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Committee to Advise on Tropical Medicine and Travel (CATMAT)*
STATEMENT ON MOTION SICKNESS

Definition and etiology

Motion sickness is known by many names, e.g., car sickness, sea sickness, air sickness, space sickness, and motion maladaption syndrome.

Motion sickness is a normal response to perception of motion where there is sensory conflict about body motion perceived by different receptors (visual, vestibular, and body proprioceptors). It can also be induced when the pattern of motion differs from that previously experienced, in the absence of expected motion, or viewing a very large screen where the viewer is not actually moving.

Symptoms and time course

The development of symptoms follows an orderly sequence that varies with the intensity of the stimulus and the susceptibility of the individual. The initial symptom is usually discomfort around the upper abdomen (“stomach awareness”), which is followed by nausea and increasing malaise. Concurrently the face or area around the mouth becomes pale and the individual starts to sweat. With rapid worsening of symptoms (“avalanche syndrome”) there can be increased salivation, feelings of body warmth, a lightness of the head, and often depression and apathy. Vomiting typically follows.

Additional symptoms are frequent, but more variable. These include belching and flatulence, hyperventilation, sighing and yawning, headache, tightness around the forehead or a “buzzing” sensation, drowsiness, lethargy and somnolence, panic or confusion. The lethargy, fatigue, and drowsiness can persist after the stimulus stops and nausea lessens.

Over time, there is a tendency to adapt (“to get one’s sea legs”). For most individuals this occurs by 2 to 3 days, although about 5% are said not to adapt and remain symptomatic if the stimulus persists. Returning to stable circumstances, as in returning to shore, can trigger an exacerbation, but this is usually shorter because readaptation is quicker.

Incidence and risk factors

Incidence varies depending upon the magnitude of the stimulus and the susceptibility of the individual. It ranges from < 1% on a large aircraft to almost 100% on a rough sea voyage under evacuation conditions. Boat travel is most likely to cause motion sickness, followed by travel by air, car, and train.

Motion sickness is rare in those < 2 years of age. It is said to peak between ages 3 and 12, with a gradual decrease thereafter. Supporting data for this appear to be mainly anecdotal[1], and where data exist, it is impossible to rule out self-selection as the reason for the observation[2]. Rates are higher in females (1.7:1 compared to males). It is increased during menstruation and pregnancy.

Within a given magnitude of stimulus, there are differences in natural susceptibility, which can be exacerbated by emotions like fear or anxiety, or by other illnesses, poor health, or some medications. Personal susceptibility tends to be a stable and enduring characteristic, and is predictive of greater susceptibility in the future[3,4].

Important physical characteristics of the stimulus include the frequency, intensity, and duration of directional changes. It is increased by visual stimuli, such as a moving horizon, or by zero gravity.

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Rates are magnified by other environmental factors, such as poor ventilation, odors, fumes, smoke, and carbon monoxide.

Differential diagnosis and complications

The differential diagnosis includes vestibular disease, gastroenteritis, metabolic disorders, and toxin exposures. At altitude, it also includes mountain sickness. Most symptoms attributed to motion sickness should resolve following termination of the motion stimulus or with adaptation to it. Some symptoms, such as lethargy, take longer to resolve[5]. Laboratory studies also show a delay in improvement in gastric motility, electroencephalographic studies, and performance[6].

Complications are infrequent, but include hypotension, dehydration, depression, and panic.

Methodologies in studies on motion sickness

There are numerous methods used to assess medications and other measures, and all have deficiencies that weaken the ability to compare studies or to apply the information to the typical traveller[7]. From reviewing the literature, it seems quite possible that for the average traveller there are several options that are of generally equal benefit[8].

There are many recommendations that appear to be based upon repeated but anecdotal observations made under real-life conditions. Where laboratory data exist, they are generally consistent with these observations.

There are a number of studies that use self-report data obtained by questionnaires. These can have rather large numbers of respondents, but to facilitate obtaining responses the questionnaire is usually simple and the responses are open to divergent interpretations. For example, in a study where 98% of travellers responded (20,029 respondents), there was a significant association between increased motion sickness and use of motion sickness medications, and between alcohol use and decreased motion sickness[2]. The investigators were unable to determine the temporal sequence or the effect of confounding factors.

