



Pharmacotherapy for Treating Tobacco Dependence

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Rationale for Pharmacological Therapy

- Success rate doubles
- Manage negative mood states
- Provides opportunity to alter behavior without withdrawal
- Reduce withdrawal symptoms

First-Line Pharmacologic Therapy

- Non-Nicotine Therapy
 - Bupropion (prescription only)
 - Chantix (prescription only)
- Nicotine Replacement Therapy
 - Nicotine patch (OTC)
 - Nicotine gum (OTC)
 - Nicotine lozenge (OTC)
 - Nicotine nasal spray (prescription only)
 - Nicotine inhaler (prescription only)

Factors for Consideration

- Contraindications
- Patient preference
- Previous patient experience
- Patient characteristics

Optimizing Pharmacotherapy

- Goals of treatment
 - Withdrawal symptom relief
 - Control of cravings/urges
 - Abstinence
- Modification of medication doses may be necessary to achieve these targets
 - Higher doses
 - Multi-drug regimens
 - Longer course of treatment

Withdrawal Symptoms

- Depressed mood
- Insomnia
- Irritability, frustration or anger
- Anxiety
- Difficulty concentrating
- Restlessness
- Shakiness
- Increased appetite or weight gain

American Psychiatric Association. (1994). Diagnostic and Statistical Manual of Mental Disorders (4th ed.)

Patch Dosing

- 40 cpd or greater = 42 mg/day
 - 21-39 cpd = 28-35 mg/day
 - 10-20 cpd = 14-21 mg/day
 - 10 cpd or less = 14 mg/day
- * If a dose >42 mg/day may be indicated, contact the patient's prescriber

Patch Dosing Schedule

- Use initial dose for 4-6 weeks
- After 4-6 weeks of smoking abstinence, taper 7-14mg steps every 2-4 wks
- Length of therapy varies based on patient response
- Withdrawal symptoms while tapering are mild to nonexistent
- Advise using overnight

