Motion sickness can occur when the sensory inputs about body position contradict what is expected. It can be provoked by abrupt changes in movement, such as occur during bumpy rides, turbulent flights, and rough seas. It can also occur when one is exposed to moving visual scenes while the body is in a relatively fixed state.

Early signs of motion sickness include pallor, restlessness, and cold sweat. In later stages, nausea, excessive salivating, and vomiting occur.1 The degree of symptoms that result from an acute exposure to provocative stimuli vary with the intensity of the stimulus and one’s susceptibility to this condition.

About one-third of the population is highly susceptible to motion sickness, one-third experience it in fairly rough conditions, and another third become sick only in extreme conditions.1 Selected groups seem particularly susceptible, including children aged 3 to 12 years,2 people who experience migraine headaches,3 and women, particularly during menstruation and pregnancy.3,4

This article provides an overview of the theories regarding the etiology of motion sickness and reviews currently available preventative treatments, including non-pharmacological remedies, over-the-counter products, and prescriptive-strength medications.

Etiology of Motion Sickness

The precise etiology of motion sickness remains a mystery. The classic “sensory conflict” explanation, posed by Reason and Brand and supported by subsequent studies, suggests motion sickness is triggered when the brain interprets sensory messages regarding movement as inharmonious.5 These messages are delivered by the parts of the body that detect motion, including the vestibular receptors, the eyes, and proprioceptors in the skin, muscles, and other tissues. Sometimes the incoming signals from these sensory sites conflict with each other; other times these signals conflict with the brain’s “positional memory.”6

The traditional sensory conflict theory does not explain motion sickness produced by all conditions. Additional sensory inputs other than those traditionally thought to trigger motion sickness may play some role. Mittelstaedt and others, for instance, recently introduced evidence suggesting inputs from visceral graviceptors may contribute to how the body determines its position.7,8 Another theory for some cases of motion sickness is the postural instability theory, based on experiments in which motion sickness was preceded by statistically significant increase in postural sway. In these cases, motion sickness symptoms were not linked to sensory conflict, but rather to a decreased ability to actively control the body’s postural motion.9,10

Motion Sickness Prophylaxis

A variety of antimotion sickness treatments is available which can protect most people if taken 1 to 2 hours prior to exposure and in sufficient dosage.11

Many non-pharmacologic remedies currently available for motion sickness are not supported by conclusive scientific evidence of efficacy. Several studies have been conducted to determine whether an association exists between cabin location and the likelihood of developing seasickness. Reviews of troops on Military Sea Transport Service ships, US Navy escort vessels, and a study of 260 passengers on an expedition ship traversing the Drake Passage during rough sea conditions documented no association between the risk of motion sickness and the location of the passenger cabin.12,13

Ingesting large amounts of ginger has long been touted as a cure by the general public; however, controlled clinical studies do not consistently document this benefit. One study compared seven commonly used agents...
for the prophylaxis of seasickness on 1,741 cruise passenger volunteers on a whale safari in Norway and concluded that ginger was as potent an agent as the others tested.\textsuperscript{14} Conflicting results were reported in a controlled clinical study.\textsuperscript{15}

Using acupressure to activate the P6 pressure point above the wrist has been shown to effectively combat nausea and vomiting associated with chemotherapy, pregnancy, and surgery\textsuperscript{16}; however, consistent results have not been documented for motion sickness. Acupressure bands worn around the wrist to apply pressure to the P6 point showed no benefit for combating motion sickness.\textsuperscript{17,18}

Some preliminary evidence suggests that electrically stimulating this point may provide some benefit. Testing 16 Chinese and 45 American subjects, Hu and colleagues found that the severity of motion sickness symptoms and gastric myoelectric activity could be reduced by placing cutaneous electrodes over the P6 point.\textsuperscript{19} In another study, involving nine healthy volunteers on a boat in open seas, Bertollucci and colleagues noted that a portable wristwatch size device that electrically stimulates the P6 point suppressed motion sickness symptoms.\textsuperscript{20} Continued research on this seems warranted for treating mild cases of motion sickness, although the cost of this treatment could be a drawback for many candidates.

Psychological therapies have also been investigated. Biofeedback does little to reduce symptoms or to increase tolerance to motion.\textsuperscript{21} Cognitive behavioral training can help to build some tolerance to provocative motion stimuli and to reduce the need for antimotion medications, but the process is quite time-consuming and thus impractical for most people.\textsuperscript{22}

One interesting study reported a significant decrease in vomiting episodes among 201 children, reportedly prone to motion sickness, when they wore prism glasses that had been prescribed to improve their mechanical reading skills. These glasses are typically worn by children with learning disabilities or Meniere’s disease. The prism glasses are thought to decrease discrepancy between visual and vestibular cues and thus to reduce the negative effects of vertigo.\textsuperscript{23} Again, further study on their usefulness in treating motion sickness seems warranted.

