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Winter ills in children

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Infectious disease patterns a major concern

Interview with Professor Diana Lennon

"Some parts of New Zealand's North Island have infectious disease patterns, which are unacceptable in a developed country such as New Zealand" says Professor Lennon, Professor of Population Child and Youth Health at Auckland University. "Young Tamariki Māori and Pacific Island children in particular are suffering the burden of these infections."

Respiratory infections are a huge problem

Infectious diseases, mainly respiratory, are the primary reason for hospital attendance in young children. The majority of these are viral infections with hypoxia being the usual reason for admission. Respiratory infections, predominantly bronchiolitis and also pneumonia, are the principle causes of hospital admission for children under two years of age.

Respiratory infections are a huge problem in the upper parts of the North Island, particularly in winter when hospital admissions peak. Part of the underlying cause is extended family living, particularly where families double up and share housing to cope with high rents.

Professor Lennon notes an increasing emergence of bronchiectasis in these disadvantaged children. A link to recurrent episodes of bronchiolitis, although being considered, has yet to be established. Historically bronchiectasis has been linked to measles, whooping cough and adenoviral infections and Professor Lennon warns that our measles immunisation rates are less than optimal making a measles epidemic possible.

Key messages for primary care:

- Recognise children with severe bronchiolitis who need hospitalisation
- Carefully evaluate chronic cough in children
- Contribute to improved measles immunisation rates
- Provide letters for housing improvement for children with recurrent respiratory infections including bronchiolitis

Rheumatic fever in some parts of New Zealand is unacceptably high

Rheumatic fever is a serious but preventable chronic disease, which is rare in most developed countries, but unacceptably common in some parts of the North Island.

Rheumatic fever in New Zealand almost always occurs in Tamariki Māori and Pacific Island children. Children of European or Asian descent and children living in the South Island rarely suffer from the illness.

Professor Lennon says 50–60% of children with rheumatic fever develop clinically apparent heart disease and 10–20% of children who get rheumatic fever will be left with permanent serious heart damage, some will require repeated surgery and have a shortened life span. Heart damage can be identified with echocardiography in up to 80% of children who suffer from the disease.

The key to the primary prevention of rheumatic fever is treating streptococcal throat infections in at-risk children

Children who have had rheumatic fever require ongoing monthly penicillin injections until they are 21-years-old to prevent further attacks of rheumatic fever, that are even more likely to cause permanent heart disease.

There is strong evidence that treating streptococcal sore throats in at-risk children is effective in preventing rheumatic fever. Streptococcal sore throats are very infectious with up to 50% risk in siblings in a household.

Crowded housing increases the risk of rheumatic fever and at-risk children often have poor access to treatment for various reasons, for example transport to primary care. The idea of developing a programme for throat swabbing children with sore throats at schools in high-risk areas, particularly metropolitan Auckland and the upper North Island, is being explored. This is based on a New Zealand research project and similar community projects overseas.

Professor Lennon has recently been involved in the development of New Zealand guidelines for the treatment of sore throats and prevention of rheumatic fever that will be published shortly (www.nhf.co.nz). She is quick to point out that she does not advocate blanket use of penicillin for sore throats, and the focus in the new guidelines is on the concept of treating children at risk of rheumatic fever and reducing antibiotic use in those at low risk.

Rheumatic fever is extremely uncommon in advantaged children, mostly of non-Māori or Pacific origin. Symptomatic treatment of pharyngitis should be paramount in these children. The carriage of *S. pyogenes* in the throats of children without sore throat or clinical pharyngitis is a distractor. It does not increase rheumatic fever risk and does not benefit from treatment.

She says that post streptococcal glomerulonephritis also persists as a problem in the upper North Island. It usually follows on from impetigo and occasionally streptococcal sore throats. However, impetigo caused by *S. pyogenes* has not been linked to rheumatic fever and as yet, there is no explanation for this curious mixture of relationships.

In New Zealand there is a different raft of serotypes of *S. pyogenes* causing rheumatic fever. This means a vaccine developed and recently trialled in the US is unlikely to be effective in this country. However other vaccines are being developed.

Key message for primary care:

- Target antibiotic treatment for sore throats to children who are at risk of rheumatic fever, not those at low risk

Immunisation preventable disease

The incidence of meningococcal disease is falling rapidly and appears to be related to the MeNZB immunisation programme. Professor Lennon is concerned, that while the programme appears very successful, the phase four evaluation has not so far been transparent. She believes more detail is needed to understand the relative contributions of the programme and the already waning epidemic.

There are currently four new immunisations competing for introduction into New Zealand:

- Pneumococcal conjugate vaccine: pneumococcal disease prevention
- Varicella: chickenpox prevention
- Rotavirus: gastroenteritis prevention
- Human papilloma virus: cervical cancer prevention

Professor Lennon supports them all, despite being expensive. She believes the priority is to immunise children against pneumococcus. Pneumococcal meningitis is a devastating disease and although febrile illnesses in children are usually viral, one of the main reasons for using antibiotics is suspicion of pneumococcal infection.

Immunising children with pneumococcal conjugate vaccine reduces the carriage of the organism in the community. This herd immunity has the added benefit of reducing pneumococcal disease in older adults.

Key messages for primary care:

- Immunisation provides effective primary prevention for many infectious diseases, which can destroy the health of children.
- The results of immunisation are best when immunisation rates are high.
- Primary care has a vital role in maintaining these rates.

Bronchiolitis

Cough in children

Fever in children

Acute gastroenteritis in children

Acute asthma in children: are nebulisers or spacers best?

Key Advisers

Dr Marguerite Dalton

Dr David Reith

1. Bronchiolitis

Most infants presenting with wheeze in the first year of life have bronchiolitis. Most cases of bronchiolitis occur between 2 and 5 months of age, in airways with very small calibre.

Bronchiolitis is usually caused by Respiratory Syncytial Virus, but can also be caused by rhinovirus, adenovirus, influenza and parainfluenza viruses. It starts with 2–3 days of coryzal symptoms and progresses to cough and wheeze with fever and tachypnoea.

Wheezes and crackles are usually heard throughout the chest. Focal chest signs suggest alternative diagnoses such as pneumonia or aspiration.

Infants with bronchiolitis often get worse for the first 72 hours of their illness and then start to improve. Symptoms may take several weeks to resolve, with a median duration of approximately 12 days. Children and parents need support during this time.

Bronchiolitis has a 1–2% mortality rate and infants with hypoxaemia related to small airways obstruction may need treatment with racemic epinephrine and steroids in addition to oxygen, intravenous fluids and nasogastric feeding.

Management of bronchiolitis is mostly supportive

Interventions such as bronchodilators, adrenaline, steroids and antibiotics have not been shown to be beneficial in uncomplicated bronchiolitis. Management is supportive but may include the need for oxygen, nasogastric feeding or intravenous fluids. Primary care clinicians need to know the features of moderate to severe bronchiolitis so that they can manage it appropriately but also so that they can educate the parents of children with bronchiolitis about recognising deteriorating illness.

Assessment of severity

Table 1: Assessment of severity of bronchiolitis

	Mild	Moderate	Severe
Respiratory rate *breaths/minute*	Under 2 months >60/min 2–12 months >50/min	>60/min	>70/min
Chest wall indrawing	None/mild	Moderate	Severe
Nasal flare	None/mild	Present	Present
Grunting	Absent	Absent	Present
Feeding	Normal	Less than usual Frequently stops Quantity >1/2 normal	Not interested Choking Quantity <1/2 normal
History of behaviour	Normal	Irritable	Lethargic

Any criterion in the severe category designates the child as severely ill

Recognising severe illness in children

- Behaviour and feeding both go from interested infant, to infant not interested
- **Respiratory rate**
  - A newborn may breathe up to 60 breaths/min
  - A 1-year-old: 40 breaths/min
  - A 5-year-old: 30 breaths/min

  If the rate is high, look for potential respiratory failure using 2 key signs
  - effort, **and**
  - effectiveness of effort
- **Increased effort** is indicated by sounds
  - Stridor in upper airway obstruction
  - Wheeze or grunting in lower airways obstruction
  - Accessory muscle use producing nasal flare, heaving chest, intercostal and subcostal indrawing
- **Effectiveness of effort** is indicated by looking at the chest movement and listening to breath sounds to judge ventilation:
  - A silent chest
  - Falling heart rate
  - Falling level of consciousness
  - Falling respiratory rate in severe illness

  are all preterminal events.

  During respiratory failure, skin colour changes from pink to pale, to mottled.

  Pale colour indicates vasoconstriction and mottled indicates terminal circulatory collapse.

Reference: Bone J. Recognising the very ill child NZ Doctor 14 Mar 2007.

When to refer with acute bronchiolitis

As a general rule **refer infants earlier rather than later**: if in doubt get specialist advice.

Refer all infants immediately with; severe illness (see Table 1), progressive dehydration, where there is clinical concern about hypoxia or a history of apnoea.

Refer early

- If less than 8-weeks-old or if birth was significantly premature (<32 weeks gestation)
- If there has been apnoea or significant comorbidity (heart and lung disorders, immune-compromise)
- If illness is getting worse after 72 hours or home care is uncertain

Management of bronchiolitis at home

Most infants with bronchiolitis can be safely managed at home. Supportive care plus careful observation for signs of deterioration are the keys.

Supportive care may include:

- Keeping the child's environment smokefree
- Keeping the child well hydrated
- Small frequent feeds
- Minimal handling
- Normal saline nasal drops before feeds
- Caregiver hand washing to prevent spread to other children

Written instructions will help caregivers to keep an eye on feeding patterns and behaviour and to monitor for:

- Respiratory rate
- Indrawing
- Grunting
- Nasal flare
- Sleepiness
- Colour

Infants with a moderate episode of bronchiolitis need to be reviewed within 24 hours and a firm appointment (time, place, person) helps to ensure the child is seen. *(For an example of written instructions for caregivers see page 23)*

2. Cough in children

Cough in children has different causes to cough in adults and symptomatic treatment is rarely needed or effective.[1] The smaller airways are vulnerable to inflammatory disease causing swelling and obstruction by mucous secretions. Coughing assists clearance of mucous, so do not attempt cough suppression.

It is reasonable to categorise childhood cough as:

- Acute cough – lasting less than two weeks
- Persistent cough – lasting two to four weeks
- Chronic cough – lasting over four weeks

Acute cough

Acute cough is usually viral

Most acute cough in children is associated with viral upper respiratory tract infections (URTI). The majority of these (70–80%) will resolve within one week although 5% will persist for more than four weeks.

No over-the-counter or prescription medicines are effective for the symptomatic relief of acute cough in children but there does appear to be a significant placebo effect. Over-the-counter cough and cold medicines are a significant cause of morbidity, especially from accidental overdose.

It follows that we should look for something soothing and safe for children with acute cough. Honey and lemon drinks have stood the test of time and can be made at home at little cost. However, water should not be boiled, firstly because children are not usually used to hot drinks and secondly because there is risk of scalding.

Aspiration may be missed

Characteristics of an acute cough may raise suspicion of specific causes such as the barking cough of croup or the paroxysmal cough of pertussis. When there are no symptoms of a viral infection, careful consideration needs to be given to an aspiration episode, particularly in younger children. Aspiration most often occurs when an older sibling has fed a young child unsuitable food.

Cough soon after birth is cause for concern

Cough that begins at, or within a few weeks of birth always raises concern. Congenital causes include tracheomalacia, tracheo-oesophageal fistula or laryngeal cleft. Cough starting within a few weeks of birth raises the additional possibilities of suppurative lung disease, aspiration, gastro-oesophageal reflux or infection with *chlamydia trachomatis*. Cough in a neonate often warrants discussion with a paediatrician.

Chronic cough

Cough continuing beyond four weeks needs careful evaluation

Although a non-specific post-viral cough is still the most likely diagnosis, children who continue to cough beyond four weeks need evaluation to exclude more specific causes. Evaluation of a significant ongoing cough includes history and physical examination with consideration of the need for chest x-ray and, if the child is old enough, spirometry.

Passive or active smoking is a common cause of cough in children. Fifty percent of children over the age of two years, with at least two family members who smoke, have cough.

Some specific causes suggested by the history and examination are described in Table 2:

Table 2: Specific causes of chronic cough suggested by the history and examination

Chronic cough	*Specific cause of cough*
Accompanying wheeze	Asthma or aspiration
Stridor	Tracheomalacia, foreign body
Moist cough, clubbing or Failure to Thrive	Suppurative lung disease, cyanotic heart disease, cystic fibrosis, immune or ciliary disorders
Aspiration episodes or swallowing difficulties	Foreign body or aspiration
Paroxysmal cough or family members with persistent cough	Pertussis
Honking cough absent during sleep	Psychogenic or habit cough
Staccato cough with or without conjunctivitis	Chlamydia

Cough from post-nasal drip, gastro-oesophageal reflux and 'cough variant asthma' are unusual in children

Studies show that post-nasal drip is unlikely to cause cough in children and the cough is more likely to be related to coexistent lower airway pathology. The use of medications to 'dry up' nasal secretions is therefore unlikely to help the cough.

Gastro-oesophageal reflux has been suggested as a common cause of cough in adults but there is no convincing evidence that it is a common cause of cough in children.

Some children with isolated persistent cough without wheeze receive a diagnosis of 'cough variant asthma'. However there is no evidence that this is really a form of asthma. Few children with isolated chronic cough have eosinophilic inflammation, atopy or airway hyperresponsiveness and they do not respond to bronchodilators or corticosteroids.

Cough may be the predominant feature of asthma but is usually accompanied by wheeze. Isolated chronic cough with no apparent underlying cause is more likely to be related to a hypersensitive cough reflex.

Treatment of chronic cough targets the cause not the symptoms

Symptomatic treatment of chronic cough is usually not effective or appropriate. It is the underlying cause, which should be the target of therapy.

- Antihistamines are proven to have no benefit in chronic cough and are associated with high levels of side effects
- Cough suppressants such as dextromethorphan, pholcodine and codeine are contraindicated in children
- Menthol inhalations are not effective and are associated with risk of scalding injuries from boiling water
- There is no evidence for effectiveness of herbal remedies
- Emetics, such as guaifenesin, ammonium chloride, ipecacuanha and squill, are used in low doses as expectorants but are not effective

Nevertheless, the significant placebo effect of cough medicines may convince parents that one is needed. A simple soothing demulcent, with ingredients such as honey and lemon, syrup or glycerol, may help reduce coughing and irritation. It is best to avoid those with high sugar content. Lozenges are associated with risk of choking for children, especially those under the age of three years.

All children with cough will benefit from a smokefree environment.

3. Fever in children

Search for a cause

Manage the symptoms

Fever is an appropriate response to infection and has some beneficial effects. For example, fever can make the environment less favourable for microorganisms to multiply and certain parts of the immune system work better at slightly higher temperatures. However, sustained high temperature adds to insensible fluid loss and risk of progressive dehydration.

Febrile convulsions occur in 3–4% of children with fever. Although they are associated with fever, they are not prevented by antipyretic medications such as paracetamol. Febrile convulsions, if they do occur, are usually brisk and not likely to cause brain damage or learning disabilities. Complex febrile seizures can occur and may be prolonged. If prolonged (>15 minutes) they should be treated with rectal diazepam.

Antipyretic medications along with physical interventions, such as cool drinks and reducing excessive layers of clothing, can be appropriate to manage discomfort which may be associated with fever.

