Pharm-10A3 Discuss the adverse effects that may occur with the administration of desflurane.

Background

Desflurane is a fluorinated volatile often used in the maintenance of general anaesthesia

Adverse effect is an unwanted effect from drug administration

Adverse effects

CVS
- Dose dependent ↓SVR (via smooth muscle Ca^{2+} channel blockade → vasodilatation)
- Reflex tachycardia → ↑metabolic demand and ↓coronary filling time in diastole → ↑risk of myocardial ischaemia
- Overall slight ↓MAP may cause organ hypoperfusion and ischaemia (e.g. ↓GFR ± AKI)

Specific to desflurane – high F\textsubscript{1} may stimulate SNS (usually FGF × %F\textsubscript{1} > 24) → tachycardia, hypertension + RAAS activation

RESP
- ↓TV + ↑RR → overall slight ↓MV
- Blunt chemoreceptor response to hypoxia and hypercapnia → risk of hypoxia and hypercapnia (together with above)

Specific to desflurane – pungent smell and airway irritant → may cause breath-holding + bronchoconstriction/bronchospasm (esp. smokers) → not commonly used in gaseous induction
May also trigger laryngospasm
Unlike other volatile agents, which often ↓airway resistance/bronchodilate → desflurane may ↑airway resistance

CNS
- vasodilate cerebral vessels (MAC > 1) → ↑CBF → ↑ICP → limited use in neurosurgery
- high doses → uncouple cerebral oxygen supply/demand balance
- high doses → EEG burst suppression

GIT
- can cause PONV
- can cause fulminant autoimmune hepatitis (much less common that halothane as relatively less hepatic metabolism)

MSK
- can trigger malignant hyperthermia
**GUT**
- ↓ uterine tone $\rightarrow$ ↑ risk of postpartum haemorrhage

**CIRCUIT**
- carbon monoxide formation esp. with dry soda lime (common to all fluoromethyl ethers), worse with low flow anaesthesia
**Examiner’s comments** (44% pass rate)

This question was poorly answered by the majority of candidates. Better answers discussed adverse effects by system or divided their response in to those effects peculiar to desflurane and those common to many volatile agents. Even better answers compared some adverse effects to other volatile agents. No marks were awarded for details which were clearly unrelated to the answer such as chemical structure and physical characteristics.

The following material needed to be covered for a clear pass.

- Desflurane is a volatile agent used mainly for the maintenance of general anaesthesia. An adverse effect is an unwanted side effect of a drug.
- Desflurane reduces systemic vascular resistance and thus mean arterial pressure in a dose dependent manner, however cardiac output is usually well-maintained by an increase in heart rate.
- Sudden increases in the inspired concentration can cause a marked sympathetic response with tachycardia, hypertension and activation of the renin-angiotensin system.
- Cerebral blood flow increases above 1.0 MAC but the rise in ICP is quite small (about 7mmHg). At higher doses there is uncoupling of oxygen supply and demand. It is not known to trigger seizure activity.
- There is a dose-dependent reduction in tidal volume and increase in respiratory rate (overall decrease minute ventilation) and an impaired response to hypoxia and hypercarbia. Desflurane is pungent and can cause coughing and breath-holding so it is infrequently used for inhalational induction.
- It can increase airways resistance (especially in smokers).
- It can cause a fulminant antibody-mediated hepatitis (like halothane) through neoantigen formation from metabolites, but this is very rare – probably due to the very low rate of metabolism.
- It reduces uterine tone (potentially worsening postpartum haemorrhage).
- It is a trigger for malignant hyperthermia.
- It can interact with carbon dioxide absorbants to produce toxic levels of carbon monoxide (especially with high temperatures and low flows over dessicated Baralyme).