bestpractice

IRRITABLE BOWEL SYNDROME
COELIAC DISEASE
LACTOSE INTOLERANCE
CONSTIPATION
RESTRICTIONS REMOVED FROM SOME EYE TREATMENTS

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Coeliac disease is a common but often unrecognised disorder, affecting about 1 in 100 people. Symptoms of coeliac disease are often vague and non-specific and may or may not include gastrointestinal symptoms. A low gluten diet in adults and a zero gluten diet in children often result in complete remission. However, untreated coeliac disease may be associated with long term health problems.

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UPFRONT

THE MANNER OF OUR DYING

Preventive health care aims to prevent premature deaths and delay the onset of the suffering caused by illness and disease (compression of morbidity). This is on the understanding that everyone is entitled to a normal life span and that anyone not achieving this has been cheated of the missing years.[1] In essence the aim is to move the survival curve towards a rectangle (Figure 1).

While we put upper age limits in place for diagnostic procedures, such as cervical smears, the theory and rhetoric of preventive healthcare has not yet addressed the problem of how medicines for disease prevention should be applied to those who have already exceeded an average life span. In the context of a rapidly ageing population, there is an urgent need to think the issues through.

Figure 1: Survival curve

Unfortunately there are too few clinical trials in older populations. Sensitivity about ageism means that preventive medicines are often applied in older groups on the basis used for younger populations. The two groups are vastly different. Multiple co-existing diseases are the rule in older populations and the risk of harm from treatment is greater.

THE NEW EPIDEMICS

In the developed world, improved social conditions, immunisation and successive generations of antibiotics have been hugely successful in stemming the epidemics of infectious disease. Individuals saved from death due to overwhelming bacterial infection are now living long enough to develop other diseases producing a new 'epidemic', this time of cardiovascular disease. Now cardiovascular disease prevention is pursued and guidelines are applied regardless of age.

However if death is to be prevented at any age from any cause, epidemic will follow epidemic. Eventual mortality is certain, so the questions is what then will be the next most common cause of death and illness – the next 'epidemic'? Our bodies have a finite functional life. If various systems wear out at a similar rate, by introducing preventive treatments in the older populations aimed at reducing the risk of a particular disease, are we simply changing the cause of death rather than prolonging life?

Several factors are influential. Firstly, single disease perspectives result in trial designs that look at outcomes for single diseases in a situation where complexity is the rule.
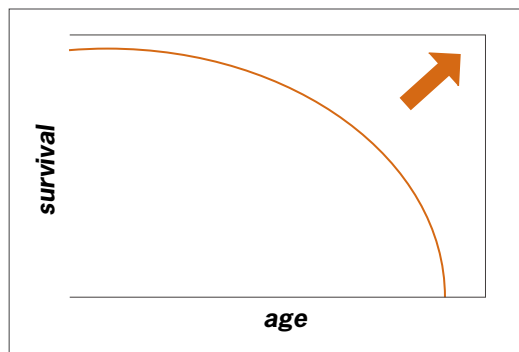
Contributed by Dr Dee Mangin

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These single disease perspectives imply that successful interventions for the index condition should be made widely available to all those with that risk factor, irrespective of the overall effect on population mortality and morbidity. Secondly, sensitivities about ageism make us feel awkward about looking at things from a different perspective when dealing with an older population. Finally there are huge commercial gains to be made by pharmaceutical companies if statistically effective interventions in relatively small population groups can be widened to larger populations.

Research estimates of differences in the absolute risk of an adverse outcome enable us to understand the potential benefits of particular treatments. In older people, the likelihood of morbidity due to multiple and compounding diseases increases and the absolute risk of dying is increased, simply because the time of death is proportionately closer. This may magnify the apparent effect of a single intervention for a specific condition while overall survival is only minimally affected.

Notwithstanding this, treatment can be justified in terms of postponement of morbidity even when there is no change in mortality. However the difficulties associated with single disease perspectives also apply here. The use of statins for cardiovascular disease prevention provides a case study for examining these issues further.
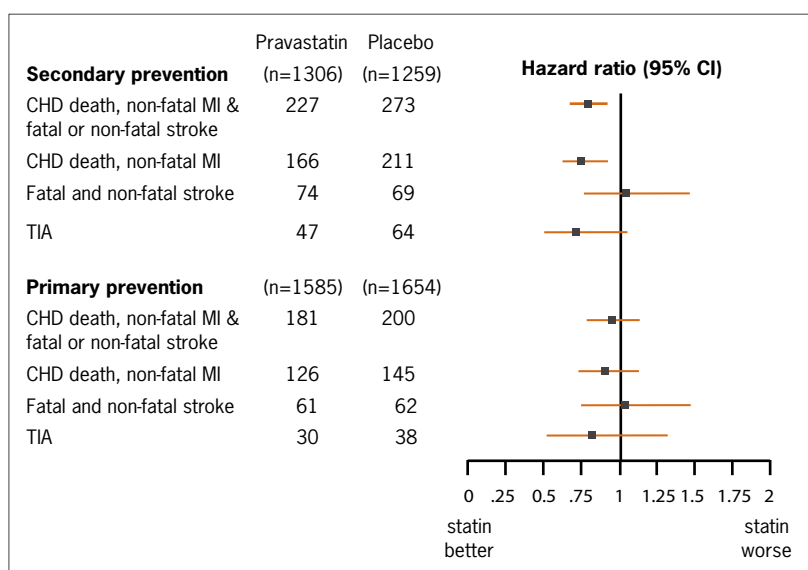
THE EVIDENCE FOR LIPID LOWERING TREATMENTS IN OLDER AGE

The framework for lipid modification at younger ages is extrapolated for those over 75. The largest trial conducted in this group is the PROSPER trial with over 5000 participants, between 70 and 82 years old, and followed up for an average of 3.2 years.[3] It is used as the basis of most recommendations for lipid lowering treatments in older populations.

There is modest but clear prevention of cardiovascular mortality and morbidity using the primary composite endpoint of CHD death or non-fatal MI (absolute risk reduction 2.1%, NNT 48). Figure 2 shows the primary and secondary outcomes underpinning the claims for the benefits of pravastatin over placebo for preventing cardiovascular morbidity and mortality. For women, the results showed no benefit over placebo for any outcome. There is also no demonstrable benefit in primary prevention yet the conclusions are that the strategy for cardiovascular risk management in middle aged people should also be applied to elderly individuals.

If the detail of the paper is examined, the other morbidity and mortality data are illuminating. Despite a change in cardiovascular composite outcomes, there is no change in all cause mortality (Figure 3). Looking at mortality and morbidity from other causes, rates of cancer diagnosis and death were increased in the treatment group compared with placebo. This did not quite reach significance for death but did for new diagnosis of cancer (NNH 59).

The efficacy of a treatment might be justified in terms of postponement of morbidity even when there is no change in mortality, in the PROSPER paper, when the scrutiny of treatment outcomes is extended beyond a single disease model, this argument does not hold. The increase in new cancer diagnoses counters any arguments of compression of morbidity. The more

Figure 2: Major cardiovascular outcomes, according to primary or secondary prevention status of participants

The primary endpoint of the study is reproduced for comparative purposes.

likely hypothesis for this effect, which is not seen in trials of younger patients, is substitution of cause of death.

This is a phenomenon which is unprecedented. The prevention of untimely death is a valid pursuit of medicine up to a point. Thus when we vaccinate children in infancy we are selecting out a cause of death for them, but in this case justifiably, because deaths from infectious disease tend to occur prematurely. It is only when we start selecting out causes of death, rather than extending life, that this endeavour becomes questionable.

Many patients fear the manner of their dying more than death itself and many regard coronary heart disease as a 'good way to go' in old age.[5] In prescribing medicines to prevent particular diseases, we may select for another cause of death unknowingly and certainly without the patient's informed consent. This is fundamentally unethical, undermining the principle of autonomous choice and the concept of *'primum non nocere'*. An older patient who has elected to *'reduce the risk of heart attack'* may make a different decision when told '*you will not extend your years of life and you will increase your risk of being diagnosed with and dying of cancer*'

Clinical decisions about prescribing for disease prevention carries additional responsibilities.[6] Preventive treatments do not relieve suffering directly, but are designed to reduce some future risk of suffering and are usually initiated by the suggestion of the physician rather then a patient request. Compared with initiation of treatment to relieve suffering, a degree of persuasion is involved in starting preventive treatments.[7] As clinicians we must therefore be reasonably certain they will fulfill their promise. There are harms other than the side effects of the actual treatments, not the least

of which is the shadow cast over a currently healthy life by the threat of disease. One might argue that this particular harm is magnified as mortality looms closer. These considerations may explain the evident discomfort of general practitioners and their apparent reluctance to follow guidelines for cholesterol measurement and lipid lowering agents in those aged 75 years or over, compared with those under 75.[8] While every treatment decision is an individual one, guidance for populations is based on population data. The PROSPER study has been acknowledged as the best available evidence for the effects of statins for prevention of cardio- and cerebrovascular disease in old age. We cannot ignore it.

The best interests of the older person, who has paid a lifetime of taxes, might be to invest that money in health care that will genuinely relieve their suffering. Cataract and joint replacement surgery, and personal care of those with dementia, provide obvious examples. A different model is required for assessing medicines for prevention in old age. One that includes duration of life extension, duration of treatment and takes account of mortality and morbidity, due to all causes as well as the harms attributable to treatment. Some preventive

Figure 3: Outcome
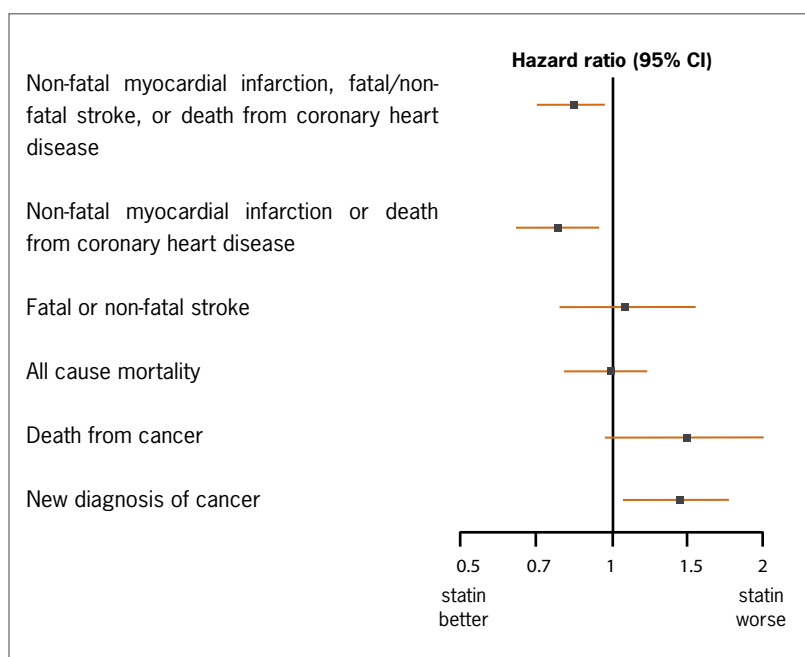
interventions that have benefits across a range of conditions will likely be of similar benefit in older populations as in younger populations using this model (flu vaccination, exercise, smoking cessation). Some may be of more benefit in older populations, some like statins, will be of less benefit.

Patients and physicians are entitled to all the information they require to make decisions with such profound consequences. The current international single disease models of research, analysis and guidelines make this unlikely. Evidence for older populations cannot be squeezed uncomfortably into models designed to best assess the benefits and harms of treatment in younger populations. Our current models of quality usually relate to 'doing something'. A better model would acknowledge confidently when not to use medicines – when best practice is 'not doing'. If we continue using the current framework the benefits will accrue only for pharmaceutical companies with increasing profits from an ageing population consumed by epidemics rather than enjoying their long life.

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SPECIALIST PRESCRIBING RESTRICTIONS
Removed for some topical eye treatments

Specialist prescribing restrictions have been removed from some topical eye treatments from 1st October 2007. These include medications from the following groups.

- Antiviral

- Antibacterial

- Steroidal anti-inflammatory

- Non-steroidal anti-inflammatory

- Intraocular pressure reducing

Key points

- Although general practitioners can now initiate some topical eye treatments, it does not mean they should.

- Significant corneal disease, intraocular inflammation and glaucoma still require specialist diagnosis and management.

- Primary care will still be involved in the ongoing support and education of people with these conditions and the continuation of the medications used to treat them.

High risk situations requiring specialist skills

Some of these medications are used when there is high risk of visual loss and their misuse can increase this risk. Initiation and monitoring require high levels of knowledge, skills and experience of a specialist nature as well as the availability and ability to use specialist equipment. For example:

- Slit-lamp examination is needed for accurate diagnosis and monitoring of intraocular inflammation, such as iritis and keratitis, and ulceration of the cornea.

- Accurate diagnosis and monitoring for adequacy of treatment of glaucoma requires accurate detailed assessment of intraocular pressure, the optic disk and visual fields.

- Accurate distinction between infective and non-infective inflammatory conditions is essential because medications, such as steroid drops, used for some conditions, will make others much worse.

- Use of steroid drops for more than ten days requires, monitoring for steroid-induced glaucoma.

Primary care role still important

Although primary care is often not equipped to initiate and monitor treatment for these conditions, it still plays a valuable role. People will still look to primary care for support, education and continuation of treatment. Clinicians, particularly prescribers, need to understand the actions of these medications and how to avoid and identify possible adverse effects. For example:

- Some topical preparations e.g. beta-blockers, are sufficiently absorbed to cause systemic effects.

- Unless medically indicated, soft contact lenses should not be used for the duration of treatment with eye drops and ointments.

- However, it is safe to replace contact lenses 15 minutes after use of some drops.