Measuring the temperature of children under five years	
√ Electronic thermometer in axilla	~~X Oral thermometer~~
√ Chemical dot thermometer in axilla	~~X Rectal thermometer~~
√ Infra-red tympanic thermometer	~~X Forehead crystal thermometer~~

Stratification of risk for serious pathology clarifies management decisions

Risk stratification for children with fever

Practitioners will always want to conduct a careful search for a focus of infection for any child with a fever and this can be combined with assessing the risk of serious pathology. Urinalysis of a clean catch urine sample is an essential part of this assessment when no obvious causes are apparent.

Table 3: High risk of serious pathology

High risk features	
Colour	Pale, mottled, ashen or blue
Activity	Weak, high-pitched continuous cry Diminished level of consciousness Appears ill Unable to rouse or if roused does not stay awake
Respirations	Grunting RR >70 breaths/min Moderate to severe chest indrawing
Hydration	Reduced skin turgor Capillary refill time ≥3 secs
Other	Non blanching rash Bulging fontanelle Neck stiffness Focal neurological signs Focal seizure Bile stained vomiting Swelling of limb or joint, non-weight bearing, not using an extremity **High temperatures** need to be interpreted with regard to other signs and symptoms, however T >39ºC should be regarded as a high risk feature

Any of the above features place a child in a high-risk category for serious pathology.

The child needs immediate admission to hospital.

Table 4: Intermediate risk for serious pathology

Intermediate risk features	
Colour	Normal
Activity	Not responding normally to social cues Wakes only with prolonged stimulation Decreased activity No smile
Respirations	Nasal flaring: age over 12 months Age 0–2 months, RR >60 breaths/min Age 2–12 months, RR >50 breaths/min Age >12 months, RR >40 breaths/min Crepitations
Hydration	Dry mucous membrane Poor feeding in infants Reduced urine output
Other	Fever for ≥5 days

In the absence of high-risk features, any of the above features places a child at intermediate risk of serious pathology.

Depending on the findings and circumstances, one or more of the following may be appropriate:

- Referral for urgent paediatric assessment
- Telephone consultation with a paediatric specialist
- Firm arrangements, time/place/person, made for a further review
- Written and verbal instructions on warning symptoms that may occur and how to respond to them

Table 6: Features of some of the serious causes of fever in children

Diagnosis to be considered	Signs in conjunction with fever
Meningococcal disease	Non blanching rash PLUS **one** of: An ill looking child, petechiae or purpura, capillary refill time >3 secs, meningism
Meningitis	Neck stiffness, bulging fontanelle, decreased level of consciousness, limpness (NB Neck stiffness and bulging fontanelle are relatively insensitive signs of meningitis)
Herpes simplex encephalitis	Focal neurological signs, focal or generalised seizures, decreased level of consciousness
Pneumonia If wheeze is present the diagnosis of pneumonia is less likely	Tachypnoea: Age 0–2 months, RR >60 breaths/min Age 2–12 months, RR >50 breaths/min Age >12 months, RR >40 breaths/min Crepitations, nasal flaring under 12 months, chest indrawing, cyanosis
Urinary tract infection	Vomiting, poor feeding, lethargy, irritability, abdominal pain or tenderness, dysuria or increased frequency, offensive urine or haematuria
Septic arthritis	Swelling of a limb or joint, not using an extremity, non-weight bearing
Kawasaki disease (very rare)	Fever >5 days WITH at least **four** of the following: Rash, conjunctivitis, lymphadenopathy, cracked lips, skin peeling

Be alert for signs of septicemia, i.e. significant fever (>38°C) ***PLUS*** lethargy (not interested, not feeding) and/or significant dehydration (dry mucous membranes, poor urine output, capillary return >2 secs) and/or fast respiratory rate with increased effort and signs of poor effectiveness of effort.

If a child becomes rapidly ill or is particularly ill, with a rash, **consider and exclude meningococcal disease**. The rash may present as a morbilliform or subtle petechial rash before progressing to a purpuric rash.

4. Acute gastroenteritis in children

Presentation of gastroenteritis may suggest cause

Viral infections cause most gastroenteritis in children in New Zealand. They usually produce low-grade fever and watery diarrhoea, without blood.

Rotavirus, the most frequent viral pathogen, tends to be seasonal, with late winter peaks, and most frequently affects children between 6 months and 2 years of age. Most children will come in contact with the virus and, as immunity is long lasting, infection is uncommon in adults.

Norovirus affects all ages, as immunity does not last long. Infection tends to occur as outbreaks in institutions such as preschools, childcare centres, hospitals and rest homes.

Bacterial infections are more likely to be associated with higher fevers and blood or mucus in the stool. They may also be associated with abdominal pain or systemic effects, from spread of the bacterial pathogens themselves or associated toxins.

Viral infections are usually transmitted by the faecal-oral route or by respiratory droplets but they can linger on contaminated surfaces. Bacterial infections are often acquired by the ingestion of contaminated food or drink which has not been properly cooked, stored or processed. Chicken, beef, pork, seafood, ice cream and reheated rice are all frequent sources of bacterial gastroenteritis.

Water may be contaminated with viruses, bacteria or protozoa.

Most Gastroenteritis in children is viral

There are many causes of acute gastroenteritis in children (Table 7)[2] but the majority are caused by rotavirus or norovirus.

Table 7: Causes of acute gastroenteritis in children

Pathogens causing acute gastroenteritis in children
Viruses – approximately 70% - Rotaviruses - Noroviruses - Enteric adenoviruses - Caliciviruses - Astroviruses - Enteroviruses
Bacteria – 10 to 20% - *Campylobacter jejuni* - Non-typhoid *Salmonella* spp. - Enteropathogenic *E. coli* - *Shigella spp.* - *Yersinia enterocolitica* - Shiga toxin producing *E. coli* - *Salmonella typhi* and *S. paratyphi* - *Vibrio cholerae*
Protozoa – less than 10% - Cryptosporidium - *Giardia lamblia* - *Entamoeba histolytica*
Helminths - Strongyloides stercoralis

Management involves considering four important questions

The following four-step approach to the management of gastroenteritis in children is based on recommendations from Starship Hospital[3] but adapted for use in primary care.

1. **Is the child shocked?**
2. **Is it really viral gastroenteritis?**
3. **Is the child dehydrated?**
4. **Can the child be managed safely at home?**

1. Is the child shocked?

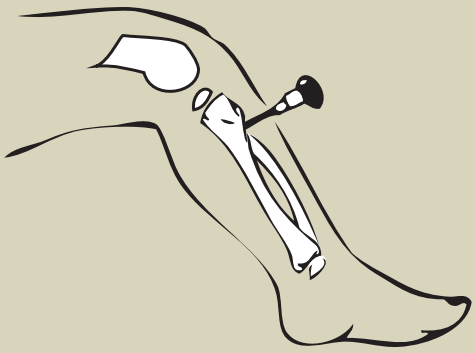
Features of shock in a child may include:

- Limpness
- Drowsy or comatose
- Rapid, thready pulse
- Cold, blue peripheries
- Hypotension
- Anuria

Skin retraction and capillary refill are less reliable signs.

Shock is an emergency and the child will need immediate hospitalisation. Consider the need for intravenous or intraosseous access if there will be any delay in getting hospital care.

Intraosseous infusion



For a detailed explanation of the technique, equipment, indications etc required for ***intraosseous infusion*** visit the following website: ***http://snipurl.com/1hr9v***

2. Is it really viral gastroenteritis?

The differential diagnosis of viral gastroenteritis is not always easy. Sometimes in the middle of an epidemic the diagnosis can be mistakenly applied to a child who has another cause for their symptoms. It is worth remembering:

- Not all vomiting is gastroenteritis
- Not all diarrhoea is gastroenteritis
- Not all gastroenteritis is viral

Not all vomiting is gastroenteritis

Vomiting may precede diarrhoea in rotavirus, but isolated vomiting always raises suspicion of another cause. Bile stained vomiting means bowel obstruction until proven otherwise.

Surgical conditions that may present with vomiting include:

- Pyloric stenosis (typical age about 6 weeks)
- Intussusception (typical age about 6–10 months)
- Appendicitis
- Intestinal obstruction

Other possible causes include:

- Infections such as urinary tract infection, otitis media, pneumonia
- Metabolic disease such as diabetic ketoacidosis and inborn errors of metabolism
- Head injury
- Poisoning

Not all diarrhoea is gastroenteritis

Other causes for diarrhoea need to be considered. These include:

- Antibiotics or other medications
- Spurious diarrhoea secondary to constipation
- First time presentations of chronic diarrhoea, such as coeliac disease

Not all gastroenteritis is viral

Bacterial gastroenteritis has higher complication rates and worse outcomes than viral gastroenteritis. Factors that may raise suspicion of bacterial gastroenteritis include:

- Blood or mucous in the stool
- Higher fevers
- Systemic toxicity
- Abdominal pain
- Association with outbreak linked to contaminated food source

Suspicion of bacterial gastroenteritis is an indication for stool culture. *Campylobacter* is the most common form of bacterial gastroenteritis. Antibiotics are not indicated for *campylobacter* gastroenteritis unless the child is systemically unwell, as they may prolong the diarrhoea or carriage of the organism.

If the child is systemically unwell, erythromycin may be considered.

3. Is the child dehydrated?

Documented recent weight loss is a good indication of the level of dehydration but these measures are often not available. Unfortunately clinical estimates are not very accurate and the categories of dehydration, which can be defined by them, are very broad.

Table 8: Signs of dehydration in a child

	Clinical signs of dehydration	**Pinch test**
No dehydration	No signs	Skin fold retracts immediately
Dehydration	Two or more of: - Restlessness or irritability - Sunken eyes - Thirst - Deep acidotic breathing	Slow retraction of skin fold – visible for less than 2 seconds
Severe dehydration with or without shock	Two or more of: - Abnormally sleepy or lethargic - Sunken eyes - Drinking poorly	Very slow retraction of skin fold – visible for over 2 seconds

4. Can the child be managed safely at home?

Children over 6 months with viral gastroenteritis of less than 24 hours duration, low-grade fever, mild levels of dehydration, no abdominal pain and minimal systemic symptoms can usually be managed safely at home. The decision is often a difficult clinical judgement and will be strongly influenced by home circumstances and ability to provide regular medical follow up.

Oral rehydration is safe and effective for most children

Oral rehydration therapy for dehydration from gastroenteritis is safer and more effective than intravenous therapy for all degrees of dehydration other than shock. However it requires a lot of input from the child's caregiver.

Vomiting is not a contraindication to oral hydration. Most children with gastroenteritis who vomit, will still absorb a significant percentage of any fluid given by mouth or nasogastric tube.

Fluid replacement occurs in two phases: rehydration and maintenance

Commercial oral fluid replacement solutions, such as Plasmalyte and Pedialyte, are mixtures of sodium and potassium salts, a base (citrate or bicarbonate) and a carbohydrate. They are designed to correct deficits in water and electrolytes caused by diarrhoea. If the child is lethargic and the skin feels dry and inelastic, dehydration is likely to be associated with low sodium. If the child has hypernatraemic dehydration, thirst is extreme and the skin feels doughy.

Breast milk, formula, cow's milk (if the child is over one year), clear soup or rice water are all suitable. Highly diluted juice or lemonade can be used if there is not a better alternative, at a dilution rate of one part juice to five parts water. Lemonade is diluted with warm water to get rid of the bubbles.

Cola, tea, coffee or sports drinks are not suitable because of their high stimulant or sugar content

Rehydration phase

During the rehydration phase, fluid is given at a rate of 5 ml per minute by teaspoon or syringe. The small volumes decrease the risk of vomiting. The rate (1 teaspoon/minute) is easy to calculate and administer for a parent sitting at the bedside. This can be changed to 25 ml every 5 minutes once the child stops vomiting.

This rate will rehydrate a moderately dehydrated 1-year-old in 2 to 4 hours and a 2-year-old in 3 to 5 hours.

Frequent review (at least 2 hourly) is advisable in the rehydration phase. A child who is not rehydrating at this rate of oral replacement will require nasogastric or intravenous fluids.

Maintenance phase

Once the child is rehydrated, hydration is maintained by giving maintenance requirements plus additional fluid to replace the fluid in every loose stool, or the child will slip back into dehydration.

Fluid requirements to maintain hydration

Table 9: Approximate fluid requirements to maintain hydration

Weight kg	Maintenance requirements ml/hour
5	20
10	40
15	50
20	60
25	70
30	75

Replacing additional fluid loss in stool

In rehydrated children whose losses are not unusually profuse, advise parents to give both maintenance fluids plus roughly 50–100 ml for each diarrhoeal stool for a child under two years and 100–200 ml for a child over two years. As with replacement, this volume should be given in small aliquots rather than as a single large bolus.

Children who have profuse ongoing diarrhoea need to have the diarrhoea measured to calculate the additional fluid replacement required.

Drug therapy rarely needed for gastroenteritis in children

Antibiotics

Even in bacterial gastroenteritis, antibiotics are not usually indicated. Antibiotics may prolong the duration of diarrhoea and are best administered on the basis of a laboratory result.

Antibiotics are required for bacterial gastroenteritis complicated by septicaemia and for cholera, shigellosis, amoebiasis, giardiasis and enteric fever.

Antidiarrhoeal and antiemetic drugs have risks of adverse effects

Anti-diarrhoeal agents, such as loperamide, should be avoided in children under the age of 12 years. They may reduce the duration of diarrhoea but adverse effects such as sedation, ileus and respiratory depression can occur.

Antiemetic medications are not recommended. They may reduce vomiting but do not reduce the need for intravenous rehydration. They may induce sedation, making oral rehydration more difficult.

Oral zinc may help

Oral zinc therapy given at onset of symptoms can reduce the duration and severity of acute diarrhoea but is usually not necessary.

Lactose intolerance is usually mild and self limiting

Although lactose intolerance is common after viral gastroenteritis it is usually mild and self-limiting and does not require treatment. If it does persist, a lactose-free formula is recommended for four to six weeks but this is not necessary as a routine for all children with gastroenteritis.

5. Acute asthma in children

aged 1–15 years: are nebulisers or spacers best?

Spacers and nebulisers are equally effective

Many clinical trials have found spacers and nebulisers to be equally effective for delivering high dose bronchodilators in acute asthma and they have comparable clinical outcomes.[4]

Spacers have the advantages of being:

- Less frightening, especially for children
- Not dependent on a power supply
- Easier to maintain
- Cheaper

The cylindrical spacers that are available on Practitioners Wholesale Supply Orders are suitable. A mask is used for young children. Depending on the individual child, they can usually manage without a mask once they are over three to five years.

Salbutamol is given through the spacer one puff at a time, and 4 deep breaths are encouraged to take up each puff. Six puffs should be given every 20 minutes up to the recommended dose. Depending on response, referral may be indicated.

The recommended dose for ***salbutamol*** in a spacer for ***acute severe asthma*** is:
Salbutamol MDI 100 microgram puffs

- Age <5 years – 6 puffs
- Age >5 years – up to 12 puffs

The use of Prednisolone should also be considered. 'Redipred' liquid 5 mg/ml is available, the recommended dose is 2 mg/kg once daily.