**Pharmacologic Treatments**

Two classes of drugs are known to be effective against motion sickness: those that are central cholinergic blockers and those that enhance dopamine-norepinephrine activity. These drugs act on various sites, including the vestibular receptors and nuclei, the cerebellum, the reticular area, and the vomiting center. All antimotion medications are also effective antiemetic agents.\textsuperscript{1}

Researchers at the Naval Aerospace Medical Institute in Florida offer the following theory of how these agents work\textsuperscript{24}: the central nervous system reacts to provocative motion stimuli and, in turn, vestibular impulses are transmitted to the vestibular nuclei, the cerebellum, and the brain stem reticular areas. In the vestibular nuclei and the reticular areas, neurons that are responsive to noradrenaline intermingle with those responsive to acetylcholine. These two neural populations appear to compete against each other. Those mediated by acetylcholine increase activity with vestibular stimulation and release a "neurotransmitter signal" which activates the vomiting center. Neurons responding to the noradrenaline promote stabilization, which staves off motion sickness. Some of the effective drugs block acetylcholine whereas others activate noradrenaline. The balance between these two neuron groups could be influenced by medications and would govern a person’s susceptibility to motion sickness. The proper use of motion sickness drugs, then, could ensure that the balance remains favorable for the patient.

Cholinergic blockers include scopolamine, atropine, dimenhydrinate, cyclizine, meclizine, and promethazine.\textsuperscript{11} The effective sympathomimetics include d-amphetamine, methamphetamine, phenmetrazine, and methylphenidate.\textsuperscript{25}

These drugs are available in a variety of forms including oral, intramuscular, and suppositories. Drugs taken orally must be taken in a sufficient dosage at least an hour in advance to be effective; otherwise, they must be administered intramuscularly in most cases if motion sickness symptoms have already surfaced.\textsuperscript{11}

**Over-the-Counter Medicines**

Over-the-counter remedies are less effective than prescription-strength medications, but provide a lesser degree of side effects and long duration of 6 to 12 hours.\textsuperscript{26} These must be taken at least an hour before exposure to be effective, since gastric motility decreases following the onset of motion sickness.\textsuperscript{11} These can be useful for travelers who experience mild to moderate cases of motion sickness. Most of these medications are antihistamines, and their initial use stemmed from reports that people being treated for allergies also experienced fewer problems with motion sickness. Although it is unclear precisely how they work to suppress motion sickness symptoms, their anticholinergic properties appear to be the important element.\textsuperscript{28}

Anecdotal reports indicate large individual differences in the effectiveness of antihistamines as antimotion sickness drugs. Dimenhydrinate (Dramamine) appears to be the most effective. The usual adult dosage is 50 mg, which typically produces some drowsiness and minor dizziness.\textsuperscript{11} It is not recommended when driving or working around machinery, but can be a good choice for long exposure to mild-to-moderate motion.\textsuperscript{23}
Scopolamine is the single most effective antimotion sickness drug, consistently providing more protection than any other single medication in clinical trials. It is particularly useful for intense motion or for patients who are very susceptible to motion sickness.

Scopolamine is a belladonna alkaloid that acts like atropine. Like the other anticholinergics, this drug acts on the muscarinic receptors, and in this case, blocks all five subtypes. It is also effective in humans at a dosage that does not produce sedation, indicating that its actions may be specific within the vestibular nuclei. The mechanism of action is thought to be associated with inhibition of vestibular input into the central nervous system (CNS), which thus inhibits the vomiting reflex. It may also directly act on the vomiting center in the reticular formation of the brainstem.

Scopolamine has been shown to be effective in all the classic cases of motion sickness, involving car, air, train, and sea travel, as well as exposure to virtual reality systems. It is currently available for prescription in two forms: a transdermal patch and a low dose tablet. Each dosage form has its respective benefits and disadvantages which warrant consideration when evaluating the needs of any particular patient.

The scopolamine patch is attached to the skin behind the ear in a hairless area and delivers 0.5 mg of scopolamine at a fairly consistent rate over 3 days. This makes the patch useful for long exposures to motion sickness, such as a prolonged sea voyage since the patient need not remember to take the shorter-acting tablets.

The patch must be applied well in advance, however, since an effective drug concentration is not achieved until 6 to 8 hours after application. This delay can be reduced to an hour or less by simultaneously administering a single dose of oral or buccal scopolamine.

Large variations in urinary excretion rates of the drug from patch-wearers, in absorption of scopolamine through the skin, and in symptom alleviation efficacy have been reported. Variable absorption and possible underdosage of large patients may have contributed to the report that topical scopolamine is effective in only 50 to 74% of users. Also, due to the fixed dosage, the patch may not be suitable for children or other small patients.

Common side effects of topical scopolamine include dry mouth (affecting about two-thirds of people) and drowsiness (affecting less than one-third). Other possible side effects of topical scopolamine include blurred vision, sore throat, confusion, disorientation, memory loss, and restlessness.

Low dose scopolamine tablets are also available in the United States. These are formulated with 0.4 mg of scopolamine per tablet, and the prescribed dosage is 1 to 2 tablets every 8 hours as needed. Although scopolamine in tablet form is readily absorbed from the GI tract, it must be taken 1 hour before exposure to motion to reach an effective concentration. The dosing flexibility provided by the tablet makes this form well suited to shorter outings such as day fishing, car rides, or plane trips.