- Application of gentle pressure to the tear duct after instilling drops increases exposure of the anterior eye tissues to the treatment and reduces systemic absorption. This is especially advisable in children .

Resource for updating primary care clinicians about eye medications

bpac^nz does not expect to see changes in the way general practitioners use topical eye medications as a result in this change in availability. However it does offer an opportunity to update knowledge in this area.

To help with this bpac^nz is producing a more detailed guide to update GPs about topical eye treatments. This will be available in the next issue of BPJ.

BE AWARE OF OTC SUMATRIPTAN USE BY PEOPLE WITH MIGRAINE

Sumatriptan 50 mg is now available for sale as a pharmacist only medicine.

Pharmacists have been given strict criteria concerning over the counter sales.

The purchaser must have an established pattern of migraine symptoms and the product can only be sold in an original pack of two tablets along with an information leaflet.

In those with a definitive diagnosis of migraine, sumatriptan is often an effective treatment. It works best when taken early in the painful phase of a migraine headache and unlike simple analgesics, is less effective when taken during the aura.

There is a significant risk of relapse with sumatriptan (within 48 hours) in up to 50% of patients. The dose can be repeated but is usually less effective the second time. Use of sumatriptan or analgesics on more than two days per week is associated with significant risk of medication overuse headache. Establishing a clear history regarding previous use is essential.

In general, it is recommended that all patients presenting with headache are questioned about their non-prescription analgesic use. Many people will have tried over the counter NSAIDS or paracetamol (and now perhaps sumatriptan) prior to a consultation. A history of self management is often useful in determining the type of headache and the treatment options.

For more information about sumatriptan and the treatment of migraine see BPJ 7.

CONSTIPATION

KEY POINTS

- *Most cases of constipation in adults are mild and intermittent and respond to lifestyle changes such as increasing fibre in the diet, increased fluid intake and exercise*

- *On assessment it is important to identify any red flags that may indicate more serious disease or the need for referral*

- *Treatment with a laxative may be required if general lifestyle advice is not helpful*

- *Choice of laxative is based on the cause of constipation, symptoms, patient preferences, potential side-effects and time to effect*

- *Constipation is also common in children and long term use of laxatives may be required when dietary measures fail - osmotic laxatives, such as lactulose, are the preferred initial treatment*

"DO NOT DISTURB"

www.bpac.org.nz   Keyword: *"constipation"*

Constipation is characterised by persistent, difficult or seemingly incomplete defaecation which may be accompanied by abdominal pain or bloating. In terms of bowel frequency, definitions differ, as bowel habits vary widely between individuals, but will usually be reported to the GP as a deviation from the norm. Constipation is more common in women than men and incidence increases with age.

International consensus (Rome II) diagnostic criteria define constipation in terms of multiple symptoms (e.g. straining, hard stools) and/or a bowel movement frequency of less than three times per week (page 14). These criteria are mainly used for research purpose and are not always applicable to general practice.[1]

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MOST CASES OF CONSTIPATION ARE NOT CAUSED BY AN IDENTIFIABLE PHYSICAL OR PATHOLOGICAL CONDITION

Most cases of constipation in adults are relatively mild and intermittent and can often be linked to lifestyle factors, poor diet, (e.g. low fibre and low fluid intake) immobility, stress and suppressing the urge to defecate.

A number of drugs (Table 1) can cause or aggravate constipation. The main mechanism is slowing of gut motility due to anticholinergic or antispasmodic effects but in some cases the mechanism is not clear. Drug induced constipation if often exacerbated, especially in older people, by comorbidities such as Parkinson's disease, reduced fluid intake, poor diet and decreased mobility. When assessing a person with constipation it is important to consider drugs (prescribed and purchased over the counter) as a possible cause or contributing factor.

Complications and consequences

Persistent constipation or inappropriately treated constipation may lead to complications of varying severity. These include haemorrhoids, faecal impaction, faecal and urinary incontinence, rectal bleeding, anal fissures, urinary tract infection and psychological disorders.

Table 1: Some drugs or drug groups that can cause or aggravate constipation (MeReC 2004)[1]

- Antacids containing aluminum or calcium
- Antispasmodics (e.g. propantheline, hyoscine-butyl-bromide [buscopan])
- Antidepressants, especially tricyclic antidepressants
- Antihistamines (especially older sedating ones such as promethazine [phenergan] or chlorpheniranine [polaramine])
- Antipsychotics
- Antiparkinsonism drugs including those with anticholinergic effects (e.g. benztropine, orphenadrine, procyclidine) and dopamine agonists (e.g. bromocriptine)
- Calcium supplements
- Calcium channel blockers, especially verapamil
- Diuretics (secondary to dehydration)
- Iron salts (irrespective of which preparation is used)
- Ondansetron
- Oxybutinin and similar drugs used for incontinence
- Proton pump inhibitors (e.g. omeprazole, lansoprazole)
- Vinca alkaloids (used in chemotherapy)

Chronic Constipation (functional)
Rome II criteria

1. Loose stools are not present and there are insufficient criteria for IBS.

2. To meet the criteria patients need to experience at least two of the following for at least 12 weeks (which need not be consecutive) in the preceding 12 months:

   - Straining >25% of the time

   - Lumpy or hard stools >25% of defaecations

   - Sensation of incomplete evacuation >25% of defaecations

   - Sensation of anorectal obstruction/ blockage >25% of defaecations

   - Manual manoeuvres to facilitate >25% of defaecations

   - <3 defaecations per week

MANAGEMENT OF CONSTIPATION

The first step in management is to gain an understanding of the possible cause for constipation and whether it is acute or chronic.

Acute constipation, for example in a younger patient immobilised from a fracture, is usually easy to manage and may only require short term treatment with a stimulant laxative.

Chronic constipation needs more careful assessment. The most common causes are medications, especially opioids, and slow transit. Less common is dyssynergia (uncoordinated rectal emptying). Patients with dyssynergia complain of prolonged and excessive straining and will often resort to digital manipulation to empty the rectum.

The steps below help formulate a management plan:

- Identify any physical or pathological cause for the constipation

- Identify any red flags which may indicate significant pathological disease or physical cause

- Consider pre-disposing conditions including causative drug treatment and manage appropriately

- Address lifestyle issues such as increasing fluid and fibre intake and increasing exercise

- Consider an oral laxative if lifestyle issues are ineffective or whilst lifestyle modifications take effect

- Choose a laxative based on the cause of the constipation, symptoms, patient preferences and prior experiences, potential side effects, time to effect and cost

- Consider a rectal laxative such as an enema if an oral preparation is ineffective or rapid relief is required

- Give the smallest effective dose of laxative and reduce or stop when symptoms resolve

DIETARY AND LIFESTYLE ADVICE

- **Increasing the fibre content** of the diet will increase the frequency of bowel motions in constipated patients. A high fibre diet consists of 18–30 g fibre per day from fruit, vegetables, wholemeal bread, cereals and grain foods. Oat bran or unprocessed bran can be taken with food or fruit juice. Benefit may be apparent in three to five days but the diet should be tried for at least a month.

- **Maintaining fluid intake** should help prevent constipation. Two litres of water daily is recommended for people on a high fibre diet. Avoid a high fibre diet if adequate fluid intake is not possible.

- **Regular exercise** encourages peristalsis in the colon and should be part of a management plan for constipation

A high fibre diet is generally less effective if constipation is secondary to slow transit (reduced gut motility). Constipation secondary to opioid analgesic use usually requires more aggressive management than just fibre supplementation.

Constipation 'Red Flags' which may indicate the need for further investigation (based on MeReC, 2004, Prodigy, 2007)[1,2]

- Blood in the stools

- New onset or worsening constipation in people aged over 50

- Concurrent weight loss, nausea, vomiting, anorexia or fever

- Severe abdominal pain

- Co-existing or alternating diarrhoea

- Persistent symptoms

- Tenesmus

- Failure of laxative treatment and lifestyle modifications

Table 2: Classes of laxatives

Class of Agent	Examples	Time to effect
Bulking Agents	Unprocessed bran	2–3 days
	Soluble fibres (mucilaginous laxatives) - Psyllium (Konsyl D, Mucilax, metamucil) - Ispaghula (Isogel)	2–3 days 2–3 days
Stimulant Laxatives	Docusate sodium with sennosides Coloxyl with Senna	8–12 hours
	*Codalax (Danthron with Poloxamer)	6–12 hours
	Bisacodyl - Oral (Dulcolax; Bisacodyl AFT) - Rectal (Dulcolax, Fleet)	10–12 hours 20–60 min
Faecal softeners	Docusate sodium (also has stimulant activity) - Oral (Coloxyl Tablets) - Enema (Coloxyl enema concentrate)	12–72 hours 15–20 mins
	Poloxamer (Coloxyl drops)	12–24 hours
Osmotic Laxatives	Lactulose (Laevolac)	Up to 2 days
	Macrogols (polyethylene glycols) (Movicol)	1–3 days
	Glycerol Suppositories (also has a stimulant effect)	15–60 min
	Sodium acid phosphate (Fleet enema)	15 min
Herbal Laxatives	There are numerous preparations available	Action often unpredictable and not generally recommended

* Currently unavailable

CHOOSING A LAXATIVE

Laxatives are categorised according to their properties (Table 2). They vary in their time to effect and mode of action.

There are very few studies which have compared the effectiveness of the various classes of laxatives, and generally the choice of agent is based on potential causes of the constipation, symptoms, patient preferences and prior experiences, potential side effects, time to effect and cost.

Constipation caused by an opioid analgesic will usually require a laxative which includes a stimulant such as senna (Table 2). A bulk former used in this situation could lead to impaction and a stool softener or osmotic preparation would not solve the underlying problem of reduced gut motility.

The prolonged use of laxatives is not usually necessary but may be appropriate in situations where constipation may re-occur if they are stopped. For example, for inactive or immobile people, those receiving opioids or other constipating drugs, those with chronic neurological conditions such as Parkinson's disease and occasionally for children.

Generally, all oral laxative preparations should be avoided in people with intestinal obstruction[2] but there is evidence of safe and effective use of macrogols in malignant obstruction.

BULK FORMING LAXATIVES

These add bulk to the stool and stimulate peristalsis. Several days are required for effect and they are not suitable for acute relief of constipation. They are useful for people with normal gut motility and uncomplicated constipation, who require long-term control.

They should be avoided in people with intestinal obstruction, colonic atony, faecal impaction or dehydration.[2] Their main side effects are abdominal bloating and flatulence.

Many bulk laxatives are now easier to mix and administer as they are formulated as a mucilaginous gel.

FAECAL SOFTENERS

These agents lower surface tension and allow water to penetrate hard dry faeces.

Softeners are often combined with a stimulant where they are especially useful for opioid induced constipation. Enemas are also available to give a more rapid action.

Docusate is a faecal softener with some stimulant activity. Oral docusate should be avoided in people with intestinal obstruction.

OSMOTIC LAXATIVES

These work in the lumen of the colon to draw water in to the gut by osmosis. Osmotic laxatives need to be taken in combination with a good fluid intake.

Lactulose, an osmotic laxative, is fermented by gut bacteria to produce short chain fatty acids with resultant beneficial effects on gut motility and flora. It is a synthetic combination of galactose and fructose which is not absorbed in the gastrointestinal tract and can be taken by people with diabetes (avoid in those with galactosaemia). It needs to be taken regularly and takes at least two or three days to work so will not give immediate relief. Abdominal discomfort and flatulence are common side effects and some people find it unpalatable.

Macrogols (e.g. Movicol) are relatively new products and appear to be at least as effective as lactulose and may cause less flatulence. However, there is no evidence that they are more effective or superior to more established, less expensive agents.[1] Macrogols should be avoided in people with severe inflammatory conditions of the gut (e.g. Crohn's disease, ulcerative colitis, toxic megacolon).[2]

STIMULANT LAXATIVES

These increase intestinal motility by direct stimulation of colonic nerves to increase the movement of faeces. They are often suitable for short term use to restore normal bowel function and are usually taken at night to produce an effect the next morning.

Bisacodyl stimulates small as well as large bowel motility. Bisacodyl suppositories can be used for rapid evacuation.

Senna is available in combination with faecal softeners and is especially useful in longer term management of opioid induced constipation. The use of danthron containing preparations is restricted to terminal care due to concerns about its potential for carcinogenicity.

Abdominal cramps are common with stimulants and they should be avoided if there is a possibility of intestinal obstruction. Prolonged use of stimulant laxatives can lead to diarrhoea and associated fluid and electrolyte imbalance (e.g. hypokalemia) particularly if fluid intake is inadequate.

RECTAL PREPARATIONS (SUPPOSITORIES AND ENEMAS)

These are used if oral preparations are ineffective or if impaction is low down the intestinal tract. Avoid rectal preparations if haemorrhoids or anal fissures are present.

The choice of product is governed by the site of the impaction and stool type.[2]

- Phosphate enemas (e.g. Fleet) are suitable for hard impacted stools
- Bisacodyl suppositories can be used for soft stools in the lower rectum
- Glycerol suppositories are often effective for both soft and hard stools in the lower rectum
- Docusate enemas (e.g. Coloxyl) can be used for clearing both hard and soft stools occurring higher in the rectum

Care is required in administering rectal agents as tears and perforations can occur.

LAXATIVE MISUSE AND EATING DISORDERS

Misuse of laxatives can occur in people with eating disorders such as anorexia and bulimia but also in normal or overweight persons. Laxative misuse in the UK has been reported at 2% in secondary school students and 13% in college students.[3] All health care providers need to be aware of the possibility of misuse, especially pharmacists, as many laxatives can be purchased easily without prescription.

The aims of treatment are to restore the normal pattern of defaecation and relieve discomfort. Generally a step wise approach is recommended in which possible causes are identified and managed, lifestyle changes tried and laxatives used if these approaches fail. If drug treatment is required, use the least number of drugs for the shortest time to avoid laxative dependence.[3]

CONSTIPATION IN CHILDREN

Constipation is common in children and can present at three important stages of childhood, in infants at weaning, in toddlers acquiring toilet skills and at school age.