Patient information on spacer use and maintenance is available from bpac^{nz} and can be ordered by faxing 0800 27 27 69 or visit www.bpac.org.nz

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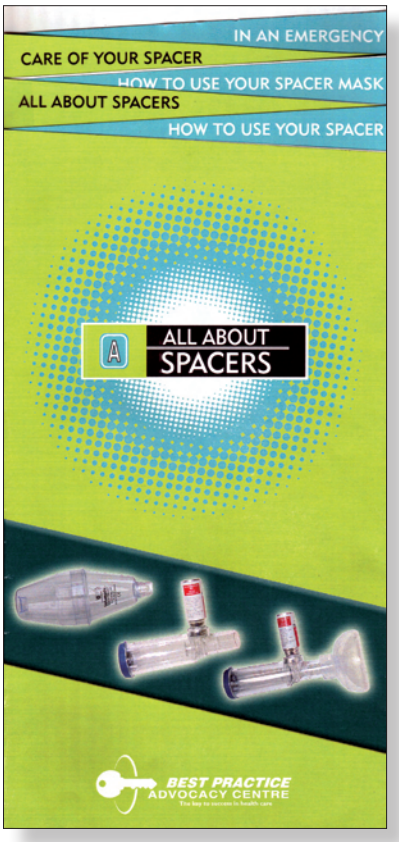

Do you have electronic notes for disorders that cover Normal expectations, Emergency signals & Timely review?

Are you willing to share these with your colleagues?

If your answers are yes and yes, please send them to us and we can make them available on our web site.

editor@bpac.org.nz

On the opposite page you will find an example of a Safety NET Note for bronchiolitis in children. Safety NET notes for viral upper respiratory infections with fever and gastroenteritis are also available from www.bpac.org.nz in .rtf format so that you can download them and incorporate them into the outbox or form letters on your PMS. You are welcome to modify them to make them more suitable for the context of your clinical practice.

PATIENT ADVICE PRINTOUTS

Electronic Safety NET Notes available at www.bpac.org.nz

Patients often remember little of what we say during consultations. Important information may be forgotten. We try to overcome this by giving out notes or pamphlets to take away.

Electronic notes have several advantages:

- They can be prewritten as form letters in our Practice Management Systems (PMS).
- They can be embedded in templates, which contain practice information such as phone numbers or after-hours contact details.
- They can be personalised, electronically or manually, for individual patients.
- A record of the note is automatically placed in patient's notes.

The Department of General Practice at the Dunedin School of Medicine has identified three essential components of information to give to patients at the time of acute presentation. For teaching purposes this has been labelled as Safety NET.

The three components are:

Normal expectation – What can be expected and when to return in normal circumstances.

Emergency signals – Signs and symptoms of a possible emergency and how to respond.

Timely review – Indications things may not be progressing as expected and urgent review is advisable.

Caregiver advice for bronchiolitis

Your child has bronchiolitis. This is very common in children under one-year-old and is caused by a virus. Bronchiolitis can usually be managed safely at home

1. *What to expect and how you can help your child*

You can expect your child to get a lot better after the first three days, although their cough may linger for several weeks.

Medicines are not helpful for children with bronchiolitis but you can help keep your child comfortable by:

- Keeping your child's environment smokefree
- Giving them small frequent feeds
- Handling them no more than is necessary
- Washing your hands before and after handling them to prevent the spread of infection

Your doctor or nurse may also advise using saline nose drops to help clear the nose before feeds.

2. *When you should get urgent advice*

You can expect your child to improve so you should get urgent advice from a doctor or nurse if they get worse. Any one of the following may be a sign of the illness getting worse:

- Breathing fast and having to use extra effort to breathe
- Flaring their nostrils to breathe
- Grunting with their breathing
- Taking less than half of their normal feeds
- Looking pale or unwell
- Vomiting
- Has not had a wet nappy for six hours

3. *Danger signals*

The following are danger signs. Dial 111 or contact a doctor immediately if your child has any of the following:

- Blue lips or tongue
- Severe breathing difficulties
- Is becoming less responsive
- Is floppy
- Has periods of stopping breathing

This note tells you:

What to expect and how you can help your child

How to recognise when you should get urgent advice

How to recognise danger signals

Healthline is available for free, confidential health advice 24 hours a day

Healthline nurses do not diagnose over the phone but will assess the situation and provide advice as to the best course of action.

Call 0800 611 116 from either a landline or a mobile phone.

Your child may need a further check up

Your Doctor or Nurse may want to check your child even if things appear to be going as expected. If you have been advised to have a check up, write the details here:

Check up time and date:

At the following location:

Name of person doing the check up:

Phone number:

For more information visit
www.kidshealth.org.nz

SAFE USE OF PARACETAMOL IN CHILDREN

Paracetamol is a safe medication for children when used appropriately. However, liver toxicity can occur with inappropriate use. For example, sustained high doses for a sick child under the age of two years can lead to toxicity within days.[1] In 2006, New South Wales Health released a mandatory policy directive on the use of paracetamol following a death related to paracetamol toxicity.[2]

Indications for paracetamol use

Paracetamol is a useful medication for symptomatic pain relief in known painful situations, such as pain following injury or an operation, migraine headaches in older children or reducing the discomfort that may be associated with fever.

Paracetamol also has a role when there is a combination of respiratory distress and fever, such as in croup, bronchiolitis or pneumonia. Fever increases the metabolic rate and oxygen requirements in these situations.

However, continued use of paracetamol for pain or fever of unknown causes is inappropriate and can lead to delays in diagnosis of conditions, which would benefit from earlier treatment.

Paracetamol is best avoided in infants under 2 months. Metabolism in the liver produces a toxic metabolite which requires glutathione to detoxify and protect against hepato cellular necrosis. Glutathione may be rapidly depleted.

Recommended doses of paracetamol for children of normal or average body build

The dose of paracetamol is based on lean body weight. The total body weight of an obese, anorectic or malnourished child is not their lean body weight. *Download a paracetamol dosage calculator (including BMI and LBW) from www.bpac.org.nz*

The recommended doses of paracetamol for children of **normal or average build are:** 15 mg/kg four to six hourly, up to a maximum daily dose of 60 mg/kg/day.

If it is difficult for clinicians to calculate these doses, it is often so much harder for parents. Careful attention to labelling advice is needed.

For children older than one month with acute pain, this may be increased to a daily maximum of 90 mg/kg/day for a maximum of two days but this is usually only in the hospital setting.

Calculating the paracetamol dose for obese children

In most situations clinicians will use a rule of thumb and err on the side of caution, remembering that the dose is based on lean body weight (LBW), not actual weight.

Paracetamol dose must take into account paracetamol as an ingredient of other medications being taken concurrently

Paracetamol is an unexpected ingredient of many over-the counter medications and must be taken into account when calculating paracetamol doses.

Paracetamol is present, for example, in preparations of:

- Codral
- Coldrex
- Dimetapp
- Lemsip
- Orthoxicol
- Sinutab
- Sudafed

Ibuprofen is not a safer alternative in children

Ibuprofen appears to be as safe as paracetamol in short term use but we do not yet have the same length of experience with using ibuprofen as we do with paracetamol. The well known risks of NSAID use are at least as great in children as in adults.

There is no evidence for the safety or efficacy of combining or alternating paracetamol and ibuprofen use in children.

References

1. Graudins L, Gazarian M. Promoting safe use of paracetamol in children. J Pharm Pract Res 2006; 36:297-300.
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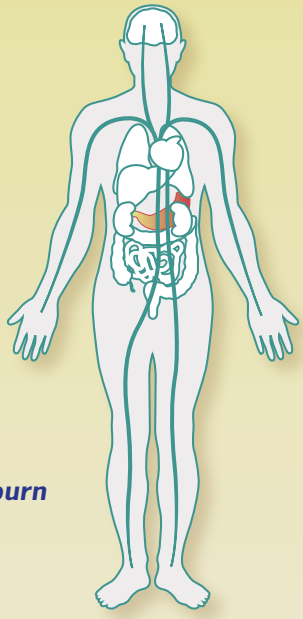
DYSPEPSIA AND HEARTBURN

QUIZ FEEDBACK



This article presents the results of the recent Dyspepsia and Heartburn quiz (BPJ 4). Commentary is provided by Professor Gil Barbezat (GB).

The participants responses were as follows:

1. Which one of the following is a red flag for serious pathology in dyspepsia presentation?

3% Early satiety

8% Father got gastric cancer aged 61 years

88% First presentation at aged 42 years in Maori

1% Recurrence of symptoms 9 months after stopping treatment

0% Paracetamol use

Q1. GB comments: Eighty eight percent of GPs opted for 'c' as the most correct answer. Gastric cancers are relatively more common amongst Māori and Asian patients, and tend to occur at a younger age (often a decade earlier) than in the European based population. Importantly, if a Māori patient is part of a family linked with gastric cancer, the disease may present at a very young age (mean age in early 30s, youngest at 14 years of age).

Although early satiety can be a symptom of gastric outlet obstruction by ulceration or cancer, it is also common in functional dyspepsia, and has poor specificity as a sign of organic disease. This could well be related to delay in gastric emptying. The context in which it arises is important; for example, it is less relevant in a young otherwise well patient, but may be more significant as a new symptom in a 60-year-old.

Although family history may be very important in assessing the risk of gastric cancer, the age at which the family member (preferably first degree) had the cancer is most important. Those presenting at a young age, usually between 20s and 40s, are far more likely to have a transmissible genetic predisposition than those presenting over the age of 50, when genetic transmission of gastric cancer is rare.

Recurrence of dyspepsia after 9 months of stopping treatment is more the rule than the exception, both for functional dyspepsia and peptic ulcer (if *H. pylori* has not been eradicated successfully). Here again, the context of the presentation needs to be considered.

2. When a patient presents with indigestion and they have no red flags or indications of alternative causes for their symptoms, which of the following features is the most important in determining management?

1% Belching

1% Bloating

1% Early Satiety

1% Feeling of fullness

97% Heartburn

Q2. GB comments: Heartburn was correctly identified as the most significant differentiating upper gastrointestinal symptom by 97% of GPs. Its positive predictive value for gastro-oesophageal reflux disease (GORD) is about 80%.

The other symptoms are part of the "dyspepsia complex" and have poor differentiating value.

If you have completed this quiz, please see the personalised feedback accompanying this journal

3. Which one of the following is an indication for H. pylori testing in dyspepsia?

1% Awaiting oesophago-gastro-duodenoscopy

1% High alcohol intake

97% High local prevalence of *H. pylori*

0% NSAID use

0% Smoking

Q3. GB comments: A test-and-treat policy in the management of dyspepsia has only been validated for cost efficacy in populations who have a high prevalence of *H. pylori* infection (estimated in the NZ Guidelines as at least 30%). There is little point in doing the test in populations where infection is as low as 5%, as found in younger populations studied in the South Island; most will be negative, and the risk of false negatives or false positives in the method used, make the results virtually uninterpretable. If a patient is already scheduled for oesophago-gastro-duodenoscopy, testing for *H. pylori* can easily and usually be done as part of that procedure, rather than as a separate test. A point could be made for a prior test in special circumstance where the waiting time for endoscopy is inappropriately long.

4. A person with low-risk undifferentiated dyspepsia without heartburn has been unsuccessfully self-medicating with antacids. Which one of the following is the most appropriate approach to management?

1% Alginates

14% Lifestyle modification and step down therapy

81% Lifestyle modification and step up therapy

1% Oesophago-gastro-duodenoscopy

3% Proton pump inhibitors

Q4. GB comments: Lifestyle modification and some form of medication were correctly chosen as the managements of choice. In this circumstance, the majority (81%) chose the step up regimen, rather than step down (14%). This is a rational choice, as undifferentiated dyspepsia does not have any one medication regimen vastly superior than any other; starting with simpler, cheaper medication and progressing on from there is favoured. This contrasts with heartburn, where proton pump inhibitors (PPIs) have a distinct therapeutic advantage over other medications, and are therefore favoured as initial treatment in the interests of proven efficacy.

Oesophago-gastro-duodenoscopy is not necessary in most patients with low risk undifferentiated dyspepsia where empiric treatment is fully justified. It should be reserved for those with danger signals, first presentation over the age of 50–55, or those with persistent, or incapacitating, severe symptoms. While PPIs are often effective in treating undifferentiated dyspepsia, they are much less effective in patients in whom heartburn has been excluded. Cheaper, simpler medications are worth using initially.

5. A person with low-risk dyspepsia and heartburn has been unsuccessfully self-medicating with antacids. Which one of the following is the most appropriate approach to management?

1% Alginates

55% Lifestyle modification and step down therapy

11% Lifestyle modification and step up therapy

0% Oesophago-gastro-duodenoscopy

33% Proton pump inhibitors

Q5. GB comments: As indicated in question 4, where heartburn is present, PPIs have a very good chance of settling the patient's symptoms. Both answers 'b' and 'e' include PPIs; answer 'b' was chosen by more responders (55%), quite correctly, as lifestyle measures always need to be considered as part of a management package. Weight control (admittedly a difficult challenge for many) may allow patients to come off all medication as the most desired end result of a step down regimen, while some may well need to stay on treatment because of weight related reflux. Avoiding fatty foods, particularly at night, smoking cessation and alcohol moderation are also worth noting. PPIs (chosen by 33%) alone would almost certainly be effective, but could influence the ongoing course of treatment options as discussed above. A step down regimen should always be considered as a part of empiric treatment.

Lifestyle modification and step up therapy is an alternative preferred by 11% of responders. This is a valid option, but there are good data to show that use of PPIs result in more asymptomatic heartburn patients after 2 weeks than after 12 weeks with H2 receptor antagonists. Ultimately, a very significant proportion of patients will need PPIs anyway, so they might as well be started on the most effective regimen as soon as possible. Patient satisfaction is significantly enhanced and the number of doctor consultations reduced. Having said that, it is vital that a step down process is followed so that patients are eventually taking the lowest dose of medication, if any, to control their symptoms. In patients not responding to empiric antacids, responders came to the reasonable conclusion that there was little benefit of trying alginates.

6. Which one of the following medications is not associated with a contribution to dyspepsia symptoms?

81% **Beta-blockers**

5% Calcium antagonists

3% Low-dose aspirin

7% Nitrates

0% NSAIDs

Q6. GB comments: The wording of the question is perhaps a bit misleading in using the words "not associated" with adverse effects. Eighty one percent of GPs correctly picked beta-blockers as the medication least associated with dyspepsia; although "gastrointestinal upsets" are listed amongst their adverse effects, they are not common. Low dose aspirin (usually about 80 mg per day) can certainly produce dyspepsia. Significant inhibition of gastric prostaglandin activity has been shown to occur with aspirin doses as low as 10 mg. Particular care is required in at risk patients taking low-dose aspirin as well as other drugs (e.g. anticoagulants, corticosteroids and NSAIDs, whether non-selective or COX-2 selective where the selectivity is virtually negated by the aspirin).

Nitrates may produce nausea, vomiting and dyspepsia, but gastrointestinal adverse effects are less common with the longer acting products.

Calcium antagonists are commonly associated with gastrointestinal symptoms, including dyspepsia.

7. Which one of the following is LEAST likely to be associated with functional dyspepsia?

9% Eating habits

71% **Hyperacidity**

10% Reduced gastric motility

1% Smoking

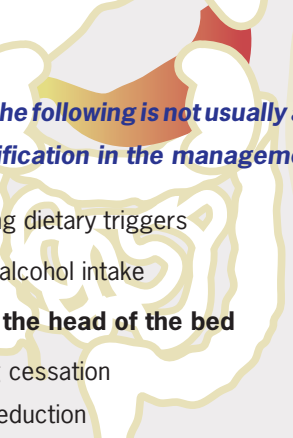
8% Stress

Q7. GB comments: As suggested by the question, all the answers can be associated with functional dyspepsia. Most GPs (71%) thought that hyperacidity was the least likely association, and it is indeed correct that many studies have failed to show any link between dyspepsia and gastric acid secretion where peptic ulceration has been excluded.

