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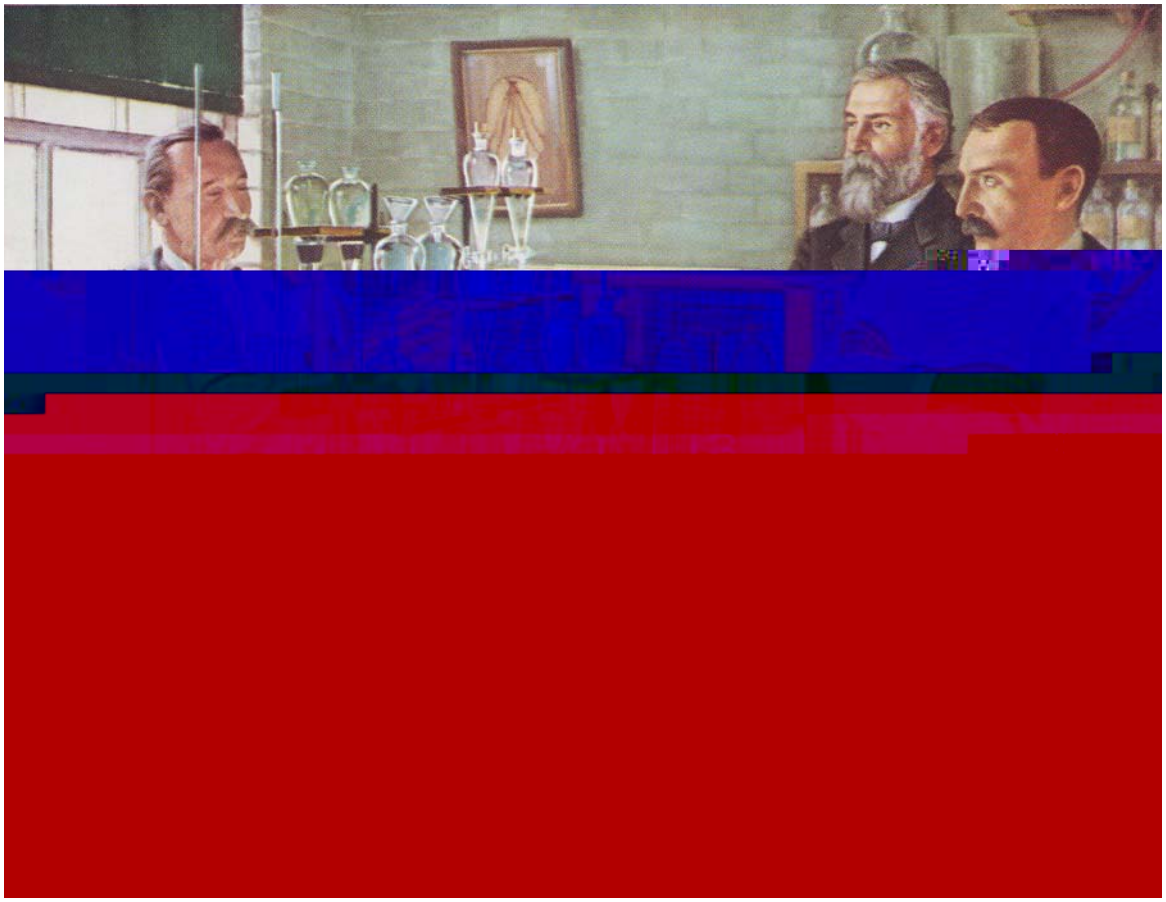

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# The Sri Lanka
# Prescriber



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**Cover picture**

**The standardization of pharmaceuticals** (About 1883)

Seldom did two preparations of 19th-century vegetable drugs have the same strength. Dr. Albert B. Lyons developed methods of accurate assay. Messrs. Parke and Davis recognized the importance of his work, began marketing of standardized medicines.

One of a series: *A History of Pharmacy in Pictures*, presented by Parke, Davis & Company.

George A. Bender, Director  Robert A. Thom, Artist

# Toxocariasis

Toxocariasis is a zoonotic helminthic infection of humans caused by the dog roundworm (*Toxocara canis*) or cat roundworm *(Toxocara cati)*. Humans are accidental hosts, usually infected by ingestion of embryonated eggs from contaminated sources. H. C. Wilder was the first to describe toxocariasis in humans, when he published a paper in 1950 describing ocular granulomas in patients thought to have retinoblastomas.

Toxocariasis is a worldwide infection. Seroepidemiological surveys show a 2-5% positive rate in healthy adults from urban western countries and 14-37% in rural areas. In tropical countries, surveys show a positive rate of 63% in Bali, 86% in Saint Lucia (West Indies), and 92% in La Reunion (French Overseas Territories, Indian Ocean).

## Clinical presentation

Most cases of *Toxocara* infection are asymptomatic, especially in adults. When symptoms do occur, they are the result of migration of second stage *Toxocara* larvae through the body.

Three syndromes of *Toxocara* infection are generally recognised.

