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Managing motion sickness

Louisa Murdin, ¹ John Golding, ² Adolfo Bronstein ³

Motion sickness is a syndrome of nausea and vomiting, pallor, sweating, headache, dizziness, malaise, increased salivation, apathy, drowsiness, belching, hyperventilation, and stomach awareness. Symptoms can be provoked by externally imposed motion, or implied self motion from a moving visual field, such as in a cinema. The condition has been recognised from the early days of sea travel and the word for sickness, "nausea," derives from the Greek word $v\alpha v\alpha c$, meaning "ship."

Travel by car, train, or other transport is part of everyday life for most people, and motion sickness is a common problem. Estimating its prevalence is complex because reported symptoms depend on variables such as previous avoidance and exposure, as well as presumed inherent susceptibility. Some estimates are presented in table 1. Motion sickness may have an important effect on occupational activity for some people, such as airline pilots, those in the armed forces, and emergency services staff. General practitioners may frequently encounter patients who report difficulties in work or daily life related to motion sickness, or those seeking advice about prevention before a forthcoming journey. We review the management of patients with motion sickness for the generalist. This article is based on evidence obtained largely from controlled studies in patients and in healthy volunteers.

Why do people get motion sickness?

There is no universally accepted explanation about why people get motion sickness. One commonly held view is that motion sickness originates from a mismatch between sensory inputs, especially between the visual and vestibular systems. For example, when travelling in a vehicle with limited outside visibility, the vestibular system reports motion to the central nervous system, but information from

the visual system suggests the individual is not moving. Other forms of mismatch, such as visual motion without actual motion—for example, in a large cinema—can have the same effect. Motion sickness itself could have evolved from a system designed to protect from potential ingestion of neurotoxins by inducing vomiting when unexpected central nervous system inputs are detected (the "toxin detector" hypothesis). This system would then be activated by modern methods of transport that cause mismatch.

Less popular alternatives to the toxin detector hypothesis propose that motion sickness could be the result of aberrant activation of vestibular-cardiovascular reflexes¹; or that it might originate from a warning system that evolved to discourage development of perceptual motor programmes that are inefficient or cause spatial disorientation²; or that motion sickness is a unfortunate consequence of the physical proximity of the motion detector (vestibular) and vomiting circuitry in the brainstem.³

Who is most susceptible to motion sickness?

Experimental evidence supports the theory that, with varying thresholds of susceptibility, almost all healthy unmedicated individuals can get motion sickness in the right conditions. Some people may be more troubled by the condition than others, and reports of motion sickness depend on lifestyles and situations. For example, a professional pilot will be more troubled by new symptoms of air sickness than someone who never needs or wants to travel by aeroplane. Bearing these difficulties in mind, various large prospective surveys have estimated the frequency of symptoms of motion sickness (table 1).

Babies and young children under 2 do not usually get motion sickness. However, motion sickness is more common in children under 15 than in adults, perhaps because of habituation—that is, reduction in symptom severity with repeated exposure. It is also more commonly reported in women than in men, although a number of potentially confounding variables related to social roles may account for this observation. Evidence from twin studies has shown that a large proportion of individual variation in susceptibility is due to genetic factors, with heritability estimates in the range 55-70%. **

Some groups of patients are particularly susceptible. Self reported motion sickness is higher in people who have migraines than in those who have other types of headache.

SUMMARY POINTS

Motion sickness is a common and potentially disabling problem, thought to be due to sensory conflict or "mismatch" involving the vestibular system

Management using behavioural methods such as habituation can be effective and has few adverse effects, but can be unpleasant and time consuming

Hyoscine is an effective preventive medication for which oral preparations and transdermal patches are established in clinical practice, and emerging evidence suggests that hyoscine nasal spray is effective in preventing motion sickness

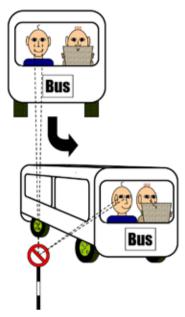
Evidence to support the use of other drugs, taking into account the trade off between efficacy and adverse effects, is weaker.