Of the abnormalities of gastric function detected on investigation of patients with functional dyspepsia, dysmotility is amongst the most common. Slow gastric emptying is found in a significant proportion of patients, but by no means all.

Eating habits (as most of us will have experienced at some time) can certainly induce dyspepsia. Bolting food, poor chewing (often associated with poor dentition), and overindulgence may all produce dyspepsia.

Stress is a common cause of dyspepsia, effecting some people more than others. This has led to the common misconception of stress being responsible for peptic ulceration. Now that accurate methods have become available to exclude peptic ulceration (endoscopy), the vast majority of people with stress related dyspepsia do not have peptic ulcers.



8. Which one of the following is not usually a recommended part of lifestyle modification in the management of dyspepsia?

13% Identifying dietary triggers

0% Limiting alcohol intake

86% **Raising the head of the bed**

0% Smoking cessation

1% Weight reduction

Q8. GB comments: Raising the head of the bed was correctly identified (by 86%) as a futile measure in the management of dyspepsia. Even in those with heartburn, analysis of the evidence for its efficacy is largely anecdotal or of very poor quality. Now that we have effective medication for reflux, appropriate prescribing is a much better alternative. Avoiding fatty meals in the evening, alcohol moderation and weight control are far more useful lifestyle changes. Having said that, a very small proportion of patients who have volume reflux (regurgitation of large volumes of non-acid fluid, especially during the night) may benefit from raising the head of the bed.

While identifying dietary triggers for dyspepsia may be notoriously difficult, some are worth considering in selected patients. These include lactose intolerance, which might result in gaseous discomfort, and even coeliac disease.

Besides vague intuition, there is no clear evidence that weight reduction benefits the treatment of dyspepsia. This contrasts with efficacy of this measure in the treatment of heartburn. However, in the many patients where weight reduction is indicated, it is likely to produce a number of health benefits, as opposed to raising the head of the bed which may well result in sleep disturbance without much benefit at all.

Remembering...
Respiratory Infections

Antibiotic use is increasing in New Zealand and around the world. Many patients expect that antibiotics will be prescribed to them for a variety of respiratory symptoms, including the common cold. This is despite the fact that the common cold is caused by a rhinovirus and in most cases antimicrobial agents are not needed.[1] Cochrane reviews of research have also found that antibiotics usually have minimal or no benefit when used for sore throat, acute otitis media, streptococcal tonsillitis and acute purulent sinusitis.[2]

Although the majority of GPs are aware that antibiotics have limited effectiveness for many upper respiratory tract infections, they may often still prescribe antibiotics for these conditions due to patient expectation or demand and their own perception of what the patient wants.[3] However the consequences of antibiotic overuse include unnecessary adverse effects, increased costs and the development of bacterial resistance, which is arguably the most detrimental effect.

An effective strategy for decreasing prescribing of unnecessary antibiotics, without damaging the patient-doctor relationship, is to give a delayed or back-pocket prescription, to be filled at a later time if the patient's condition does not improve. A recent study reported that 50% of patients given delayed prescriptions did not fill them.[4] Delayed prescribing also enables GPs to practice more patient-centred medicine by educating patients to take more responsibility for their own health care management. It also assists the GP in dealing with pressure they may experience from patients expecting antibiotics, by giving them something to take home and preventing them from visiting another GP to obtain a prescription.[5] However, more work is needed in developing uniform guidelines on when delayed prescriptions are most appropriate.

Education campaigns, targeting both the general public and health care professionals, are one of the most important tools in reducing unwarranted prescription of antibiotics. PHARMAC launched a campaign in 1999 ('Wise Use of Antibiotics') in response to the growing volume of antibiotics being prescribed in New Zealand. Following this campaign, there was a national reduction in antibiotic use, attributed in part to changes in the behaviour of both doctors and patients.[6]

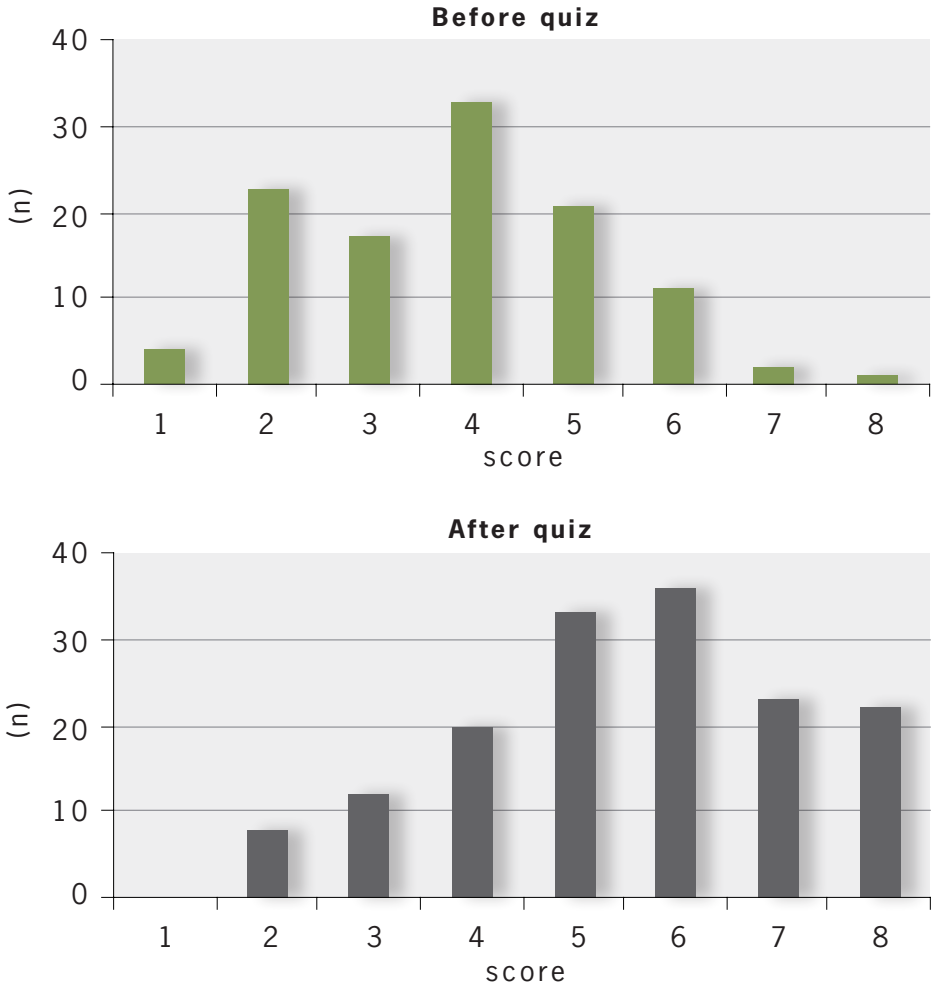
In July 2006, bpac produced and distributed an education programme to promote appropriate antibiotic treatment of respiratory tract infections and to reduce the prescription of antibiotics for viral infections. In order to evaluate the effectiveness and impact of this campaign, two groups of GPs were randomly selected and asked to participate in a 'Before/After' quiz or a 'Remembering' study.

"Before/After Quiz"

One month before the bpac campaign was released, a random sample of 150 GPs were contacted by email and asked to complete a web-based questionnaire testing their knowledge of antibiotic treatment of upper respiratory tract infections. The questionnaire contained eight clinical scenarios which the GP was asked to consider and then indicate which antibiotic they would prescribe – amoxicillin, amoxicillin-clavulanate, erythromycin, penicillin V or no antibiotic. Seventy-five percent of GPs (112) completed the quiz, with an average test score of 3.8 out of 8 (range 1–8). Several patterns emerged such as selecting amoxicillin-clavulanate where amoxicillin was considered more appropriate and indicating an antibiotic would be given when antibiotics were not deemed necessary.

One month after the campaign had concluded, the 112 GPs who participated in the "Before Quiz", along with an additional randomly selected group of 150 GPs were asked to complete the quiz. The response rate was 59% (76 of the original GPs and 78 of the new group). The average quiz score after the campaign was 5.5 out of 8 (range 2–8). This was a significant ($p = 0.01$) increase in score. There was no significant difference between the two groups.

Although there are several limitations in using this methodology, it can be considered that the bpac campaign increased GPs knowledge of the antibiotic treatment of respiratory infections. It is anticipated that this may result in a decrease in the volume of antibiotics being prescribed by these GPs.



'Remembering' study

A web based questionnaire surveying GPs on their recollection of the bpac Respiratory Infections campaign and subsequent changes they made to their clinical practice, was emailed to a random sample of 200 doctors, one month after the conclusion of the campaign. 76 of the 200 GPs responded.

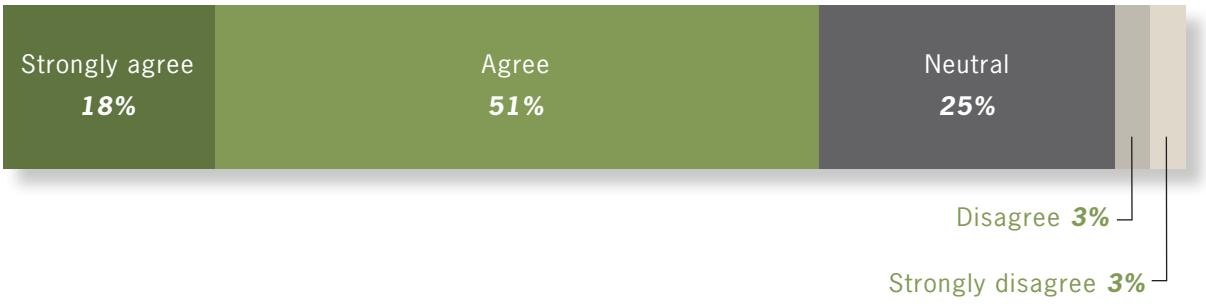
Remembering key messages of the campaign

- Almost all GPs (92%) remembered at least one key message
- Of those who remembered, 55 (79%) remembered one message and 15 (21%) remembered two or more messages
- The most frequently recalled message was; antibiotics aren't always necessary and their use should be limited and doses carefully considered
- Other recalled messages included; antibiotics shouldn't be prescribed for viral infection – many infections are viral and narrower spectrum antibiotics should be used in preference to broader spectrum antibiotics

Making subsequent changes to clinical practice

- Two thirds of the GPs (66%) made at least one change to their clinical practice as a result of the campaign
- Of those who made changes, 39 (78%) made one change and 11 (22%) made two or more changes
- The most common change was prescribing less broader spectrum and more narrower spectrum antibiotics
- The second most frequent change was reducing use of antibiotics and applying more caution in prescribing. Other changes included; becoming more aware of the issues surrounding antibiotic use and applying this to practice, changing dose and duration of treatment to follow recommendations and using 'back-pocket' prescriptions
- The most frequent reason given by those who did not make any changes was 'already carrying out campaign recommendations'

'The bpac^{nz} campaign has improved my knowledge of treating respiratory infections'



The 'Hygiene Hypothesis'

Is there a link between childhood antibiotic use and asthma?

Evidence is emerging of a possible causal association between the increased use of antibiotics and the increased prevalence of asthma. Asthma is now the most common chronic disease of childhood. The reasons for the asthma epidemic are not yet fully known. One hypothesis suggests that infections during infancy may protect against asthma by down-regulating production of immune response cells (IgE). Protection against microbial exposure by using antibiotics may negate this effect by increasing the immune response. This is known as the 'Hygiene Hypothesis'.

Researchers from the University of British Columbia undertook a systematic review and meta-analysis of eight studies (including two New Zealand studies) which investigated the link between antibiotic use in early infancy and subsequent development of childhood asthma. Their analysis found that exposure to at least one course of antibiotics in the first year of life was a risk factor for the development of asthma (OR 2.05; 95% CI 1.41–2.99). However the positive association was largely seen in the results of retrospective studies. These studies relied on data from parent-completed questionnaires and it is possible that information was influenced by recall bias, as parents of children with asthma may be more likely to report an earlier exposure to antibiotics. There is also the issue of confounding by indication i.e. children with asthma are more likely to suffer from respiratory infections in their infancy, requiring antibiotics. Further research should focus on antibiotics prescribed for non-respiratory tract indications and validated measures of antibiotic exposure, to eliminate these confounding factors.

The authors concluded that there is some evidence of a relationship between early antibiotic use and development of asthma in childhood, however further large-scale, population-based studies are needed to determine whether this is due to the 'Hygiene Hypothesis' of antibiotic exposure or simply due to the fact that children with asthma are more likely to suffer from early respiratory infections treated with antibiotics.

*The full meta-analysis study is available from: http://snipurl.com/1g097

Reference: *Marra F, Lynd L, Coombes M, et al. Does antibiotic exposure during infancy lead to development of asthma?: A systematic review and meta-analysis. Chest 2006;129(3):610-18.*

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Fighting immunisation preventable disease in primary care

Dr Nikki Turner, Director Immunisation Advisory Centre, University of Auckland

Coverage and timeliness maximise success of immunisation

Childhood immunisation is one of the most cost-effective activities in health care. In New Zealand, the immunisation programme has eliminated polio and controlled tetanus and diphtheria. However, disease persists, as seen with high rates of pertussis and recurrent epidemics of measles. The burden of disease disproportionately affects Māori and Pacific children. With better coverage and improved timeliness of immunisation, the gains could be higher.

Immunisation Coverage

While much of New Zealand historical coverage data has not been accurate, there are three coverage surveys using robust methodology involving random sampling of geographical clusters to ascertain children's immunisation status.

Coverage Survey Results

Children Fully Immunised At the Age of 2 Years

	All Children	Māori	Pacific
1991 National Survey[1]	56%	-	-
1995/6 North Health Survey[2]	72%	47%	53%
2005 National Survey[3]	77.4%	69%	82%

Timeliness of Immunisation

Achieving good disease control requires not just high coverage, but immunisation events to be delivered on time. Delay in receiving the first immunisation in the primary series is one of the strongest predictors of subsequent incomplete immunisation.[4] Also a delay in timeliness affects disease control. A child with delayed immunisation in the primary course has a 4.5 times increased risk of being admitted to hospital with pertussis.[5]

Overcoming barriers to immunisation coverage and timeliness

The major factors leading to incomplete immunisation are socioeconomic factors (poverty), provider and system factors, and parental/community attitudinal factors.

Provider commitment is the key

The commitment of the provider is the most important determinant of immunisation coverage. Effective, motivated primary care can achieve good immunisation uptake, even in the face of socioeconomic deprivation and parental low confidence. Despite mediocre national coverage, some primary care providers with strong commitment to immunisation delivery can, and do, achieve high coverage rates.

Provider knowledge overcomes false immunisation beliefs

Health provider knowledge is a significant factor in obtaining high immunisation coverage. While GP attitudes to immunisation in New Zealand are positive, our knowledge base is not as strong. A national survey reviewing GP knowledge revealed significant knowledge gaps around false contraindications.[6]

Genuine contraindications to immunisation

Children with minor illness (without an acute systemic illness and with a current temperature below 38.5ºC) may be vaccinated safely.