- In children, covert toxocariasis is a mild, subclinical, febrile illness. Symptoms include cough, difficulty sleeping, abdominal pain, headaches, and behavioural problems. Examination may reveal hepatomegaly, lymphadenitis, and wheezing.
- Visceral larva migrans is caused by the migration of larvae through the internal organs of humans and the resulting inflammatory reaction. A constellation of symptoms develops, including fatigue, anorexia, weight loss, pneumonia, fever, cough, bronchospasm, abdominal pain, headaches, rashes, and, occasionally, seizures. Examination may reveal hepatomegaly, lymphadenitis, and wheezing. Occasionally, pleural effusions develop. Chronic urticaria has been described. Severe cases can lead to myocarditis or respiratory failure.
- Ocular larva migrans, which is caused by larval migration into the posterior segment of the eye, tends to occur in older children and young adults. Patients may present with decreased vision, red eye, or leukokoria (white appearance of the pupil). Granulomas and chorioretinitis can be observed in the retina, especially at the macula. Unilateral visual loss, retinal fibrosis, retinoblastoma, and retinal detachment occur. Serum antibodies to *Toxocara* are often absent or present in low titres.

Because the anti-*Toxocara* immunoglobulin-positive population is much higher than the prevalence of clinical toxocariasis, most patients are thought to have subclinical infection.

## Transmission

Transmission of *Toxocara* to humans is usually through ingestion of infective eggs. Both *Toxocara canis* and *Toxocara cati* eggs require a long incubation period outside of a host before becoming infective, so fresh eggs cannot cause toxocariasis. Many objects and surfaces can become contaminated with infectious *Toxocara* eggs. Flies can act as mechanical vectors for *Toxocara*, but most infections occur without a vector. In tropical countries eggs can mature to the infective stage after 2 weeks outside of a host. *Toxocara* eggs can remain infectious for years, as they are very resistant to the effects of chemicals, as well as changes in temperature.

## Diagnosis

Diagnosis of toxocariasis is difficult because confirmation of infection requires demonstration of larvae by biopsy. Clinicians use serologic testing (eg, enzyme-linked immunosorbent assay [ELISA] and immunoblot) to infer diagnosis.

## Laboratory studies

- The diagnosis of toxocariasis requires a high index of suspicion and depends on serologic testing.
- Peripheral blood eosinophilia is the most important finding; however, it may be absent in patients with ocular or covert toxocariasis.
- Serum total IgE: Patients with toxocariasis often have a marked increase in total IgE levels.
- ELISA with *Toxocara* excretory-secretory antigen (TES-Ag)
    - An elevated anti-TES-Ag IgE level indicates acute infection or progressive inflammation caused by toxocariasis.

- An increase in the immunoglobulin G (IgG) level confirms a past or present infection with minimum inflammation.
- In ocular toxocariasis, IgG or IgE titre is lower because the worm burden is smaller.

ELISAs are much more reliable and currently have 78% sensitivity and 90% specificity.

## Treatment

Toxocariasis will often resolve without treatment, because the *Toxocara* larvae cannot mature within human hosts. Chemotherapy is the treatment of choice in most patients with liver, lung, or eye involvement. Occasionally, ocular involvement requires ocular surgery. Treatment includes mebendazole or thiabendazole and specific organ treatment. Fortunately, toxocariasis usually carries a good prognosis.

In general, blood eosinophilia combined with a positive serologic test result indicates active toxocariasis and requires treatment. Deciding whether to treat covert or subclinical toxocariasis that does not show eosinophilia is controversial. Consider treatment in patients with a total serum IgE level over 500 IU/ml.

Albendazole, mebendazole, thiabendazole and diethylcarbamazine kill the nematode larvae. Albendazole 400 mg daily for seven days is the preferred treatment. It is important to advise the pharmacist in this regard as albendazole is usually given as a single dose for all the other helminthic infections and the uninformed pharmacist might hesitate to dispense a one week course of albendazole. Prednisolone is used as an adjunct to antihelminthic therapy in patients with visceral larva migrans, wheezing or other signs of tissue inflammation.

Granulomas in the eye can be surgically removed, or laser photocoagulation and cryoretinopexy can be used to destroy ocular granulomas. For liver or lung involvement, no surgical care is required.

## Consultation

- A consultation with an ophthalmologist is indicated in cases of ocular larva migrans.
- Consultation with a neurologist is indicated in cases of brain involvement with neurologic symptoms or seizures.
- Consultation with an infectious disease specialist may be indicated when questions exist regarding treatment for visceral larva migrans.

## Public health and prevention

Pet faeces should be picked up and disposed of or buried, as they may contain *Toxocara* eggs. Practicing this measure in public areas, such as parks and beaches is especially essential for decreasing transmission. Hand-washing before eating and after playing with pets, as well as after handling soil will reduce the chances of ingesting *Toxocara* eggs. Washing all fruits and vegetables, keeping pets out of gardens and thoroughly cooking meats can also prevent transmission. And, teaching children not to place non-food items, especially dirt, in their mouths will drastically reduce the chances of infection. Since pregnant or lactating dogs and cats and their offspring have the highest active parasitic load, these animals should be placed on a deworming program.