Nicotine Patch – Person smoked 30 cpd

Patient A

- 28 mg x 4 weeks
- 21 mg x 4 weeks
- 14 mg x 3 weeks
- 7 mg x 2 weeks

Patient B

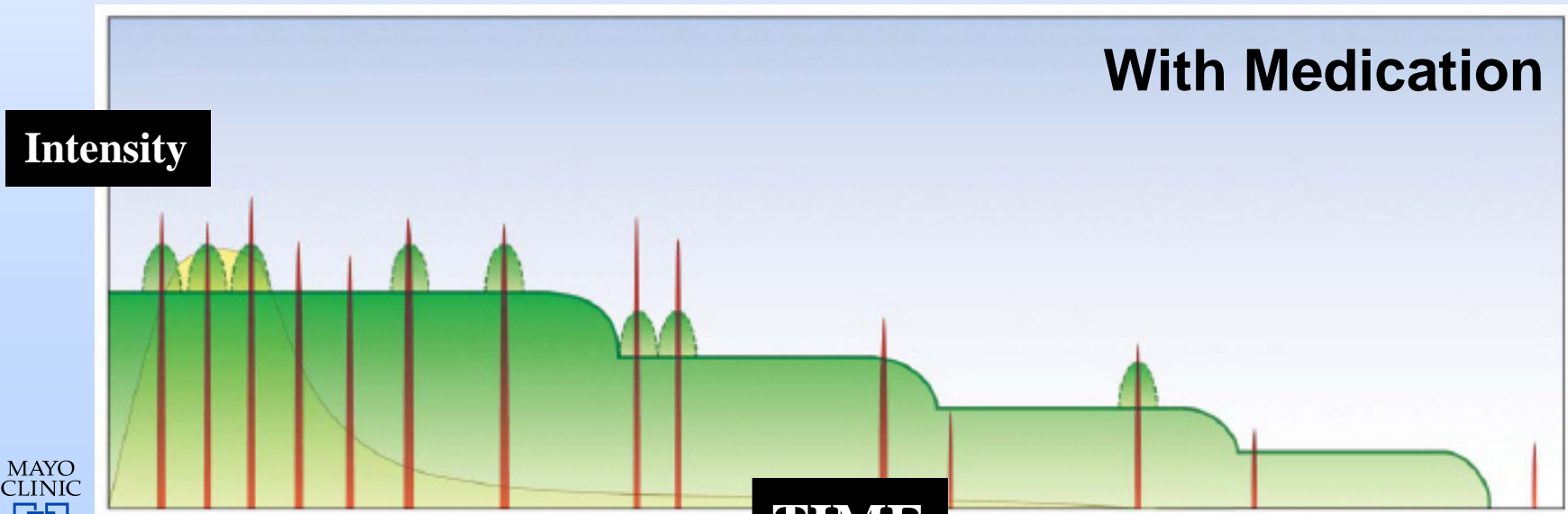
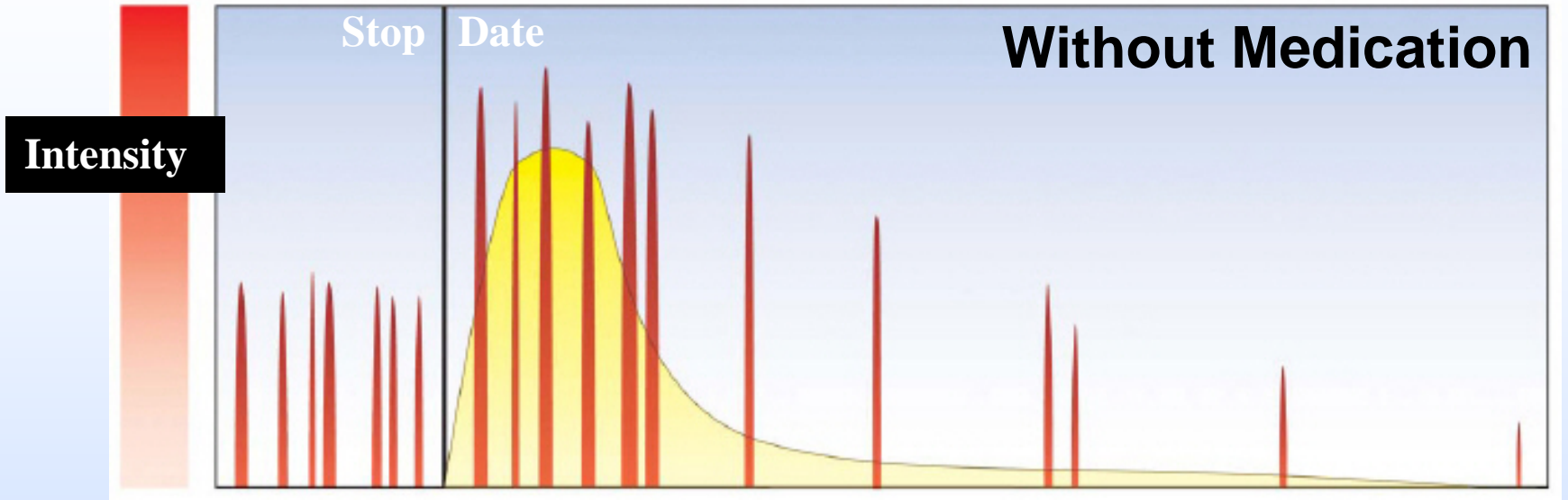
- 28 mg x 6 weeks
- 21 mg x 4 weeks
- 14 mg x 4 weeks
- 7 mg x 4 weeks

Combination NRT rationale

Combine long-acting patch with *ad libitum* short-acting medication (gum, lozenge, inhaler, nasal spray)

- Encourages patient to be in control of cravings and withdrawal symptoms, while keeping a consistent baseline
- Improves compliance with treatment plan
- Achieves higher drug concentrations
- Allows further dose adjustments
- Replace tactile stimulus by mimicking smoking

Medication:

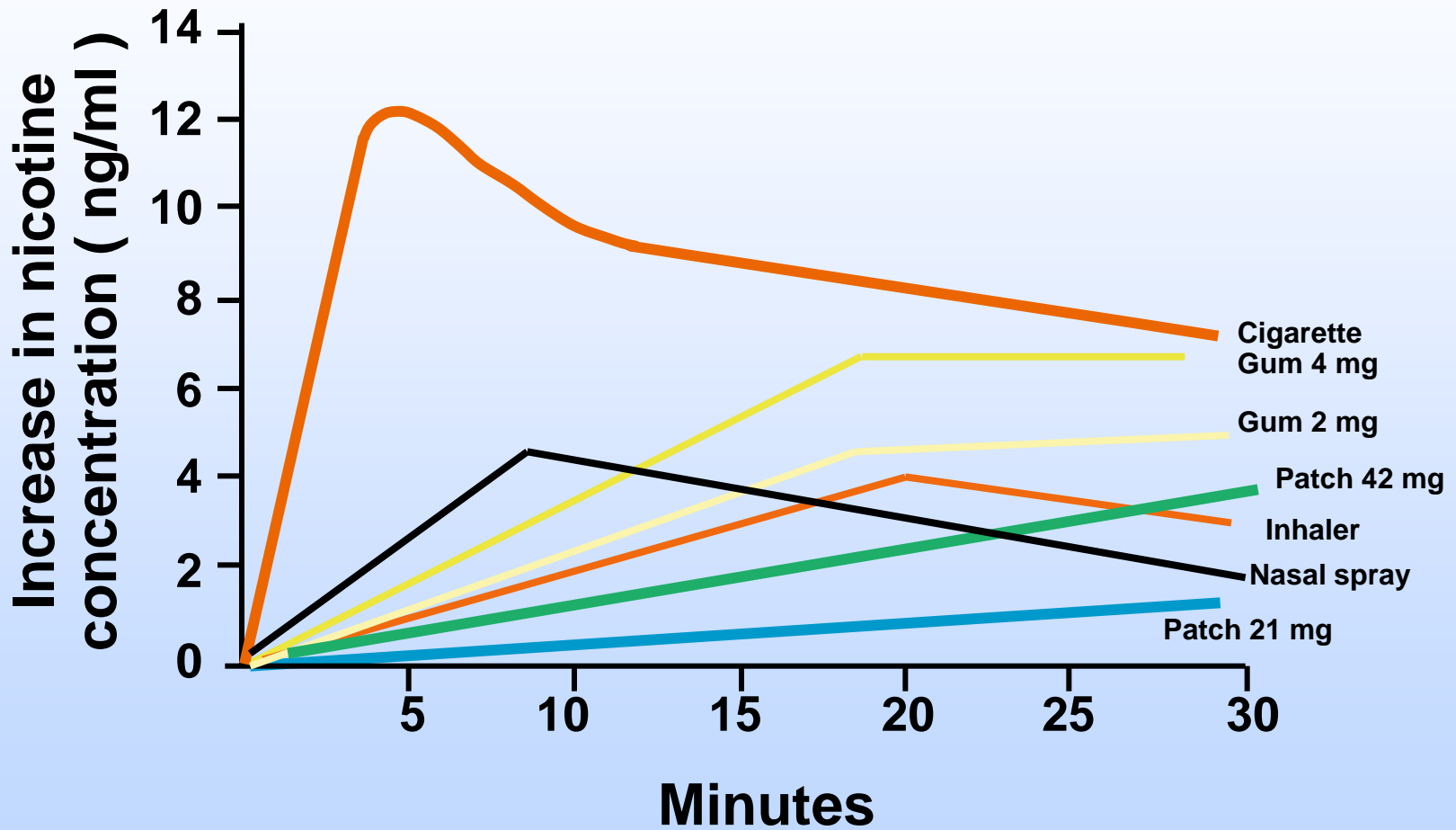


TIME

Immediate-release NRTs

- Nicotine gum, lozenge and inhaler
 - Buccal mucosal absorption
 - Affected by pH
 - Technique important with NG, NL
 - Peak absorption in 15-20 min.
- Nicotine nasal spray peak absorption in 5-10 min.

Smoking produces much higher nicotine levels and much more rapidly than NRT



Source: Balfour DJ & Fagerström KO. Pharmacol Ther 1996 72:51-81.