Major illness or high fever may be confused with vaccine side effects and increase the discomfort for a child. In this case the vaccination should be postponed 2–3 days until the child is well. It is a good idea to make a return appointment at the time of deferral.

A practice visit is an opportunity for immunisation

A visit to primary care when a child is due a vaccination but does not receive it, is a missed opportunity. This is one of the most important factors contributing to decreased immunisation coverage and timeliness. Missed opportunities are happening almost universally in New Zealand primary care. Recent research[7] has shown that on auditing a subgroup of children in 62 practices, 97% of practices had missed opportunities to vaccinate. Of the records audited, 30% of the children had had a missed opportunity, with the most common reason being a visit for an URTI. Genuine contraindications were shown in less than 5% of cases. Surprisingly 10% of the missed opportunities occurred at well child visits.

Guide to the contraindications for vaccination

Vaccine	Contraindications
All	Fever greater than 38.0ºC
	Moderate to severe acute illness without fever >38.0ºC
	Anaphylaxis, allergy, or anaphylaxis reaction to any vaccine component or previous dose
Diphtheria, tetanus, acellular pertussis	Previous encephalopathy within 7 days after diphtheria, tetanus, whole cell pertussis vaccines, and haemophilus influenza type b vaccine
	Evolving, undiagnosed neurological problem
Measels, mumps and rubella vaccine	Other than simultaneously administered vaccines (at different injection sites), the patient having had a previous live virus vaccine within the last 4 weeks
	The patient having received blood or human immunoglobin within the last 6 months, or is about to in the next 3 weeks
	Immune suppressed patient
Influenza, yellow fever	Anaphylaxis to eggs or chicken

Some conditions increase the risk of complications from infectious diseases and children and adults with such conditions should be vaccinated as a matter of priority

These conditions include:

- Asthma
- Chronic lung and congenital heart conditions
- Downs Syndrome
- HIV infection
- 'Small for date babies' and premature babies

Practice systems impact on immunisation rates

A range of practice policies and systems have considerable impact on immunisation uptake. Vital systems for high immunisation rates include:

- A clear enrolment policy
- Early enrolment of children
- Good data entry of records
- Systematic precall* & recall
- Regular audit

**Precall is a reminder sent prior to the vaccination being due*

While around 60–70% of children receive immunisation with a simple precall system and organised practice, the other 20–30% requires extra time and effort in tracking and recalling. This requires committed staff time, a good understanding of how to use a PMS and effective use of National Immunisation Register (NIR) status queries. Practices with high staff turnover or inexperienced staff are likely to have greater problems with entering quality, accurate data.

There are significant numbers of errors occurring in immunisation data entry at the practice level. Recommendations to improve this include early enrolment of infants, standardised approaches to entering data, checking data entry quality, improving staff training in use of the PMS, and developing a focus on timeliness, as well as coverage, with regular audits. Performance feedback to the practice has been shown internationally and locally to improve coverage rates.

Other important ways to improve immunisation coverage and timeliness include making immunisation services available at all possible hours, and having staff available at all times who can vaccinate (including GPs if the practice nurse is not present).

Parent/Community knowledge and attitudes

In New Zealand it is known that 20% of parents consider that good healthy living will be enough to prevent disease without the need for vaccination.[8]

Caregiver's knowledge and attitudes impact on immunisation uptake to a lesser extent than practice characteristics but the impact is still significant.

The media, fuelled at times by the anti-immunisation lobby, can have dramatic effects on parental confidence in vaccination as has been seen with the abiding myth that MMR may be linked to autism despite the lack of any scientific backing.

The importance of the primary care provider relationship with the parent is vital to parental confidence. A knowledgeable, committed and confident provider with a good relationship with their patients, is likely to overcome many parental myths and concerns.[9]

Practice Strategies that Promote High Coverage/Timeliness

Improving immunisation coverage and timeliness of delivery is a practice-level issue. The answers lie in good practice systems, dedicated staff time and regular commitment of all clinical staff to regularly review progress.

Key factors are:

1. Enthusiastic and committed staff
2. Enrolling children as early as possible
3. Accurate immunisation data entry in the PMS
4. Using NIR status queries to update records
5. Timely precall system
    a. Attractive, engaging precall and recall letters
    b. Early and systematic recall follow up, first recall within 2 weeks of the due date
    c. A broad recall approach – letters and telephone
6. Regular practice audit, preferably monthly
7. Dedicated staff time to recalls, audits and data entry
8. Regular feedback of results
9. Vaccinate at all times, do not turn children away
    a. All clinical staff available to vaccinate, including GPs
10. Take every opportunity
    a. Flags, electronic reminders on notes
    b. High staff awareness, regular awareness raising
    c. Vaccinate children with mild illnesses
11. Improve our knowledge base
    a. Attend regular updates**
    b. Access and use the Immunisation Handbook

***The Immunisation Advisory Centre, University of Auckland, is launching a web-based online update course in April 2007. Visit www.icomet.org.nz*

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OVER-THE-COUNTER

MEDICATION IN CHILDREN: FRIEND OR FOE?

Cranswick N, McGillivray G. Over-the-counter medication in children: friend or foe? Aust Prescr 2001;24:149-51. Reprinted with permission from Australian Prescriber.

SYNOPSIS

Over-the-counter medications are often taken by adults, and given to children, to relieve minor ailments. Despite being freely available from a pharmacy or supermarket, many preparations are of unproven benefit. Some have the potential for harm, especially in the young. Health professionals, as well as parents, have a responsibility to be cautious about giving drugs to children.

INTRODUCTION

The use of over-the-counter (OTC) medications has become commonplace in Australia. Not only do we, as adults, frequently medicate ourselves with OTC preparations, we give them to our children. The health professions and the community at large often assume that, because these drugs are not regulated by prescription, they are safe, even in overdose. However, the truth may be somewhat more sinister. While some are harmless placebos, others may be causing much more harm than good. Even the ubiquitous paracetamol may slow the body's response to viral infections and, in overdose, it can result in liver failure. Health professionals need to know about the efficacy and safety of OTC preparations in as much detail as they do about prescription medications. All too often, practitioners will recommend a preparation without sufficient knowledge of its potentially serious adverse effects or the evidence (or lack of) for its use.

MEDICINES IN CHILDREN

There are fundamental differences between children and adults. Previous generations have treated children as small adults, often with dire consequences.[1] Drug regulatory history is littered with therapeutic misadventure involving children.[2] Nowhere is this plainer than in the story of Reye's syndrome and its association with aspirin, previously thought to be a useful and safe OTC medication for children.

Sugar-free preparations: Much is made of the importance of sugar-free preparations in the marketing of medicines for children. There is a general concern in the community about the effects of sugars upon children's behaviour. However, the only objective harmful effects of sugar are related to the development of dental caries and childhood obesity. Some preparations contain excipients which can be harmful to children with inborn errors of metabolism, e.g. phenylketonuria (PKU).

DECONGESTANTS

There is little evidence for the use of either local or systemic decongestants in the symptomatic relief of viral infections. However, they are widely promoted for relieving the symptoms of cold and influenza.

Oral decongestants: A large number of OTC preparations include decongestants. These may be helpful for symptomatic relief of the symptoms associated with viral illnesses. However, prescribers should be aware that many preparations have age restrictions and some are contraindicated in children less than two years old. Often this group of medications is given by parents for their sedative properties. Occasionally, however, children react paradoxically with hyperactivity. Parents should be warned that this effect may last several hours and that further attempts at chemical restraint may only prolong the reaction. ***Promethazine*** is worthy of special mention. Although it is sedating and is used as a remedy for many ailments in children, it can cause paradoxical reactions with hyperactivity in toddlers. Children with epilepsy should use promethazine with caution as it may precipitate seizures. The product information also specifically warns against giving the drug to children under two years old, as its use has been linked to sudden infant death syndrome.[3]

Nasal decongestants: Topical nasal vasoconstrictors have been recommended in the past for babies and children with nasal congestion. In the short term, they will result in the clearing of the nasal passages. Unfortunately, tachyphylaxis may occur after a few days of regular use, and rebound nasal congestion can occur after cessation of the medication. In general, these formulations should be avoided. Intranasal saline solution is a safer alternative (for example 0.5 ml per nostril, one nostril at a time), however, it should be prewarmed to room temperature (for example in the parent's hands) in case the infant has a particularly sensitive diving reflex leading to bradycardia.

ANTITUSSIVES

Cough is a common symptom in childhood and is usually related to viral bronchitis and upper respiratory infections.

These conditions are self-limiting and the cough probably serves a useful function in clearing mucus and preventing secondary infection. If a cough is particularly troublesome, other diagnoses should be considered before using an antitussive. Most cough medicines contain a mucolytic, antitussive, decongestant or some combination of these. The only proven antitussives are those containing opioids such as dextromethorphan and codeine. These work by suppressing the cough reflex centrally. Paediatricians do not recommend the routine use of these drugs. Overdose can cause drowsiness.

ANALGESICS AND ANTIPYRETICS

Paracetamol: Paracetamol is often overused in the treatment of childhood fever[4] and there is a danger of liver toxicity.[5] In spite of these concerns, it should still be considered as first-line treatment for analgesia in children.

Aspirin: Aspirin is contraindicated in children less than 12 years old. Although it is a well-documented analgesic, anti-inflammatory and antipyretic, it has a strong association with Reye's syndrome. Now that the use of aspirin in children has all but ceased, Reye's syndrome has disappeared.[6]

Ibuprofen: Ibuprofen is a non-steroidal anti-inflammatory drug which has recently been marketed as an OTC preparation for children. Its efficacy is probably similar to that of paracetamol and it is currently used as an alternative to paracetamol for the management of pain and fever. While the drugs have similar safety profiles, ibuprofen is associated with a slightly increased risk of gastrointestinal bleeding, even at the low doses used in OTC formulations.[7] There have also been reports of renal toxicity and aspirin-like sensitivity reactions. There is limited experience with this drug in Australia.

TEETHING GELS

An assortment of gels are commonly recommended for relieving the pain and discomfort of teething. While there are complications associated with teething, including drooling, teething gels have failed to demonstrate any specific benefit. It may be that the observed therapeutic effect is related to the actual gum massage. The gels commonly contain salicylic acid, lignocaine, tannic acid, menthol, thymol, glycerol and up to 40% ethanol. Some of these substances have the potential to be harmful in overdose, however teething gels are safe if used as recommended.

TOPICAL APPLICATIONS

Topical moisturising creams and ointments are among the commonest preparations used by parents on their children. However, they are often not considered 'medications' and may not be reported to their physician. Fortunately, most of these products are emollients which can be safely applied to the face and body, and systemic absorption is minimal. They are particularly useful for dry skin and for atopic eczema. In general, ointments are best for dry skin while creams are used for moist lesions. For atopic eczema, aqueous creams should be applied at least three times a day to all the affected skin. The creams can be used with steroid-containing ointments. They can be used as alternatives to soap for washing, and should also be applied within three minutes of finishing a bath, to the whole body, and face. For very dry lesions, ointments may be more appropriate for trapping moisture in the skin. This can be achieved by adding 10% olive oil or 10% liquid paraffin to the aqueous cream. In severe eczema, especially if it wakes the child or if there is persistent redness or itching, wet dressings may be appropriate. An alternative is the application of a mixture of 50% liquid paraffin and 50% white soft paraffin (made up by the pharmacist). Adverse effects are uncommon, but some children experience stinging, and blocked pores or pimples and may require temporary discontinuation of the treatment.

Topical steroids: Most of the useful topical steroids are prescription medicines. However, low-potency preparations containing 0.5% hydrocortisone are available OTC. These preparations can be a useful adjunct to moisturisers in cases of mild eczema. Before recommending hydrocortisone a specific diagnosis should be made, and conditions exacerbated by steroids, such as fungal infections, should be excluded. Parents should be advised to seek early review if the treated skin condition fails to respond or worsens.

Antifungal drugs: Infants and children are prone to a range of fungal infestations. Oral infection or secondary infection of nappy rash by Candida albicans is common. Topical antifungal drugs such as nystatin or miconazole cream are effective, but need to be continued for a few days after clinical resolution. Ringworm can occur anywhere on the body and is caused by a range of dermatophytes. The diagnosis can be confirmed by microscopy and culture of skin scrapings. Most cases in children can be treated with topical antifungals such as miconazole. Terbinafine cream is very effective in adults, but is not currently recommended for use in children. Resistant cases, or those involving the scalp or nails, may require systemic therapy.

REHYDRATING FLUIDS

One of the great advances in the treatment of gastroenteritis has been the recognition that appropriate oral rehydration is the best form of therapy. Balanced electrolyte solutions can easily be prepared by parents, but the instructions should be carefully followed as over-concentrated solutions can cause osmotic diarrhoea. Compliance may be enhanced by the use of one of the flavoured solutions and by pre-chilling the drink.

ANTICOLIC PREPARATIONS

Persistent crying, or 'colic' is common in the first three months. Any suspicions of underlying organic disease, especially of the gastrointestinal (failure to thrive) or urinary tract (fever), should be investigated and excluded before making the diagnosis of colic. Colic has not been proved to be due to 'wind' or 'gas' and may well be a normal developmental phase for many infants. The currently available products contain either simethicone (an anti-gas agent) or a combination of anticholinergics, but none of these has been shown to be effective. In the majority of cases, clinical exclusion of serious pathology and parental reassurance and support is all that is required. However, in severe cases, parental distress exceeds the infant's distress and an effective treatment regimen may include either in-patient or outpatient attendance at a mother/baby unit

TREATMENTS FOR REFLUX

Many infants vomit, this is usually associated with a poorly or incompletely developed lower oesophageal sphincter. In most cases, this is mild and resolves spontaneously with age. In mild cases, posturing and thickened feeds with one of the many available anti-reflux infant feeding formulae may provide symptomatic relief. Severe or persistent cases should be investigated particularly if there is weight loss or failure to thrive.

COMPLEMENTARY AND ALTERNATIVE MEDICINES

Complementary medicines such as echinacea and aloe vera are not OTC medicines and are not registered as such. Specific product information is not generally available. Currently in Australia, there is a listing system for these products. This ensures that the manufacturing process complies with certain standards, but no review of efficacy or safety in children is included. Medical practitioners and pharmacists should be aware of the widespread use of complementary medicines.

SOURCES OF INFORMATION*

There are few reliable sources of information on OTC preparations. Practitioners should initially consult the product information[8] and dosing information for many of the medications is available.[8,9,10,11] A few indications covered by the reviews of the Cochrane Collaboration are nasal decongestants for the common cold,[12] topical antifungals[13] for skin infections and vitamin C for the common cold.[14] In cases of overdose, the local poisons information centre should be consulted.

CONCLUSION

OTC medications are commonly used for the temporary relief of minor ailments in children. Some, such as topical moisturisers and oral rehydration fluids, have a real place in therapy. Many, such as the nasal decongestants, are of little use and may have unwanted adverse effects. Others, such as aspirin, are contraindicated in children. Practitioners should question parents about all the therapies that they are giving their children. They should also consult appropriate references before recommending OTC medicines for children.