## Further reading


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# Management of chronic constipation in children

Chronic constipation is a relatively common problem in children, with the highest incidence in the 2-4 year age group. Childhood constipation is characterised by infrequent bowel evacuations, unusually large or hard stools, and difficult or painful defecation. This may be associated with involuntary passage of liquid or semisolid faeces in clothing, due to overflow from the faeces loaded rectum. The term soiling is used to describe this type of incontinence, which may be mistakenly diagnosed as diarrhoea. Chronic constipation with faecal soiling can have a significant effect on the social and emotional development of the child and family dynamics. Management demands time and commitment from the doctor as well as from the parents. The cultural beliefs and practices in the community could add to the difficulties of management. Although a number organic causes can lead to chronic constipation (panel 1), more than 90% of children have no identifiable organic cause and considered as having 'functional constipation'. When an organic cause is suspected on the history and examination they could be confirmed by special investigations (panel 1). Management of constipation in these children involves the management of specific conditions and is beyond the scope of this article.

**Panel 1. Organic causes of chronic childhood constipation**

| Type | Cause | Investigations |
|---|---|---|
| Anorectal abnormalities | Congenital | |
| | Anal anomalies | Examination under anaesthesia |
| | Hirschsprung disease | Imaging studies, barium enema, biopsy |
| | Acquired | |
| | Anal fissure | |
| | Perianal infections | Clinical examination only |
| Neurological | Spina bifida | Imaging studies |
| | Cerebral palsy | |
| Endocrine / Metabolic | Hypothyroidism | Thyroxine, TSH level |
| | Hypercalcaemia | Serum level |
| | Hypokalaemia | Serum level |
| | Lead poisoning | Serum level |
| Gastrointestinal | Cystic fibrosis | Sweat test |
| | Motility disorders | Motility studies |
| | | Biopsy |

The factors which predispose to chronic functional constipation in children include

- Low fibre diet
- Reduced fluid intake
- Poor toilet training
- Painful defecation
- 'Holding on' (withholding defecation due to fear of pain)
- Social and behavioural problems (home environment, school)
- Drugs (cough medication, anticholinergic drugs, opiate analgesics)
- Sexual abuse (rarely)

Normally the rectum remains empty most of the time and fills with faeces usually following a 'mass action' of the colon, and stretching of the rectum, which is responsible for the feeling of a desire to defecate. If there is no voluntary inhibition, this will result in complete evacuation of rectum. Constipation can be triggered by any event that causes a delay in bowel evacuation, which includes an acute illness, a period of immobility, a dislike to the unfamiliar school toilet, or simply being too engrossed in activities to go to the toilet. When there is a failure of complete evacuation over a period of time the rectum becomes chronically filled with faeces and dilates to form a "megarectum" which may not sense the faecal matter, and diminish the desire to defecate. At the same time, there may be formation of a hard, large diameter faecal mass, which will be difficult and painful to pass, setting up a vicious cycle. These children may develop recurrent colicky abdominal pain, and treatment with anticholinergic antispasmodic drugs is likely to worsen the constipation.

**Diagnosis**

The criteria recommended by the Paris Consensus on Childhood Constipation Terminology (PACCT) Group for the diagnosis of chronic constipation, has simplified precise diagnosis [1]. It is important to accurately identify the presence or absence of constipation as well as the predisposing factors. It is not difficult to diagnose functional constipation based on a detailed history and examination without any special investigations. According to the PACCT Group, one would diagnose chronic constipation when 2 or more of the following criteria are present in a child for more than 8 weeks.

1. < 3 stools/week
2. > 1 faecal incontinence (soiling)/week
3. Large stool in rectum or palpable in the abdomen
4. Passage of large (increased diameter) stools
5. Displays retention posturing and withholding behaviour
6. Painful defecation

At the age of 4 years 98% of normal children are toilet trained and expected to pass 1-2 stools a day [2]. This could vary from 3/day to 3/week. As there is a normal individual variation of stool frequency and consistency, the effect constipation has on the child and the family should be taken into account when making the diagnosis.

Digital examination of the rectum can be distressing to the child and is usually unnecessary. Inspection of the perineum is sufficient to check for anal fissures, perianal infections, anal anomalies, and faecal soiling.

**Treatment**

Establishment of a rapport with the parents and the child is the critical first step for successful treatment. The clinician should be prepared to spend time and explain the pathophysiology in an appropriately simplified way, so that the parents are convinced that the child was born with normal anatomy and function, and the constipation and the associated soiling if present, are due to the result of one or more of the factors mentioned above, which could be corrected by relatively simple measures.

It is essential to develop a treatment plan with the parents and the child, which should emphasise that the plan extends for a period of 3-6 months, and needs the active participation of the parents.

**The objectives of the treatment**

1. Remove the fecal impaction.
2. Restore a normal bowel habit, where soft formed stools are passed without any discomfort, at an appropriate place and time.
3. Maintain normal defecation and prevent relapses.

***Removal of impacted faeces***

The aim is to clear the rectum of retained faeces and keep it empty at most times of the day. This could be achieved by one or more of the following methods, depending on the severity of the impaction. The measures recommended to achieve restoration of healthy bowel habit (given below) also should be started at the same time, and continued for a much longer period.