Most current controlled studies are conducted under laboratory conditions where healthy, typically young male individuals are subjected to strong stimuli, e.g., a rotating chair, over a short time, with the intention of rapidly inducing some degree of motion sickness. These studies usually have a small number of subjects, and the results may not have full relevance to the typical traveller since they are usually used to study aspects of space sickness or effects under extreme sea conditions.

Many older studies[7,9], but few recent studies, have used more realistic settings, either in induced sea-like conditions, or under real sea-based conditions[8]. It is almost impossible to control all key variables in these latter studies, but they may provide the most useful information.

General measures for prevention of motion sickness

The support for the following measures is based on observations from laboratory manipulations and repeated anecdotal experience. Scientific support is generally B II-III (see Appendix I)[10].

1. Minimize exposure:
   - be located in the middle of the plane or boat where movement is least
   - be in a semi-recumbent position
   - minimize head and body movements.
2. Restrict visual activity:
   - fix vision on the horizon or some other stable external object
   - avoid fixation on a moving object
   - avoid reading
   - close eyes, if below deck or in an enclosed cabin.
3. Improve ventilation and remove noxious stimuli.
4. Reduce the magnitude of the motion stimulus:
   - avoid or minimize acceleration and deceleration, and turning or moving of the vehicle.
5. Engage in distracting activity:
   - be in control of the vehicle
   - perform mental activity.

Recommended dietary manipulations include decreasing large oral intakes, taking frequent small feedings, and avoiding alcohol. The scientific support for these observations is less certain.

Medications for prevention of motion sickness

1. Important variables

There is no one standard approach that is ideal for everyone in all circumstances. Important variables that may influence the choice include individual susceptibility, the amount of time available before the stimulus will start (e.g., planned travel versus a sudden exposure), the severity of stimulus, the duration of the stimulus (e.g., a brief exposure versus a trip of several days or more), whether medications are being used for prophylaxis or once symptoms have begun, tolerance to individual medications, the need to maintain total alertness, and other underlying medical conditions.

2. Potential routes of administration

There are a variety of routes of administration. These include by mouth (tablet to swallow or chew), sublingual (tablet or sachet under tongue), buccal (sachet or tablet in mouth cavity), intramuscular, rectal (suppository), and transdermal (patch).

3. Timing of medical use

Oral regimens must be taken prior to the exposure, both to allow absorption and to attain adequate levels. Regimens are usually considerably less effective once symptoms of motion sickness have begun. With the onset of symptoms, absorption becomes less effective, and with vomiting, becomes close to impossible. Once severe manifestations have begun, rectal suppositories may still be an option if intramuscular injections are not possible.

4. Classes of medications used

Travellers commonly use two classes of centrally acting medications; muscarinic receptor antagonists and histamine H_1-receptor antagonists. Despite intensive study, their site(s) of action remains poorly defined and their effectiveness does not parallel their receptor-blocking potency.

Under conditions of intense stimuli there is a role for centrally acting sympathomimetic substances, e.g., dextroamphetamine[11].

These are typically used in conjunction with either of the first two classes of agents.

There are a number of other classes of agents that have or are being studied and for which data are very conflicting (e.g., ginger)[12–15], or preliminary (e.g., antidepressants and anti-convulsants). Much of the effort with new compounds, such as doxepin[16] and phenytoin[17,18], is based on an attempt to decrease adverse reactions, particularly those that could compromise functioning under conditions of space travel or maritime operations.

5. Adverse reactions to medications used for motion sickness

Motion sickness itself may contribute to some of the symptoms attributed to the medications, but drowsiness is common with all except those that include sympathomimetic agents. Symptoms are usually dose-related and it may be possible to strike a balance between efficacy and adverse reactions (e.g., in most individuals scopolamine 0.3 mg will produce significant protection with minimal side effects).

