OTC advice on travel sickness

With Easter coming up and families going on holiday, travel health will be a frequent subject in community pharmacies. In this article, Alan Nathan looks at motion sickness.

Travel (motion) sickness is a condition for which pharmacists are frequently asked to provide advice and to recommend preventive treatment. All medicines licensed for this indication are pharmacy medicines so pharmacists have good options to offer.

What is motion sickness?
Motion sickness includes all forms of travel sickness (e.g., sea-sickness, air-sickness, car-sickness). It can be defined as a characteristic syndrome brought on by being transported by a means of conveyance (including fairground rides) as opposed to self-propelled motion, such as walking, running or cycling. The condition also can also be caused by simulated motion, such as being in a flight simulator or watching wide-screen projected images.

Panel 1 lists the symptoms of travel sickness. In some people the symptoms can last for some time after the journey ends.

Almost anyone can suffer from motion sickness if exposed to sufficient stimulation. Even airline pilots and astronauts are not immune. Almost all ship passengers can become seasick in rough conditions but up to 30 per cent of the population may be particularly prone to motion sickness. Panel 2 (p396) describes the prevalence of motion sickness and factors that can predispose to it.

What causes motion sickness?
The causes of motion sickness are not fully understood but the explanation currently widely accepted is the sensory conflict or neural mismatch theory. This describes the condition in terms of an individual’s response to discordant sensory information regarding motion. The theory suggests that people carry an internal expectation of motion in common situations (e.g., walking, running, jumping, etc) and this involves the correlation of sensory experience with movement.

Information about movement is obtained from several sources, including the eyes, vestibular apparatus in the ear and mechanoreceptors in the skin, muscle and joints (known as the somatosensory system). The information is stored in the brain and compared with other experiences of motion, allowing for normal function when undertaking the movements needed for everyday living. Motion sickness occurs when the signals from the senses do not match the expectations associated with the body’s actual state of movement. Symptoms of motion sickness will continue until the information has been updated to accommodate the new situation.

The sensory conflict theory appears to be borne out by common experience. For example, the person in control of a vehicle will rarely suffer from travel sickness — the driver of a car has a clear view of the route and can anticipate movements (e.g., bends in the road). In comparison, a passenger in the back of the car is more likely to be car-sick. Similarly, somebody standing on the deck of a ship is less likely to become seasick than a passenger in a cabin who can feel movement but cannot see the moving panorama, especially if the cabin is located on the outside of the vessel where the ship’s movements are more pronounced.

The exact mechanism connecting sensory conflict theory with motion sickness symptoms is uncertain but several pathways appear
**Panel 2: Factors associated with motion sickness**

**Gender** Females are more susceptible to motion sickness than males, in a ratio of 1.7:1. Susceptibility increases with use of oral contraceptives and during menstruation or pregnancy.

**Age** Children under two years of age are rarely affected. Susceptibility increases rapidly with between the ages of three and 12 years and declines gradually thereafter.

Other predisposing factors include:
- Recent ingestion of food, particularly dairy products and foods high in sodium, protein or calories
- Aerobic exercise and fitness (The reasons are not known but research has shown that aerobic capacity is specifically linked to signs and symptoms of vasomotor origin including stomach discomfort, nausea and vomiting, headache and profuse sweating.)
- Anxiety
- Tendency to facial flushing
- Migraine
- Schizophrenia
- Gastrointestinal disorders
- Unpleasant odours
- Spatial disorientation

Motion sickness can be explained by the sensory conflict or neural mismatch theory

Hyoscine and first-generation antihistamines are used. Pharmacists can also suggest strategies to minimise the effects of travel sickness (see Panel 3).

Few treatments are effective for travel sickness once the symptoms have occurred. In addition, these require a prescription and are normally administered by medical staff. Severe motion sickness symptoms are treated with intramuscular injections of hyoscine or promethazine hydrochloride.

**Hyoscine** Hyoscine hydrobromide is a naturally occurring alkaloid that competitively inhibits acetylcholine at muscarinic receptors of autonomic effector sites innervated by parasympathetic nerves. It has a central as well as a peripheral action because it is lipid-soluble and crosses the blood–brain barrier. The quaternary derivative hyoscine butylbromide (used for gastrointestinal spasm) is poorly absorbed from the gastrointestinal tract and does not readily cross the blood–brain barrier.

Hyoscine is probably the most effective drug for prevention of motion sickness. However, it is relatively short-acting when taken orally and has more pronounced antimuscarinic side-effects than the antihistamines (see below).