1. Suppositories of stimulant laxatives (daily for 5-10 days)
   Glycerol suppositories are recommended for infants.
   Bisacodyl suppositories are recommended for older children [2].
2. Enemas
   Saline, sodium citrate (micro-enema), or phosphate enema.
   Soap and water enemas are potentially toxic and should be avoided.
3. Polyethylene glycol orally or by nasogastric tube (1g/kg/day for 3 days).
4. Manual evacuation under sedation or general anaesthesia (rarely).

If there is no significant fecal impaction, skip this stage and commence with the next stage.

***Restoration of a healthy bowel habit***

1. Toilet training.
   Get the child to sit on the toilet at a fixed time of the day for about 5 minutes, preferably after a meal (to get the benefit of the gastro-colic reflex)
   Do this twice a day at the beginning.
2. Increase the fibe and the fluid content of the diet.
3. Laxatives. Orally
   - Osmotic. lactulose, polyethylene glycol
   - Stimulant. bisacodyl, senna
   - Combination of osmotic and stimulant laxative
   - Behavioural modifications in addition to toilet training [3]. System of rewards with positive feedbacks
   - Avoid blaming and punishing the child
   - Child and the parents are encouraged to keep a bowel chart or diary.
5. Repeat the use of suppositories or enemas in case the child retain stools for >48 hours.

***Maintain the healthy bowel habit for a minimum period of 3-6 months***

The activities mentioned above should continue with appropriate adjustments. The dose of laxatives should be reduced gradually, as abrupt withdrawal of laxative support could result in a relapse [4]. Up to 30% of children may need laxative support for periods much longer than 6 months. Assessment by a paediatric specialist is necessary only when an organic cause is suspected in the initial assessment or if the well planed treatment is unsuccessful [2].

**Indications for surgical interventions in functional constipation**

Faecal impaction resistant to medical measures may need manual disimpaction under general anaesthesia. Manual dilatation of the anus may give temporary relief but has no long term benefit [5]. In rare instances where conservative management continues to fail, and the child is distressed and incapacitated due to soiling, formation of a caecostomy to facilitate the insertion of a catheter to practice antegrade continence enemas may be indicated [2].

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## Panel 2. Key points

- In healthy children there is a wide variation in the frequency and consistency of stools.
- Organic causes for chronic childhood constipation are rare.
- Faecal soiling is most likely due to chronic constipation.
- Functional constipation can be diagnosed without special investigations.
- Good rapport with the parents and child is essential for effective treatment.
- Disimpaction of the rectum should be achieved at the beginning.
- Osmotic laxatives should be tried before stimulant axatives.
- Laxatives may be needed for long periods, and should be tailed off gradually.

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**Further reading**


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# Treating dementia

## Summary

**With increasing numbers of elderly patients, general practitioners are uniquely placed to investigate and treat dementia. Screening tests can be used, but a thorough history and physical examination are usually needed to make the diagnosis. Other conditions such as delirium and depression should be excluded. Both pharmacological and non-pharmacological treatments are important, depending on the particular problems facing the patient and their carer. The treatment of concurrent chronic disease may need to be modified as dementia progresses.**

Key words: Alzheimer's disease, cholinesterase inhibitors, memory.

*(Aust Prescr 2009,32:9-12)*

### Introduction

The prevalence of dementia approximately doubles with every five years of age beyond the age of 65. By 2050, the estimated number of new diagnoses in Australia will reach 175 000 annually compared with 45 700 in 2001.[1]

General practitioners are often the first point of contact for patients or families who have concerns about memory and cognitive function. They are also in a unique position to suspect the diagnosis of dementia when a patient presents with other problems.

The variation in presentation can make diagnosis of cognitive impairment or early dementia difficult. However, early diagnosis may enable planning for the future, decrease anxiety with appropriate education and allow consideration of treatment.

A multinational survey of carers for people with Alzheimer's disease showed a delay of 12 months from first symptoms to diagnosis, including a delay of four months in making an appointment. In the Australian component of this survey, 30% of patients were diagnosed by their general practitioners. In 93% of the Australian cases, general practitioners were the first point of contact.[2]

### Diagnosis

The diagnosis of dementia is made on clinical assessment using formal criteria.[3] These include a history of the gradual onset of impairments in two or more cognitive domains, which cause difficulty in everyday function. These impairments should not be attributable to another cause, such as a drug effect or depression. Cognitive domains which are commonly impaired include memory, language and decision-making ability.

A detailed history with a collateral history from family and friends is essential in making the diagnosis, determining a pattern of progression and assessing any impact on daily living. As this is a time-consuming process, a screening test is often used to determine whether this is necessary.

The most commonly used screening test is the Folstein Mini-Mental State Examination (MMSE). Its validity has been demonstrated in many populations, however in patients of non-English speaking background the Rowland Universal Dementia Assessment Scale (RUDAS) may be more appropriate. The Mini-cog and General Practitioner Assessment of Cognition tests also have reasonable sensitivity and specificity and may take less time to administer.[4]

### *Differential diagnoses*

It is worth deliberately excluding other conditions that may appear to cause cognitive impairment such as delirium, depression and the adverse effects of some drugs such as antipsychotics. The clinical features of these conditions are usually different from those of dementia when considered closely (see Table 1). Blood tests to help exclude illnesses mimicking dementia would include measurement of full blood count, biochemistry, thyroid stimulating hormone, vitamin $B_{12}$ and folate. A CT scan of the brain is useful in excluding conditions that may be amenable to treatment, such as subdural haemorrhage and normal pressure hydrocephalus. Although there may be reversible elements for many with abnormal tests, reversible causes of dementia are extremely rare (less than 1.5%).[5]

### *Identify the type of dementia*

There is no 'cure' for most dementias. However, if the diagnosis includes information about the subtype of dementia (see Table 2) it allows a patient and their family to:

- access information that may help them deal with functional difficulties
- benefit from specific treatments (for example cholinergic therapies)
- avoid drugs known to aggravate problems (for example, anticholinergics, and antipsychotics in dementia with Lewy bodies)
- make plans for the future.