ACKNOWLEDGEMENT

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In New Zealand the following sources can be used for information on OTC medicines:

- MIMS New Ethicals. January 2007 Edition. Auckland. CMP Medica (NZ) Ltd. 2007.
- Medicine Data Sheets. Wellington. Medsafe. Ministry of Health.
  Available from http://www.medsafe.govt.nz/profs/Datasheet/dsform.asp

etc

evidence that counts

Inhaled vs. Oral Steroids for Children with Mild-to-Moderate Acute Asthma

Journal Watch , Volume 26, Number 19, Oct 1, 2006
— ***Howard Bauchner, MD***

Bottom Line: These results reaffirm the superiority of oral steroids compared with inhaled steroids for treating children with acute asthma, including those with mild-to-moderate disease. Oral steroids remain the agent of choice.

Inhaled corticosteroids are less effective than oral corticosteroids in children with severe acute asthma, but what about children with mild-to-moderate acute asthma? In a double-blind, randomised clinical trial, 69 children (age range, 5–17 years) who presented to the emergency department (ED) with mild-to-moderate acute asthma (FEV_1, 50% to 79% of predicted) received either fluticasone (2000 µg by metered dose inhaler, followed by 500 µg twice daily for 10 doses after discharge) or oral prednisolone (2 mg/kg, followed by 5 daily doses of 1 mg/kg). All children also received albuterol in the ED and salmeterol after discharge.

Children who received oral steroids had significantly greater improvement in FEV_1 at 4 hours than children who received inhaled steroids (mean change, 91% vs. 82%), and more were judged to have had an excellent response to treatment, defined as an increase in FEV_1 >30% (proportions responding, 77% vs. 47%). At 48 hours, FEV_1 no longer differed significantly between groups.

References: *Schub S et al. High-dose inhaled fluticasone does not replace oral prednisolone in children with mild to moderate acute asthma. Pediatrics 2006 Aug; 118:644-50.*

Involving Patients in Their Own Care Improves BP Control

Journal Watch , Volume 26, Number 19, Oct 1, 2006
— ***Richard Saitz, MD, MPH, FACP, FASAM***

Bottom Line: This study cannot tell us whether the clinician education and alerts were necessary for the patient education to have its effect. And it is puzzling that the patients who had the best control were not more likely than others to have had their medication regimen intensified. Nonetheless, it makes sense that involving patients in the care of their own chronic illness can improve outcomes.

Hypertension is commonly poorly controlled in the U.S., despite the availability of effective treatments. Researchers compared three interventions for improving control in a randomised trial involving 1341 veterans who were taking only one antihypertensive medication, and their 182 clinicians.

One group of clinicians received an email message that contained a link to national hypertension guidelines (JW June 15 2003, p.93, and JAMA 2003; 289:2560) and an alert in the patient's electronic medical record that noted recent blood pressure readings, guideline recommendations, and therapeutic options. A second group received only the email with the link. The third group received the link and the alert, and their patients received a letter that described behavioural strategies for BP control and the possible need for more than one medication.

Among the 73% of patients who had repeat BP measurements in the next 6 months, the systolic BP goal of ≤140 mmHg was achieved by significantly more patients in the group that included the patient letter than in the other two groups (60% vs. 42% and 41%, respectively). Interestingly, patients in the group with the best outcomes were no more likely than those in the other two groups to have had their BP medication regimen intensified (about 30% in all three groups).

References: *Roumie CL et al. Improving blood pressure control through provider education, provider alerts, and patient education: A cluster randomised trial. Ann Intern Med 2006 Aug 1; 145:165-75.*

Report: Comparative effectiveness of second-generation antidepressants in treatment of adult depression

National electronic Library for Medicines - Yuet Wan

This report 'Comparative Effectiveness of Second-Generation Antidepressants in the Pharmacologic Treatment of Adult Depression,' is the newest analysis from the Effective Health Care programme of the Agency for Healthcare Research and Quality (AHRQ) in the U.S. This programme aims to help patients and healthcare practictioners choose the most effective treatments.

The analysis examined 293 published studies looking at use of second-generation antidepressants in adults, of which 187 were judged to be of good or fair quality. It compared the drugs' benefits and risks in the treatment of major depressive disorder, dysthymia (a chronic, less-severe form of depression), and subsyndromal depression (an acute mood disorder that is less severe than major depression). The drugs analysed were bupropion, citalopram, duloxetine, escitalopram, fluoxetine, fluvoxamine, mirtazapine, nefazodone, paroxetine, sertraline, trazodone and venlafaxine. The main findings from the report were as follows:

- Six in 10 adult patients get some relief from the drugs; about 6 in 10 also experience at least one side effect, ranging from nausea to sexual dysfunction.
- In controlled studies, about 38% of patients saw no improvement and 54% had only partial improvement.
- 25% to 33% of patients will improve with the addition or substitution of a different drug.
- 61% of patients taking second-generation antidepressants experience at least one side effect; the most common are nausea, vomiting, constipation, diarrhoea, dizziness, headache, and sleeplessness.
- Venlafaxine is associated with a higher incidence of nausea and vomiting than SSRIs and is also more likely than SSRIs to be discontinued due to adverse events.
- Sertraline is more likely to cause diarrhoea than bupropion, citalopram, fluoxetine, fluvoxamine, mirtazapine, nefazodone, paroxetine, or venlafaxine.
- Mirtazapine leads to higher weight gains than fluoxetine, paroxetine, venlafaxine, or trazodone.
- Trazodone is associated with higher rates of sleeplessness than bupropion, fluoxetine, mirtazapine, paroxetine, or venlafaxine.
- Paroxetine and venlafaxine have the highest rates of discontinuation, fluoxetine has the lowest.
- Second-generation antidepressants work at different rates; 7 studies funded by the maker of mirtazapine claimed that the drug works faster than citalopram, fluoxetine, paroxetine, or sertraline.
- Bupropion is less likely to cause sexual dysfunction than fluoxetine, paroxetine, or sertaline.
- Paroxetine has higher rates of sexual dysfunction than fluoxetine, fluvoxamine, nefazodone, or sertraline.

The report concludes that "current evidence on the drugs is insufficient for clinicians to predict which medications will work best for individual patients."

A Sneeze May Launch a Thousand Staph.

Journal Watch , Volume 26, Number 23, Dec 1, 2006 — ***Abigail Zuger. MD***

Bottom Line: Sneezing is often dismissed as a relatively trivial reflex, but this research suggests that it may have potentially serious consequences, transmitting not only upper respiratory pathogens, but also the pharyngeal colonisers, such as *S. aureus* and pneumococcus, that can cause severe illness. Further studies will define the risks more precisely, but in the interim, prudence suggests that sneezing healthcare workers, especially those with respiratory allergies, should use tissues, masks, and antihistamines to minimise the cloud of organisms they generate.

In most respiratory infections, the cough is considered the prime culprit in generating airborne infectious particles. Now researchers point out that the sneeze should not be underestimated as a means of launching pathogens from the pharynx into the atmosphere.

Eleven healthy college students identified as chronic pharyngeal *Staphylococcus aureus* carriers were inoculated with rhinovirus to induce cold symptoms; they also received daily intranasal histamine challenges to provoke additional sneezing. At baseline, bacterial cultures of the air around them yielded minimal *S. aureus*, and only a slight, insignificant rise in colony counts was demonstrated with cold symptoms alone. However, during bouts of histamine – induced sneezing, the airborne *S. aureus* counts increased dramatically, as did the percentage of small (<5 µm) particles carrying *S. aureus*. The emission of staph per sneeze was particularly robust for participants with respiratory allergies.

References: *Bischoff WE et al. "Gesundheit!" Sneezing, common colds, allergies, and Stapbylococcus aureus dispersion. J Infect Dis 2006 Oct 15; 194:1119-26.*

etc

evidence that counts

Rescreening People with STDs

Journal Watch , Volume 26, Number 23, Dec 1, 2006
— ***Richard Saitz, MD, MPH, FACP, FASAM***

Bottom Line: How many times, or for how long, should people be retested after having a documented STD? The answer is unknown, but the current study suggests that repeat testing of high-risk patients is warranted because, presumably, the risk persists. Also, it is important to counsel patients to prevent reinfection. How these results may apply beyond high-risk young adults remains to be seen.

Because treatments for chlamydia and gonorrhea are highly effective, the CDC does not recommend repeat testing to ensure a cure. However, having had a sexually transmitted disease (STD) increases the risk for having another STD, raising the possibility that repeat testing might be warranted. In this study, 2419 sexually active (i.e., having anal or vaginal sex with an opposite sex partner), HIV–negative young adults were evaluated at public STD clinics and reassessed every 3 months for up to a year.

Twenty-six percent of women developed one or more new infections (chlamydia, gonorrhea, or trichomonas); 15% of men developed new infections. Two thirds of these infections were diagnosed at scheduled visits, and two thirds of diagnosed patients were asympotomatic. Among 265 women with infections at study entry. 20% had a new infection in 3 months. Similarly, among the 205 men with infections at study entry, 16% had a new infection in 3 months. The rate of new infections during 1 year of follow-up remained high.

References: *Peterman TA et al. High incidence of new sexually transmitted infections in the year following a sexually transmitted infection; A case for rescreening. Ann Intern Med 2006 Oct 17; 145:564-72.*

SSRIs may increase risk of osteoporotic fracture

National Electronic Library for Medicines

Bottom Line: Based on their analysis, the authors conclude that daily use of SSRI is associated with an increased risk of fragility fractures. Given the frequency of both depression and osteoporosis in this age group, they suggest that the association may be a significant public health issue.

An epidemiological study suggests that use of Selective Serotonin Reuptake Inhibitors (SSRI) is associated with an increased risk of fragility fracture. The authors of the study note that both fractures and depression are common in older people. SSRIs are commonly used for treatment of depression, and the authors therefore aimed to determine whether SSRI use was associated with increased fracture risk. They carried out a prospective cohort study in people aged 50 and over, living in the community, and followed them for five years. Fragility fracture was defined as proven fractures associated with minimal trauma; risk of fracture was calculated for reported SSRI use, controlling for relevant confounding factors.

There were 5,008 people in the study cohort, and SSRI use was reported by 137 of these. After adjustment for potential confounders, daily SSRI use was associated with substantially increased risk of incident clinical fragility fracture (hazard rate, 2.1; 95% CI, 1.3–3.4). Daily SSRI use was also associated with increased odds of falling (odds ratio, 2.2; 95% CI, 1.4–3.5), lower bone mineral density at the hip, and a trend toward lower bone mineral density at the spine. These effects were dose dependent and were similar for those who reported taking SSRIs at baseline and at 5 years' follow-up.

Reference: *Richards B, Papaioannou A, Adachi J et al. SSRIs may increase risk of osteoporotic fracture. Arch Intern Med 2007;167:168-174.*

Smoking Accounts for Most of the Socioeconomic Inequalities in Mortality in Men

Journal Watch , Volume 26, Number 19, Oct 1, 2006. — ***Bruce Soloway, MD***

Bottom Line: Although this analysis is limited by its indirect statistical methods, these data suggest that higher mortality rates among middle-aged men in lower socioeconomic groups are largely attributable to smoking.

In many countries, smoking prevalence and mortality rates are higher among men in low economic strata than among those in higher strata. To estimate smoking's contribution to differences in mortality, researchers employed indirect statistical methods in which absolute lung cancer rates in a population are used to estimate the proportion of mortality from other diseases attributable to smoking. These methods were applied to 1996 mortality data for men aged 35 to 69 in three social strata in four countries: England/Wales (strata defined by occupation). Canada (strata defined by residence), and the United States and Poland (strata defined by education level).

In each country, overall death rates were about twice as high in the lowest social stratum as in the highest social stratum, and the proportion attributed to smoking was greater in the lowest stratum. In each country, smoking accounted for more than half (51%–65%) of the differences in mortality rates between strata. Across the four countries, the probability that a middle-aged man would die from smoking was 5% in the highest social stratum and 17% in the lowest social stratum.

Reference: *Jha P et al. Social inequalities in male mortality, and in male mortality from smoking: Indirect estimation from national death rates in England and Wales, Poland and North America. Lancet 2006 Jul 29; 368:367-70.*

Reviews - treatments for stroke

National Electronic Library for Medicines

Two review articles in the Lancet themed issue look at established and potential future treatments for stroke.

The review of established treatments gives an overview of the total management of acute stroke, starting with pre-hospital care. The authors comment that ambulance paramedical staff can be trained to recognise possible stroke with a high degree of accuracy, improving the likelihood that the patient will be transported rapidly to hospital. They discuss the initial diagnosis and investigations, and focus on neuro-imaging, which is needed to differentiate ischaemic from haemorrhagic stroke. General medical care is discussed, followed by a more detailed coverage of thrombolysis.

Thrombolysis is currently the most important treatment for acute ischaemic stroke, and for this reason it is necessary to determine the time of onset as accurately as possible. Alteplase is currently proven to be beneficial if started within three hours of onset; there is evidence that use outside this window may be beneficial in some patients, however this is still experimental. Some work is looking at local placement of thrombolytic at the site of occlusion using a micro-catheter, however this is technically complex and is currently investigational. Anticoagulants (oral or heparin) do not seem to be useful, however there is evidence for benefit from antiplatelet drugs (although they may increase the risk of bleeding after thrombolysis).

The authors discuss the complication of stroke management, including the complications of thrombolysis, acute medical complications, and acute neurological complications. Finally, they conclude by noting that acute stroke is a medical emergency requiring timely and appropriate therapy; in suitable patients, thrombolysis can improve outcomes. Antiplatelet drugs are beneficial in those not suitable for thrombolysis, and all stroke patients require good general medical care.

The second review covers experimental treatments for stroke. A wide range of drugs and techniques are being studied, however these break down into a number of groups. Strategies aimed at better thrombolysis include augmentation with other agents such as glycoprotein IIb/IIIa inhibitors, longer time windows, and newer thrombolytic agents. Studies into mechanical techniques such as ultrasound and endovascular devices show promise. Techniques to improve cerebral perfusion could reduce neuronal injury; they include induced hypertension and mechanical devices currently in clinical trials.

A wide range of agents have been investigated for neuroprotection, on the basis that much of the neuronal loss occurs after the acute event, in areas of tissue surrounding the core lesion. Many of these have been high-profile failures, however others continue to show promise and further investigation of the reasons for failures suggest where therapy may be better applied. In particular, cerebral ischaemia is a complex process, and it is likely that a combination of therapies will be necessary to bring benefits.

Reference: *Lancet 2007; 369: 319-30 (established treatments), 331-41 (experimental treatments)*

Bandolier

Independent evidence-based thinking about health care

Eggs and eyes

Bandolier 155, Volume 14, Issue 1 www.ebandolier.com

Age-related macular degeneration (AMD) is the leading cause of blindness in the developed world. In the USA 200,000 new cases are diagnosed each year, and nearly six million Americans have suffered some vision loss from AMD. A rapidly aging and longer living population suggests that the prevalence of AMD is likely to triple over the next 25 years as our populations contain increasing numbers of older people.

Age is the biggest risk factor, but diets low in antioxidants low in substances like lutein and zeaxanthin may also contribute to both low serum and retinal levels of these antioxidants (Bandolier 123). Higher serum levels are associated with lower incidence of AMD, as are diets high in antioxidants. Spinach and other green and yellow vegetables, as well as egg yolk, have high contents of lutein and zeaxanthin. Recently there has been something of an interest in eggs, so Bandolier has done a quick review.

