DRUG INTERACTIONS with SMOKING

PHARMACOKINETIC DRUG INTERACTIONS with SMOKING

Drugs that may have a *decreased effect* due to induction of CYP1A2:

- Bendamustine
- Caffeine
- Clozapine
- Erlotinib
- Fluvoxamine
- Haloperidol
- Olanzapine
- Riociguat
- Ropinirole
- Tacrine
- Tasimelteon
- Theophylline
- Irinotecan (clearance increased and systemic exposure decreased, due to increased glucuronidation of its active metabolite)

Drug that might have an *increased effect* and efficacy due to induction of CYP1A2: Clopidogrel

Smoking cessation will reverse these effects.

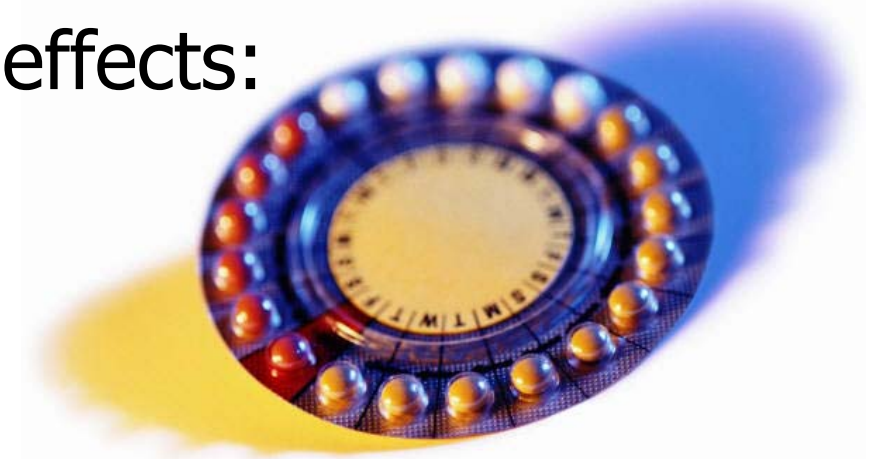
DRUG INTERACTION: TOBACCO SMOKE and CAFFEINE

- Constituents in tobacco smoke induce CYP1A2 enzymes, which metabolize caffeine
  - Caffeine levels increase ~56% upon quitting
- Nicotine withdrawal effects might be enhanced by increased caffeine levels
- Decrease caffeine intake by 50% when quitting; no caffeine after 1PM for individuals with a typical bedtime

PHARMACODYNAMIC DRUG INTERACTIONS with SMOKING

Smokers who use combined hormonal contraceptives have an increased risk of serious cardiovascular adverse effects:

- Stroke
- Myocardial infarction
- Thromboembolism



This interaction **does not** decrease the efficacy of hormonal contraceptives.

Women who are 35 years of age or older AND smoke at least 15 cigarettes per day are at significantly elevated risk.

DRUG INTERACTIONS WITH TOBACCO SMOKE

Many interactions between tobacco smoke and medications have been identified. Note that in most cases it is the tobacco smoke—not the nicotine—that causes these drug interactions. Tobacco smoke interacts with medications through pharmacokinetic (PK) and pharmacodynamic (PD) mechanisms. PK interactions affect the absorption, distribution, metabolism, or elimination of other drugs, potentially causing an altered pharmacologic response. The majority of PK interactions with smoking are the result of induction of hepatic cytochrome P450 enzymes (primarily CYP1A2). Smokers may require higher doses of medications that are CYP1A2 substrates. Upon cessation, dose reductions might be needed. PD interactions alter the expected response or actions of other drugs. The amount of tobacco smoking needed to have an effect has not been established, and the assumption is that any smoker is susceptible to the same degree of interaction. **The most clinically significant interactions are depicted in the shaded rows.**

DRUG/CLASS	MECHANISM OF INTERACTION AND EFFECTS
Pharmacokinetic Interactions	
Alprazolam (Xanax®)	▪ Conflicting data on significance, but possible ↓ plasma concentrations (up to 50%); ↓ half-life (35%).
Bendamustine (Treanda®)	▪ Metabolized by CYP1A2. Manufacturer recommends using with caution in smokers due to likely ↓ bendamustine concentrations, with ↑ concentrations of its two active metabolites.
Caffeine	▪ ↑ Metabolism (induction of CYP1A2); ↑ clearance (56%). Caffeine levels likely ↑ after cessation.
Chlorpromazine (Thorazine®)	▪ ↓ Area under the curve (AUC) (by 36%) and serum concentrations (by 24%). ▪ ↓ Sedation and hypotension possible in smokers; smokers may require ↑ dosages.
Clopidogrel (Plavix®)	▪ ↑ Metabolism (induction of CYP1A2) of clopidogrel to its active metabolite. ▪ Clopidogrel's effects are enhanced in smokers (≥10 cigarettes/day): significant ↑ platelet inhibition, ↓ platelet aggregation; while improved clinical outcomes have been shown, may also ↑ risk of bleeding.
Clozapine (Clozaril®)	▪ ↑ Metabolism (induction of CYP1A2); ↓ plasma concentrations (by 18%). ▪ ↑ Levels upon cessation may occur; closely monitor drug levels and reduce dose as required to avoid toxicity.
Erlotinib (Tarceva®)	▪ ↑ Clearance (24%); ↓ trough serum concentrations (2-fold).

DRUG INTERACTIONS with SMOKING: SUMMARY

Clinicians should be aware of their patients' smoking status:

- Clinically significant interactions result the combustion products of tobacco smoke, not from nicotine.
- Constituents in tobacco smoke (e.g., polycyclic aromatic hydrocarbons; PAHs) may enhance the metabolism of other drugs, resulting in an altered pharmacologic response.
- Changes in smoking status might alter the clinical response to the treatment of a wide variety of conditions.
- Drug interactions with smoking should be considered when patients start smoking, quit smoking, or markedly alter their levels of smoking.