There is a good correlation between the clinical diagnosis of Alzheimer's disease and the neuropathology at autopsy. This association is less certain with other subtypes of dementia, but even a putative diagnosis may allow a patient and carer to make sense of the patient's symptoms. An example is the severe fluent aphasia seen in a younger patient with frontotemporal dementia.

*Table 1*

**Alternative causes of cognitive impairment**

| Condition | Clinical features |
|---|---|
| Delirium | Disorder of attention<br>Fluctuation of symptoms over hours<br>Recent onset (usually days to a few weeks) |
| Depression | Low mood is predominant feature<br>May have biological features of mood disturbance<br>May be motivated to improve performance on testing for a short time<br>Often coexists with dementia<br>May have history of depression |
| Drug effects | Common offenders are:<br>• anticholinergics<br>• sedatives and hypnotics<br>• antipsychotics<br>• analgesics<br>Usually cause features of delirium, but the duration of symptoms may be very long |

*Table 2*

**Subtypes and features of dementia**

| Dementia subtype | Important features |
|---|---|
| Alzheimer's dementia | Clinical diagnosis requires memory impairment and impairment of language, executive function, motor function (dyspraxia) or agnosia |
| Vascular dementia | Stepwise progression, associated with physical signs of stroke or history of transient ischaemic attack |
| Mixed dementia | Most commonly mixed Alzheimer's disease and vascular dementia |
| Dementia with Lewy bodies | Progressive dementia with at least two of the three features of fluctuating cognition, visual hallucinations, and Parkinsonism<br>Falls common<br>Severely intolerant of the adverse effects of antipsychotic drugs<br>Some evidence for benefit from cholinesterase inhibitors |
| Parkinson's disease with dementia | Ability to function can also be related to adequacy of dopa replacement and is often worse in 'off' periods<br>May be part of a spectrum of disease with dementia with Lewy bodies |
| Frontotemporal dementia | Younger patients (less than 65 years of age)<br>Family history of frontotemporal dementia often found<br>'Dysexecutive syndrome' with change in behaviour and personality common<br>Delusions common<br>Also includes progressive fluent and nonfluent aphasia types<br>Memory relatively spared<br>Mini-Mental State Examination unreliable<br>Deteriorates with use of antipsychotics |
| Post-traumatic | History of injury with consistent imaging<br>Not progressive<br>Appears to increase the risk of later developing Alzheimer's type dementia |
| Toxic encephalopathy (e.g. alcohol) | History of toxin exposure |

***Assessment and planning***

Assess how the patient and their carer are coping and what formal and informal supports and help are available. This assessment can be time consuming and a home visit (perhaps by associated nursing or allied health staff) may be an efficient way of getting this information. Reimbursement for gaining collateral information may be included in a comprehensive health assessment which may be reimbursed under Medicare*. If there are areas of need identified, an Aged Care Assessment Team (ACAT) evaluation may enable access to a range of services.

*Medicare Benefits Schedule – Items 700 and 702
www9.health.gov.au/mbs Search for 700 and 702
[cited 2009 Jan 13]

People with dementia may be irritable and aggressive. They can experience delusions and hallucinations. Look for challenging behaviours as they are common and burdensome.They warrant a specific assessment and management approach.[6]

Ask about the making of wills, enduring powers of attorney and advance health directives. If these arrangements are not in place and the patient is competent to make these decisions they should be encouraged to do so. If capacity to perform these actions has been lost, the carer may have to apply for these powers through guardianship legislation.

Give the patient information about managing their disease and consider referring them to a local patient support organisation. Education of the carer can be invaluable. Ask if the patient is still driving. The ability to drive safely is affected by many factors including visuospatial attention, switching of attention between tasks, and judgement. These are difficult to assess in a routine medical assessment. A specialist off-road and on-road assessment may be required. There may be state-funded access to these assessments, but the waiting lists can be very long and legal requirements vary from state to state.

Incontinence, increased nocturnal activity, impaired mobility[7] and aggressive behaviour increase the burden on carers.These problems are also predictors of nursing home placement within one year, independent of the level of cognitive impairment.

## Referral

Sending the patient to a memory clinic or specialist (geriatrician, psychiatrist or neurologist) may be required to access some treatments or to confirm the diagnosis. Offer referral if the diagnosis is in doubt, if the patient is young, the presentation is unusual or if requested by the patient or the family.

## Non-drug therapy

Monitor the patient's general health and other chronic conditions, especially vascular risk factors, to optimise health and independence. Should there be unexpected changes in cognition or behaviour, reconsider the possibility of incident delirium or depression. Other problems that can cause aggravated behaviours or distress in patients with dementia include pain, constipation, reduced vision and hearing loss.