DEFINITION OF CONSTIPATION IN CHILDREN

The diagnostic criteria are different to those of adults. There have been various attempts to define chronic constipation in children and the most commonly adopted is the Rome III criteria (see opposite)[4,5]

- The most common cause for constipation in children is functional (90–95%)
- Most children with constipation are developmentally normal
- Performing a thorough history and examination is sufficient to diagnose functional constipation in most cases

Many conditions may pre-dispose children to constipation including ADHD, autism, coeliac disease, cystic fibrosis, dehydration, metabolic conditions, psychological conditions and dietary factors.

INVESTIGATION OF CONSTIPATION IN CHILDREN

Careful questioning about the frequency of stooling is important, as well as the shape and consistency of the stool.

Infants under six months often strain or become distressed when stooling (dyschezia), which in a healthy infant can be considered normal, and should not be mistaken for constipation.

Some older children may also withhold defaecation, which causes the stool to become hard and defaecation painful. This compounds the problem and the constipation may reach a stage where there is overflow incontinence.

- Growth parameters should be checked to ensure there is normal growth
- Abdominal examination should check for distension and palpable stool particularly in the left lower quadrant and lower abdomen
- The perianal area should be checked for sensation, anal fissures and the position of the anus
- Rectal examination is controversial. It will confirm constipation if the rectal vault is full of firm stool and it does allow assessment of anal tone, however it is invasive
- Occasionally an abdominal x-ray is useful to confirm significant faecal retention
- Rectal biopsy and rectal (balloon) manometry are the only tests that can reliably exclude Hirschsprung's disease

Diagnosis of constipation in children using Rome III criteria (Rubin 2006)[6]

For diagnosis of functional constipation under the Rome III criteria symptoms must include at least two of the following;

- Two or fewer defaecations per week
- At least one episode per week of faecal incontinence after the child has acquired toileting skills
- History of excessive stool retention or retentive posturing
- History of painful or hard bowel movements
- Presence of large faecal mass in rectum
- History of stools with a large diameter which may obstruct the toilet
- In infants and children up to age four, these symptoms must be present for at least one month, in children aged over four, symptoms must be present for at least two months, with insufficient criteria for the diagnosis of irritable bowel syndrome

MANAGEMENT

The data for effectiveness of the various treatments (fibre, biofeedback, behavioural modification, laxatives) for constipation in children is not robust.

Initially dietary measures may be tried if constipation is not too severe or longstanding. Increasing fruit and vegetable consumption as well as drinking plenty of fluids may be useful. Regular toileting after dinner, by sitting on the toilet for five minutes, may establish a habit and provide the opportunity for daily bowel evacuation, taking advantage of the gastro-colic reflex.

If general measures are not helpful, laxatives will be required and treatment may be necessary for several months or years depending on the severity and duration of symptoms.[7] Once regular bowel function has been restored, laxatives can be gradually withdrawn but relapse may occur. It is therefore important to inform parents of this and explain that progress can be slow.

For significant faecal impaction, the use of a short course of glycerine suppositories for infants and enemas for children (e.g. microlax) may help to dislodge the stool, allowing laxatives to work more effectively and faster.

Lactulose is commonly used in children and the dose can be split into two divided doses if there is an increase in bloating or flatulence.

Suggested initial doses of lactulose in children (adjust according to response):[7]

1 month–1 year	2.5 mL twice daily
1–5 years	5 mL twice daily
5–10 years	10 mL twice daily
10 years and above	15 mL twice daily

If osmotic laxatives or softeners fail to resolve the constipation, the addition or substitution of a stimulant laxative (senna or bisacodyl) may be required, but their chronic use is controversial and they are best prescribed on the advice of a paediatrician. Prolonged use of stimulant laxatives can give rise to atonic colon and hypokalaemia and consequently it has been suggested that they are used intermittently to avoid impaction.[7]

Macrogols (e.g. Movicol) are effective both for faecal disimpaction and also as maintenance therapy for constipation that is difficult to manage.

Referral to a paediatrician should be considered when treatment fails, when there is concern that there is organic disease or if management is complex.

"It is important that constipation and faecal retention are recognised early as treatment may be less prolonged. When a child reaches the stage of soiling, treatment is likely to be much more prolonged, than parents expect. Slowly down titrating the lactulose dose is important as relapse is not uncommon."

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USEFUL WEBSITES

- Best Treatments http://snipurl.com/1rabc
- Constipation in childhood. CORE. http://snipurl.com/1rabe

COELIAC DISEASE

SUMMARY POINTS

- Coeliac disease is a common but often unrecognised disorder, affecting about 1 in 100 of the general population. Prevalence in those with a first-degree relative with coeliac disease is about 1 in 10

- Many people presenting with coeliac disease have vague or non-specific symptoms and gastrointestinal symptoms may even be absent

- Coeliac disease causes inflammation of the small intestine which may affect absorption of important nutrients including iron, folic acid, calcium and fat soluble vitamins

- The diagnosis of coeliac disease should be considered in a wide range of clinical situations

- Appropriate initial tests for coeliac disease are anti-tTG and a total IgA level. The gold standard for diagnosis is duodenal biopsy

- A zero gluten diet in children usually results in complete remission. In adults, the amount of gluten that can be tolerated is variable. Symptomatically some adults are sensitive to extremely small amounts of gluten, while others can tolerate low levels (page 24)

- Untreated coeliac disease can be associated with the development of long term health problems although some patients remain completely asymptomatic

COELIAC DISEASE IN ADULTS

Coeliac disease is a chronic inflammatory condition of the small intestine in genetically susceptible individuals. It typically presents with gastrointestinal symptoms but may also present with a wide range of non-specific symptoms.

Many studies report a prevalence of coeliac disease in adult populations as 1 in 100 but this varies with the ethnic composition of the population being studied. A study in Canterbury, NZ gives a prevalence of 1 in 82.[1] This is one of the highest rates reported in the literature. A 30-year review of coeliac disease in Canterbury reports that prevalence is increasing[2] but cautions that this may be due to increased awareness, specific serological tests and availability of endoscopic duodenal biopsies, rather than a true increase.

Diagnosis can be made at any age but the majority of people present for the first time as adults.[3,4] Both sexes can be affected by coeliac disease, although most studies indicate a higher proportion of females, particularly during the reproductive years. The Canterbury study showed a female to male ratio of about two to one.[2]

Coeliac disease occurs in almost all ethnic groups, but appears to be rare in black Africans and people of Chinese or Japanese origin. There is little information on prevalence rates in Māori but it is generally considered to be lower than in Europeans.

Expert Reviewers

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Samuel Gee, a physician at St Bartholomew's Hospital, London gave the first detailed description of coeliac disease in 1887 although the physician, Aretaeus of Cappadocia described a malabsorptive syndrome, with persistent diarrhoea, during the 2nd century AD.[5] As the years went by, some researchers suspected that carbohydrates were involved in the development of coeliac disease, but the specific link with wheat was not confirmed until the 1940s, with work done by a Dutch paediatrician, Professor Willem-Karel Dicke.[6] In 1950 he published a classic thesis on the deleterious effects of wheat on the gut. Biopsies of the upper bowel have been performed since 1956, although the use of fibre-optic endoscopy over the last 25 years has made this much easier. During the 1970s genetic markers were identified and the haplotypes HLA-DQ2 and DQ8 which are seen in more than 99% of patients have now been well characterised. Serological tests have made recognition of coeliac disease much easier over the last 20 years.

SUMMARY OF PRIMARY CARE INVESTIGATIONS IN COELIAC DISEASE

Scenario 1
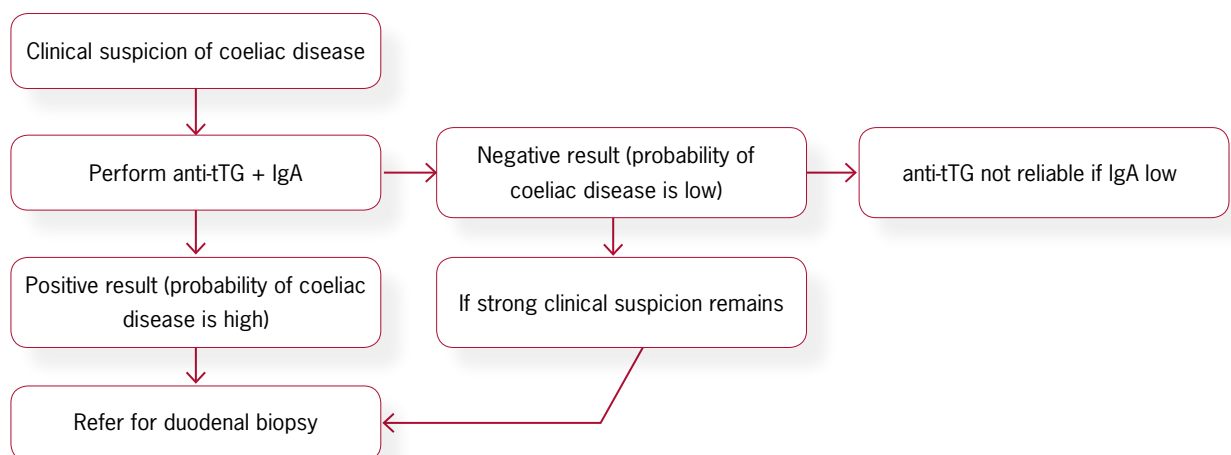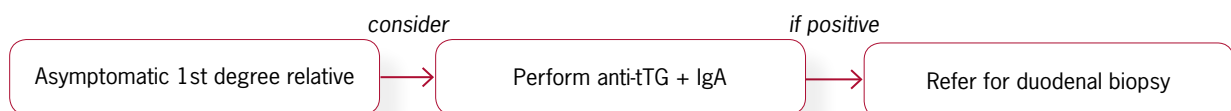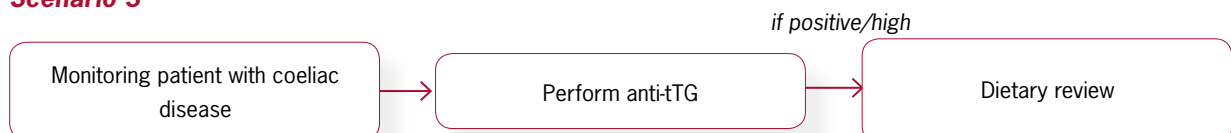
Clinical suspicion of coeliac disease

Perform anti-tTG + IgA → Negative result (probability of coeliac disease is low) → anti-tTG not reliable if IgA low

Positive result (probability of coeliac disease is high)

If strong clinical suspicion remains

Refer for duodenal biopsy

Scenario 2

Asymptomatic 1st degree relative → *consider* → Perform anti-tTG + IgA → *if positive* → Refer for duodenal biopsy

Scenario 3

Monitoring patient with coeliac disease → Perform anti-tTG → *if positive/high* → Dietary review

Coeliac disease is a chronic inflammatory condition of the small intestine in genetically susceptible individuals

Active consideration of the diagnosis of coeliac disease in general practice will help identify those with non specific symptoms

Coeliac disease remains under-recognised because of the non-specific way in which people with coeliac disease present to their GP. The 'classical' presentation of coeliac disease reflects its effect on the small bowel with resulting malabsorption producing steatorrhoea, abdominal cramps, bloating and weight loss. In practice however, people with coeliac disease often present with diarrhoea and can be overweight. Symptoms may be similar to those attributed to irritable bowel syndrome and some gastroenterologists routinely test people with suspected irritable bowel for coeliac disease.[4]

For those diagnosed with coeliac disease as adults, it is presumed that the disease has been silent or unrecognised during childhood. The proportion of people with latent or early symptomatic coeliac disease who go on to develop more classical coeliac symptoms is still not known.[7] Unless coeliac disease is considered, it will remain undiagnosed.

As well as presentations caused by malabsorption, a wide range of symptoms are associated with dysmotility, autoimmunity or the systemic effects of nutritional deficiency. Some people with coeliac disease may have temporary secondary lactose intolerance due to the intestinal damage, which then resolves as the gut heals.

Some common presentations of coeliac disease are;

- Iron or folate deficiency anaemia[3,8]
- Tired all the time ('TATT') or chronic fatigue[9]
- Unexplained diarrhoea[3,8]
- Dental enamel defects[10,11]
- Recurrent mouth ulcers[9,10]

Coeliac disease is more prevalent in those with;

- First degree relative with coeliac disease (risk 1 in 10)[4,8]
- Type I diabetes (risk 1 in 20)[4,9]
- Auto-immune thyroid disease[4,9]
- Osteoporosis[8,9]
- Infertility/recurrent miscarriage[4,7]
- Unexplained neurological disease (particularly peripheral neuropathy, ataxia and epilepsy)[8,9]
- Unexplained liver disease[4,9]
- Addison's disease[3,9]
- Sjogren's syndrome[3,8]
- Dermatitis herpertiformis[3,9]
- Down and Turner syndromes[3,10]
- Primary Biliary cirrhosis[3,8]

APPROPRIATE INITIAL TESTS ARE ANTI-tTG AND TOTAL IgA LEVELS, WITH PATIENT STILL ON GLUTEN

An appropriate initial test for coeliac disease is anti-tissue transglutaminase antibodies (anti-tTG) plus a total IgA level.[9,12] The patient should still be taking a gluten containing diet, as a negative result does not exclude coeliac disease if the person has had a gluten free diet prior to testing.[13] Testing the total IgA level is necessary because the likelihood of IgA deficiency is up to ten times higher for people with coeliac disease than in the general population[14] and this may give a misleadingly low result to the anti-tTG level. There should be a lower threshold for performing duodenal biopsy in people with IgA deficiency.