Management of motion sickness with traditional remedies such as ginger and acupressure bands has not been shown to be effective.

SOURCES AND SELECTION CRITERIA

We searched *Clinical Evidence*, PubMed, Medline, and Embase for articles using the keywords "motion sickness." Articles were limited to studies in people published in the past 10 years (2000-11), focusing on clinical trials and review articles. We consulted a Cochrane Review on prevention and treatment of motion sickness. We also consulted personal reference collections.

Visual-vestibular conflict. As the bus turns, the passenger on the left has a fixed external visual reference and has no visual-vestibular conflict. The passenger on the right, who is reading the paper, experiences a conflict because the visual input is still but the vestibular system is sensing motion (modified from Bronstein and Lempert **6*)



Furthermore, migraineurs characteristically report heightened sensitivity of all senses⁷—for example, phonophobia and photophobia—including vestibular and visual-vestibular inputs. Many symptoms of motion sickness are reminiscent of a migraine attack. One large observational study of female yacht racers found that that individuals with migraine are more susceptible to motion sickness, and are prone to develop migraine headaches during provocative motion exposure. Patients with vestibular migraine, in which vestibular symptoms and migraine are strongly associated, "a report greater susceptibility than those with other forms of migraine (see "A patient's story"). ¹⁰

Many patients with vestibular disorders also report symptoms during external motion. ¹¹ By contrast, patients with absent vestibular function do not normally become motion sick, ¹² although they are still partially susceptible to visually induced motion sickness. ^{w4}

How should the patient with motion sickness be assessed?

The diagnosis of motion sickness is made on the basis of reported symptoms in externally imposed motion. It is rare for motion sickness to be the presenting symptom of serious disease. Vestibular disease (peripheral or central) can present with motion sickness, but dizziness or vertigo will usually exist between exposures. Unilateral vestibular disease can be suggested by a positive head thrust test or positional manoeuvre. We central vestibular disease can present with cerebellar symptoms and signs, so an eye movement and gait examination is essential. Mal de debarquement is a distinct presentation, which is discussed later in this article.

How can motion sickness be treated?

Behavioural counter measures

Simple behavioural counter measures can be effective treatments for patients who experience motion sickness. A within person comparison showed that sickness was reduced when a stable visual reference point, such as

the horizon, was provided, minimising visual-vestibular conflict during sea travel¹³ (figure). Forward visibility is particularly helpful in coach or bus travel.⁶ Alternatively, laboratory based observations showed that lying supine, where practical, reduces symptoms of motion sickness and is preferable to an upright seated posture.¹⁴ Controlled studies have shown that deliberate restriction of head movements is helpful, as is avoidance of tasks that enhance visual-vestibular conflict, such as reading when travelling.

Prospective controlled studies have shown that repeated exposure to the nauseogenic stimulus (habituation) is an effective treatment for motion sickness. ¹⁵ ¹⁶ Habituation programmes pioneered by the military are effective but time consuming. For maximum efficacy, the exposure to the stimuli needs to be frequent and graded. The exposure is initially gentle, and is then increased by gradual increments to maximise acceptability and speed up recovery between sessions, and to avoid the undesirable effect of sensitisation to the stimulus. Habituation is specific to a particular stimulus: tolerance to car travel may have no effect on susceptibility to seasickness.

A prospective controlled study of healthy volunteers has shown that coping strategies such as controlled regular breathing or listening to music are more effective than placebo in reducing nausea. However the effect size was small, with provocative stimuli tolerated for around 10% longer. A small but well designed prospective placebo controlled study showed no benefit of acupressure bands over control, although a small trial showed Korean hand pressure to be more effective than sham pressure in reducing subjective nausea for emergency patients transported in ambulances. B

Motion sickness is increasingly reported in the context of virtual environments, with head mounted or large field of view displays, when it is known as cybersickness or visually induced motion sickness. These devices are potentially useful tools for various research, health, training, and leisure activities. Cybersickness can be treated with habituation.¹⁸