Psychosocial interventions for carers, such as teaching them specific problem-solving skills, are more effective if the patient is also involved. Other factors that appear to be important include structured individual counselling, involvement of the extended family and consistent professional long-term support. These interventions can help to reduce the psychological burden and can reduce the need for institutional care of the patient. However, there is little impact on the carer's overall burden.[8] Interventions that do not improve outcomes include single interviews and interventions not associated with long-term contact such as short educational programs and support groups alone.

There is some evidence for the cost-effectiveness of community-based occupational therapy aimed at improving the patient's daily function.[9] Cochrane reviews have found no supportive evidence for the use of aromatherapy, music therapy, transcutaneous electrical nerve stimulation (TENS) or bright light therapy.

In practice, maintaining cognitive, physical and social activity appears to help in improving quality of life for the patient and reducing the burden of care. This burden is also improved by education about symptom progression, burden management and enabling appropriate access to services including respite care. Local patient support organisations can be useful resources for this. It is also important that carers maintain a relationship with their own general practitioner so that their own needs are addressed.

## Drug therapy

Dementia is a progressive disease. Drug treatment at best only slows the decline in cognitive function.

### *Cholinesterase inhibitors*

The drugs available in Australia are donepezil, galantamine and rivastigmine (also now available in a topical formulation). Patients must meet specific criteria to be eligible for subsidised treatment under the Pharmaceutical Benefits Scheme (PBS).

There is a statistical benefit of cholinesterase inhibitors in mild to moderate Alzheimer's disease, however the clinical benefit remains uncertain and all the studies are short term.[10] There is no evidence that one drug has a benefit over another. Many specialists switch to another cholinesterase inhibitor if there is no efficacy or tolerance of the first. If required, a trial of memantine may then be appropriate.

A study of patients taking one of several cholinesterase inhibitors (donepezil, tacrine and rivastigmine) showed improvement in cognition and function at one year and delay in nursing home placement.[11] However, some randomised controlled trials have shown the drugs do not delay placement.

There is also some evidence for the efficacy of cholinesterase inhibitors in vascular dementia and dementia with Lewy bodies.[12,13] The drugs have not been approved for these indications.

Common adverse effects include nausea, vomiting and diarrhoea. These are less troublesome with dose titration. Other adverse effects include bronchoconstriction (particularly in patients with asthma), bradycardia, cramps and vivid dreams.

### *Memantine*

Memantine is a non-competitive antagonist of the N-methyl D-aspartate (NMDA) receptor. It is available on the PBS and may be an alternative for those patients unable to tolerate cholinesterase inhibitors.

Placebo-controlled trials have shown benefit in patients with moderate to severe Alzheimer's disease. Memantine has been used in combination with cholinesterase inhibitors in clinical trials. As with the cholinesterase inhibitor studies, the outcomes measured do not translate easily into clinical practice. Memantine requires dose titration over a month to minimise the adverse effects of agitation, hallucination and headache. It may also increase the risk of seizure activity. Memantine is excreted in the urine and is probably not suitable for use in those with renal impairment.

### *Other drugs for dementia*

Hundreds of different drugs are currently in various stages of clinical testing including vaccines and monoclonal antibodies against amyloid protein. There is no consistent evidence of efficacy or safety for drugs such as vitamin E, selegiline, vitamin $B_{12}$ or ginkgo biloba.

## Disease progression

While the patient's functional state is still intact, treatment of chronic conditions can improve symptoms and life expectancy. As dementia progresses the benefits are reduced and the need for investigations or therapy should be discussed with the carer. A previously completed advance health directive can be very valuable to guide therapy.

Timing of cessation of drug therapy for dementia is controversial, but should be considered if the patient is completely dependent in their care needs. Cessation should be discussed with the patient's family, particularly as they may notice some deterioration in the patient's functional abilities.

## Conclusion

Most cases of dementia are diagnosed on clinical assessment. Excluding treatable causes of cognitive impairment is vital. Management of the patient and their care needs should be individualised. Consider the needs of the carers as well as the patient themselves. Early education and planning for future events can assist both the patient and their support network.

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# Management of psoriasis

Psoriasis is a chronic inflammatory disease affecting the skin and the joints. It has substantial physical and psychosocial consequences on the quality of life. Over the past few decades several new agents have been added to the list of psoriasis therapies. This article describes the management of psoriasis affecting the skin.

**Aim of treatment**

A permanent "cure" for psoriasis remains elusive, but it is important to explain that it is treatable, and to educate patients about the relapsing-remitting nature of the disease. Treatment is aimed at induction and maintenance of remissions. The therapeutic measures used have to be safe, effective, affordable and convenient to use.

Therapeutic agents for psoriasis include (i) topical agents and (ii) systemic therapies.

**Topical therapies**

These are effective as monotherapies in mild disease and as adjunctive treatment in severe disease.

*Coal tar*: This time honoured medication is available as a shampoo, lotion, ointment and paste. Tar acts by inhibiting DNA synthesis. In developed countries newer drugs have replaced coal tar. However it is relatively inexpensive and widely used in the management of chronic plaque psoriasis in Sri Lanka. Due to its irritant properties it cannot be used on the face and sensitive areas.