Nicotine Lozenge and Gum Dosing

- Based on time to first cigarette
 - < 30 minutes = 4 mg
 - > 30 minutes = 2 mg

Based on cpd

- >20 cpd = 4 mg
- ≤20 cpd = 2 mg

- Monotherapy:
 - 1-2 pieces every 1-2 hours
 - Minimum of 9 lozenge/day or 10-12 gum/day
 - Taper over 12 weeks (or as tolerated)
- Consider in Combination with other NRT
(Use 2 mg lozenge or gum)



Nicotine Nasal Spray

- 1 dose = 1 spray in each nostril
- Starting dose: 1 dose 1-2 times/hr, Up to 5 times/hr or 40 times/day
- Most average 14-15 doses/day initially
- Length of Rx: 12 weeks but can be shorter
- Can taper or stop abruptly, as tolerated



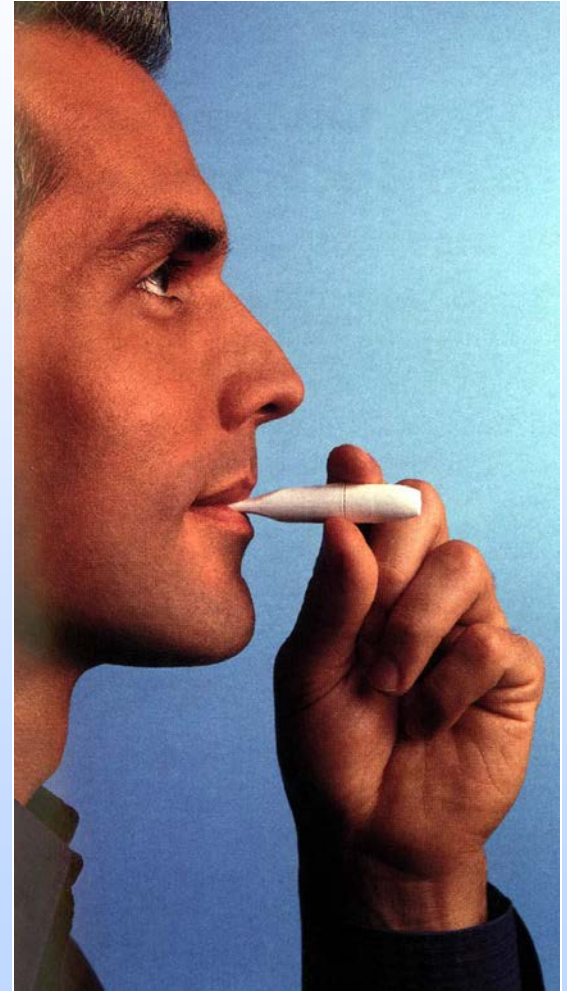
Nicotine Nasal Spray

- Side Effects -
 - moderate to severe nasal irritation (81-94%)
 - nasal congestion
 - transient change in sense of smell/taste
- Dependency profile between other NRT and cigarettes
- Contraindication - severe reactive airway disease

Nicotine “Inhaler”

Dose Instruction

- Puff on inhaler several times a minute
- Each cartridge will last about 30 minutes of active puffing
- 1 cartridge = as much nicotine as 2-3 cigarettes
- Monotherapy: At least 6 cartridges each day, up to 16/day
- Can be used alone or in combination with other NRT



Nicotine Inhaler: Side Effects

- local irritation throat/mouth (40%)
- coughing (32%)
- rhinitis (23%)

“puff” not “inhale”



Combination NRT Compared With Single Agent NRT

- Nicotine patch + short-acting NRT
 - Patch provides steady baseline
 - NG, NL NNS, NI respond to urges
- Withdrawal may be improved
- Overall abstinence rates at 6 mos. better
 - OR 1.35 (95% CI 1.11-1.63)*

*Cochrane Database of Systematic Reviews 2009

How to use Combination Rx

- Use NP at dose adjusted for CPD
- Assess patient preference for immediate-release NRT
- Use IR NRT scheduled or ad lib
 - Every 1-2 hours while awake
 - In response to urges to smoke
- Taper per individualized plan



Bupropion SR

Wellbutrin
Zyban



Bupropion SR prescribing

- Set target quit date 1 week from start of medication
- Begin with 150 mg daily for 3 days
- Increase to 150 mg twice daily at least 8 hrs apart
- Evening dose before 6PM
- Treat for 8-52 weeks

