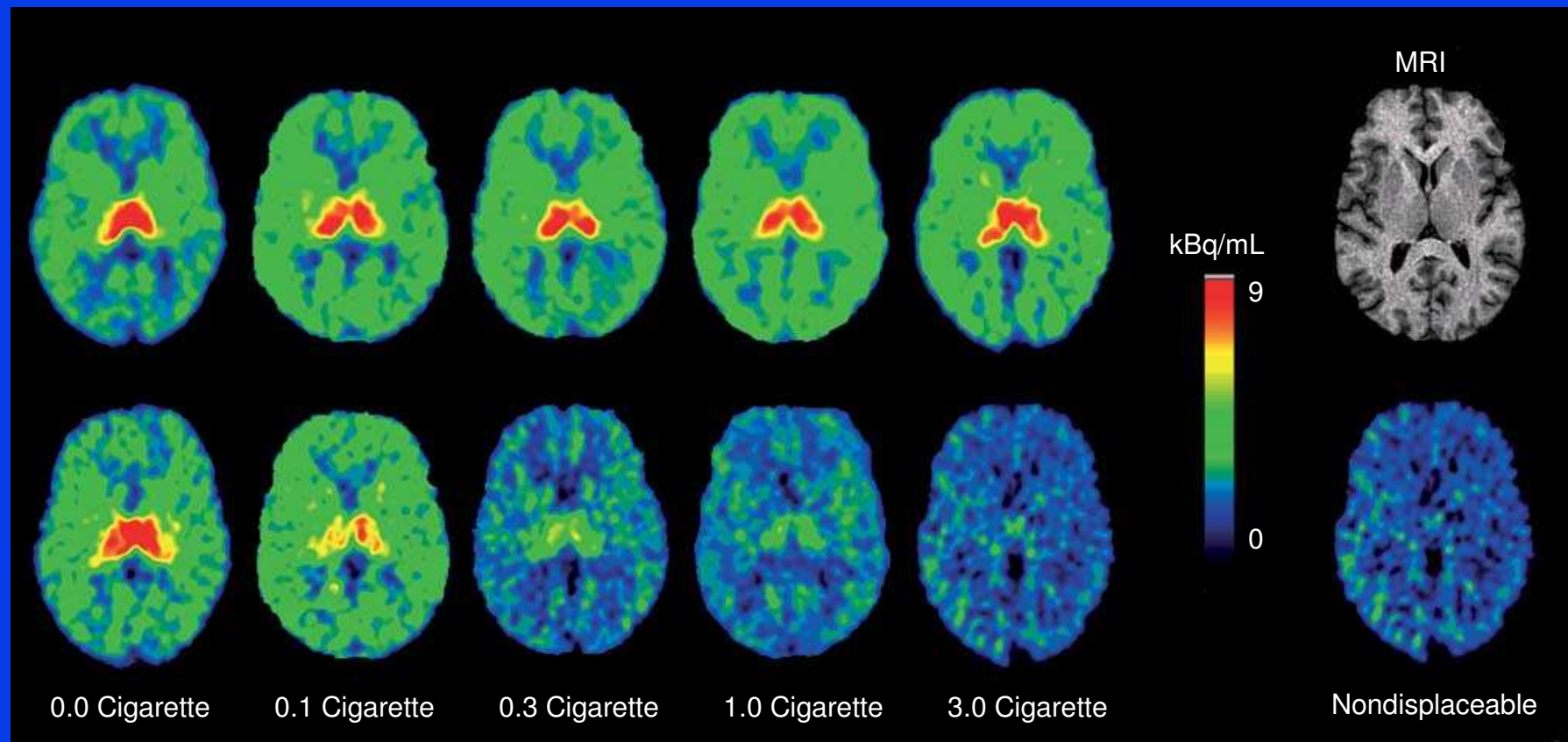
I-III IV V VI

B. Smoker



Perry, DC, et al. J Pharmacol Exp Ther, 289:1545, 1999

Smoking Saturates Nicotinic Receptors



Brody, A.L. Arch Gen Psychiatry. 63;907-915, 2006

Treating Tobacco Dependence

Basic Concepts

- **Treat tobacco dependence for the serious medical problem it is**
- **Motivational counseling plus pharmacotherapy**
- **Dose response to counseling**
- **Higher nicotine patch doses for heavier smokers**
- **Combination pharmacotherapy**
- **Longer treatment is better. This is not strep throat nor a UTI**

Mayo Clinic Nicotine Dependence Center

Treatment Program

- **Established April 1988**
- **Integrated approach – behavioral, addictions, pharmacotherapy, relapse prevention and motivational interviewing**
- **Outpatients- Individual counseling by Tobacco Treatment Specialist**
- **Inpatients- Hospital Nurse Tobacco-Use Intervention Protocol and hospital-based TTS**
- **Residential Treatment Program**