Hyoscine is available as tablets and as a transdermal patch. Doses for tablets vary slightly between products, but the British National Formulary recommends, for adults, hyoscine hydrobromide 300µg 30 minutes before travelling, followed by 300µg every six hours if required, to a maximum of three doses in 24 hours. The recommended dose for children over 10 years is 150–300µg, and for children aged four to 10 years, 75–150µg. The patch is effective for up to 72 hours but it needs to be applied five to six hours before travelling. It should be applied to a clean, hairless area of skin behind the ear.

**Antihistamines** The antihistamines marketed in the UK for travel sickness prophylaxis are cinnarizine, meclozine, promethazine hydrochloride and promethazine teoclate. First-generation antihistamines have anti-allergic, antipruritic, antitussive and anti-emetic properties. Anti-emetic action also results from blockade of dopamine 2 receptors in the brain. However, it has been proposed that the anti-emetic activity also results from blockade of dopamine 2 receptors in the brain.

All four compounds are probably of similar efficacy — there appear to be no comparative trials. When selecting an antihistamine to prevent motion sickness several factors, such as length of action and side-effects, can be taken into account (see Table, p398 for summary). The second-generation antihistamines, having much lower lipid solubility than first-generation compounds, do not cross the blood–brain barrier to a significant extent and exert little or no central activity. Tests have shown them to be of no value as prophylaxis for motion sickness.

Most people adapt to new types of motion stimuli after repeated or extended exposures, although the length of time it takes varies between individuals. Each experience is added to a neural store. This might be why children are more prone to car-sickness than adults and why first-time flyers are more likely to suffer air-sickness than those who fly frequently. In the same way, individuals with greater spatial and motor control (eg, athletes and soldiers) are less susceptible to motion sickness.

Hyoscine and first-generation antihistamines are used. Pharmacists can also suggest strategies to minimise the effects of travel sickness (see Panel 3).
Hyoscine is probably the most effective drug for prevention of motion sickness.

Cinnarizine Cinnarizine is a piperazine derivative and compounds in this group generally possess anti-emetic properties. Cinnarizine causes some drowsiness, but antimuscarinic side effects do not appear to be a problem. Peak plasma concentrations occur two to four hours after administration, and the half-life is three to six hours. For adults, a loading dose of 30mg is recommended two hours before the start of a journey, followed by 15mg eight-hourly during the journey. Half this dose may be given to children aged between five and 12 years, but cinnarizine is not licensed for use in younger children.

Meclozine Meclozine hydrochloride is a piperazine. It is considered to be among the least sedating compounds in this group and to have low antimuscarinic activity. It is long-acting. The adult dose is two 12.5mg tablets of meclozine hydrochloride taken at least one hour before travelling, and repeated once every 24 hours if necessary. The dose for children between six and 12 years is half the adult dose, and for children from two to six years, one-quarter the adult dose.

Promethazine Promethazine teoclate and promethazine hydrochloride are phenothiazines. They have marked anti-motion sickness activity but also marked antimuscarinic properties and sedation is common. Both compounds have been widely used for the treatment of nausea, vomiting and vertigo. The sedative effect of promethazine hydrochloride is sometimes considered to be an advantage in young children on long journeys. Promethazine teoclate is long-acting, with an initial dose for an adult or child over ten years of one 25mg tablet, taken two hours before a short journey or the night before a long journey, with further 25mg doses every 24 hours if required. Half the adult dose can be given to children between five and 10 years old. Promethazine hydrochloride is also long-acting, and it is licensed for use in children from the age of two years. It has the advantage of being available as tablets in two strengths (10mg and 25mg) and as an elixir (5mg/5ml). Dosage schedules are as for promethazine teoclate, but one 10mg tablet is recommended for five- to 10-year-olds, and a 5mg dose of the elixir for children between two and five years.

Cyclizine Cyclizine is also a pharmacy medicine licensed for motion sickness, but it is subject to abuse (for its euphoric effects) and is not marketed for OTC use.

Adverse effects and contraindications Antihistamines and hyoscine have similar adverse effects, including sedation. This effect may be useful for children (so promethazine is an option), but adults may prefer a product that is less likely to cause drowsiness (eg, meclozine or cyclizine). Antimuscarinic side effects include:

- Dry mouth
- Blurred vision
- Urinary retention
- Constipation

At the low doses and short periods of use in motion sickness, antimuscarinic effects do not normally cause problems. However, antihistamines and hyoscine should still be avoided in patients suffering from glaucoma or prostatic hypertrophy. They should also be used with caution generally in the elderly and in patients with epilepsy or cardiac or cardiovascular disease.