Common adverse events reported in 40 controlled clinical trials of bupropion SR

<u>AE</u>	<u>Mean %</u>	<u>Range</u>	<u>Studies</u>
Insomnia	32.3	(10 to 53)	25
Dry mouth	23.9	(6 to 62)	17
Headache	21.5	(6 to 56)	9
Anxiety	20.3	(10 to 31)	4
Nausea	19.8	(10 to 44)	5
Diarrhea	17.5	(6 to 50)	5

Serious adverse effect with bupropion SR

- Seizure rate about 1/1000 treated
 - 7/6409 subjects on active therapy in RCT's
 - Post marketing studies show seizures in people with known predisposition
 - Contraindications: known seizure (ever); structural brain abnormality; serious closed head injury

Bupropion: Seizure Screen

- Known seizure history: epilepsy, febrile seizure, withdrawal seizure
- Structural brain lesion: tumor, stroke, previous brain surgery
- Drugs that lower seizure threshold: phenothiazines, benzodiazepines, theophylline, ethanol
- Anorexia/Bulimia
- Significant head trauma: prolonged LOC, skull fracture, intracranial bleeding

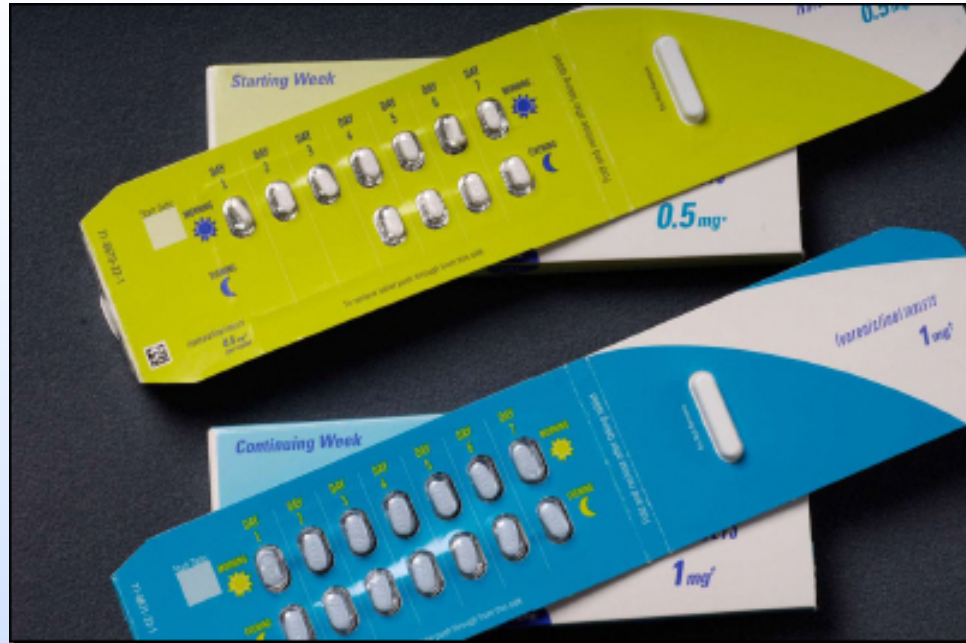


MAYO
CLINIC



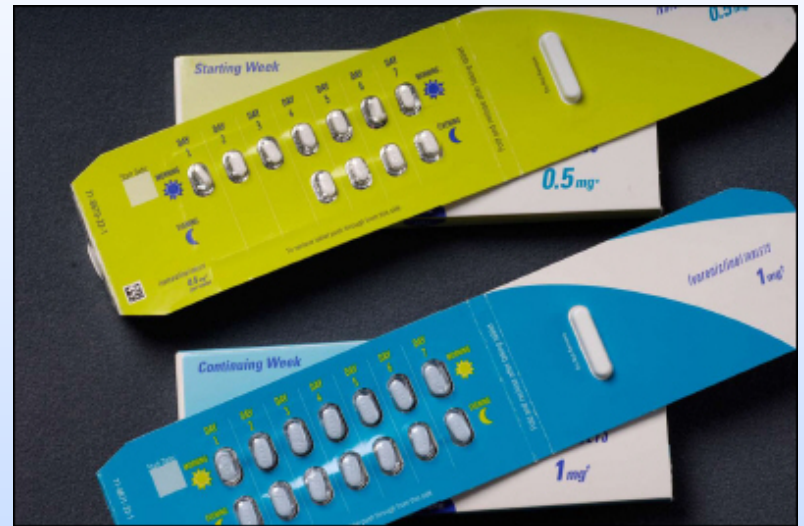
Varenicline

Chantix



Varenicline Dosing

- Taken with full glass of water after eating
- Start one week prior to Target Quit Date
 - Days 1-3: 0.5 mg once daily
 - Days 4-7: 0.5 mg twice a day (morning and evening)
 - Day 8 and for 11 weeks: 1.0 mg twice daily
- If abstinent at 12 weeks, continue twice daily for an additional 12 weeks



Common Adverse Events in Clinical Trials (%)

	Varenicline	Placebo
Nausea	35.8	11.2
Insomnia	22	12.7
Abnl dreams	14.4	5
Headache	16.8	14.3
Other GI	22.5	11.8
Discontinued	12	8.1

Conclusions

- **NRT**
 - Patch dosing matched to CPD is safe and effective
 - Combined NRT's are efficacious
 - Length of therapy guided by patient response (longer may be better)
 - Safe in smokers with CHD

Conclusions

- **Bupropion**
- Safe and effective in most populations at 300mg per day
- Increased efficacy combined with NP
- Can be safely combined with SSRI's
- Attenuates post-cessation weight gain

Conclusions

- **Varenicline**
- Varenicline is efficacious for the treatment of tobacco dependence
- Side effects have been generally mild and well-tolerated
- Trend in increased cessation with duration of use

E-Cigarette