Hurt RD, et al CA Cancer J Clin 59:314, 2009

Treating Tobacco Dependence in a Medical Setting

Pharmacotherapy

- **Clinical decision-making using clinician skills and knowledge of pharmacology to guide medication selection and doses**
- **Patient involvement: past experience and/or preference**
- **Nicotine patch, varenicline and/or bupropion used as “floor” medications**
- **Short acting NRT products for withdrawal symptom control**
- **Combination pharmacotherapy the rule**

Hurt RD, et al CA Cancer J Clin 59:314, 2009

Tailoring Pharmacotherapy

Long Acting + Short Acting

Long acting

Pick 1 or 2 from here

- Nicotine patch
- Bupropion
- Varenicline

Short acting

Plus 1 or 2 from here

- Nicotine gum
- Nicotine inhaler
- Nicotine lozenge
- Nicotine nasal spray

Summary

- **Treat tobacco dependence for the serious medical problem it is**
- **Supportive counseling plus pharmacotherapy**
- **Combination pharmacotherapy is the rule (long acting plus short acting)**
- **Pharmacotherapy for “as long as it takes”**

50 y/o man with Buerger's Disease

- **Started smoking as a teenager**
- **1987 Non-healing toe ulcerations**

30 CPD

Dx Buerger's Disease

- **1988 Thoracic Sympathectomy**
- **1989 Amputation, right 5th toe**

Auto amputation, right thumb

Stopped smoking (5 years)

- **2000 Hazelden Alcohol/drug Dependence Treatment**

50 y/o man with Buerger's Disease (cont.)

- **2002 Residential Treatment at NDC (20 CPD)**
- **Ulcerations right heel & right lateral malleolus**
- **“Like someone pounding nails in my leg and foot”**
- **Bupropion started before admission**
- **Nicotine patch therapy at 35 mg/d**

50 y/o man with Buerger's Disease (cont.)

- Reluctant to use two patches
- Baseline serum cotinine 300 ng/mL
- Steady state cotinine 188 ng/mL on 21 mg/d patch
- Eventually ↑ patch dose to 35 mg and then to 42 mg/d → much improved – less withdrawal

50 y/o man with Buerger's Disease (cont.)

- **Post Residential Treatment**
- **Continued 42 mg/d nicotine patch dose for 6 weeks then slowly tapered**
- **Continued bupropion for 2 years**
- **Panelist at our Conference May 2010**
- **Still abstinent from smoking**

35 y/o Man from Texas

Residential Patient 2010

- **Heavy smoker (up to 30CPD) since starting at age 15**
- **Average 20-40 CPD over past year**
- **Stopped smoking 1x for 8 months – non-smoking girlfriend**
- **Efforts to cut down → nicotine withdrawal despite nicotine gum or nicotine patches.**
- **Bupropion → ↓ libido**

35 y/o Man from Texas (cont.)

- **Resisted idea of nicotine patch therapy. Wanted to consider no pharmacotherapy**
- **Varenicline 1mg on day 1 with rapid ↑ + nicotine inhaler**
- **Day 2-Severe nicotine withdrawal – disheveled, tremulous, no sleep, cut himself shaving.**
- **Considered checking out of program**
- **Baseline serum cotinine 396 ng/mL**

35 y/o Man from Texas (cont.)

- **Declined nicotine patch dose of 56 mg/d. Agreed to 42 mg/d dose → improved w/d relief by afternoon of Day 2. ↑ varenicline to 1 mg BID**
- **Day 3-Markedly improved. Tremor gone, less irritable, but not sleeping well.**
- **Day 4-Slept better. Less w/d**
- **Day 5-Steady state serum cotinine 323 ng/mL Discussed safety margin if more NRT needed**
- **Day 7-“Best night sleep I’ve had in many years”**

52 Y/O Married Man With Back Pain

- **Smoker since age 14 smoked 40 cpd until a 2 months ago, now smoking 20-30 cpd.**
- **Wife is an ex-smoker but very supportive.**
- **Smokes first cigarette within 5 minutes of arising in the morning.**
- **Longest period of smoking abstinence 1 month 21mg nicotine patch but had w/d.**
- **Nicotine gum and bupropion did not relieve cravings. Varenicline no help in stopping smoking.**

52 Y/O Married Man With Back Pain

Telephone call f/u at 2 weeks

- **Started 2-21 mg nicotine patches + nicotine inhaler for ad lib use.**
- **Good initial response with w/d relief most of the day. Stopped smoking for 10 days.**
- **Frequency of inhaler use increased toward early evening as cravings seemed to increase and continue until he goes to bed.**
- **Next steps?**

52 Y/O Married Man With Back Pain

Phone call 2 weeks later

- **14 mg patch @ 4PM. Evening cravings resolved**
- **Less frequent inhaler use**
- **Continue on 2-21 mg patches in the AM and a 14 mg patch at 4 PM**
- **Continue ad lib nicotine inhaler**
- **Phone back in 2 weeks**
- **Encouraged to use the medications until he is very comfortable in ability to abstain then ↓ morning patch dose**