When combined with salicylic acid it is effective in treating thick lesions. The keratolytic property of salicylic acid facilitates the action of coal tar. Strength of tar can be adjusted to suit the patient. Folliculitis is a known side-effect but it is rare. If the psoriatic plaques become erythrodermic, tar should be discontinued. To elicit a response tar has to be applied for several weeks.

*Emollients*: Preparations such as aqueous cream, emulsifying ointment, soft paraffin and liquid paraffin are used topically in erythrodermic psoriasis when other applications are contraindicated because of their irritant effects.

*Dithranol*: Dithranol acts by inhibiting keratinocyte proliferation. It is available in a cream base or as a paste. It is effective in treating intractable plaque psoriasis limited to small areas. Irritation of the skin and brownish staining of clothes limit its use. It is too irritant to be used on the face, flexural areas and the genital region.

*Topical corticosteroids:* Mild topical steroids are effective in treating psoriatic lesions on the face, and genital and flexural areas. Potent steroids are useful in treating palmoplantar and scalp psoriasis. In several countries such as the USA, topical steroids are the mainstay of treating psoriasis. However, the rebound effect on withdrawal and tachyphylaxis are problems. Intermittent use can reduce these. Steroids can be effectively combined with coal tar, calcipotriol and retinoids.

*Calcipotriol:* This vitamin D analogue acts by binding to vitamin D receptors on keratinocytes, regulating their proliferation and T cell activation. It is cosmetically more acceptable but occasionally causes irritation. It is applied twice a day and the weekly dose should not exceed 100g. It is contraindicated in abnormalities of calcium metabolism, renal insufficiency and pregnancy. High cost restricts its use. It is successfully combined with topical steroids and PUVA.

*Tazarotene:* Though this retinoid is expensive and not currently available in Sri Lanka, it is useful in treating moderately severe psoriasis. Due to its teratogenic potential it is best avoided in pregnancy. It is available in gel or cream formulations, and is successfully used in combination with steroids and UVB.

*UVB phototherapy:* Ultraviolet rays of 290-320 nm are delivered in a phototherapy chamber. UV rays have anti-inflammatory and antiproliferative effects. It cannot be used in photosensitive individuals. It can be used in combination therapy with methotrexate or acitretin. Narrow band UVB (at 311 nm) is more effective than the usual broadband UVB.

*Excimer laser:* This delivers an intense 308 nm radiation. It is useful for treating isolated plaques of recalcitrant psoriasis. As it targets only the affected area it has an advantage over other therapies. It is costly and is not available in Sri Lanka at present.

**Systemic therapies**

These are indicated in moderate and severe disease poorly responsive to topical therapy.

*Photochemotherapy* (PUVA): This treatment is used for adults with severe psoriasis poorly responsive to conventional therapy. Because of possible long term side-effects it is avoided in children. It is also contraindicated in pregnancy, lactation and in the presence of photodermatoses, skin malignancies, cataract, severe cardiovascular disease and debility.

Psoralens capsules are ingested 2 hours before the UVA exposure. UVA activates psoralens which then reacts with DNA and reduces epidermal turnover. UVA is delivered within a specialised chamber. The dose and duration are calculated according to the skin type. Wearing of UV protective goggles and covering of male genitals are mandatory during treatment. Phototherapy equipment is costly and available only in a few centres.

*Methotrexate:* Methotrexate has both anti-inflammatory and immunomodulatory properties. It is widely used in severe psoriasis. It is not expensive, and is readily available. Pretreatment evaluation is essential and includes medical history, drug history, complete physical examination and assessment of renal, liver and haematological functions. It is contraindicated in pregnancy and in the presence of liver disease, renal disease and active infections. It is administered on a weekly basis, and dose ranges from 7.5 to 22.5 mg. Side-effects such as nausea, vomiting and abdominal discomfort are counteracted by administering folic acid 1 to 5 mg/day. Regular assessment of blood counts, liver and renal functions are necessary. Generally it is well tolerated and safe in the long term. The cumulative dose that is considered as safe is 1.5 grams.

*Hydroxyurea:* This antimetabolite is not hepatotoxic. However blood counts need monitoring. The initial dose is 500mg b.d. Later it can be increased to 1gram b.d.

*Acitretin:* This retinoid is a potent teratogen. Pregnancy needs exclusion before starting treatment and has to be avoided for a period of 2 years after the last dose. It can cause derangement of liver functions, hyperlipidaemia and glucose intolerance, and these should be assessed before treatment and during it at regular intervals. Marked dryness of the skin and mucous membranes is a common side-effect. Hepatitis and benign intracranial hypertension may occur rarely. Intermittent therapy over a long period is possible with this drug. It can be effectively combined with PUVA.

*Ciclosporin:* Ciclosporin inhibits cytokine production by T helper cells and is highly effective in inducing a rapid remission in patients with severe psoriasis. It is important to record pre-treatment blood pressure, renal function and liver functions. It is contraindicated in the presence of malignancies, pregnancy and active infections. The starting dose is 2.5 mg/kg/day; it can be raised to 5 mg/kg/day depending on the response. Blood pressure, renal functions and electrolytes need monitoring. Gingival hyperplasia and hirsutism are known side-effects. Intermittent short courses of treatment are effective and safe. Discontinuation is recommended after a period of 2 years. It is expensive.