An interesting problem, particularly with long-acting agents is that, under stimuli that rarely produce motion sickness, symptoms of the medication are likely to be worse than the placebo. In contrast, with progressively more intense symptoms of motion sickness, symptoms often attributed to the medication may be much more intense in placebo recipients[19–21].

6. Summary of reported results

Table 1 lists common regimens that have been shown to be effective in one or more controlled trials. The support for efficacy compared to the placebo is A I (see Appendix I) for all. Much of the older literature on these regimens is summarized in references 7 and 9.

The table includes information on the amount of time required to attain effective protection, the duration of the effectiveness, commonly experienced adverse reactions, and the severity of the motion for which it is likely to be most effective.

None of the regimens provides total protection for everyone under all circumstances.

Comments about individual medications, including their availability in Canada, dosage, and adverse reactions are given in Tables 1 and 2.

The intervals between doses and the recommendations for use in children and for use in pregnancy listed in Table 2 and discussed below are summarized from information in the literature and recommendations in standard reference texts such as Martindale and the 1996 *Compendium of Pharmaceuticals and Specialties (CPS)*. These are not always consistent and, particularly for use in pregnancy, are not clear. For many, use at very young ages is not recommended. Since children < 2 years of age are said to rarely develop motion sickness, this may not be of major practical significance.

a. Dextroamphetamine

Amphetamine and related agents have significant effects on motion sickness[11,22]. Their main usefulness appears to be under conditions of extreme stress where they have been used in conjunction with scopolamine or promethazine to provide additional benefit and counteract adverse effects[6,23,24]. For prevention of motion sickness in the routine traveller, there is little indication for its use. In Canada it is marketed as Dexedrine®, which is available as a short-acting and a long-lasting preparation.

These agents are not recommended for use in pregnancy, or in children < 3 years of age. If ever used for motion sickness prevention in childhood, the recommended dose for ages 3 to 5 years is 1/4 of the adult dose, and from ages 6 to 12 years, 1/2 of the adult dose, which is 5 mg to 10 mg.

They are not routinely used, particularly on a repeated basis, because of the adverse reactions which include restlessness and talkativeness, plus the potential for abuse. They interact with numerous medications, particularly those with cardiac or CNS effects.

Table 1
Effective oral* regimens for the prevention of motion sickness

Drug	Oral Dose (mg)*	Interval to be Effective (hrs)	Duration of Effectiveness (hrs)	Major Adverse Reactions	Severity of Motion that Drug is Effective Against
Amphetamine	5-10	1-2	8	Talkative, restlessness Abuse potential	Mild
Cinnarizine	30	2-5	6-8	Drowsiness	Mild to severe
Cyclizine	50	1-2	4-6	Slight drowsiness	Mild
Dimenhydrinate	50-100	1-2	6-8	Drowsiness, vertigo	Moderate
Meclizine	25-30	2	6-12	Drowsiness	Mild
Promethazine	25	1.5-2	24-30	Extensive drowsiness	Moderate to severe
Promethazine/ephedrine	25/25	1-2	12		Moderate to severe
Scopolamine	0.3-0.6	0.5-1	4-6	Dry mouth, drowsiness, blurred vision	Severe
Scopolamine patch (TTS)	1.5	6-8	72	Dry mouth, drowsiness, blurred vision	Moderate to severe
Scopolamine/amphetamine	0.3-0.6/5-10	1-2	6	Slightly dry mouth	Severe

Table 2
Regimens available in Canada or the United States for the prevention of motion sickness