The oral route offers certain advantages over the scopolamine topical patch. In a study conducted for the National Aeronautics and Space Administration, oral scopolamine was twice as effective as the topical form in preventing motion sickness symptoms. Another study showed that motion-induced symptoms decreased 75% with oral scopolamine compared with 63% with the patch variety. This may be due to greater consistency in dosage with the oral delivery system.

Another advantage of tablet form is cost. One dose of scopolamine tablet costs less than 10% of the cost of the patch.

Like the patch, the standard dosage of oral scopolamine also produces some dry mouth and drowsiness. However, as documented in a double-blind, placebo-controlled study involving 12 male volunteers aged 19 to 38, performance side effects occurred less frequently with the oral form. These include decrements in tasks involving continuous attention or performance, memorizing new information, and self-rated feelings of alertness and sociability. Again, this may be due to the dosing flexibility of the tablet formulation, meaning practitioners can prescribe the lowest dosage needed to achieve the needed travel comfort.

Although some drowsiness may be a welcome side effect for travelers who are not operating a vehicle or equipment, this and other performance side effects of scopolamine can be eliminated by adding 5
to 10 mg of the sympathomimetic medication d-amphetamine (Dexedrine). The drowsiness produced by scopolamine and the excitement produced by d-amphetamine effectively cancel each other. This combination also produces the fastest rate of habituation in motion sickness, but also leads to increased dry mouth symptoms.

**d-Amphetamine and ephedrine.** Because the sympathomimetics, such as d-amphetamine and ephedrine, increase the release of norepinephrine into the CNS, they appear to counter the increased activity of acetylcholine-sensitive neurons stimulated by vestibular activation. d-Amphetamine has been shown to protect against motion sickness when used alone and to act synergistically when combined with scopolamine or promethazine. It reduces the sleepiness and performance decrement produced by scopolamine. The routine use of this controlled drug is unjustified, however, considering its addiction potential.

Ephedrine, which is not a controlled drug, could be used instead, although in combination with the anticholinergics, it is much less effective than d-amphetamine and its usefulness is questionable based on available laboratory studies.

**Promethazine.** In the typical 25 mg oral dose, promethazine (Phenergan), which is an antihistamine, is slightly less effective than 0.6 mg scopolamine at preventing motion sickness. Promethazine is also the only phenothiazine that is effective against motion sickness, perhaps because it reportedly has the strongest central anticholinergic action among this class of drugs.

The onset of effectiveness occurs at 2 hours and its duration ranges from reported 6 hours to as long as 18 hours. Side effects include significant drowsiness, but less dry mouth and dizziness than occurs with scopolamine. Like scopolamine, adding d-amphetamine or ephedrine to the promethazine regimen can reduce drowsiness.

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**Figure** Drugs and combination of drugs ranked according to their effectiveness. Reproduced with permission from Wood CD and Greybiel A.
Cinnarizine. Cinnarizine is a piperazine derivative with the actions and uses of antihistamines. A study conducted by the British Royal Navy compared cinnarizine to scopolamine for seasickness prophylaxis in both laboratory and sea-trial conditions. This study documented that scopolamine was more effective than cinnarizine, but cinnarizine had a lower incidence of side effects. This comparative superior tolerability of cinnarizine, but cinnarizine had a lower incidence of side effects. This comparative superior tolerability of cinnarizine decreased as motion sickness increased.44 A separate study involving 25 volunteers who were exposed to rapid and abrupt movements associated with a rotating chair and parallel swing demonstrated that the combination of domperidone and cinnarizine was superior to either agent individually or placebo as prophylaxis for motion sickness.45

Comparison of Efficacy

The relative effectiveness of sixteen medications in reducing susceptibility to acute motion sickness was compared by Wood and Graybiel using a slow rotation room where stressful accelerations were under quantitative control. Fifty subjects were enrolled, each serving as his own control.46 The Figure ranks the medications according to their effectiveness. Scopolamine hydrobromide was identified as the most effective single agent, and the summation effect of d-amphetamine sulfate and scopolamine hydrobromide provided significantly better protection than any single drug.

Summary

Although the precise etiology of motion sickness is still unclear, several effective treatments are available to prevent its symptoms. Numerous clinical trials support the anticholinergic drug scopolamine as the most effective treatment to prevent motion sickness. This prescription medication, available in both tablet and topical form, is particularly useful for people who suffer moderate to severe symptoms. The shorter-acting (8-hour) tablet allows one to control the precise dose of scopolamine received and should be taken 1 hour before travel. The scopolamine patch dispenses the medication over 72 hours and is convenient for long exposures. However, variable skin absorption and a fixed patch dosage that may not be suitable for all patients result in reduced efficacy and increased incidence of side effects compared with scopolamine tablets.

For more mild cases of motion sickness, over-the-counter remedies have been proven useful. Most of these medications are antihistamines, and dimenhydrinate appears to be the most effective of this class. The use of nonpharmacologic remedies, such as ingesting ginger supplements and applying acupressure to the wrists, is supported by promising, but inconsistent data and awaits confirmation with controlled clinical studies.

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