

# RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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## Smoking, smoking cessation and medications

Tobacco smoking, and cessation of tobacco smoking, is known to affect the handling of various medications. However the significance of the effect smoking can have on medications may not always be considered in clinical practice. As many hospitals and health services (including RGH) work towards becoming smoke-free environments it is timely to highlight potential interactions involving smoking, smoking cessation and medications.

Pharmacodynamic interactions alter the expected response or actions of other drugs. In the case of tobacco smoke, these interactions are largely due to nicotine. Pharmacodynamic interactions with medications and smoking include:

- Combined hormonal contraceptives - risk of cardiovascular disease is increased for women who smoke
- Inhaled corticosteroids - cigarette smoking in asthma is associated with a reduced sensitivity to corticosteroids
- Beta blockers - nicotine stimulation of the sympathetic nervous system may counteract the effects of these drugs

Pharmacokinetic interactions are those that affect the absorption, distribution, metabolism, or elimination of other drugs, potentially causing an altered pharmacologic response. Polycyclic aromatic hydrocarbons (PAHs) are products of incomplete combustion of organic matter, and are some of the major lung carcinogens found in tobacco smoke. Induction of hepatic cytochrome P450 isoenzymes (primarily CYP1A2) caused by PAHs is responsible for the majority of pharmacokinetic drug interactions associated with tobacco smoking.

Induction of CYP1A2 enzymes can increase metabolism of the many drugs that are CYP1A2 substrates, causing a decrease in pharmacological effect and potentially resulting in a requirement for higher doses of these drugs in smokers. Smoking cessation can conversely result in increased drug effects and necessitate a reduction in drug dose as the decrease in CYP1A2 activity occurs. Research suggests that this may begin immediately on cessation of smoking and can occur over approximately one week, however full normalisation of hepatic function may take much longer. The most significant interactions will be with drugs extensively metabolised by CYP1A2 and with a narrow therapeutic index. Studies have demonstrated the following effects of smoking on CYP1A2 substrates:

- Theophylline clearance up by 58-100% in smokers; within 7 days of smoking cessation clearance falls by 35%
- Clozapine - plasma concentrations 18% lower amongst smokers
- Olanzapine - clearance increased by 98% and serum concentrations 12% lower in smokers

General principles to consider:

- Always obtain a history of the patient's smoking status
- Monitor smoking and advise patients to seek advice from a health professional if smoking status is to change
- Assess clinical significance potential interactions, monitor efficacy and side effects and adjust dose if necessary
- As smokers often make multiple quit attempts, it is important to educate patients regarding the potential impact that variations in smoking can have on medication effects

There are many other potential drug-smoking interactions. For more information refer to: Zevin S, Benowitz NL. Drug interactions with tobacco smoking. *Clinical Pharmacokinetics*. 1999;36(6):425-438 and Kroon LA. Drug interactions with smoking. *American Journal of Health-System Pharmacy*. 2007;64(18):1917-1921

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