Drug	Available		Oral Dose (mg)	Interval to be Effective (hrs)	Dose Frequency (hrs)	Use in Pregnancy	Use in Children
	Canada	United States					
Amphetamine	Yes	Yes	5-10	1-2	q 4-6	No	not < 3 years
Cinnarizine	No	Yes	30	2-5	15 mg q 6-8	?No	? not < 5 years
Cyclizine	No*	Yes	50	1-2	q 4-6	?No	Yes
Dimenhydrinate	Yes	Yes	50-100	1-2	q 4-6	?No	not < 2 years
Meclizine	Yes	Yes	25-50	2	q 6-24	?No	Yes
Promethazine	Yes	Yes	25	1.5-2	q 4-6	Yes	not < 2 years
Scopolamine patch (TTS)	Yes	Yes	patch	8	q 72	No	No

b. Cinnarizine

Used as 30 mg 1 to 2 hours before exposure and 15 mg every 6 to 8 hours thereafter, it has been shown to be significantly more effective than a placebo[3] and similar to scopolamine 0.3 mg every 6 to 8 hours in a much smaller study[25]. The standard dose is the one used in the study. It is not available in Canada, but is in the United States.

Its use is not recommended in pregnancy, and no dosage recommendations are offered < age 5. For children aged 5 to 12 years, half the adult dose is recommended.

The major adverse reaction is drowsiness.

c. Cyclizine

Cyclizine has been shown to be inferior to scopolamine, but significantly better than a placebo[19]. The standard dose is 50 mg orally every 4 to 6 hours. Cyclizine is only available as an intramuscular preparation in Canada (Marzine®) but is available in the United States as an oral preparation.

It is not recommended for use in pregnancy, but can be used in children. In children the recommended dose is 1/4 of the adult dose up to age 6 years and 1/2 of the adult dose from 6 to 10 years of age.

In recommended doses, its major adverse reaction is slight drowsiness.

d. Dimenhydrinate

This has long been considered one of the treatments of choice for the degree of motion sickness that travellers might experience[7,9,26-29]. Dimenhydrinate is available under numerous trade names (e.g., Gravol®) in over the counter preparations, and comes as tablets, chewable tablets, filmkote preparations, long-acting capsules, liquid preparations, suppositories, and injectable preparations.

It should not be used in children < 2 years of age and is not recommended for use in pregnancy. The standard adult dose is 50 mg to 100 mg orally every 4 to 6 hours, to a maximum of 400 mg in 24 hours. For children 2 to 6 years of age, the oral dose is 15 mg to 25 mg every 6 to 8 hours, to a maximum of 75 mg in 24 hours. For children 6 to 12 years of age, the oral dose is 25 mg to 50 mg every 6 to 8 hours, to a maximum of 150 mg in 24 hours. For children > 12 years of age, the oral dose is 50 mg every 4 to 6 hours, to a maximum of 300 mg in 24 hours.

Compared to the scopolamine patch, dimenhydrinate's major deficiency is the need for frequent administration. The major adverse reactions are drowsiness and vertigo. In children there can be excitement.

e. Meclizine

This has also long been considered an effective regimen[7,9,29], but does not appear as effective as the scopolamine patch[30]. Meclizine (Bonamine®) is available in a tablet that can be swallowed, chewed or allowed to dissolve in the mouth.

Its use in pregnancy is not recommended, but it can be used in children. The standard adult dose is 25 mg to 50 mg orally, but recommendations for dose intervals range from every 6 to 12 hours to every 12 to 24 hours. Based on the duration of action shown in Table 1, intervals longer than 12 hours would seem inappropriate if rough conditions are being encountered. Half the adult dose is recommended for children.

The major adverse reaction is drowsiness.

f. Promethazine

Promethazine, with or without an amphetamine-like agent, has largely been used in situations of severe stimuli, and for treatment of established motion sickness[5,31]. Promethazine is available in several brands (e.g., Phenergan®), including tablets and syrups.

It can be used in pregnancy but should not be used in those < 2 years of age. The standard dose for prevention is 25 mg orally every 6 hours. Based on its long duration of activity (Table 1), this frequency seems unnecessarily high. The dose recommended for children > 2 years of age is 0.25 to 0.5 mg/kg of body weight every 4 to 6 hours.