Table 1: Summary of six trials examining dietary egg and changes to serum lutein and/or zeaxanthin concentrations

Reference	Study	Results
Handelman et al. American Journal of Clinical Nutrition 1999 70: 247-251	Uncontrolled study of 11 subjects aged 48-78 years, mean LDL cholesterol 4.3 mmol/L Two diets for 4.5 weeks separated by 2 weeks, with or without supplementation with 1.3 egg yolks daily	Significant increases in plasma lutein and zeaxanthin: plasma lutein by 28% and 50%, and zeaxanthin by 142% and 114%
Surai et al. European Journal of Clinical Nutrition 2000 54: 298-305.	Randomised, double blind, placebo controlled study in 44 healthy adults aged 26 to 59 years, mean total cholesterol 5.4 mmol/L, HDL cholesterol 1.2 mmol/L Diets were either commercial eggs or "designer" eggs from chickens fed supplemented diet rich in lutein (15x greater lutein content); one egg per day for 8 weeks	No increase in plasma lutein with standard egg, but 100% increase with supplemented egg No significant change in total cholesterol or HDL cholesterol
Chung et al. Journal of Nutrition 2004 134: 1887-1893.	Randomised, open, comparison of four lutein diets in 10 healthy men aged 26 to 75 years, all with total cholesterol below 6.2 mmol/L Four diets tested, lutein and lutein ester supplement, spinach, and egg yolk, each with 6 mg lutein daily for 10 days	Serum lutein increased with all diets: lutein 82% lutein ester 83% spinach 141% egg 323%
Goodrow et al. Journal of Nutrition 2006 136: 2519-2542.	Randomised, open, comparison of two diets in 33 older individuals, mean age 78 years, mean LDL cholesterol 3.1 mmol/L, total cholesterol 5.1 mmol/L Diet periods consisted of no eggs and 1 egg daily for 5 weeks	Serum lutein and zeaxanthin increased by 26% and 38% on 1 egg per day compared with no egg No change in cholesterol in total or subfractions
Wenzel et al. Journal of Nutrition 2006 136: 2568-2573.	Open comparison of placebo pill with diets of standard and high lutein eggs for 12 weeks in 24 women aged 24 to 59 years (randomisation not stated). Initial mean LDL cholesterol 2.6 mmol/L, total cholesterol 4.7 mmol/L	Change in lutein: placebo -10% ordinary egg +23% high lutein egg +26% Change in zeaxanthin: placebo -15% ordinary egg +30% high lutein egg +60% Significant increase in macular pigment optical density with both egg groups No change in serum cholesterol subfractions
Herron et al. Journal of Nutrition 2006 136: 1161-1165.	Randomised comparison of 91 people, mean age 31 years, mean total cholesterol 4.3 mmol/L. Analysis according to genetic subtypes Comparison of 3 eggs daily versus placebo, for 30 days	In 40 patients in whom they were measured, serum lutein increased by about 30% and zeaxanthin by 20%

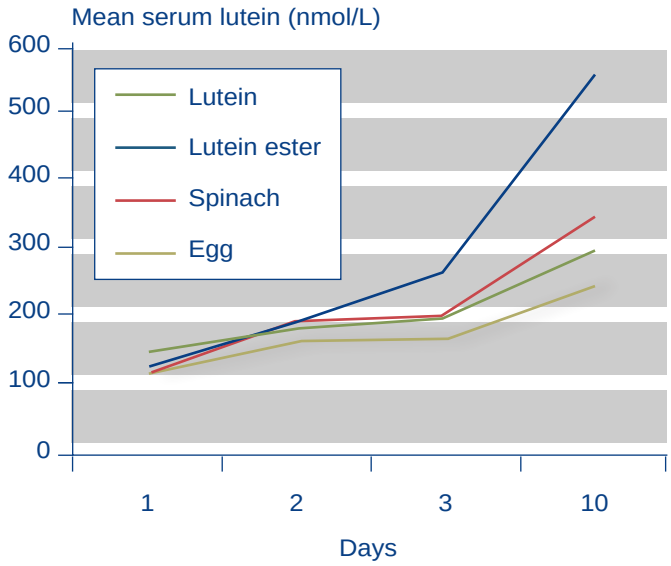
Egg evidence

Table 1 contains information from six comparative studies of egg supplementation to diets. Most of these were randomised, and most examined dietary supplementation with one egg per day, measuring serum or plasma concentrations of lutein and zeaxanthin, as well as plasma cholesterol subfractions.

Most studies showed that eating about one egg a day increased serum or plasma lutein by about 20-30%. Only one [1] failed to show any increase in plasma lutein with a standard egg, though it showed a large increase with a "designer" egg from chickens fed a supplemented diet, with 15 times more lutein per egg (1.9 mg) than a standard egg.

Two other results are interesting. One of them [2] compared four diets containing the same amount (6 mg) of daily lutein as a lutein supplement, lutein ester supplement, in spinach, or egg. While the study was small, involving only 10 healthy men in the crossover study, it

Figure 1: Change in serum lutein concentrations in 10 healthy men with different sources of dietary lutein



showed a much higher increase in serum lutein for eggs compared with spinach or supplements for the same daily lutein dose (Figure 1).

Only one study has examined the effects of dietary eggs on the retina [3]. Individuals with low macular pigment optical density may be at greater risk of retinal disease because more potentially harmful short wavelength light reaches tissue at the back of the retina. Higher macular pigment optical density is considered, therefore, to be protective. In 24 healthy younger women given placebo or one of two egg diets for 12 weeks, the change in macular pigment optical density was greatest in those with low initial levels (Figure 2).

Comment

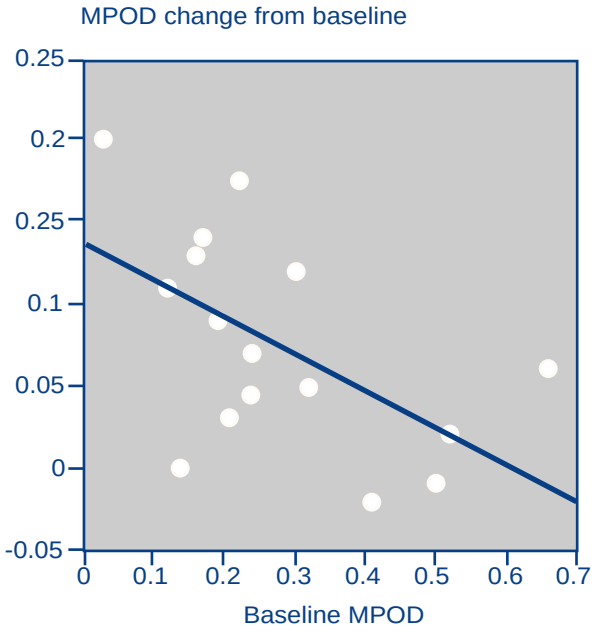
Before anyone rushes off to stuff themselves with eggs, it needs to be said that these are early days, though many Internet sites would try and convince readers otherwise. There is no evidence that eggs are a miracle for preventing or curing macular degeneration. What we are seeing is a reasonably consistent response for useful surrogate markers (serum concentrations of lutein and zeaxanthin or macular pigment optical density), without any major change in serum cholesterol or its subfractions.

What is interesting is that lutein in eggs seems to be more readily available, and that any protective effects are likely to be greatest in those with the greatest risk, in this case those with the lowest macular pigment optical density. A good diet, which includes all those leafy greens and some eggs, is still the right advice, for macular degeneration and all sorts of other ills [4].

References:

1 PF Surai et al. Designer egg evaluation in a controlled trial. European Journal of Clinical Nutrition 2000 54: 298-305.
2 HY Chung et al. Lutein bioavailability is higher from lutein-enriched eggs than from supplements and spinach in men. Journal of Nutrition 2004 134: 1887-1893.
3 AJ Wenzel et al. A 12-wk egg intervention increases serum zeaxanthin and macular pigment optical density in women. Journal of Nutrition 2006 136: 2568-2573.
4 JD Ribaya-Mercado, JS Blumberg. Lutein and zeaxanthin and their potential roles in disease prevention. Journal of the American College of Nutrition 2004 23: 567S-587S.

Figure 2: Change in macular pigment optical density in 24 women over 12 weeks according to baseline value



Almotriptan for acute migraine

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Migraine is one of those conditions where continuous improvements have been made to outcomes, in this case largely at the prompting of the International Headache Society. Originally the outcome of interest was migraines with initial moderate or severe pain becoming mild pain or no pain by two hours (headache response at two hours).

Later, pain free at two hours was used. Then the goalposts moved to incorporate not just these two hour outcomes, but the additional requirement that patients with the two hour outcome should maintain at least that level of pain relief for 24 hours without additional analgesic medication.

This represents moving goalposts. The hurdle for effectiveness is increasingly higher. One consequence or measure of the increasing difficulty is that response rates with placebo fall from about 40% with the original outcome of two-hour headache response to about 5% for pain free at two hours maintained to 24 hours. An individual patient analysis of almotriptan [1] takes things one step further.

Meta-analysis

The analysis was of four randomised, double-blind, placebo-controlled trials of almotriptan for acute migraine. Several different doses were used, and all analyses estimated efficacy for the first migraine attack.

Results

The four trials had 2,294 patients, of whom 86% were women, and the mean age was 41 years. The main results calculated from data in the paper [1] are shown in Table 1. As expected from other migraine trial data, NNTs were lower (better) with both higher dose of almotriptan, and more easily attained outcome.

One new outcome was the proportion of patients who were pain free at two hours, who were without recurrence of moderate or severe headache pain, who had no additional analgesics before 24 hours, and who reported no adverse events. For this outcome, almotriptan 12.5 mg was successful for 22% of patients, compared with 11% with placebo.

Comment

What we can say is that almotriptan 12.5 mg is about as effective for treating acute migraine as sumatriptan 100 mg, based on short-term outcomes at two hours. As the hurdle gets higher, placebo responses fall (Table 1), just what we have seen before.

What is new is that, using individual patient data, we can now have at least one outcome that has real relevance for patients. We know that 1 in 5 patients who have an acute migraine attack and take the medicine will be pain free at two hours, remain pain free up to 24 hours with no additional analgesic use, and will not have any adverse events.

Pharmaceutical companies may not like the message, because this way of looking at outcomes implies that their drugs are not as good as they would like to think. So be it. But there is another message for people who run or impose formularies: highly limited formularies will mean that only a minority of patients may get the benefits they want, for which of us can say whether those who do not benefit with almotriptan would not benefit with another headache therapy, including other triptans?

References:

1 GC Dahlöf et al. Efficacy, speed of action and tolerability of almotriptan in the acute treatment of migraine: pooled individual patient data from four randomized, double-blind, placebo-controlled clinical trials. Cephalalgia 2006 26: 400-408.

Table 1: Pooled analysis of four randomised trials of almotriptan compared with placebo in a migraine episode with moderate or severe pain

Outcome	Almotriptan dose (mg)	Percent with outcome		NNT (95% CI)
		Almotriptan	Placebo	
Headache response 2 hours	6.25	55	35	5.0 (3.7 to 7.5)
	12.5	61	35	3.8 (3.1 to 5.1)
	25	64	35	3.5 (2.8 to 4.7)
Sustained response 24 hours	6.25	41	27	7.0 (4.8 to 13)
	12.5	45	27	5.5 (4.1 to 8.2)
	25	51	27	4.0 (3.2 to 5.6)
Pain free 2 hours	6.25	29	14	7.0 (5.1 to 11)
	12.5	35	14	4.8 (3.8 to 6.3)
	25	40	14	3.9 (3.1 to 5.1)
Sustained pain free 24 hours	12.5	26	11	6.8 (5.2 to 9.9)
Sustained pain free without adverse events	12.5	22	10	8.5 (6.2 to 14)

Mobile phones and cancer

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Many of us use mobile telephones to a greater or lesser extent. Because mobile phones emit radio frequencies that can penetrate several centimetres into the human brain, it has been hypothesised that their use could possibly lead to tumours of the head and neck.

This possibility has led to a number of 'scare' stories in the popular press. Typically, debunking the scare involves trying to prove a negative, never an easy thing at the best of times. About the only way to prove a negative is to have very large amounts of data, but also demonstrating the lack of any sort of dose-response as well as no biological plausibility. A large Danish study goes most of the way to doing that for mobile phones and cancer [1].

Study

In the period 1982 to 1995 over 700,000 Danish citizens subscribed to a mobile telephone service. After eliminating those in which individual users could not be identified because they were corporate subscriptions, had incorrect addresses, were from Greenland or the Faroe islands, had a history of previous cancer, or were under 18 years, the final cohort consisted of 420,000 identified subscribers.

Because Denmark has a system of personal identification numbers, cohort members could be linked to files of a cancer registry that is virtually complete, and using a nationwide system of cancer classification. Follow up began from the first day of subscription, and ended on date of diagnosis of any cancer, death, emigration, or end 2002.

Numbers of cancers found were compared with the number expected in the general Danish population, for men and women, and in five-year age groups. Mobile phone subscribers were omitted from this comparison group.

Results

Most (85%) of the 420,000 subscribers were men. The median time of mobile telephone subscription was 8.0 years. Mobile subscribers had 14,250 cases of diagnosed cancer, against an expected number of 15,000, giving an overall standardised incidence ratio of 0.95 (95% confidence interval of 0.93 to 0.97).

For men and women analysed separately there was no difference from expected in all brain and nervous system cancers, or cancers of the salivary glands or eye. For men and women analysed together, there was no increased risk of any type of intracranial cancer, with a hint of a decreased risk for parietal lobe tumours. There was no increase in brain and nervous system tumours and leukaemias according to time from first subscription (Table 1).

There was no increased risk of any other type of cancer for men, with hints of decreased risk for lung, bladder, buccal, oesophageal and liver cancers, as well as other cancers and unspecified cancers. For women the numbers of individual cancers were small, and none had any large increase or decrease in incidence over expected.

Comment

What is good about this study is that it was large, of long duration, covered a whole population, and was performed in Denmark. Denmark has an almost unique ability to successfully link different databases through the use of personal identification numbers.

The results all but eliminates the concept that the use of mobile phones can cause cancer. And not just cancer, because the study allows detailed diagnosis of particular cancer types, including acoustic neuromas and cancers of temporal and parietal lobes which would be the parts of the brain closest to a mobile phone antenna, and hence most at risk.

The paper has a wonderful discussion, which not only puts these results into the context of others, but tells us that the authors could find no studies indicating any biological plausibility for a link between mobile phones and cancer. This comes a close to proving a negative as we are ever likely to get, but even more data will come out in future from continuation and extension of the study.

If you Google mobile phones and cancer, you will find links to over nine million sites. Some are good, some are up to date, but many are not. They should all reflect on the data from Denmark.

Reference:

1 J Schüz et al. Cellular telephone use and cancer risk: update of a nationwide Danish cohort. Journal of the National Cancer Institute 2006 98: 1707-1713.

Table 1: Brain and nervous system cancers, and leukaemias, by years of mobile phone subscription, compared with non-subscribers in Denmark

		Standardised incidence rate (95%CI)	
Years of subscription	Person years	Brain and nervous system	Leukaemia
<1	420,000	0.9 (0.7 to 1.2)	1.1 (0.8 to 1.5)
1-4	1,656,000	1.0 (0.9 to 1.2)	1.1 (0.9 to 1.2)
5-9	1,327,000	1.0 (0.8 to 1.1)	0.9 (0.8 to 1.1)
10	170,000	0.7 (0.4 to 0.95)	1.1 (0.7 to 1.5)

Dear Dave

Dave and other members of the bpac[nz] team answer your clinical questions

If you have a clinical question email it to
dave@bpac.org.nz

Can Proton Pump Inhibitors cause vitamin B_{12} deficiency?