Some centres follow a positive anti-tTG result with a request for endomysial antibodies and some use endomysial antibodies as the initial test. A recent review published in the BMJ found that the use of anti-tTG was adequate and cost effective.[12]

Anti-gliadin antibodies are no longer routinely used for initial testing.

Serological tests are most useful as a preliminary step in testing symptomatic people and those with increased risk, or to monitor the condition. There is some controversy in the literature as to whether asymptomatic people should be screened.

HLA typing is available but it is expensive and can be difficult to interpret. It can be useful to rule out coeliac disease when the diagnosis is uncertain or endoscopy cannot be performed. HLA typing leads to a high false positive rate in those identified as having the gene, resulting in unnecessary further testing and possibly gluten free diets.

If serology is equivocal and/or there is a high suspicion of coeliac disease, then upper GI endoscopy and duodenal biopsy should be considered.

The characteristic histological changes in a duodenal biopsy are decreases in the height of villi, crypt hyperplasia, a chronic inflammatory cell infiltrate of the lamina propria, lymphocytic infiltration of the epithelium, and a decrease in the epithelial surface-cell height. This is often referred to as villous atrophy.

Biopsy remains the gold standard for diagnosing coeliac disease

If serology is positive, the patient should be referred to a gastroenterologist for a duodenal biopsy to confirm the diagnosis.[9] This is still considered to be the gold standard despite the availability of the highly specific blood tests.

There are three major reasons for seeking a secure diagnosis.

1. A life-long dietary change usually has a significant effect on the quality of life of people with coeliac disease and also financial implications.

2. Baseline histology can be useful for later comparison, particularly if there is no response to the change in diet, or if the initial histology is not diagnostic of coeliac disease.

3. PHARMAC currently requires a biopsy proven diagnosis to approve a special authority for gluten free products.

Other Investigations

A number of routine blood tests are required at diagnosis, during symptomatic relapse, and during pregnancy to identify nutritional deficiencies. Tests include haemoglobin, vitamin B_{12}, folate, iron studies, LFT's, vitamin D and calcium. They may also be done at annual follow-up if dietary adherence needs checked or the response to the dietary change has been poor. There is no clear agreement on when bone densitometry should be requested but a recent article suggests symptomatic patients be referred at the time of diagnosis.[15]

MANAGEMENT OF COELIAC DISEASE

Treatment is based on permanent removal of gluten from the diet

Adherence to a gluten free diet remains the key step in the management of coeliac disease. This means the exclusion of all foods containing wheat, rye and barley. Avoiding these cereals can be difficult as they are found in bread, biscuits, cakes, pastries, breakfast cereals, pasta, beer, and most soups, sauces and puddings.[16] Gluten is often present as an additive or contaminant in foods.[7]

Prescription gluten free products include gluten free flour, bread, biscuits, and pasta. Most patients with coeliac disease tolerate these products well. Gluten free products are now available in most supermarkets.

A low gluten diet may be tolerated by some adults with coeliac disease. Low gluten foods must have less than 20 mg of gluten per 100 g of the food (or <2.5–5 g per day). For this category there is no prohibition on oats and malts. Children, however, should have a zero gluten diet (page 27).

Therapeutic trials of a gluten free diet are generally not indicated without confirmation of the diagnosis, if coeliac disease is suspected.

Removal of gluten from the diet improves symptoms and long term health for people with coeliac disease

Most adults respond promptly to a gluten free diet, showing improvement of symptoms within days or weeks. Histological improvement usually takes many months. Once established on a gluten free diet, eating gluten-containing food can cause an almost immediate return of symptoms and histological changes within a few weeks. There may however be no direct relationship between the amount of gluten in the diet, the extent of the small bowel damage and the severity of the symptoms.

Referral to a dietician is important to ensure a balanced, varied gluten free diet through assessment and education. Dieticians can also provide advice on food labelling, product availability, tips for eating out and travelling and unusual sources of gluten (medication, sweets etc).

For most people strict adherence to a gluten free diet not only resolves the majority of presenting symptoms but also improves the long-term health outcome. Untreated coeliac disease can lead to a number of other health problems including poor growth in childhood, osteopenia, osteoporosis, anaemia and possibly autoimmune disorders. It has been linked to the development of malignancy but there is still debate regarding the strength of these associations.[17,18] Experts generally believe that adherence to a gluten free diet reduces this risk of malignancy.

People with coeliac disease benefit from regular follow-up

After diagnosis, patients are initially seen at three and six months. If the patient is well, it is recommended that they be reviewed annually. People with coeliac disease should be reviewed during pregnancy.

Vaccination against pneumococcus and haemophilus influenzae type b and meningococcus should be offered to the minority of people with coeliac disease who develop hyposplenism.[3,9,19] Hyposplenism is suggested by abnormalities on the blood count and blood film.

Effective management requires a team approach

Information and support is vital to help people make the change to a gluten free diet. Adherence to a gluten free diet is not easy, even in ideal circumstances. For individual patients this task can be complicated by family and professional commitments, as well as peer pressure. People may find they manage well at home and when they have control over their food choices but have difficulties while socialising and travelling. Adolescence can be a particularly difficult time.

As with any chronic condition, careful explanation, the provision of written information and ongoing encouragement are very important. Supervision by a dietician may be essential, at least initially. People with coeliac disease are encouraged to join the Coeliac Society of New Zealand (www.coeliac.co.nz). Booklets listing gluten free products specific to New Zealand are available.

WHEN TO REFER TO A SPECIALIST

-    For duodenal biopsy and confirmation of the diagnosis

-    If serology is negative but suspicion of coeliac disease remains

-    Failure of a patient with coeliac disease to respond to a gluten free diet

-    New symptoms arising in a patient with coeliac disease, already on a gluten free diet

Check of coeliac disease status after diagnosis

-    BMI

-    Symptoms, including gastrointestinal symptoms, rashes, lethargy.

-    Blood tests for haemoglobin, folate, iron studies, vitamin D, calcium, vitamin B_{12}, LFT's.

-    Consider an annual check of anti-tTG to assess poor adherence to diet or relapse.

-    Consider bone densitometry scan after one year of gluten free diet, during the perimenopausal period for women, age 55 for men and at any age if fracture occurs.[15]

-    Consider testing first-degree relatives, who have a 1 in 10 chance of developing coeliac disease.

SOME CONDITIONS ASSOCIATED WITH COELIAC DISEASE

Osteoporosis - Most people with coeliac disease have bone mineral loss due to inadequate absorption of calcium. Bone densitometry scan should be considered at the time of diagnosis, especially in patients with symptoms of malabsorption.[15] Adequate intake of calcium and vitamin D should be encouraged. Patients should be advised to stop smoking, avoid excessive alcohol and take regular weight bearing exercise.

Bone densitometry is also recommended for people with coeliac disease at 55 years for men and at menopause for women. Other causes of osteoporosis should always be considered.

Dermatitis Herpetiformis - This is a disorder characterised by an itchy blistering skin eruption that frequently affects the knees, elbows, buttocks and back. It is found in 2–5% of people with coeliac disease.[19] Treatment with a gluten free diet may control the dermatitis over six to twelve months, although dapsone may be needed in some cases.

Malignancy - Several types of malignancy may be increased in adults with coeliac disease.[3,20] The strongest links are with T cell lymphomas and gastrointestinal malignancies[20] specifically small intestinal carcinoma, oesophageal and pharyngeal carcinoma.[21] Interestingly there has been recent evidence of a reduced risk of breast cancer in coeliac patients.[20,22]

Ulcerative Jejuno-ileitis: This is an unusual complication in which unresponsive coeliac disease is associated with ulceration and stricture formation. This change can signify the development of T cell lymphoma.

COELIAC DISEASE IN CHILDREN

The symptoms of coeliac disease vary widely depending on the age at presentation.

Classically there is a gradual failure to gain weight or a loss of weight after the introduction of cereals in a previously well child aged 9–24 months, accompanied by anorexia, irritability, alteration in stools, abdominal distension, muscle wasting and hypotonia. This 'text book' presentation is not the norm and in practice coeliac disease presents more frequently in children between 5 to 9 years of age or older. A retrospective review of children diagnosed at Starship Hospital showed a median age of 6.9 years.[23]

These older children present with a range of symptoms such as recurrent non specific abdominal pain, constipation, intermittent loose stools, tiredness, mouth ulcers, vomiting and poor appetite. Significant poor growth may not be seen although sometimes children present with short stature alone.

Coeliac disease can also present in infants younger than nine months although rarely. In this age group, vomiting, diarrhoea and abdominal distension are more marked.

WHICH CHILDREN REQUIRE TESTING?

Testing is recommended for all symptomatic children.

Testing in asymptomatic children includes siblings of an index case (although because the tests may be unreliable, avoiding this until the child is 2–3 years of age, may be preferable, unless there are symptoms), those with Type I diabetes, and children with Down's syndrome.

HOW TO TEST FOR COELIAC DISEASE IN CHILDREN

The basic approach to testing is the same as in adults. However, in young children, antibody tests are less reliable for excluding coeliac disease. It may be appropriate to do a duodenal biopsy for every child where there is a clinical suspicion of coeliac disease despite negative serology.

Before any testing is done, parents or caregivers need to be aware of the risks of biopsy and of untreated coeliac disease, and the need for a lifelong gluten free diet if the tests are positive.

Children should not be started on a gluten free diet on the basis of an antibody test unless there are reasons why an endoscopy cannot be performed.

MANAGEMENT IN CHILDREN REQUIRES A ZERO GLUTEN DIET

A zero gluten diet is usually recommended for children as opposed to the low gluten diet tolerated by most adults (Chin S. personal communication, September 2007).

Oats are not recommended because their safety is still unproven and there is a risk of cross contamination from gluten containing products. Adherence to a gluten free diet can be enhanced by involvement of caregivers and teachers in playgroup and school environments. This will help prevent 'cheating' or experimentation with the diet, contamination (e.g. eating play dough) or accidental exposure to gluten.[11] Compliance in the teenage years can be particularly troublesome.

Symptoms and signs found in coeliac disease in children (both GI & non GI)[10]

- Persistent diarrhoea
- Abdominal pain, vomiting, constipation, abdominal distension
- Unexplained anaemia or iron deficiency
- Lassitude/weakness
- Dermatitis herpetiformis
- Dental enamel defects
- Faltering growth, idiopathic short stature
- Osteoporosis, rickets, pathological fractures
- Delayed menarche
- Recurrent aphthous ulcers
- Unexplained raised transaminases

Associated conditions (estimated lifetime prevalence)[10]

- Type I diabetes (≥8%)
- Selective IgA deficiency (1.7–7.7%)
- Down's, (5–12%) Williams' (8.2%) and Turner's (4.1–8.1%) syndrome
- Autoimmune thyroiditis (5–15%)
- Relatives of coeliac patient. First degree relative (10%), HLA matched sibling (30–40%), monozygotic twin (70%)

Children should be followed up regularly (12 monthly) to ensure they are growing normally and complying with the diet and that there are no persistent symptoms. Formal dietary advice about a gluten free diet should be sought from a paediatric dietician.

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Other resources

Coeliac Society of New Zealand
www.coeliac.co.nz

Coeliac Society of Australia
www.coeliacsociety.com.au

Coeliac Society in United Kingdom
www.coeliac.co.uk

Australian New Zealand Coeliac Research Fund
www.coeliacresearch.com

NZ Manufactured Food Database
www.mdf.co.nz

THE IMPORTANCE OF BEING REGULAR

Assessing the risk and benefit of alternative therapy for GI conditions

The regularity of our bodily functions has been used as the 'canary in the mine' for health and wellbeing, since early times. Ancient Egyptians first introduced the concept of 'autointoxication' which suggests that undigested food in the colon produces toxic substances that circulate through the body, causing illness.[1] Autointoxication is not supported by scientific evidence and is disregarded by most of the medical fraternity today. Waste material does not adhere to the colon wall or produce toxins. However, many people still place faith in 'detoxifying' their digestive system as an important process for their health and well-being. Detoxifying may include a combination of fasting, cleansing ('natural' laxatives) and colonic irrigation (by enema or machine). While short periods of fasting and laxative use are likely to be harmless, enema and colonic irrigation are associated with some serious health risks.

The greatest risk associated with colonic irrigation is perforation of the wall of the colon by mechanical penetration or excessive pressure from liquid forced into the bowel. Risk factors for perforation include older age, recent bowel surgery and conditions such as diverticulitis, inflammatory bowel disease, Crohn's disease and haemorrhoids. Three cases of perforation of the rectum after a colonic irrigation procedure were recently documented in Australia. It was concluded that the potential harm of colonic irrigation outweighs any obvious benefit.[2]

There is also some concern that introducing large amounts of water into the bowel may result in depletion of electrolytes. People with kidney or heart failure have a higher risk of this.[3] Improper sterilisation techniques also contribute to a risk of transmission of pathogens. There have been several cases of amoebiasis reported after colonic irrigation.[4] Enemas may be associated with many of the same risks as colonic irrigation, if not performed under medical supervision. In addition, coffee, wheat grass, herbs and other substances may be added to the enema solution. This increases the risk of adverse effects including toxicity and allergic reaction.[3]

Many patients are reluctant to reveal to GPs that they are using complementary therapies. As a general reminder;[5]

- Routinely question patients about their use of alternative therapies

- Discuss the safety, efficacy and merits of commonly used alternative treatments

- Provide information on the risks of some treatments

- Help patients make informed decisions about alternative treatments e.g. find a qualified/licensed provider

For a full version of this article, please visit www.bpac.org.nz   Keyword '*colonic*'

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LACTOSE INTOLERANCE

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Key Points:

- Most lactose intolerance is due to primary lactase deficiency which is genetically determined

- Secondary lactase deficiency is transient and occurs mainly as a result of gastrointestinal illness

- Lactose intolerance can normally be diagnosed through dietary challenge

- Lactose intolerance is initially treated by minimising or avoiding lactose containing foods, however most people can tolerate one to two glasses of milk per day, in divided doses with food

- People with primary lactose deficiency should be encouraged to gradually and regularly increase their intake of milk until a level of tolerance is achieved

- Children who have developed secondary lactose intolerance as a result of infectious diarrhoea, may still safely receive milk

www.bpac.org.nz   Keyword: *"lactoseintolerance"*

BACKGROUND

Lactose intolerance is the clinical syndrome that occurs, when the inability to digest lactose results in gastrointestinal symptoms. It is estimated that around 70% of the world's population are deficient in lactase.[1] However not all lactase deficiency results in lactose intolerance and it is likely that its prevalence is over estimated.