*Biological agents:* These drugs target specific steps in the immunopathogenesis of psoriasis. Their side-effects can be quite severe. Administration of these needs expertise. T cell response modifiers such as efalizumab and alefacept as well as TNF alpha inhibitors such as infliximab and etanercept are effective in treating psoriasis. Most patients improve by 4 weeks of therapy. These drugs are very expensive. However, they are of proven value in treating severe psoriasis unresponsive to standard drugs.

**Combination therapies**

When standard monotherapy does not control the disease effectively, combination therapies are used.

In conventional combination therapy, agents with synergistic or complementary actions are used concomitantly. eg. acitretin + UVB/PUVA, or methotrexate + UVB.

In rotational therapy, cumulative doses and toxicities of the drugs will be reduced eg. UVB/PUVA/methotrexate/ acitretin.

In sequential therapy, initial efficiency and subsequent safe maintenance are optimised. eg. initial rapid control with ciclosporin, followed by acitretin, later maintained on UVB/PUVA.

**Treatment of different types of psoriasis**

*Plaque psoriasis:* If mild, coal tar and salicylate ointment is the first choice. Calcipotriol also can be used. For delicate areas topical steroids are indicated. If rapid clearance is needed, a combined preparation containing calcipotriol and a potent topical steroid is effective. If lesions are few and recalcitrant, dithranol is suitable. Severe plaque psoriasis is treated with UVB, methotrexate or PUVA. Hydroxyurea, ciclosporin and acitretin also are effective. Selection of the therapy depends on the availability, cost and the presence of contraindications.

*Erythrodermic psoriasis and pustular psoriasis:* Need admission to hospital, treatment of the provocative factors and supportive care. Systemic drugs are indicated. Irritant topical applications should be avoided. *Guttate psoriasis* is treated with coal tar or UVB. Scalp lesions are treated with cetrimide shampoo or tar containing shampoos. Coconut oil compound (containing tar, salicylic acid, coconut oil in emulsifying ointment) is useful when there are thick scales. *Palmoplantar* lesions are treated with coal tar and salicylate ointment and potent steroids.

Treatment of nail plate involvement is difficult. Injection of potent topical steroid to the matrix is effective. Severe nail psoriasis may be treated with methotrexate.

**Further reading**


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# Self-assessment questions

*(And clinical physiology in small doses)*

Select the **best** response in each question

1. Regarding toxocariasis caused by the ingestion of dog roundworm (*Toxocara canis*) or cat roundworm (*Toxocara cati*) eggs:
   a. Freshly laid eggs are more infective than eggs incubated in soil for a long period.
   b. The larvae can mature into adult worms in human body tissues.
   c. Albendazole 400mg daily for 7 days is the preferred treatment in adults.
   d. In ocular larva migrans a very high peripheral blood eosinophil count is a characteristic feature.
   e. ELISA with *Toxocara* excretory-secretory antigen (TES-Ag) has a 95% sensitivity and 98% specificity for progressive inflammation caused by toxocariasis.

2. The following precautions are recommended when using acitretin in the treatment of psoriasis.
   a. Avoid concomitant PUVA therapy.
   b. Avoid in palmoplantar pustular psoriasis.
   c. Avoid concomitant methotrexate therapy.
   d. In women in the childbearing age, avoid pregnancy 1 month before starting, during therapy, and for 6 months after the last dose of acitretin.
   e. Acitretin may be prescribed by family physicians and specialists who are not dermatologists.

3. The following substances produced by vascular endothelium and their functions are correctly matched
   a. Nitrous oxide – vasoconstriction
   b. Angiotensin converting enzyme – vasodilation
   c. Endothelin – vasoconstriction
   d. Prostacyclin ($PGI_2$) – vasoconstriction
   e. von Willebrand factor – inhibits platelet aggregation

**Answers to self-assessment questions**

Question 1. The correct response is **c,** and the daily dose for children has to be adjusted according to age and body weight. Fresh eggs are not usually infective, as they have to undergo a long incubation period outside the worm's body before becoming so. Larvae cannot mature into adults in human tissues; man is only an 'accidental host'. In ocular larva migrans the eosinophil count is usually not raised. ELISA (TES-Ag) has only about 78% specificity and 90% sensitivity, but is still the most reliable laboratory investigation. (See article by Professor Weerasinghe, in this issue)

Question 2. The correct response is **c**. Acitretin therapy is for extensive severe psoriasis and palmoplantar pustular psoriasis. It can be effectively combined with PUVA. Women should avoid a pregnancy for at least 2 years after the last dose; and acitretin therapy should be given only under a specialist dermatologist's supervision. (See article by Dr Sirimanne in this issue, and BNF March 2009 page 634-5)

Question 3. The vascular endothelium has been described as a 'cardiovascular endocrine organ, which occupies a strategic interface between blood and other tissues'. The correct response is **c.** (Read Clinical Medicine. Editors P Kumar and M Clark, 7the Edition, pages 685-7).

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