Promethazine causes more drowsiness than most of the other standard agents and its use is reported to result in significant decreases in performance scores, psychomotor function, information processing, and alertness, but results are conflicting, and under conditions of motion sickness there may be less impairment than that attributable to the motion sickness itself[23].

g. Scopolamine hydrochloride

This preparation is not currently available on the Canadian or American market in an oral form. It is, however, often the standard against which other medications have been compared[19,23,25,32]. It is not apparent why it is not available, but presumably manufacturers believe that the scopolamine patch has replaced it. In Canada there is a preparation, scopolamine butylbromide (Buscopan®), that does not have an indication for motion sickness.

The major adverse reactions with scopolamine are similar to those discussed for the scopolamine patch.

h. Scopolamine patch

The scopolamine transdermal patch is applied to the skin behind the ear at least 8 hours prior to exposure to the stimulus, with replacement every 72 hours. It has been extensively studied and reviewed[21,30]. Studies show overall efficacy similar to oral scopolamine and oral dimenhydrinate[26-28,30,32]. Its main advantages are its practical ease of administration and long duration of activity. Problems with its use include adverse reactions which may outweigh the benefit when there are minimal stimuli to induce motion sickness, the long period before onset of activity, and the inconsistency of effects in different individuals and in the same individual at dif- ferent times[21,34]. There is a concern that it may decrease adaptation to motion sickness, although this has not always been apparent[20]. It should be avoided in pregnancy and should not be used in children. The scopolamine patch (Transderm-V®) is available in Canada.

Use of the scopolamine patch is contraindicated in glaucoma; should be avoided in the young, the elderly, during pregnancy, and when there is urinary or pyloric obstruction. The scopolamine patch can interact with sedatives, such as antihistamines, alcohol, antidepressants, and anticholinergics-like belladonna alkaloids. Hands should be washed after applying it to avoid inadvertent contact to the conjunctiva with resultant pupillary dilatation and blurred vision. Commonly reported adverse effects include dry mouth, drowsiness, and blurred vision (even without direct contact). The visual problem may increase with continuous use[21]. It can cause confusional states and/or visual hallucinations, particularly in elderly individuals.

Numerous approaches likely provide comparable activity

A recent study assessed seasickness on a whale-watching trip where 80% without prophylaxis typically become sick. It compared many of the available preparations that travellers might use[8]. The following regimens were taken up to 2 hours before departure: meclizine (12.5 mg) plus caffeine (50 mg), ginger root (250 mg), and cinnarizine (20 mg) plus domperidon (15 mg). Two regimens were started the night before: scopolamine patch, and cinnarizine (25 mg) (with a second dose at least one hour before). There were 1,741 individuals recruited and 1,489 (85.5%) completed the evaluation. There were no significant differences between regimens, with 4.1% to 10.2% reporting vomiting and 16.4% to 23.5% that they were at least slightly seasick. There was a slight trend towards the scopolamine patch having a weaker action ($p = 0.14$), and slightly more visual problems. The authors concluded that all but the scopolamine patch may be recommended for prophylaxis in this setting of short-term, but potentially intense exposure.

Recommendations for travellers, using regimens available in Canada

The following are recommendations for preventive use by travellers who do not need to drive or perform skilled tasks, using medications available in Canada. All medications are effective compared to a placebo [A I (see Appendix I)], but none will work for all travellers. If one approach is not effective, or not tolerated, another should be tried.

There are no studies that definitively support or refute the following recommendations. Based on factors such as cost, willingness to tolerate adverse reactions, and prior experience, individual travellers may wish to choose one regimen over another.

For longer-term travel many would prefer the scopolamine patch, but it has several disadvantages. The recommendation to use alternatives (*see below) as needed for mild stimuli is based on the observation that, with use of the patch, symptoms (adverse reactions) are more frequent than symptoms attributed to motion sickness when minimal or no rough conditions are encountered[21,34].