Most lactase deficiency is genetically determined. In general, people of Northern European descent have lower rates of lactase deficiency (2–30%) and people of Mediterranean, South American, African and Asian descent have higher rates (60–100%).[2,3] Both males and females are affected equally.[4] There have been two studies in New Zealand, reported in the 1980s, which suggest that people of Māori and Pacific origin have a higher prevalence of lactase deficiency than New Zealand Europeans.[5,6] A literature search did not reveal any recent follow-up studies to confirm these results.

Other physiological and psychological factors can contribute to gastrointestinal symptoms that mimic lactose intolerance.[7] Many people may believe they are lactose intolerant, but do not actually have impaired lactose digestion.[2]

- Lactose intolerance is NOT a milk allergy.

- A milk allergy is related to the protein in milk rather than the lactose.[2]

- Human breast milk contains 7% lactose and cow's milk 4.8%.[7]

THERE ARE FOUR TYPES OF LACTASE DEFICIENCY

Primary lactase deficiency is the most common reason for lactose intolerance (sometimes referred to as adult or late onset lactose intolerance). Lactase concentrations are at their greatest shortly after birth and rapidly decline after the usual age of weaning. The timing and rate of this decline is genetically determined. Primary lactase deficiency has a higher prevalence in those ethnic/geographical groups whose ancestors did not drink milk as a nutrient.[4,7] Onset of primary lactase deficiency is typically subtle and progressive over several years; however acute development is possible. The age of onset varies among ethnic populations, but it would be uncommon to be seen before two to three years of age (or before four or five years of age in European children).[1] Lactose intolerance may not become clinically evident until late adolescence.[8]

Secondary lactase deficiency (acquired) is transitory and can occur as the result of any gastrointestinal illness that alters the nature of the gut mucosa.[2] This is common in children with rotaviral (and other infectious) diarrhoea.[1] Giardiasis, cryptosporidiosis and other parasitic infections of the proximal small intestine often lead to lactose malabsorption.[1]

Secondary lactase deficiency may occur with coeliac disease, Crohn's disease and immune-related illnesses such as HIV.[1,4] In addition, drugs such as tetracycline and methotrexate can cause villous atrophy, resulting in secondary lactase deficiency. Alcohol is known to inhibit lactase and other enzymes, initiating or worsening lactose intolerance.[4]

Congenital lactase deficiency (alactasia) is the life-long absence of lactase.[2] This is an extremely rare condition that is apparent at birth, with the development of persistent diarrhoea soon after milk is introduced. Children with alactasia have otherwise normal intestinal mucosa.[9] This condition has been diagnosed in less than 50 people world-wide.[7]

Developmental lactase deficiency (neonatal) occurs in premature infants. This condition is usually temporary and rapidly improves as the intestinal mucosa matures.[9] Lactase and other disaccharidases are deficient until after 34 weeks gestation.[1]

GASTROINTESTINAL SYMPTOMS CHARACTERISE LACTOSE INTOLERANCE

In general, the symptoms of lactose intolerance are non-specific, highly individual and mild.[7] Symptoms usually occur between 30 minutes and two hours after ingestion of lactose.[2,7] Vomiting is rare[4] and severe gastrointestinal symptoms would be an indication to investigate other causes.[7]

Symptoms result from two main causes:[4]

1. Undigested lactose acts as an osmotic laxative (diarrhoea, abdominal pain)

2. Intestinal bacteria use lactose as a growth substrate (flatulence, dyspepsia, abdominal distension, stomach rumbling)

Symptoms are influenced by the degree of lactase deficiency and are dose dependent – the larger the amount of lactose consumed, the more frequent or severe the symptoms. The minimum dose of lactose to cause symptoms is variable but most people can ingest up to one or two cups of milk daily, without symptoms.[2]

Diarrhoea is more pronounced in children with secondary lactose deficiency than in those with primary lactose deficiency. Perianal excoriations due to acidic stools are common.[9]

Pathophysiology of lactase deficiency

Lactase is an enzyme that is located in the microvilli of the small intestine. Lactase splits and hydrolyses dietary lactose (a disaccharide sugar) into glucose and galactose (monosaccharide sugars) for transport across the cell membrane. In the absence, or deficiency, of lactase, unabsorbed lactose causes an influx of fluid into the bowel lumen, due to osmotic pressure. Unabsorbed lactose then enters the colon and is used as a substrate by intestinal bacteria, producing gas and short-chain fatty acids via fermentation. The fatty acids cannot be absorbed by the colonic mucosa, therefore more fluid is drawn into the bowel. A proportion of the lactose can be absorbed but the overall result of ingestion is a substantial rise of fluid and gas in the bowel, causing the symptoms of lactose intolerance.[2,7,9]

LACTOSE INTOLERANCE IS USUALLY DIAGNOSED BY DIETARY CHALLENGE

Step 1: Rule out other causes

Step 2: Dietary challenge

Step 3: Further investigation, if dietary challenge inconclusive

Accurate diagnosis of lactose intolerance can significantly relieve patient anxiety and avoid inappropriate investigation and treatment. Dietary challenge is the best way to achieve this in most situations. Laboratory testing will often not provide a definitive diagnosis and the availability of tests throughout New Zealand is variable.

Dietary Challenge

Lactose intolerance can be suspected in people who exhibit gastrointestinal symptoms following ingestion of milk or milk products. This can be confirmed by manipulation of diet. This diagnosis can be made by a GP and further investigation is rarely needed in clinical practice.[9]

The American Academy of Paediatrics recommends that when lactose intolerance is suspected, a lactose-free diet should be trialled for two weeks. However it is important that during this trial, all sources of lactose are eliminated – food labelling should be closely studied. If symptoms resolve over this two week period and then return with subsequent reintroduction of lactose containing foods, then lactose intolerance can be diagnosed.[1]

Self-diagnosis is not recommended as it could lead to unnecessary dietary restrictions and expense, lack of essential nutrients and most importantly, failure to detect a more serious gastrointestinal problem.[7]

If dietary challenge is inconclusive or self-reported symptoms are unreliable, then further investigation may be required.

Laboratory diagnosis of lactose intolerance

The role of laboratory tests in diagnosing lactose intolerance in New Zealand is limited. Although laboratory testing is often cited to aid in the diagnosis, many of these tests are not widely available and some lack sensitivity and/or specificity.

The breath hydrogen test is often referred to as the method of choice for laboratory diagnosis of lactose malabsorption but is not widely available throughout New Zealand. Breath hydrogen levels are measured after ingestion of 25–50 g of lactose (2 g/kg in children, maximum 50 g) after fasting overnight. Positive results are seen in up to 90% of patients with lactose malabsorption but false-negative results can occur and other factors such as gut motility disorders, small bowel bacterial overgrowth, a high fibre diet or smoking may increase breath hydrogen secretion unrelated to lactose digestion.[2,7,9] A specialist should be consulted to interpret the results of this test. The breath hydrogen test is technically difficult to perform in younger children and infants, for whom other tests may be more appropriate (faecal pH, reducing substances).

The lactose tolerance test is used infrequently, as it is less reliable than other diagnostic tests. Blood glucose levels are measured after ingestion of lactose – in lactase deficiency, glucose levels will not increase at a normal rate. False positives and false negatives occur in 20% of normal subjects due to the influence of variable gastric emptying and glucose metabolism.[2,9]

Faecal pH test is less commonly used as it is a non-specific marker for lactose (or other carbohydrate) malabsorption.[1] A pH of <5.0 suggests lactose intolerance.

Faecal reducing substances is a simple but non-specific test to detect the presence of lactose, glucose and fructose. A positive test suggests an absence of the corresponding enzyme. This is not offered in all areas of New Zealand because transportation delays (>3 hours from time of collection to testing) can cause false negative results.[10] A trace of positive reducing substances in a healthy breast fed infant is not uncommon and does not necessarily signify clinically significant lactose intolerance.

Small bowel disaccharidases is an invasive test involving duodenal biopsy and is very rarely used. It is not readily available throughout New Zealand. It is difficult to perform and results can be difficult to interpret. Results may be normal if lactase deficiency is confined to patches of the bowel.[8] This test may occasionally be considered in the context of secondary lactose intolerance where a gastroscopy is being performed to determine an underlying cause (e.g. coeliac disease, Crohn's disease, patient with protracted diarrhoea).

New diagnostic tests are also being developed, including a breath test using Carbon-13 labelled lactose.[9]

Differential diagnoses

When dietary challenge and laboratory tests prove inconclusive, alternative diagnoses should also be considered (see below).[2] Diagnostic tests are usually not needed for secondary lactase deficiency as it resolves upon treatment of the primary cause.

Differential diagnoses for lactose intolerance (adapted from Swagerty et al)[2]

Irritable bowel syndrome
Inadvertent laxative ingestion
Regional enteritis
Coeliac disease
Ulcerative colitis
Viral or bacterial infection
Cystic fibrosis
Parasitic disease e.g. giardiasis
Bowel neoplasm or polyp
Mechanical bowel compromise
Diverticulitis

LACTOSE INTOLERANCE CAN BE MANAGED IN MOST CASES BY DIETARY RESTRICTION

Step 1: Confirm diagnosis of lactose intolerance

Step 2: Determine how much lactose can be tolerated without symptoms

Step 3: Encourage gradual reintroduction of milk - this usually improves symptoms and tolerance

Initial treatment of lactose intolerance is to minimise or avoid lactose containing foods. However, it is important to retain an adequate calcium intake, including actual dairy products.[2]

Most people with primary lactose intolerance do not require a totally lactose free or severely restricted diet. One or two glasses of milk per day can usually be tolerated, if divided into small portions and taken with food (e.g. cereal).[11]

Yoghurt with live culture, curds and cheese (especially aged) is better tolerated because the lactose is partially hydrolysed by bacteria during preparation and gastric emptying is slower due to their thicker consistency.[9] Skim milk (green top) causes more severe symptoms than whole milk.[4]

Children may also tolerate up to one or two glasses of milk a day without symptoms.[1]

Chocolate milk and ice cream are better tolerated because their fat content delays gastric emptying.[2] Cow's milk substitutes are generally free of lactose and may be used (e.g. rice, soy) however their nutrient content is not equivalent to cow's milk and they should not be used in very young children. All mammalian milk, for example goats milk, contains varying amounts of lactose.[1]

Some people may choose to use lactase enzyme supplements, however these may not completely relieve symptoms and it is difficult to determine the effective dose. Enzyme supplements should be an adjunct, not a substitute for dietary restriction.[2] If milk is able to be tolerated in small amounts, enzyme supplements are unnecessary. Low-lactose milk is generally not necessary unless large quantities of milk are consumed, or in the rare case of non-tolerance to even small amounts of milk. In New Zealand, lactose-free, soy and goat's milk infant formulae are available on the pharmaceutical schedule, under special authority for children less than three years of age. Lactase enzyme supplements are not subsidised.

It is important to reassure patients that ingestion of lactose-containing products may cause symptoms, but these are transient and no harm is caused to the gastrointestinal tract.[1]

Increasing tolerance by exposure to lactose

People with primary lactose deficiency should be encouraged to gradually and regularly increase their intake of milk. Continual exposure often enhances the number and efficiency of colonic bacteria to metabolise lactose, thereby producing fewer symptoms. Total elimination of lactose from the diet may actually worsen the symptoms of intolerance when lactose is inadvertently ingested or reintroduced.[12]

Managing secondary lactose intolerance

Short periods of lactose intolerance are common in children after bouts of infectious diarrhoea. This can lead to unnecessary antibiotics and unwarranted avoidance of milk.[9] A meta-analysis of clinical trials found that most children with acute diarrhoea can safely continue to receive breast or undiluted animal milk.[13]

In children younger than three months, or in malnourished children, lactose intolerance after a bout of infectious diarrhoea may however be a significant factor that will influence recovery from the primary illness.[1] Lactose avoidance may be required for a short period.

LACTOSE INTOLERANCE IS NOT AN ALLERGY TO MILK

In cow's milk allergy, children are allergic to the protein in milk.

Cow's milk allergy is one of the most common food allergies in young children (prevalence between 2–6% of infants between 1 and 3 months of age).[1] The incidence in adults is much lower (0.1–0.5%).[14] Most children outgrow their milk allergy between 1 and 3 years of age.[1] However there is a strong trend in children who recover from a milk allergy, to develop an allergy to other food proteins (e.g. egg, soy, peanut) or an inhalant (e.g. pollen, dust mites, cat). Milk allergy is a strong risk factor for predicting children who will develop asthma, eczema or allergic rhinitis.[4, 14]

It is thought that exposure to cow's milk proteins commonly occurs prenatally. Breast fed infants are exposed to cow's milk and other food proteins ingested by the mother. In children who develop an allergy, the immune system becomes sensitised to the milk proteins and mounts an inflammatory response. It is thought that this is a hereditary condition, however the expression of this trait is dependent on both genetic and environmental factors.[14]

Despite possible in utero sensitisation, breast feeding is the best prevention for cow's milk allergy. There is no evidence to support the restriction of dairy intake during pregnancy or lactation to prevent cow's milk allergy.[14]

There are three types of clinical manifestation of cow's milk allergy;[4, 14]

Type 1 IgE mediated (Immediate): Develops within minutes to one hour of a small volume of cow's milk. Symptoms may be; eczema, urticaria, runny nose, cough, wheezing, vomiting, diarrhoea. Life threatening anaphylaxis is possible but rare.