As yet there are no clear guidelines on routine monitoring for vitamin B_{12} status in people taking long term acid suppressant drugs. For people who have been taking proton pump inhibitors (PPIs) for more than 3–4 years, especially the elderly, it would be a reasonable precaution to occasionally check vitamin B_{12} status particularly if there are associated signs and symptoms. This also probably applies to people taking long term H2RAs.

Vitamin B_{12} requires gastric acid and pepsin to release it from its protein bound form in food and allow binding with intrinsic factor. PPIs do not reduce the secretion of intrinsic factor, but reduced acid secretion may lead to vitamin B_{12} malabsorption.

Several studies have demonstrated that omeprazole can reduce vitamin B_{12} absorption[1,2]. The effects of long-term PPI administration on vitamin B_{12} status has been examined in a number of studies but these are of variable design and quality, making firm conclusions difficult. Most studies have been relatively short (1–4 years) which may be of insufficient duration to deplete body stores of vitamin B_{12} and reflect a deficiency. There is also the difficulty in separating out the underlying pathology as a possible cause of reduced vitamin B_{12} concentrations and most of the longer term studies have been performed in people with Zollinger-Ellison Syndrome (ZE), which may not be applicable to people with other conditions.

Who is Dave?

Pharmaceutical Programme Manager Dave Woods is a graduate of Manchester University (B.Sc. [Hons]) and the University of Otago (MPharm). Dave has extensive experience in hospital pharmacy, drug information, rational use of drugs and quality assurance. He has published on a range of subjects and holds editorial positions for several international journals.

If you have a clinical question email it to
dave@bpac.org.nz

Conflicting results

For these reasons the results of studies are conflicting. A small study[3] in 34 patients with peptic ulcer disease and a prospective study in patients with ZE (Maton, 1989) found no significant change in vitamin B_{12} concentrations with chronic PPI treatment over 1–4 years. However, Termanini et al[5] found that vitamin B_{12} concentrations were reduced in 11% of patients with ZE who had two concentrations measured at least five years apart. A recent case control study[6] showed that chronic (≥12 months) use of PPIs and H2RAs was associated with a significantly increased risk of vitamin B_{12} deficiency (OR 4.45; 95% CI 1.47–13.34) in patients aged 65 years and older with a variety of reasons for acid suppressant use. The elderly are already at increased risk of B_{12} deficiency due to the increased prevalence of atrophic gastritis and reduced acid secretion. The latter two studies have identified the possibility that the elderly may be at increased susceptibility of PPI induced vitamin B_{12} deficiency.

H2RAs as well?

The long term use of H2RAs (e.g. rantitidine, famotidine) has also been associated with vitamin B_{12} deficiency[6]. The evidence is weaker and it could be expected that the effect on vitamin B_{12} absorption is less as acid suppression is of a shorter duration.

References

1. Schenk BE, Festen HPM, Kuipers EJ, et al. Effect of short and long-term treatment with omeprazole on the absorption and serum levels of cobalamin. Alimentary Pharmacol Therap. 1996;10:541-45
2. Saltzman JR, Kemp JA, Golner BB, et al. Effect of hypochlorhydria due to Omeprazole treatment or atrophic gastritis on protenin bound vitamin B_{12} absorption. J Amer Coll Nutr 1994;13:584-91
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4. Maton PN, Vinayek R, Frucht H, et al. Long-term efficacy and safety of omeprazole in patients with Zollinger-Ellison syndrome: a prospective study. Gastroenterology. 1989;97(4):827-36
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6. Valuck RJ, Ruscin JM. A case control study on adverse effects: H2 blocker or proton pump inhibitor use and risk of vitamin B_{12} deficiency in older adults. J Clin Epidemiol 2004;57:422-428

Correspondence

Dear Editor

I have a hypothesis about the prescribing of PPIs for GORD and dyspepsia, which may or may not have any basis in fact, but is based on my observations as a GP over the past 9 years.

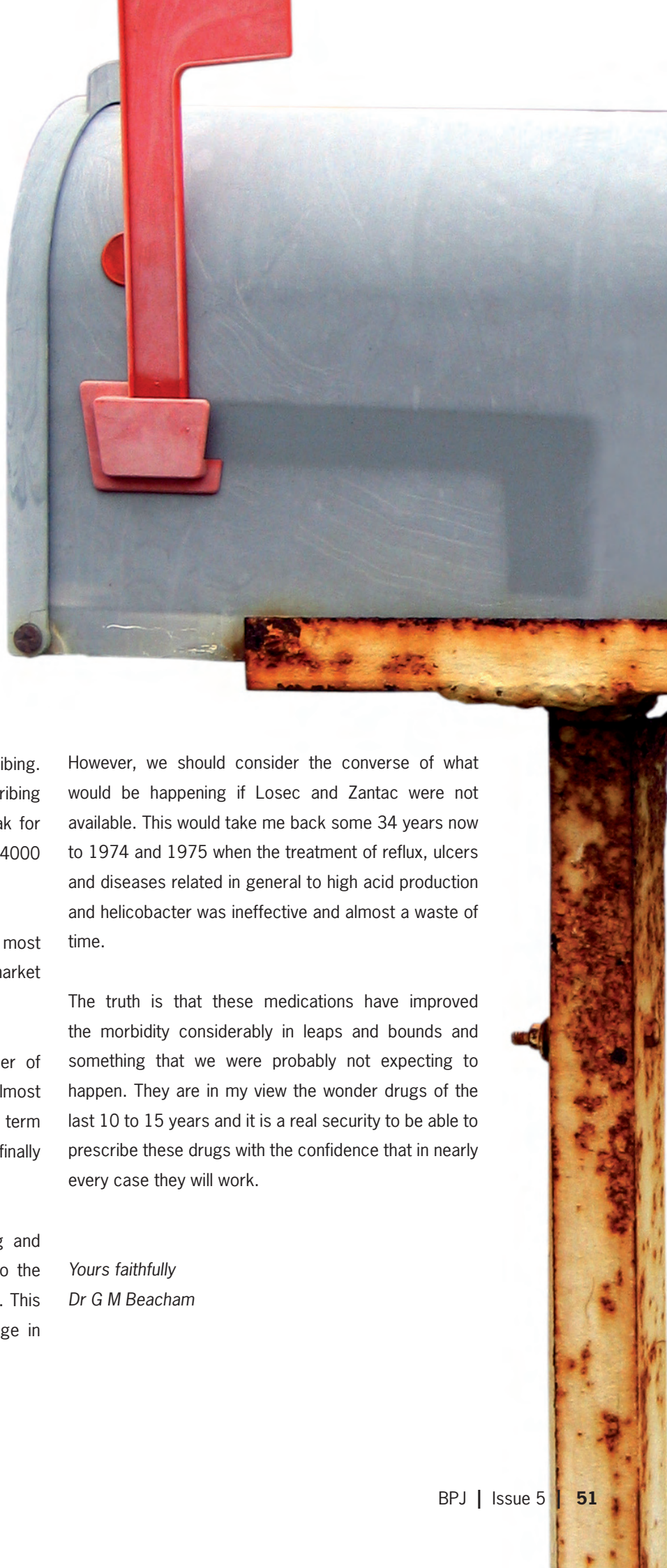
PPIs are extremely effective drugs. Usually, by the time that people consult me with GORD or dyspepsia, they have already tried at least one non-prescription drug: either antacids, or in many cases also an H2RA (recommended by the pharmacist after the antacids were not sufficiently effective). Having established they have no 'red flags', and discussed lifestyle factors, I prescribe a PPI. The effectiveness of this is such that after a period of time, the patient usually stops taking it every day. After a few days, their symptoms return, but they have their trusty PPI on hand to take again for another few days. For those patients who are in the habit of taking drugs every day, they include it as part of their routine, and are reluctant to stop or reduce it for fear of their symptoms returning. For those patients who 'don't like taking pills', they know that taking a PPI will be effective on an intermittent basis (in a way their antacids and H2RAs weren't), so they continue to ask for prescriptions for it when they run out. Your figures show that the average patient who has been prescribed a PPI takes it on 203 days out of 365 per year, with the peaks for the groups 'under 90 days' and 'over 270 days' being the two different groups I outlined above.

I hypothesise that a similar 'effectiveness trap' applies to inhaled corticosteroids for asthma. Beclomethasone is effective for asthma prevention, but the level of compliance required to achieve that effect is higher than with fluticasone. I believe very few asthmatics take their preventer as prescribed (i.e. 14 times per week, if prescribed as a twice daily dose). With beclomethasone, the effect of incomplete compliance is that their asthma remains poorly controlled. With fluticasone, they experience good asthma control even without good compliance. The unfortunate corollary is that once they perceive that fluticasone "works", they actually take their preventer inhaler more frequently and this is not ideal as they end up getting more steroid than they need.

Thus I fear bpac may be fighting a losing battle with trying to reduce prescribing of PPIs and high-dose inhaler corticosteroids. I acknowledge that these are merely observations, and would require studies to be done to see if they have any basis in fact.

Yours sincerely,
Dr Julyan Lawry

Send your letters to
'Correspondence'
PO Box 6032
Dunedin,
or email *editor@bpac.org.nz*



Dear Editor

I refer to your comments regarding Losec prescribing. You continue to be perplexed by the prescribing habits of General Practitioners. I can only speak for my own practice which is Low Access with over 4000 patients.

The simple answer is that Losec is one of the most effective drugs that has been presented to the market over the last 15 years.

In my view, it has literally reduced the number of acute ulcerations and subsequent morbidity to almost zero, has with continued use prevented long term complications of excess acid production, and finally has probably reduced gastric surgery by 90%.

The truth is that this is a very effective drug and General Practitioners by nature always move to the most effective drug when treating their patients. This is the simple answer to why there is no change in prescribing habits.

However, we should consider the converse of what would be happening if Losec and Zantac were not available. This would take me back some 34 years now to 1974 and 1975 when the treatment of reflux, ulcers and diseases related in general to high acid production and helicobacter was ineffective and almost a waste of time.

The truth is that these medications have improved the morbidity considerably in leaps and bounds and something that we were probably not expecting to happen. They are in my view the wonder drugs of the last 10 to 15 years and it is a real security to be able to prescribe these drugs with the confidence that in nearly every case they will work.

Yours faithfully
Dr G M Beacham

Correspondence

Dear Editor

RE: Vitamin D

Your advice on vitamin D was probably fine for the elderly who I generally find are happy to take vitamin D almost without question. However **virtually all of my young patients (including children) are at risk** – 'People unable to obtain regular sun exposure for any reason'. I have tested perhaps too many people and found nearly all of them have low Vitamin D levels (less than 50) and of the remainder most are in the low part of the normal range (50 to 90) and I note some experts recommend levels over 60 or even over 90 – **you made no comment on optimal levels and no comment on how to interpret tests at different time of the year.**

My experience suggests persons with unexplained fatigue particular with seasonal – late winter or just post winter flares in fatigue benefit a lot from vitamin D supplementation – (I concede it could be placebo) – is there any research on this? Also with muscle weakness from low vitamin D and evidence coming out for cancer reduction with vitamin D and even better treatment results for cancer with vitamin D supplementation I think that whilst most vitamin supplementation is dubious it looks as though vitamin D supplementation is worth while. **In young persons we are likely to be facing several problems including recommending doses for life, and fluctuating sun exposure.**

The first issue is convincing someone to take Vitamin D – if they are to take it for life the $50 cost of the test is small over a lifetime – I find a blood test convinces people where my best attempts don't. The other reason to check a level is if they are tired and the level is low a top up dose depending on the level is in my opinion useful rather than just maintenance.

I would give the 10 tabs mentioned in your article at levels less than 30 and 5 tabs for those above 30 but less than 50 – then after that I would give maintenance doses – **can we instead give a top up dose to everyone and avoid the need for the test or would that risk toxicity?**

Daily pill taking is not appealing to most people for life (even those already on pills) and regimens for maintenance probably can include 2 (stat) 1.25 mg cholecalciferol tabs each 3 months or even 4 (stat) each 6 months from what I have read – scripting each 6 months on recalls is a lot less problematic than each 3 months and more cost effective for everyone – is scripting each 6 months adequate – i.e. can the body store it for that long – **you made no comment on evidence for monthly Vs each 3, 4 or 6 months dose regimens** – it would be helpful if you would as I am now getting hospital doctors taking my patients off my 2 pills each 3 months and putting patients on one a month and I would like someone to summarise the evidence appropriately which is what I thought you were going to do when I verbally asked you about this topic last year. **If someone increases there sun exposure purposefully or by chance can toxicity occur at usual maintenance doses? And if so at what maintenance dose would we be free of that risk?**

I would appreciate your comments on the above issues and I suspect other GPs would too.

Dr Steve Searle
Dunedin

We asked Professor Ian Reid, University of Auckland, to answer Steve's questions.

Optimal Vitamin D Levels *There is considerable controversy regarding the optimal levels of 25-hydroxyvitamin D. There is general agreement that they should be greater than 50 nmol/L, but some authorities suggest levels greater than 75 nmol/L or even greater than 100 nmol/L. The latter values are based on observational data that may well be confounded by the fact that individuals with other illnesses spend less time outside and therefore have less sunshine exposure. This does not establish that their other illnesses are caused by the low vitamin D; rather the reverse may be the case. Also, to establish levels greater than 100 nmol/L would require medication of virtually the entire population. Such a step should not be taken without clear trial evidence that this is both safe and effective. At the present time neither is available. In the absence of authoritative data, my belief is that we should go for the conservative minimal value which is 50 nmol/L, and apply this to both children and adults. In order to maintain this level throughout winter, individuals not taking supplementation, need to reach higher levels during summer, since the seasonal fluctuation may be as much as 40 nmol/L.*

Vitamin D and Fatigue *Serum 25-hydroxyvitamin D levels <25 nmol/L are associated with clinical osteomalacia, which causes muscle weakness and pain. Therefore, it is likely that sub-clinical osteomalacia will have some associated muscle fatigue. Conversely, individuals who feel fatigued for other reasons are less likely to exercise and therefore less likely to get sun exposure, so may develop vitamin D deficiency as a secondary problem. Therefore, it is sensible to treat vitamin D deficiency in subjects with or without fatigue, but it should not necessarily be assumed that this will be associated with symptomatic improvement.*

Intermittent Dose *The half-life of serum 25-hydroxyvitamin D after dosing with oral calciferol is of the order of 90 days. Therefore, intermittent dosing is certainly acceptable, and many European countries have used annual dosing at the beginning of winter as a way of preventing deficiency developing during the period when sunlight exposure is least. The optimal dosing is likely to be different for each vitamin D preparation and for each region, where sunlight exposure will influence the required vitamin D dose. Therefore, if individual practitioners wish to try a variety of different dosing intervals, they probably need to validate them with serum 25-hydroxyvitamin D measurements. In Auckland, it is well established that monthly dosing with 1.25 mg (50,000 U) calciferol produces 25-hydroxyvitamin D levels greater than 50 nmol/L in almost all adult subjects.*

Toxicity *The seasonal variation in 25-hydroxyvitamin D levels in New Zealand is of the order of 20–40 nmol/L. The reference range is usually given as 50–150 nmol/L, though toxicity doesn't usually occur until much higher levels than this are reached. Therefore, there is a substantial safety margin, and changes in sunlight exposure are most unlikely to lead to toxicity in individuals who are being maintained within the laboratory reference range.*

Professor Ian Reid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