A. Short-term exposure (≤ 6 hours)
   I. Mild to moderate stimulus
      1. Recommended
         – dimenhydrinate
      2. Alternatives
         – meclizine
         – promethazine
   II. Intensive stimulus
      1. Recommended
         – promethazine plus amphetamine
      2. Alternatives
         – dimenhydrinate
         – scopolamine patch

B. Longer-term exposure (> 6 hours)
   I. Mild stimulus
      1. Recommended
         – dimenhydrinate as needed*
      2. Alternatives
         – scopolamine patch
         – meclizine as needed*
         – promethazine as needed*
   II. Moderate to intensive stimulus
      1. Recommended
         – scopolamine patch
      2. Alternatives
         – repeated doses of dimenhydrinate
         – repeated doses of promethazine
         – repeated doses of meclizine

Treatment of established symptoms

For treatment of established symptoms, options are more limited. Once vomiting has commenced, no oral regimen that is swallowed is likely to be effective[35]. Intramuscular promethazine (25 mg to 50 mg) appears to be the most effective means of managing already developed severe motion sickness[23,31,35], but most travellers will not be able to administer intramuscular injections. Rectal suppositories are available with dimenhydrinate. Several preparations can be dissolved in the mouth, but their effectiveness in the presence of vomiting is likely significantly compromised.

If the exposure is likely to be prolonged, a scopolamine patch can also be applied[36], but this will not provide immediate benefit.

Alternative approaches to prevention of motion sickness

Acupressure, using a commercially available product applying pressure at a point above the wrist, has not been shown to be effective[4].

Compounds like caffeine alone do not appear effective, but may counteract some of the drowsiness seen with common agents like the antihistamines.

Appendix 1

Categories for strength of each recommendation	
CATEGORY	**DEFINITION**
A	Good evidence to support a recommendation for use.
B	Moderate evidence to support a recommendation for use.
C	Poor evidence to support a recommendation for or against use.
D	Moderate evidence to support a recommendation against use.
E	Good evidence to support a recommendation against use.
Categories for quality of evidence on which recommendations are made	
GRADE	**DEFINITION**
I	Evidence from at least one properly randomized, controlled trial.
II	Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytic studies, preferably from more than one centre, from multiple time series, or from dramatic results in uncontrolled experiments.
III	Evidence from opinions of respected authorities on the basis of clinical experience, descriptive studies, or reports of expert committees.

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International Notes

SCIENTIFIC CONSULTATION ON HUMAN AND ANIMAL SPONGIFORM ENCEPHALOPATHIES

A scientific Consultation of 18 human and animal neurologists, neuropathologists and scientists from 14 countries, all experts in the transmissible spongiform encephalopathies (TSEs), met at WHO headquarters in Geneva from 14 to 16 May, 1996. The Consultation examined in detail the clinical, neurologic and neuropathologic findings associated with the newly recognized variant of Creutzfeldt-Jakob Disease (V-CJD), compared these findings with data on other human TSEs, and further examined their relationship to the animal TSEs including bovine spongiform encephalopathy (BSE). In addition, the Consultation evaluated the need for worldwide surveillance of CJD, and reviewed TSE research to date, including diagnostic tests, in order to identify areas where further research is required.

The group considered that this recently described disorder is part of the CJD spectrum; it is a new variant form of CJD on grounds of its unique clinical and pathologic features. BSE has been transmitted naturally and experimentally to a range of other animal species by the oral route, and it has been suggested that the emergent cluster of the new variant form of CJD may be a consequence of exposure of the human population to the BSE agent. It should be emphasized that such a link has not been proven on epidemiologic grounds. After a thorough review of the characteristics of natural and experimental TSEs, the Consultation concluded that the type of lesions and clinical presentation of the new variant form of CJD do not provide information on the possible origins of this disorder. Further data are urgently required from scientific studies on these variant cases, including animal transmission and strain typing experiments.

Based on the recommendations of the Consultation, WHO will coordinate an intensified worldwide system for CJD surveillance and ensure training in clinical and neuropathologic diagnosis on CJD and the other human TSEs at selected collaborating centres throughout the world. In collaboration with the *Office international des Epizooties* (OIE), WHO will likewise ensure worldwide surveillance for the animal TSEs. Underlying these activities, WHO will continue to provide a scientific forum for exchange on research issues related to the TSEs as well as stimulate and facilitate research.

Source: *WHO Weekly Epidemiological Record, Vol 71, No 21, 1996.*

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