Panel 3: Advice to minimise travel sickness

**General**
- Avoid heavy meals before travelling
- Avoid pungent odours
- Avoid alcohol

**Road travel**
- Drive if possible — drivers very rarely suffer from travel sickness
- If you do not or cannot drive, sit in the front passenger seat if possible
- Sit near the front in a bus or coach
- Keep vehicle windows open
- Do not read. Try to keep looking out of the window, at the road ahead. Children can be distracted and made to look out with games, such as "I-Spy"
- Listen to the radio or talk to other passengers
- Use a seat booster for children so that they can see out of the car

**Sea travel**
- If possible, stay on deck
- Below deck, stay in the centre of the ship and lie down, remain still and keep the eyes closed

**Air travel**
- Try to sit by the wing of the aircraft (where less turbulence is felt)
Paradoxical stimulation of the central nervous system can occur with antihistamines in children, resulting in insomnia and excitement and, rarely, nightmares, hallucinations and even convulsions. Photosensitivity reactions have been reported with promethazine.

In pregnancy, use under medical supervision is advised for antihistamine travel sickness products, due to fears regarding possible congenital malformations although no causal link has been established. Similar fears have not been expressed about hyoscine products and no warnings have been issued against their use in pregnancy. However, it is prudent to avoid any medication in pregnancy, if possible, and certainly in the first trimester.

Interactions
Antihistamines and hyoscine interact with other drugs that cause sedation or have antimuscarinic effects, including tricyclic antidepressants, monoamine oxidase inhibitors, phenothiazines, hypnotics, nefopam, amantadine and disopyramide. Dry mouth caused by the antimuscarinic effects of antihistamines and hyoscine may reduce the effect of sublingual nitrates. Alcohol should be avoided when taking any anti-motion sickness preparations.

Other options
A wide range of herbal, homoeopathic and non-pharmacological treatments have been recommended for motion sickness, but there is no reliable clinical evidence to support the use of most of these. There are three complementary therapy approaches to travel sickness available in community pharmacies.

Ginger
The most popular herbal preparation for nausea is ginger root, marketed in the UK as a food supplement in tablet or capsule form. There is much anecdotal evidence that ginger is an effective prophylactic; several laboratory and clinical trials have been carried out but with conflicting results. Any beneficial effect appears to be due to direct action on the gastrointestinal tract rather than on the central nervous system. The recommended adult dose is 500mg one hour before travelling followed by 500mg every two to four hours as necessary. For children over two years, the dose is calculated by weight.

**Table: Comparison of hyoscine and the antihistamines for travel sickness**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Efficacy</th>
<th>Drowsiness</th>
<th>Antimuscarinic effects</th>
<th>Minimum age</th>
<th>When the first dose should be taken</th>
<th>Approximate duration of action (frequency of dosing)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyoscine</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td>5 years</td>
<td>Tablets 30 minutes before travel</td>
<td>Tablets up to 6 hours</td>
</tr>
<tr>
<td>Cinnarizine</td>
<td>+ +</td>
<td>++</td>
<td>+</td>
<td>5 years</td>
<td>2 hours before travel</td>
<td>Up to 8 hours</td>
</tr>
<tr>
<td>Meclozine</td>
<td>+ +</td>
<td>+</td>
<td>+</td>
<td>2 years</td>
<td>At least 1 hour before travel</td>
<td>Up to 24 hours</td>
</tr>
<tr>
<td>Promethazine</td>
<td>+ +</td>
<td>+ + + +</td>
<td>+ +</td>
<td>5 years (tablets) 2 years (syrup)</td>
<td>The night before travel Up to 24 hours (teoclate)</td>
<td>6–8 hours (hydrochloride)</td>
</tr>
</tbody>
</table>

**Acupressure** It has been suggested that acupressure can reduce symptoms of travel sickness. A knitted elasticated wrist band is available that operates by applying pressure on the “nei kuan” (P6) acupressure point on each wrist by means of a plastic stud. However, clinical trial results have been disappointing. It has been postulated that there is insufficient movement of the wrist to provide the continuous stimulation needed to make wearing the bands effective.

**Homoeopathic medicines** Several homoeopathic medicines are indicated for travel sickness. The appropriate substance is best recommended by a registered homoeopath after taking into account individual factors. A compound preparation, containing most of the homoeopathic substances used to treat travel sickness, is available.

**References**

**Further reading**