Antiemetic Drugs

Most drugs in common use for motion sickness have been used for more than 30 years. Some of these drugs have been examined in small but well designed studies. However, most data have been obtained in studies involving healthy adults, usually men. Data on the effectiveness of these drugs for treating motion sickness in women and children are scarce, although these groups are generally more susceptible than men. Many of the drugs cause drowsiness and other adverse effects. Also, evidence suggests that some (for example, hyoscine) may delay habituation either directly or indirectly via sedative effects. 19 Consider drug treatment carefully in patients who could benefit from using habituation methods to overcome motion sickness, and discuss this disadvantage of using drugs with them before embarking on treatment. Some drugs in common use are shown in table 2.

Gastric stasis occurs with motion sickness before the vomiting phase, so non-oral routes of administration, such as transdermal patches, are advantageous. Medication is

Table 2 Common anti-motion sickness drugs (adapted from Benson, 2002 ³⁶)				
Drug	Route	Adult dose	Time to onset	Duration of action (h)
Hyoscine OTC	Oral	0.3-0.6 mg	30 min	4
Hyoscine	Injection	0.1-0.2 mg	15 min	4
Hyoscine	Transdermal patch		6-8 h	72
Promethazine OTC	Oral	25-50 mg	2 h	15
Promethazine	Injection	25 mg	15 min	15
Promethazine	Suppository	25 mg	1 h	15
Dimenhydrinate	Oral	50-100 mg	2 h	8
Dimenhydrinate	Injection	50 mg	15 min	8
Cyclizine	Oral	50 mg	2 h	6
Cyclizine	Injection	50 mg	15 min	6
Meclizine	Oral	25-50 mg	2 h	8
Buclizine	Oral	50 mg	1 h	6
Cinnarizine OTC	Oral	15-30 mg	4 h	8
OTC=over the counter; available	without prescription in UK.			

most effective when taken before exposure rather than after the onset of symptoms. Drugs are useful in situations where habituation is impractical, such as solitary or infrequent journeys.

Antimuscarinics

Hyoscine (scopolamine) is available as tablets or liquid for oral ingestion, intravenous and subcutaneous injection, and transdermal patches. Its potential adverse effects include drowsiness, blurred vision, dry mouth, and dizziness, which reflect its muscarinic anticholinergic properties. However, many studies have reported that it is safe and well tolerated.

Patches are applied to the mastoid area 6-8 hours before exposure. Patch users should wash their hands thoroughly both before and after touching the patch, since hyoscine can be spread to the eyes by hand, which can cause blurred vision and pupil dilatation. Patches should never be cut into pieces, as this interferes with the drug release mechanism. One small randomised, crossover, double blind study in healthy young men reported on double dose hyoscine patch therapy as a potential treatment for those in whom a single patch is ineffective, and concluded that two patches were safe and well tolerated in this group. 20 Faster onset of action may be obtained through administration as a nasal spray.²¹ A small randomised, placebo controlled, double blind crossover trial using experimentally induced motion sickness in young adults showed the nasal preparation to be effective, with no significant decrease in alertness.²² A Cochrane systematic review concluded that hyoscine is more effective than placebo in treating the symptoms of motion sickness, but that its effectiveness compared with other treatments for the condition is unclear.23 Selective M3 or M5 muscarinic receptor antagonists may also be effective against motion sickness.24

Antihistamines

Antihistamines—including cinnarizine, meclozine, dimenhydrinate, cyclizine, chlorphenamine, and promethazine—are the other main group of drugs frequently used to treat motion sickness. These are available as prescribed and over the counter preparations. Cinnarizine at a dose of 50 mg was more effective than placebo at reducing symptoms in a double blind placebo controlled study, although 25 mg

was not.²⁵ According to a small placebo controlled study of healthy young men, promethazine is effective given as a 50 mg intramuscular injection, but at the cost of considerable sedative effects.¹⁶ Dimenhydrinate was found to be no more effective than placebo in another study of susceptible individuals.²⁶ Cetirizine and fexofenadine are ineffective, probably owing to a lack of central nervous system effects.