Type 2 (Intermediate): Develops several hours after modest volume of cow's milk. Symptoms usually are vomiting and diarrhoea.

Type 3 (Delayed): Develops more than 20 hours after a large volume of cow's milk. Symptoms include diarrhoea with or without eczema.

Skin prick or specific IgE (RAST) tests can be used to diagnose a milk allergy in children with type 1 reactions. However nearly 60% of milk reactions in children are type 2 or 3 and are unlikely to give positive results. Diagnosis in this case is made by the 'elimination challenge test' (eliminating then reintroducing milk to the diet).

Differentiating between lactose intolerance and cow's milk allergy:

- Cow's milk allergy manifests during breast-feeding (due to cow's milk ingested by mother) or shortly after weaning. Lactose intolerance is usually seen after 2 years of age.

- Children with lactose intolerance can usually tolerate small amounts of dairy products, whereas in milk allergy, small traces usually cause symptoms.

- Differentiation is usually possible on the basis of clinical symptoms

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IRRITABLE BOWEL SYNDROME

KEY POINTS

- The diagnosis of IBS can be made from the clinical history as long as there are no alarm features of other pathology

- In primary care, the mainstays of treatment are explanation and reassurance, coupled with sensible advice about lifestyle, diet and stress

- Treatment is tailored to the predominant symptoms

- People with IBS often report a close relationship between stress and their bowel symptoms and both anxiety and depression are common in people with IBS

- Psychological support is an integral part of the management of IBS in primary care and there is some evidence more formal psychological therapies can be effective

- The results of pharmaceutical interventions for IBS are often disappointing but some individuals will get good responses

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www.bpac.org.nz Keyword:*"IBS"*

Irritable Bowel Syndrome (IBS) affects approximately one in ten of the population, mostly women between the ages of 20 and 50 years.

The diagnosis of IBS can be made from the clinical history as long as there are no alarm features of other pathology. However a firm diagnosis cannot be made until symptoms have been present for the previous three months with onset of symptoms at least six months before diagnosis. IBS has a prolonged course and over half of people with it still get symptoms seven years after diagnosis.

Although symptoms may occur over a long period of time, with no risk of life threatening complications, making a diagnosis as early as possible is useful. It helps prevent exacerbation of the anxiety many people with IBS experience and prevents additional costs and risks from unnecessary investigations.

CAUSES OF IBS ARE NOT YET WELL DEFINED

Although the causes of IBS are not well defined, there is some understanding of contributory factors.

Parental influences appear to be environmental rather than genetic

There is a definite familial association with IBS, however this appears to be related to environmental factors, such as parental influences on illness behaviour, rather than genetic factors. Any genetic contribution to IBS is currently thought to be minor.

Altered gastrointestinal motility: associated but not necessarily causative

Altered gastrointestinal motility occurs frequently in people with IBS. Different patterns of gastric, small bowel and colonic motility appear to be related to different symptom complexes. For example people with IBS and diarrhoea generally have increased colonic motility while those with constipation have reduced motility.

However, it has not been established that altered motility causes the symptoms of IBS, and at least 25% of people with IBS change their gastrointestinal motility pattern at least once per year.

Visceral hypersensitivity appears to be important

Visceral hypersensitivity, caused by peripheral and central sensitisation, appears to play an important role in IBS and can be demonstrated experimentally in approximately one-third of people with IBS. It may explain why some people report their symptoms began with an episode of gut inflammation due to gastroenteritis.

Distress response strongly associated with IBS

There is a strong association between IBS and psychological distress. Approximately half of people with IBS who seek medical care are depressed or anxious, and approximately two-thirds of patients attending an out patient clinic for IBS reported anxiety provoking incidents or episodes of psychiatric illness preceding the onset of symptoms. Anxiety and depression also appear to predispose people to developing IBS following a bout of gastroenteritis.

People with IBS often report multiple somatic complaints and this may indicate that somatisation or abnormal pain perception are contributing to their symptoms.

Post-infective IBS

Prevalence studies reveal between 6–12% of patients develop IBS after an infection, and it may be associated with a number of different pathogens. It is 11 times more likely that a person will develop IBS in the year following if they have experienced a bout of gastroenteritis. Female gender, as well as the adverse psychological factors previously mentioned, increase this risk.

CLINICAL FEATURES OF IBS

History is key to making a diagnosis of IBS

The diagnosis of IBS can almost always be made on the basis of the history. A good history will identify:

- Diagnostic features of IBS

- Predominant symptoms

- Health anxieties

- Precipitating or aggravating factors

- Psychological factors

- Relevant family history

- Dietary manipulations

- Presence or absence of alarm symptoms for other pathology

Diagnostic features of IBS

IBS is recurring abdominal pain or discomfort associated with disturbed bowel habit, lasting for at least six months in the absence of structural abnormalities, likely to account for these symptoms.

Disturbance of bowel habit needs clarification. Many of the symptoms experienced in IBS can be described as diarrhoea or constipation by patients. These terms may be being used when there is change in stool frequency or consistency, straining, a feeling of incomplete evacuation, passage of mucus per rectum, urgency or bloating.

The pain or discomfort of IBS is usually associated with bowel habit. For example, it may occur with changes in stool frequency or consistency or be relieved by defaecation. Pain that is not associated with bowel habit or is constant raises the possibility of other causes.

ROME III diagnostic criteria* for IBS

Recurrent abdominal pain or discomfort** at least 3 days per month in the last three months associated with two or more of the following:

- Improvement with defaecation

- Onset associated with change in frequency of stool

- Onset associated with change in form (appearance) of stool

*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

**Discomfort means an uncomfortable sensation not described as pain

Predominant symptoms

IBS is not a homogenous condition and people with it may experience a range of symptom patterns. The pattern often varies from time to time in the same patient. Treatment is tailored to the predominant symptoms.

The history often reveals one of the following as the most troublesome symptoms:

- Pain

- Diarrhoea

- Constipation

- Bloating with distension

- Bloating without distension

Health anxieties

As many as 50% of people with IBS are concerned they have cancer or some other serious underlying pathology. Anxiety about this may be the most troublesome feature of IBS and may lead patients to want invasive investigations. Discussion of these anxieties can help patients avoid unnecessary procedures.

Precipitating or aggravating factors

Some patients will be able to identify an event, which preceded the onset of their IBS, such as a bout of gastroenteritis (page 37).

Patients may be able to identify factors, which aggravate their symptoms. These may include menstruation, antibiotics, NSAIDs and statins.

Psychological factors

Anxiety, stress and other psychological factors, are common accompaniments to IBS. Their presence has been shown to negatively impact on response to treatment and they require careful management.

Relevant family history

A family history of bowel disorders may raise patient anxieties, sometimes appropriately, about a serious underlying pathology.

Dietary manipulations

Most people with IBS will have tried some form of dietary manipulations and some may be on diets, which contain excessive amounts of fruit, bran, dairy products, caffeine or other foods in efforts to control their symptoms.

Alarm signals

Alarm signals, which may indicate other pathology, such as gastrointestinal cancers and inflammatory bowel disease, must be excluded before a confident diagnosis of IBS can be made. Alarm signals include:

- Aged over 50 years at first presentation
- Male
- Short history of symptoms
- Nocturnal symptoms
- Significant family history of colon cancer
- Rectal bleeding
- Recent antibiotic use
- Unexplained iron deficiency anaemia

Physical examination in IBS usually reveals no relevant abnormality

Physical examination is usually normal in IBS; any abdominal tenderness, as with abdominal pain, is generalised, as it is visceral in origin. Examination may reveal signs of another cause for the abdominal pain such as localised abdominal wall tenderness or tenderness over the gall bladder or other organs.

More extensive examination may be indicated by any alarm signals identified.

Investigation

The diagnosis of IBS is made from the pattern of symptoms as previously discussed. It is not a diagnosis of exclusion. Investigation to exclude other causes are not needed, particularly for young people with straightforward symptoms, unless there are features which suggest other causes.

Initial investigation is usually complete blood count to check for iron deficiency anaemia and CRP. Further investigations, such as thyroid function tests, glucose and coeliac serology will be indicated if there are any alarm signals, suspicion of coeliac disease (page 20) or persistent diarrhoea.

Referral for colonoscopy is usually not indicated in a young patient. In specialist practice, partial investigation of the colon (flexible sigmoidoscopy) may be useful to obtain biopsy specimens, however this is not often required or performed. Occasionally management outcomes appear to be improved by performing these procedures and confirming a normal colon, but there are always risks associated with over investigation.

TREATMENT

In primary care, the mainstays of treatment are explanation and reassurance, coupled with sensible advice about lifestyle, diet and stress.

Psychological factors are best raised at the first consultation and clinicians in primary care can build upon their ongoing relationships with their patients. Fears of cancer and other serious organic pathology are often easily allayed if handled sensitively.

Pharmaceutical interventions are available but their efficacy is limited and they need to be used judiciously.

Dietary treatment

Adjusting the intake of fibre, carbohydrate and fats in the diet is a simple and sometimes effective intervention in IBS. Effects of changes in the diet may be delayed for one to five days, or longer if the patient has constipation.

Alterations in fibre intake needs careful management

The majority of therapeutic trials in secondary care examining the effect of fibre in the diet do not show much benefit. Cereal fibre may make the majority of patients worse. Soluble fibres, such as psyllium (Mucilax, Konsyl D) and ispaghula can be better.

In primary care, it is worthwhile trialling soluble fibres for patients in whom it seems to be indicated, but reducing or stopping them if there is no improvement. Some patients will need to be cautioned against excessive fibre intake.

Alterations in carbohydrate intake

Lactose and fructose intolerance have been associated with IBS-like symptoms. Reliance on history and trials of low intakes of either lactose or fructose may give the diagnosis. However, there appears to be little difference between the prevalence of carbohydrate intolerance in people with IBS and the general population.

Alteration in fat intake often helps

Fat in the gut can induce flatulence and bloating and people with IBS are often particularly aware of this because of their visceral hypersensitivity. It is often worth decreasing the fat intake.

Some patients may respond to food exclusions

Some patients appear to respond to food exclusion but a systematic review has concluded that there is insufficient evidence to use this routinely. It may however be worth trying when other options have failed.

The most frequently reported food intolerances in IBS are dairy and wheat products.

People who undertake food exclusion diets are at risk of a nutritionally inadequate diet so this is probably best supervised by a dietician. It is important to re-challenge with the excluded food to confirm any association.

Psychological therapies

People with IBS often report a close relationship between stress and their bowel symptoms and both anxiety and depression are common in people with IBS. Psychological support is an integral part of the management of IBS in primary care and there is some evidence more formal psychological therapies can be effective. These are less likely to be effective for patients who have constant pain or bowel upsets or have depression. Lack of availability and cost often limit the use of formal psychological therapies.

Psychodynamic interpersonal therapy

Psychodynamic interpersonal therapy shows signs of being successful. Its goal is to provide insights into why symptoms developed in association with life events or changes and to provide an understanding of the link between bowel symptoms and emotions. This uses the therapeutic relationship to help patients recognise the association between present stressors and symptoms. It appears to lead to significant improvement in quality of life and reduction in symptoms.

Cognitive behaviour therapy

Studies suggest that cognitive behaviour therapy helps people with IBS cope with their symptoms but does not relieve the symptoms themselves.

Hypnotherapy

Hypnotherapy has evidence of effectiveness for people with symptoms refractory to standard treatments but its use as a first line treatment is not proven.

Relaxation therapy

Relaxation therapy appears to be useful when exacerbation of symptoms is associated with stress.

Pharmaceutical interventions are guided by the predominant symptoms

The results of pharmaceutical interventions for IBS are often disappointing but some individuals will get good responses. The targets of drug therapy include relaxing the smooth muscle of the gut wall, altering gut transit patterns and reducing visceral sensation. There appears to be a significant placebo response, which is enhanced by more frequent dosing and therapeutic doctor/patient interactions.

Pharmaceutical interventions are targeted at the predominant symptoms and are more likely to be effective for diarrhoea or constipation than they are for pain, discomfort and bloating.

Antispasmodics

Cochrane Reviews have confirmed the efficacy of anti-spasmodic therapies in controlling pain in IBS sufferers. As with all trials in IBS therapies there is a significant placebo response and large numbers of patients require treatment to benefit one patient.

Peppermint oil, in capsule form or from tea, has proven antispasmodic properties. Many IBS sufferers report benefit from peppermint but large scale trials are lacking.

Antidepressants

Tricyclics reduce pain   Low-dose tricyclics can be effective at reducing pain associated with IBS (NNT 5.2) and appear particularly effective when pain is associated with diarrhoea. Unfortunately, even at low doses, adverse effects such as constipation, dry mouth, drowsiness and fatigue can be troublesome (NNH 22) and affect adherence to medication. Warning patients about the possibility of transient adverse effects, starting with a low dose (e.g. nortriptyline 10 mg) at night, increasing slowly and sticking to the medication for at least four weeks can improve results.

PSYCHODYNAMIC-INTERPERSONAL THERAPY

Psychodynamic-interpersonal therapy (formerly known as the Conversational Model of Therapy) assumes that symptoms and problems arise from, or are exacerbated by, disturbances of significant personal relationships. It explores feelings using cue-based responses and metaphor; links distress to specific interpersonal problems and uses the therapeutic relationship to test out solutions in the 'here and now'.