A battery-powered device that provides inhaled doses of vaporized nicotine solution. It is used as an alternative to smoking tobacco product

“Vaping”





U.S. Food and Drug Administration
Protecting and Promoting *Your Health*



- E-cigarette cartridges labeled as “no nicotine”
 - Low levels of nicotine present in all cartridges tested, except one.
- 3 different E-cigarette cartridges with same label
 - Markedly different amount of nicotine with each puff
- One high-nicotine cartridge delivered 2 x as much nicotine as the nicotine inhaler



ENDS

- “E-cigarettes”- electronic nicotine delivery systems
- Deliver nicotine solution by heating and vaporizing for inhalation
- Safety concerns have been raised
- No evidence to support use as a treatment to help smokers stop smoking
- Legal status in the US– regulated as tobacco
 - FDA yet to reveal regulations

Case Study - “Karla”

- 42 year old divorced female
- Patient reports the following:
 - COPD-bronchitis
 - Type II diabetes
 - Seizure disorder
 - Hearing impaired
- Smoked for past 25 years, 2 1/2 ppd
- Reports several quit attempts
 - Hypnotized once and quit for 9 days
 - Longest abstinence was 3 weeks with patch
- Motivation: health concerns, role model for children, tired of the ‘control’ of the addiction

Case Study

“Travis”

- 52-year old divorced male
- Medical History
 - Chronic back pain
 - Migraine headaches
 - Arthritis
- 35 yr hx of smoking, 20 cpd
- In recovery from alcohol for past 3 months
- No “serious” quit attempts
- Wife and sponsor are both smokers

Case Study

“Colleen”

- 33-year old married female
- Patient reports following:
 - Recurring skin rash
- 15 yr hx of smoking, 20 cpd, but down to 10 cpd for past week
- Quit 6 years ago “cold turkey” for 10 months (pregnancy was motivation)
- Relapsed after birth of child
- Several serious quit attempts in the past 4 years – never abstinent for more than 1 day.

References

Treating Tobacco Dependence in a Medical Setting, Richard D. Hurt, Jon O. Ebbert, J. Taylor Hays, and David D. McFadden *CA Cancer J Clin* 2009; 59;314-326; *originally published online Aug 25 2009*

Treatment of Tobacco Dependence, Michael V. Burke, EDD; Jon O. Ebbert, MD, MSC; and J. Taylor Hays, MD
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