Central nervous system stimulants

Sympathomimetics such as dextroamphetamine have been documented to have efficacy in the prevention of motion sickness, either alone or in combination with other drugs, but their usefulness is limited by the potential for abuse and legal problems. Amphetamine has been discontinued as an anti-motion sickness treatment, apart from some limited use in special circumstances for the military. Modafinil, an alternative central nervous system stimulant, was recently evaluated as a potential treatment for motion sickness, but was not found to be effective alone in a double blind, placebo controlled study.^{w9}

Ondansetron

Individuals with a history of motion sickness are at higher risk for postoperative and chemotherapy induced nausea

A PATIENT'S STORY

I had mild motion sickness when travelling by car as a child, but my symptoms dramatically worsened when I developed acute labyrinthitis about 10 years ago. Since then I have become much more sensitive to motion, especially when travelling by bus. It's best for me to be the driver, but the next best option is to sit in the passenger seat, and the back seat is worst of all. I've also developed troublesome vestibular migraine, and have noticed that travel and motion sickness can trigger a bad migraine attack a few hours after the journey. My migraines are managed with amitriptyline, and although they are still fairly frequent (a few episodes a week) I have learnt to manage them. They are less severe than they were. There is a definite relation between the migraine and the motion sickness, and the motion sickness is better when the migraines are under better control. I've had some physiotherapy, which has been helpful at times when the migraines have been well treated. It's also been really helpful for me to see a specialist who has an interest in these problems, as I have found that some professionals haven't appreciated the connections between my motion sickness, vertigo, and migraines.

and vomiting. Because 5-HT3 receptor antagonists such as ondansetron have revolutionised the management of nausea and vomiting, experts hoped they would be efficacious in the management of motion sickness. However, initial results of placebo controlled studies have not shown ondansetron to be effective among small groups of healthy volunteers^{w10} or larger groups of people with a history of high susceptibility to motion sickness.²⁶

Non drug remedies

Ginger is a popular traditional remedy for nausea. One small trial suggested that ginger was better than placebo in treating motion sickness²⁷ but another has shown it to be ineffective compared with hyoscine.²⁸ Supplemental oxygen may reduce motion sickness in patients being transported by ambulance, but does not alleviate the problem in individuals who are otherwise healthy.²⁹ This apparent paradox is perhaps explained by the suggestion that supplemental oxygen may work by ameliorating internal states that sensitise for motion sickness.

Combination treatments

Combinations of agents have also been selected with the aim of increasing efficacy and others to increase tolerability. One small study examined the combination of chlorpheniramine with ephedrine to combat the drowsiness which is so frequently a problem in managing motion

TIPS FOR NON-SPECIALISTS

- Exclude central and peripheral vestibular disease in patients who report marked motion sickness
- Motion sickness is linked to migraine. It is worth asking specifically about migraine symptoms in patients who present with motion sickness, since uncontrolled migraine can be treated prophylactically as well as acutely.
- Habituation is a highly effective treatment when exposures are specific, graded, and frequent
- Drug treatments can be selected according to factors such as desirability of sedation and duration of expected exposure
- The most effective treatments for motion sickness are used in advance of an expected exposure
- Gastric stasis occurs with motion sickness before the vomiting phase, so non-oral routes of administration, such as transdermal patches, are advantageous

QUESTIONS FOR FUTURE RESEARCH

- Are selective M5 muscarinic receptor antagonists effective treatments?
- Can motion sickness be alleviated pharmacologically after symptoms are established, perhaps by using faster routes of administration?
- Can the addition of alternative stimulant drugs to proved agents such as antihistamines and anticholinergics improve tolerability, especially with respect to drowsiness?
- How can the known link between migraine, vestibular migraine, and motion sickness be exploited to better manage patients?
- How do vestibular disorders contribute to motion sickness?
- How can virtual reality technologies be adapted to avoid cybersickness, and do they have a role in preventing motion sickness in other settings?