Predominant symptom pattern	Medication
Pain	1. Antispasmodics 2. Tricyclics
Diarrhoea	Loperamide
Constipation	Ispaghula, Psyllium
Bloating with distension	1. Dietary manipulation 2. Macrogols (only if constipation present)
Bloating without distension	1. Antispasmodics 2. Tricyclics

Selective serotonin re-uptake inhibitors improve quality of life SSRIs in standard doses appear to improve the health-related quality of life in people with chronic IBS, but with no significant changes in bowel symptoms or pain. This may well be a result of influencing associated depression, anxiety or somatisation.

Anti-diarrhoeals reduce diarrhoea in IBS

Loperamide reduces diarrhoea in IBS but has little effect on abdominal pain. It can be used as required or, if needed, on a regular basis. Regular use does not lead to a reduced effect.

Codeine is best avoided because of the potential for dependence.

Fibre and laxatives

Psyllium (Mucilax, Konsyl D) and ispaghula, soluble fibres, are usually the laxatives of choice in IBS. However, although this may improve constipation it does not usually improve abdominal pain. Insoluble fibres, such as bran, aggravate the symptoms of half of people with IBS and are associated with increased incidence of flatulence and bloating.

Stimulant laxatives are recommended for occasional, short term use only and have not been demonstrated to be effective in IBS.

Other pharmaceutical treatments

Other treatments, not funded in New Zealand or under investigation, include drugs which act through serotonin (5-HT) receptors. Serotonin plays a significant role in gastrointestinal motility, sensation and secretion and drugs, such as tegaserod, alosetron and cilansetron, which influence selected 5-HT receptors are proving to be effective.

Antibiotics and probiotics are also under investigation for the management of IBS, but no clear role has yet been identified.

Herbal remedies

Some trials of herbal remedies have shown significant improvement for some people with IBS. Most of these trials appear to relate to mixed plant preparations. For example a trial of a combination of bitter candytuft, chamomile flower, peppermint leaves, caraway fruit, liquorice root, lemon balm leaves, celandine herbs, angelic root and milk thistle fruit demonstrated improvement in IBS scores and abdominal pain.

RONGOA MAORI

Rongoa is the Māori term for medicines produced from native plants in New Zealand. Rongoa is enthusiastically used within a number of communities throughout the country, sometimes in conjunction with other Māori and mainstream health services.

There are numerous plants used for rongoa to treat gastrointestinal complaints. Two of the more common are Koromiko (Hebe) and Harakeke (NZ Flax):

Koromiko (Hebe)

The young leaves and shoots are chewed to relieve diarrhoea and dysentery. The active ingredient is phenolic glycocide.

Harakeke (NZ Flax)

Flax root is considered by users to be an effective remedy for constipation, diarrhoea and dysentry. The root is chewed or crushed and boiled with water. The harakeke rhizome has been shown to contain a red crystalline substance which is thought to be a purgative anthraquinone.

http://pharmacy.otago.ac.nz/rongoa/inex.html

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qi4gp

Ensuring quality patient care

qi4gp (Quality Information for General Practice) is a 'grass roots' initiative with a vision to provide a new information environment which will make comprehensive patient information accessible to all practitioners.

It has the backing of the four major general practice organisations: Independent Practitioners Association Council, the New Zealand Rural General Practice Network, the Royal New Zealand College of General Practitioners and the New Zealand Medical Association, and has been given seeding funding by the Ministry of Health.

An improved information environment would have lots of benefits for general practices and their patients. For example, it would be possible to quickly identify whether people have a condition excluding them from certain medicines. Shared assessment would be much easier, and patients would not have to repeat their story to a number of health professionals. Health records would be completely up to date at all times. In simple terms, the right information would be available to all clinical staff where and when it was needed.

The final form of the new information environment will be determined by the feedback received.
Some suggestions include:

- the introduction of electronic patient records allowing information to be exchanged between providers

- a health information network for general practice teams that includes information about available health services and how to access them, protocols and guidelines for general practice teams; as well as information for patients, including on clinical matters, self-management and how to access health services

- an overview at practice and PHO levels of population health and practice activity

- patient access to parts of their medical records

A discussion document, A Quality and Information Perspective for General Practice has been circulated, and feedback received from a number of stakeholder groups. The final report was due in late August 2007.

qi4gp wants to work with general practice to identify a vision for quality and information, and we need feedback on the best way to achieve that vision. What would your ideal information environment look like? What do you think of the qi4gp project's aims? What do we need to know about the problems you face and how the project could help address them?

The more feedback we can get, the better we can plan an information environment that best meets all needs.

You can find out more about qi4gp at **www.qi4gp.org.nz**

Making Ethnicity Data Count

Key points:

- Knowing ethnicity allows us to have a more comprehensive and complete understanding of peoples' health experiences and outcomes, and is an important factor in providing appropriate and responsive healthcare.

- The best method of collecting ethnicity data is to allow people to complete the ethnicity question themselves

- The ethnicity question used to collect ethnicity information in the health sector should be the 2001 Census ethnicity question

- Ethnicity data should be used to help inform the development of effective interventions

How will collecting accurate ethnicity data in primary care help address New Zealand's well-documented and long-standing ethnic disparities in health?

The need for accurate and consistently collected ethnicity data is becoming increasingly recognised. At a PHO and practice level, ethnicity data helps to inform the development of targeted programmes to address health inequalities, to ensure all patients are recalled for appropriate preventative health measures, and to inform decision making during consultations.

What is ethnicity (and what is it not)?

Ethnicity is a complex concept that reflects a country's historical, social and political environment. In New Zealand, ethnicity data is based on the concept of self-identification, that is, ethnicity is the group or groups that a person affiliates with.

There are a number of related concepts, including ancestry, citizenship, and nationality that overlap with ethnicity. However, ethnicity is not the same as nationality or citizenship, nor is it a measure of biology or genes.

Key Contributor: Donna Cormack, Senior Research Fellow, Te Rōpū Rangahau Hauora a Eru Pōmare, University of Otago, Wellington

Why collect ethnicity data?

A quality health system should be able to measure and monitor what is happening for different population groups, in terms of exposures to risk and protective factors for health, experiences of the health system and health outcomes. In New Zealand, as internationally, there are well-documented and long-standing ethnic disparities in health.[1,2,3] In order for us to understand these disparities, with the ultimate goal of eliminating them, high-quality and complete ethnicity data are essential.

'Degrees of blood' or self-identification of ethnicity?

Historically, official definitions of ethnicity in New Zealand have employed a biological 'degrees of blood' approach.[4] Since 1986, ethnicity in the population census has been collected based on the notions of self-identification and cultural affiliation. In line with this, it has been official policy to collect self-identified ethnicity for hospitalisations since 1996.[5]

There has been a greater emphasis in recent years on improving the quality of ethnicity data on routine datasets such as hospitalisations and the NHI, issues with mismatch and undercount of ethnicity remain.[6,7]

Figure 1: 2001 Census ethnicity question

Which ethnic group do you belong to?
Mark the space or spaces that apply to you

- New Zealand European
- Māori
- Samoan
- Cook Island Māori
- Tongan
- Niuean
- Chinese
- Indian
- Other *(such as DUTCH, JAPANESE, TOKELAUAN)*. Please state:

How should ethnicity data be collected and recorded?

1. Ethnicity data protocols developed by the Ministry of Health guide the collection, input and output of ethnicity data within the health and disability sector in New Zealand. In particular, they emphasise the importance of data collection practices that are consistent, standardised, and appropriate.

2. **Ask the right question**

   The standard ethnicity question (Figure 1: 2001 Census ethnicity question) should always be used.

   This question allows people to identify with one or more of the listed ethnicities and/or write in their own response. Using this question consistently gives us the ability to compare across datasets and over time.

2. **Ask in the right way**

   Ask people to **self-identify** by self-completing the question. It is not appropriate to guess a person's ethnicity based on their name or appearance, or to not give people the opportunity to complete the ethnicity question themselves.

   In instances where an individual is not able to self-complete the question, it is important that the data is collected from next-of-kin using the standard question.

3. **Avoid aggregating ethnicity data at the input stage**

   Ideally, ethnicity data should be recorded at the most detailed level. Aggregating ethnicity data at the recording or input stage should be avoided where possible, as this means that the original level of detail is lost. For example, recording Samoan as Pacific.

4. **Make sure to record multiple ethnicities**

   As people are able to identify with more than one ethnic group, it is important to record multiple ethnicities.

How can we improve our ethnicity data?

- Make ethnicity data collection routine. This includes checking that ethnicity data is recorded, complete and current

- Have policies and systems that ensure accurate data collection practices

- Make the data useful by using it to:

  - Develop policies and procedures

  - Ensure appropriate recalls for preventative care

  - Audit practice to see that everyone is getting appropriate care

  - Assist decision making in consultations

Summary

Ethnicity data allows us to have a more comprehensive and complete understanding of people's health experiences and outcomes. It is an important factor in developing responsive policies and procedures and providing appropriate healthcare.

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7. Swan J, Lillis S, Simmons D. Investigating the accuracy of ethnicity data in New Zealand hospital records: still room for improvement. NZ Med J 2006;119(1239).

Further reading:

Ministry of Health. Ethnicity data protocols for the health and disability sector. Wellington: Ministry of Health.

NZHIS training information http://snipurl.com/1rqdy

Where is Bandolier?

Statement from Bandolier

Bandolier to close print editions

Bandolier will cease publishing its monthly print editions after July 2007, making Bandolier 161 the last to appear in print. This was not a decision taken lightly.

One reason was external pressures, particularly several recent hikes in postal charges against a background of never having changed the price from £36 annually. Moreover, many people find it more convenient to download PDF versions from the Internet.

There were internal reasons for making a change, and relieving some of the demands imposed by a monthly printing schedule. Internal changes have combined with different priorities to mark a change in direction.

The Bandolier website will continue, and, we hope, flourish in other ways. Right now Bandolier is looking at how best to continue to re-invent itself electronically after having, to some extent, pioneered universal free access to knowledge.

Looking back, 161 monthly issues of Bandolier will look an awful lot. The initial idea was for three.

A huge thank you to faithful readers and correspondents.

Dr Andrew Moore, Professor Henry McQuay and the Bandolier Team

Now online – the new look Bandolier, with a host of new material written especially for the web.

New for September 07

Book review:	Medical writing – A prescription for clarity
Risk:	Aspirin or car? Comparing drugs risk with life risk
	Attitudes to risk in OA
	Citizens have inadequate medical knowledge
Arthritis:	Prognostic factors for progression of OA knee
	Intra-articular hyaluronic acid for knee osteoarthritis: update
Complementary:	Update on honey therapy: 2007
Labour:	Intrathecal opioids and foetal bradycardia in labour

Go to www.jr2.ox.ac.uk/bandolier

etc

evidence that counts

Systematic review: Low-dose aspirin sufficient for prevention of cardiovascular disease

A systematic review published in the Journal of the American Medical Association has investigated the mechanism of action of aspirin and the clinical literature for relationships among aspirin dosage, efficacy, and safety. The review included data from clinical trials using various doses of aspirin for cardiovascular disease, ranging from 81 mg/day to 325 mg/day, and concluded that long-term aspirin therapy at doses greater than 75 to 81 mg/day does not enhance the prevention of cardiovascular events but does increase the risk of gastrointestinal bleeding.

They conclude that currently available evidence does not support the routine, long-term use of aspirin dosages greater than 75 to 81 mg/day for cardiovascular disease prevention.

Reference
Campbell et al. Aspirin Dose for the Prevention of Cardiovascular Disease: A Systematic Review. JAMA 2007;297:2018-2024.

Pharmacist intervention can improve medication adherence in patients with heart failure

National Electronic Library for Medicines

Bottom Line: An educational intervention delivered by pharmacists can improve patients' adherence to medication for heart failure, but only as long as it is ongoing according to a controlled trial from the US.

A major proportion of the cost of caring for patients with heart failure comes from the treatment of exacerbations: appropriate medication can reduce the frequency of exacerbations, however regimens are often complex with a number of drugs to be taken. Patients may find adherence to such regimens difficult, and this study aimed to determine whether an educational intervention delivered by the pharmacist dispensing the patient's routine medication could improve adherence. It was carried out in a large academic primary care centre in an economically disadvantaged area and involved patients with heart failure seen by general medical or cardiology clinics or after hospital discharge, who were randomised to intervention or usual care.

Patients receiving their care from the centre get prescribed medicines from a central pharmacy or one of several associated satellites. For the purpose of the study, the central pharmacy was moved to be adjacent to the general medicine clinics treating heart failure patients: it was staffed with two pharmacists, the study pharmacist who saw all intervention patients, and another pharmacist who saw usual care group. The study pharmacist reviewed each intervention patient's medication history and their level of medication knowledge and skills. Based on this, they were provided with personalised verbal and written education about their medication and how to take it. Primary outcomes were medication adherence (measured using electronic container lids) and clinical exacerbations requiring emergency department treatment or hospitalisation. Study duration was one year overall, with a nine month intervention period and three months post-intervention.

A total of 314 patients were randomised from 1,512 potentially eligible. Study patients were slightly younger (63 vs. 67) and more likely to be women (67%

vs. 59%) than those in the potentially eligible group, however they were similar to heart failure patients seen by the centre overall (n=3,034). Of the study group, 192 were randomised to usual care and 122 to the intervention. Adherence to medication was significantly greater in the intervention group than in the control: 78.8% vs. 67.9% (difference 10.9 percentage points; 95% CI, 5.0 to 16.7 percentage points) actually took their medication and 53.1% vs. 47.2% (difference, 5.9 percentage points; 95% CI, 0.4 to 11.5 percentage points) took their medication near the scheduled times. The effect dissipated fairly rapidly, however, as the differences were not significant by the end of the post-intervention period. Patients in the intervention group were 19.4% less likely to have an exacerbation requiring emergency department visit or hospitalisation (incidence rate ratio, 0.82; 95% CI, 0.73 to 0.93) and had lower healthcare costs over the study period.