METHODS for QUITTING

- Nonpharmacologic
  - Counseling and other non-drug approaches

WISCONSIN TOBACCO QuitLine 800-QUIT-NOW

- Pharmacologic
  - FDA-approved medications

Counseling and medications are both effective, but the combination of counseling and medication is more effective than either alone.

Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline.* Rockville, MD: USDHHS, PHS, May 2008.

PHARMACOTHERAPY: Use in SPECIAL POPULATIONS

Pharmacotherapy is **not** recommended for:

- Pregnant smokers
  - Insufficient evidence of effectiveness
- Smokeless tobacco users
  - No FDA indication for smokeless tobacco cessation
    - Study by Fagerstrom (2010; BMJ 2010; 341:c6549) using varenicline showed favorable results
- Individuals smoking fewer than 10 cigarettes per day
- Adolescents
  - Nonprescription sales of NRT products (i.e., patch, gum, lozenge) are restricted to adults ≥18 years of age
  - NRT use in minors requires a prescription

Recommended treatment is behavioral counseling.

NONPHARMACOLOGIC METHODS

- Cold turkey: Just do it!
- Unassisted tapering (fading)
  - Reduced frequency of use
  - Lower nicotine cigarettes
  - Special filters or holders
- Assisted tapering
  - QuitKey (PICS, Inc.)
    - Computer developed taper based on patient's smoking level
    - Includes telephone counseling support

Sad fact: A 2017 study found that when one quit method was used, smokers used 1) cold turkey, 2) assisted taper, 3) e-cigs and then 4) FDA approved products to help them quit.

SCHEDULED GRADUAL REDUCTION of SMOKING

- Gradual reduction of the total number of cigarettes smoked per day
- Computerized unit facilitates reduction:
  - QuitKey
    - Tapering curve developed based on patient's smoking level
    - 19–24% abstinent at 1 year
    - Includes telephone counseling support

Who is a candidate for scheduled gradual reduction?

- Anyone who wants to quit smoking
- Particularly useful in persons for whom medications might not be a first-line choice, such as pregnant women or teens
- Spit tobacco users (18.4% abstinent after 1 year)

Ordering information

www.quitkey.com or 1-800-543-3744
($37.19 on Amazon)

Stage 1 (7 days)
- Push the SMOKE button every time you smoke, to record smoking habits

Stage 2 (14–34 days)
- Smoke only when you hear the tone or see the SMOKE SIGNAL; tapers smoking over time
- Press the SMOKE button every time you smoke

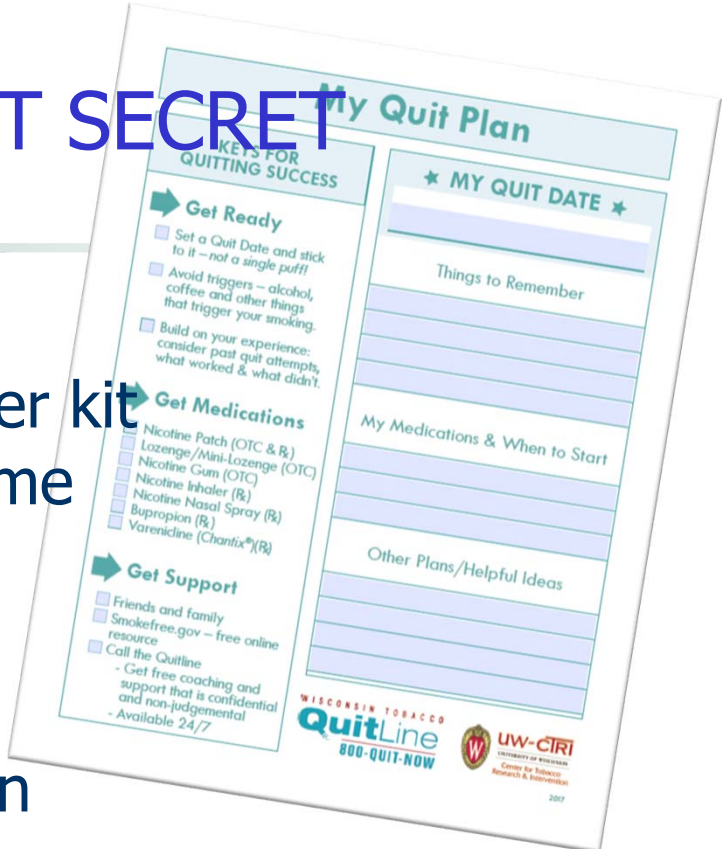
NONPHARMACOLOGIC METHODS (cont'd)

- Formal cessation and behavioral counseling programs
  - Self-help programs
  - Individual counseling
  - Group programs
  - Telephone counseling
    - 1-800-QUITNOW
    - (1-800-784-8669)
  - Web-based counseling
    - www.smokefree.gov
    - www.quitnet.com
    - www.becomeanex.org

- Acupuncture therapy
- Hypnotherapy
- Lasers
- Massage therapy

- Behavioral programs have evidence of their effectiveness which is enhanced further when pharmacologic agents are also used.
- Alternatives, such as acupuncture and hypnotherapy, lack supporting evidence.
- Massage therapy may be useful as adjunct therapy to alleviate cravings and anxiety.

QUITLINES: A WELL-KEPT SECRET



- Free cessation services, including counseling, self-help kits, 2-week starter kit of patch, gum or lozenge mailed to home (1 per 12 mo), and cessation information

- Success rates double for those using a quitline, compared with quitting on own

- 1) Identify triggers: re-learn daily routines;
  2) Recognize how powerful nicotine addiction is; and
  3) Engage social support