ADDITIONAL EDUCATIONAL RESOURCES

For healthcare professionals

Motion Sickness Susceptibility Questionnaire Short-form (www. westminster.ac.uk/__data/assets/pdf_file/0010/47539/MSSQ-short.pdf)—questionnaire useful for quantifying susceptibility to motion sickness

Medical Aspects Of Harsh Environments: Motion Sickness (www.bordeninstitute.army.mil/published_volumes/harshEnv2/HE2ch35.pdf)—a more detailed review of the topic 36

For patients

NHS Choices (www.nhs.uk/Conditions/Motion-sickness/ Pages/Introduction.aspx)—information for patients about motion sickness

Vestibular Disorders Association (www.vestibular.org)—support for patients with vestibular disorders and doctors treating them *Travel Sickness* (www.bbc.co.uk/health/physical_health/conditions/travelsickness1.shtml)—overview and advice on BBC Health site

sickness. A modest reduction in drowsiness was reported. ³⁰ In another study of the prevention of air sickness, the combination of promethazine with caffeine was more effective than placebo, meclizine, or hyoscine and had fewer adverse effects. ³¹ Although no longer available for legal reasons, combinations of hyoscine or promethazine with amphetamine are highly effective.

Other drugs

5-HT receptor agonists

Given the well known connections between migraine and motion sickness, w11 and the revolution in migraine management that has taken place thanks to the advent of 5-HT 1B/1D receptor agonists (triptans), experts hoped that these drugs might be useful in motion sickness, both in migraineurs and in non-migraineurs. Rizatriptan has been evaluated for efficacy in motion sickness in migraineurs in a double blind randomised placebo controlled study. Although the majority of participants with complete data reported a reduction in symptoms, the effect was small and not repeatable. 32

Phenytoin

A number of small placebo controlled double blind studies have evaluated the effectiveness of phenytoin for treating motion sickness and found it to be effective on some, but not all, measures. ³³ At the dose that is appropriate for treatment of epilepsy (approx 4-7 mg/kg daily for adults) the adverse effects of phenytoin are well known, including nausea, dizziness, constipation, mood changes, and blood dyscrasias. However, the doses required to prevent motion sickness would be smaller (previous studies used from 200 mg up to levels used for anticonvulsant treatment) and less frequent, which may be more tolerable.

Loperamide

Loperamide, a μ -opiate receptor antagonist known for its role in managing diarrhoea, has been evaluated in a small study of motion sickness. A statistically significant reduction in nausea was found, although in clinical terms the effect size was small. ³⁴

What is mal de debarquement?

Mal de debarquement (from the French for "sickness of disembarkment") is the persistence of imbalance or a rocking sensation after exposure to passive motion, especially a sea voyage. A transient sensation of this kind is normal, but some individuals report persistent and troublesome symptoms. ³⁵ Mal de debarquement is usually managed along the same principles as other vestibular disorders, using customised vestibular rehabilitation exercises, but no studies have prospectively evaluated the efficacy of this approach. Consider referring patients with symptoms extending beyond one month to an audiovestibular physician or other specialist in vestibular disorders.

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CASE REPORT

An unconscious patient

- 1 This patient has hyperosmolar hyperglycaemic state, previously known as hyperosmolar non-ketotic state. This is one of the most serious acute diabetic complications with a mortality of 10-50%.
- 2 After initial resuscitation, the remainder of the fluid deficit should be replaced gradually. Frequent clinical assessment and electrolyte monitoring are needed to prevent rapid osmolar shifts.
- 3 Insulin should be administered by continuous intravenous infusion at a low infusion rate to provide a steady and gradual fall in plasma glucose concentrations. This approach reduces the risks of hypoglycaemia, hypokalaemia, and cerebral oedema.
- 4 Infection and myocardial infarction are two major precipitants. In addition, the omission of insulin or the introduction of new drugs, such as corticosteroids, can contribute to hyperglycaemia and lead to this condition.

STATISTICAL OUESTION

Cohort studies: sources of bias

Answers b, c, and d are true, whereas a is false.

ANATOMY QUIZ

Anatomy of the bones of the foot

- A Cuneiforms (medial and intermediate superimposed)
- B Navicular
- C Talus
- D Lateral cuneiform
- E Cuboid
- Calcaneum