Based on their results, the authors conclude that a pharmacist intervention for outpatients with heart failure can improve medication adherence. This can reduce exacerbations and consequently costs, however it probably needs to be ongoing as the effect dissipated rapidly after the end of the study. The cost of the intervention was associated mainly with setting it up, and as more patients received it, the cost per patient reduced: the authors calculate that it gave a return on investment of 14 times. They suggest that the results are consistent with those of previous studies looking at similar pharmacist and multidisciplinary interventions, however the intervention in this study was less comprehensive or intensive than most previous work.

Reference

Murray MD, Young J, Hoke S et al. Pharmacist intervention to improve medication adherence in heart failure: a randomized trial. Ann Intern Med 2007; 146:714–25.

Nicotine replacement does seem to help smokers quit in the real world

National Electronic Library for Medicines

A multinational cohort study indicates that use of nicotine replacement therapy (NRT) does seem to help smokers quit, even without other support. Many clinical trials have shown that NRT can improve quit rates, however there is doubt over whether these benefits can be replicated outside the supportive environment of the controlled trial. Apart from the lack of support, smokers making self-initiated attempts to quit unsupervised may not use NRT products effectively. Previous reports have shown limited success, however it is suggested that these are based on inappropriately designed studies. The authors of this report carried out a prospective multinational cohort study that controlled for baseline nicotine dependence and was intended to examine a range of issues around smoking cessation.

At enrolment, participants were smokers aged 35-65, smoking five or more cigarettes daily, and intending to quit within the next three months. They were followed-up at three months and asked whether they had made a serious quit attempt lasting at least a day since enrolment. Those who responded yes were asked to indicate which supportive methods they had used (if any) during that attempt; they were subsequently followed up at six months. Those who had formal behavioural support or used bupropion were excluded as this study was intended to examine only unsupported effectiveness. Users were compared with non-users of NRT, with the main outcome measure being self-reported abstinence at six-months follow-up. The study had two phases that were carried out to the same protocol.

A total of 5,654 participants were recruited (2,009 in phase 1 and 3,645 in phase 2). Of these, the three month interview identified 357 (of 492 who quit) and 732 (of 906) who reported quit attempts and were followed up. About a third overall used NRT (36.5% in phase 1, 29.6% in phase 2), and those who reported NRT use were more likely to have remained abstinent as six months. Odds ratios for abstinence for NRT users vs. non-users, adjusted for degree of dependence, were 3.0 (95% CI 1.2 to 7.5) for Phase 1 sample and 2.1 (95% CI 1.0 to 4.1) for those in phase 2. Adjusted difference in likelihood of successful quitting was 6% for phase 1 and 3.7% for phase 2. Combining the results from the two phases gave an overall risk ratio for achieving six months abstinence for NRT users vs. non-users of 2.2 (95% CI 1.3 to 3.9, $p < 0.005$); adjusted difference in success rates was 4.3%. No significant differences could be identified between users and non-users (e.g. in motivation, loss to follow-up) that would account for the difference.

Based on their results, the authors conclude that unsupported NRT has a small but statistically and clinically significant benefit in helping smokers to quit. They suggest that although the effect is relatively modest, the potential benefit is large and the cost small: it is therefore one of the most cost-effective healthcare interventions available.

Reference

West R and Zhou X. Is nicotine replacement therapy for smoking cessation effective in the "real world"? Findings from a prospective multinational cohort study. Thorax (online) 15 June 2007.

etc

evidence that counts

Statins for all middle-aged people with type-2 diabetes?

National Electronic Library for Medicines

An effective and efficient strategy for primary cardiovascular disease (CVD) prevention in patients with type 2 diabetes would be to treat all men over 40 and all women over 45, according to a modelling study from Nottingham.

The authors note that type 2 diabetes is viewed as a risk factor for CVD itself, and this had led to recommendations that all patients with type 2 diabetes should routinely receive statin treatment irrespective of their cholesterol levels. This approach, however, ignores the fact that even within this patient group, there will be a spread of baseline CHD risk: a blanket approach will expose many patients to life-long therapy with consequent risk of adverse events, polypharmacy and reduced adherence to overall treatment. It is therefore appropriate to use some form of risk assessment to trigger treatment. The aim of this cross-sectional cohort study was to determine which of four possible strategies, including blanket use, gave the best balance between efficiency and effectiveness.

Strategies considered were (1) blanket treatment of all patients with type 2 diabetes; (2) a baseline risk strategy (as advised by NICE) treating those with moderate or high baseline risk; (3) an individual risk factor strategy treating those with total cholesterol >5 mmol/l; and (4) an age cutoff strategy treating patients at a sex-specific age, in effect combining the first two strategies. The study cohort was derived from the THIN dataset, which contains anonymous patient data from 304 UK general practices. Using this, the authors calculated for each strategy the number of patients treated with a statin, its effectiveness (potential number of CVD events that could be prevented), and its efficiency (the number needed to treat to prevent one CVD event). Values were extrapolated to national figures based on an estimated national prevalence of 3.6%. The relationship between age and CVD risk was plotted to determine the age at which patients moved from lower (<10%) to moderate-high CVD risk (>10%):

this gave ages for transition from low risk to moderate to high risk of just over 40 for men and 44 for women. These values were therefore used for calculation.

The study cohort consisted of 60,258 patients with type 2 diabetes aged between 30 and 75. In this group, there were 11,005 who had complete datasets and were not taking any lipid-lowering agent and had no CVD history, and were thus eligible for primary prevention. Using this study group and extrapolating to national figures, the authors calculate that the four strategies would result in giving statin treatment to 352,160 (strategy 1), 172,736 (strategy 2, high baseline risk), 264,608 (strategy 2, moderate/high baseline risk), 127,456 (strategy 3), and 278,800 (strategy 4, using the new age cutoff criteria) patients respectively. In the study cohort, the most effective strategies were 1 (blanket), 2 (moderate/high baseline risk), and 4 (age cutoff), resulting in 12,050, 11,214, and 11,094 CVD events avoided respectively. The most efficient and most cost-effective strategies were treatment at moderate to high risk, and age cutoff (NNT 24 and 26 respectively). Treatment of only those with total cholesterol >5mmol (strategy 3) was most efficient (fewest treated) but least effective (smallest number of events prevented).

The authors conclude that statin prescribing for primary prevention in patients with type 2 diabetes should aim to avoid the most events while treating the fewest patients. According to their study, treating according to calculated moderate to high CVD risk is the optimal strategy. However, as age is the most important determinant of baseline risk, treating based on a simple sex-specific age cutoff gives similar results with greater simplicity. They therefore suggest that statin therapy for primary prevention should be started in all men with type 2 diabetes at age 40 and all women at age 45, regardless of other factors.

Reference

S Siyambalapitiya, Uditha Bulugahapitiya, Jabulani Sithole et al. Combining Population Health and Baseline Risk Strategy by Determining an Age Cutoff for Initiating Statins in Patients With Diabetes. Diabetes Care. 2007 Aug;30(8):2025-9.

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DECISION SUPPORT FOR HEALTH PROFESSIONALS

Dear Dave

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

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

My patient was started on timolol eye drops a week ago for glaucoma. He is now complaining of feeling tired and coldness in his hands and feet. Could this be due to the timolol eye drops, and how can the situation be managed?

It is known that drugs can be absorbed in to the systemic circulation from ophthalmic preparations such as eye drops and solutions.

The nasopharyngeal mucosa is the primary site of systemic absorption of drugs applied topically to the eye. The extent of absorption depends on several factors including drop size, blink rate, physical capacity of the lacrimal sac and physicochemical properties of the drug. The conjunctival sac has a capacity of only 10 µL and an average eye drop is 25–50 µL, so 60–80% of an eye drop can overflow and enter lacrimal drainage.[1] Peak drug levels typically occur much more rapidly (similar to an intravenous bolus) than with oral administration.[2]

Absorption through the nasopharyngeal mucosa also avoids a first pass through the liver and for some drugs this will increase the proportion of drug reaching the systemic circulation. Timolol, which exhibits extensive first pass metabolism is such a case.

All the adverse effects associated with oral administration of timolol have also been reported with ophthalmic administration. This includes CNS, cardiovascular and respiratory effects so topical timolol has the potential to cause bradycardia and bronchospasm in susceptible people. As glaucoma is more prevalent in the elderly, who are also more likely to have co-morbidities, it is especially relevant to consider the potential effects of topical beta-blockers on any pre-existing conditions.[1]

Generally, the same precautions and contraindications should be observed with topical beta-blockers than those advised with oral administration. Relatively rare idiosyncratic adverse reactions such as hair loss have also been reported with timolol and other beta-blocker eye drops. This indicates that it is also possible for unpredictable (non-dose related) systemic reactions, such as hypersensitivity, to occur following administration of any eye drop preparation. An eye drop preparation should be avoided if it contains a drug which has previously caused a hypersensitivity or 'allergic' reaction in that person.

The systemic absorption of drugs from eye drops can be significantly reduced by simple advice

Digital nasolacrimal occlusion for three minutes or eyelid closure for two minutes immediately after instillation of the drops have both been shown to reduce plasma concentrations significantly. Digital nasolacrimal occlusion involves applying gentle pressure over the tear duct with a clean finger. Either of these methods can be used to reduce the absorption of any drug for which systemic absorption may be problematic such as corticosteroids, beta-blockers and cholinergic agents. They will reduce dose related adverse effects such as bradycardia with a beta-blocker but as they do not block systemic absorption completely and contraindications and precautions should still be observed. In addition, neither of these techniques remove the risk of non-dose related effects such as hypersensitivity.

Management of this case

Firstly it is important to examine the persons technique as people often use more drops than prescribed, 'just to make sure' or because they have difficulty telling how many drops they have instilled. This may lead to an excessive dose of the drug and more being available for absorption. A second person to check technique is useful and especially important to someone new to eye drop administration.

This person's side effects may be dose related so digital nasolacrimal occlusion or eyelid closure could be tried initially to try and stop or reduce them. Betaxolol is an alternative beta-blocker which is available as an eye drop. This is cardioselective (timolol is non-cardioselective) and is less well absorbed from eye drops than timolol. In this case it may be better tolerated than timolol.

Finally, if side effects are still troublesome a non beta-blocker agent, such as a prostaglandin analogue may be preferred.

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1. Rait JL. Systemic effects of topical ophthalmic ß-adrenoceptor antagonists. Aust NZ J Ophthalmol 1999;27:57–64.

2. Lama PL. Systemic adverse effects of beta-adrenergic blockers: An evidence-based assessment. Am J Ophthalmol 2002;134:749–760.

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

Correspondence

Could I have some CoQ10 please?

Dear Editor

I refer to your article about co-enzyme Q10 in "Upfront", Best Practice September issue. This article was very well presented and I'm quite sure that we'll have to "watch this space" on CoQ10 as research emerges and pharmaceutical companies grapple on how to curb the profits made by supplement manufacturing companies.

The importance of CoQ10 as an anti-oxidant in cell membrane protection and mitochondrial protection is well established. It is also known to be an "energy stimulant" and "has a potential role as a neuroprotectant" (quotes from your article). It is also well established that oxidative stress or free radical damage plays a major part in degenerative disease. The statin drugs inhibit HMG-CoA reductase (the rate limiting enzyme for the synthesis of mevalonic acid), this results in decrease in mevalonic acid, which consequently leads to a decrease in cholesterol and CoQ10.

I would therefore agree with your author that statins lower CoQ10 and I will accept that it is not the low Q10 levels that are the cause for myopathy or myalgic pains. However, it still lowers CoQ10 (an important anti-oxidant). It will therefore make "perfect sense" to advise our patients to take it as a supplement because we are giving them a drug that lowers their bodies' production of this important nutrient. Do we really have to wait for "evidence" when we advise "common sense" in GP practice all the time?

Send your letters to...

Correspondence, PO Box 6032, Dunedin
or email editor@bpac.org.nz

While I could agree with the author that a healthy diet should provide enough Q10 for the healthy person, I do not agree that the diet will be providing enough of this nutrient if we are giving a drug that lowers CoQ10. You could just the same argue that pregnant women should get enough folate from green-leaf veggies or red meat is enough to treat iron-deficiency anaemia or rest home patients should spend their afternoons bathing in the sun for their vitamin D needs.

I believe that knowing of this potentially harmful effect of statin drugs, it may in future be unethical or even negligent not to advise patients of using co-enzyme Q10.

Yours truly

Dr Werner Pohl
Gore Medical Centre

As always, we welcome alternative points of view on our material.

However scientific evidence can often be interpreted in opposing ways. It may be that a role for CoQ10 is found in the future but currently there is a lack of evidence for the claims being made. The ethical responsibility of a clinician, is to provide unbiased evidence in order for the patient to make a fully informed decision about their health.

Betaloc CR change

Dear Editor,

While we fear that feedback from the supplier of Betaloc CR is likely to be *a priori* discredited we would like to nonetheless offer the following feedback.

First, the Cardiovascular Sub-Committee of PTAC at their March 2007 meeting noted with respect to dividing anti-hypertensive medications that: "the Subcommittee was concerned about elderly patients who may not be able to break the tablet and pharmacists not providing them with divided tablets without an extra charge." This practical concern is arguably worth noting with respect to Slow-Lopresor as it would potentially directly impact on patients either clinically or financially.

Second, the quality of the advice is somewhat diminished by omitting a cost comparison with other key options. A number of the suggested alternatives are in fact more expensive than Betaloc CR. For example, the cost of Lopresor 50 mg bid is $0.33 versus Betaloc CR 47.5 mg od at $0.26. Similarly, Lopresor 100 mg bd costs $0.66 versus Betaloc CR 95 mg od at $0.44

We hope that these comments assist in your ambition for "Better Medicine".
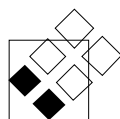
Dr Lance Gravatt, AstraZeneca