

February - March 1979

Clinical Implications of Surgeon General's Report on Smoking and Health

The recently released Surgeon General's Report on Smoking and Health has important implications for physicians' routine diagnostic and prescribing practices.

The report contains an unprecedented compilation of information on the effects of smoking on health. One of its conclusions is that the widely recognized smoking-related medical problems, such as lung cancer, other respiratory problems, and cardiovascular disease, represent only some of the medical issues health professionals need to consider.

The report brings to attention four other important areas related to smoking:

1. **Prescribing practices:** Smokers may experience altered therapeutic effects from some drugs, and the toxicity of drugs may be affected by smoking habits. The report notes several drugs for which smokers require higher doses or more frequent doses than nonsmokers.

2. **Use of diagnostic tests:** There may be significant differences in normal values for smokers and nonsmokers in various routine biochemical clinical tests.

3. **Treating and preventing nutritional deficiencies:** Smoking alters the absorption and metabolism of important macronutrients and micronutrients, such as protein and vitamins—with clear implications for nutritional management of smokers, especially pregnant women.

4. **Smoking and estrogen use:** Smokers who take oral contraceptives have an increased risk of myocardial infarction.

The following discussion on smoking interactions with drug therapy, diagnostic tests, and nutrition summarizes one major section in the Surgeon General's Report. Complete scientific literature citations are available in the full text of the Report (which can be purchased from the Government Printing Office).

Prescribing Practices

Smoking has significant implications for the drug therapy of a wide variety of conditions.

- For certain drugs, smokers need different doses or a different frequency of administration than nonsmokers.

- When patients stop or reduce cigarette consumption, their drug regimen may need adjustment.

- Doctors should expect smokers sometimes to have more numerous adverse reactions and sometimes fewer, or even to have different reactions to certain drugs than nonsmoking patients.

Mechanisms of Tobacco-Drug Interaction

The dominant effect of smoking on drug pharmacology is the ability of nicotine and other tobacco constituents to enhance drug disposition by inducing microsomal enzyme systems responsible for the metabolism of many drugs and chemicals.¹ The clinical effects of inducing these systems in smokers can include accelerated rates of drug disposition, decreased intensity,

and duration of effect, and therefore, decreased therapeutic efficacy of drugs.

Two drugs for which the metabolic interaction with smoking can be a critical factor in a patient's therapy are theophylline and pentazocine. Theophylline is an important bronchodilator for treating acute and chronic asthma or bronchitis. This drug has a narrow therapeutic index, and smokers on the average are reported to need one and one-half to two times as much of the drug as nonsmokers to achieve the same effects—either through larger doses or more frequent administration.² The half-life of theophylline is reduced to about 4 hours in smokers, from about 7 hours in nonsmokers.

Hunt et al. have also reported that in patients using theophylline who stopped smoking, it took more than 3 months for the effects of chronic tobacco use on theophylline disposition to dissipate.³ Therefore, close monitoring for altered dosage needs of theophylline is required in patients who make any changes in their smoking habits.

Another significant factor in considering theophylline-tobacco metabolic interactions is the frequency of adverse reactions with the drug. Smokers frequently experience reduced toxicity from theophylline apparently because of the increased biotransformation rate, and the frequency of adverse reactions correlates negatively with the smoking habit.⁴ However, the large maintenance doses heavy smokers require in comparison to nonsmokers could put them in jeopardy of toxicity if they discontinue smoking without adjusting their dosage regimen.

In a study of pentazocine dosage requirements for supplementing nitrous oxide general anesthesia, investigators found that smokers needed larger priming and maintenance doses, up to 50 percent higher than nonsmokers.⁵ Other research has confirmed that smokers metabolize 40 percent more pentazocine than nonsmokers—therefore, often necessitating larger and more frequent doses for analgesia.⁶

Other examples of drug-tobacco pharmacokinetic interactions are less dramatic than theophylline and pentazocine but appear with widely used drug classes—tranquillizers, analgesics, and antidepressants.

The following tables on interactions between smoking and drugs summarize clinical pharmacological data in humans and clinical observational studies from the Boston Collaborative Drug Surveillance Program.^{7,8}

Table 1. Interactions between Smoking and Drugs in which Biotransformation Is Not Affected by Smoking

Meperidine	Ethanol
Phenytoin	Chlordiazepoxide
Nortriptyline	Phenobarbital
Warfarin	