Pharmacological Agents Affecting Emesis
A Review (Part I) *

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* A complete reference list will appear in Part II of this article in the next issue of the Journal.
Summary

The availability of radiolabelled ligands selective for various putative neurotransmitter receptor sites and the development of quantitative autoradiography has led to a greater understanding of the neuronal pathway and receptor subtypes involved in the vomiting reflex induced by various mechanisms both within the central nervous system and the periphery. Receptors for acetylcholine, dopamine, histamine and serotonin have been detected in a number of brain regions associated with the vomiting reflex, and provide a rational basis for the antiemetic action of drugs that inhibit receptor subtypes for these neurotransmitters. The basis of the antiemetic action of other drugs such as dexamethasone and the cannabinoids is still obscure.

Some drugs act on more than one receptor subtype. Metoclopramide may inhibit both dopamine D2- and 5-HT3 receptors in producing its antiemetic effect. Both metoclopramide and domperidone appear to have additional peripheral actions that contribute to their effectiveness. The cannabinoids are effective in cytotoxic-induced vomiting, perhaps acting via endorphin receptors or by inhibiting prostaglandin synthesis. The effectiveness of 5-HT3 receptor antagonists may depend on the block of both central and peripheral neuronal 5-HT3 receptors.

Vomiting constitutes a major disadvantage to the use of many drugs; vomiting induced by aminoglycoside antibiotics appears to be due to ototoxicity and is relieved by histamine H1-receptor antagonists. The protracted vomiting associated with the use of some cytotoxics in cancer chemotherapy may involve psychic components, the chemoreceptor trigger zone and peripheral sensory neurons. Both 5-HT3 and dopamine D2-receptor antagonists exert some control, the former being more effective with cytotoxics of high emetogenic potential, such as cisplatin. Serotonin 5-HT3 receptor antagonists or high doses of metoclopramide in combination with anxiolytics and steroids as well as greater attention to pharmacokinetic profiles of the drugs involved would appear to offer improved control.

The use of dopamine receptor antagonists in controlling emesis induced by dopamine agonists used in Parkinson's disease poses theoretical problems which can be overcome by using drugs with selectivity for the chemoreceptor trigger zone, such as domperidone or metoclopramide. However, higher doses of these drugs may produce some impairment of therapeutic responses to the agonists.

Muscarinic and nicotinic agonists currently under investigation in Alzheimer's disease pose another therapeutic dilemma as emesis is due to a central action of these compounds. Several sites may be involved including the chemoreceptor trigger zone and frontal lobes. Opiates may act through dopamine receptors or μ-receptors on dopaminergic nerves, but serotonergic mechanisms may also be involved in the action of some opiates.

Part II of this article discusses treatment of migraine, morning sickness, motion sickness, postoperative vomiting, radiation-induced emesis and nausea from labyrinthine disorders.

The question of why vomiting occurs is of considerable clinical importance given the distress associated with prolonged vomiting and the wide range of conditions and drugs that can induce the effect.

A protective reflex against the ingestion of various toxins could be proposed for the vomiting following gastric irritation, but the presence of such a reflex is not essential for life.

The evolutionary basis for the vomiting reflex induced by pregnancy or certain types of motion is still obscure. In the case of motion sickness, Triesman (1977) proposed that certain stimuli may induce conflicting information in several sense organs concerned with detecting motion. The resulting sensory conflict may elicit a similar pattern of central stimulation to that obtained following ingestion of a neurotoxin; vomiting then occurs due to the false perception that a neurotoxin is involved.