Overview of disease state management

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Introduction

Learning Objectives:

1. To understand brief pathophysiology of the disease states being discussed.
2. To recognise signs and symptoms of the disease states being discussed.
3. To understand various non-pharmacological and pharmacological management of the disease states discussed

Disease states being discussed:

- Orthostatic hypotension
- Thyroid issues in older people
- Management of UTI in older people
- Polymyalgia Rheumatica

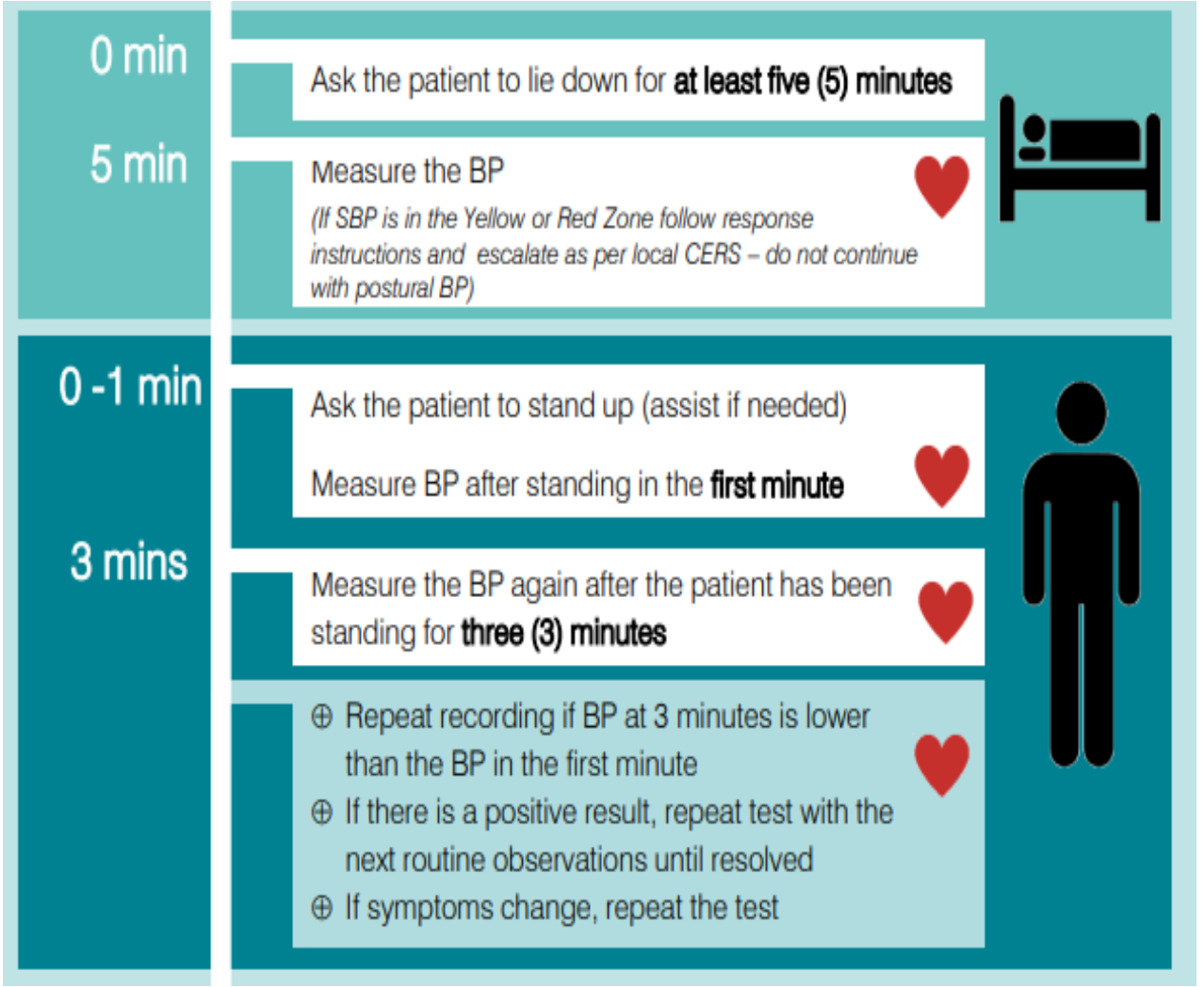
Orthostatic Hypotension (OH)

- Common in older people
- Incidence increases with age
- Independent predictor of mortality
- increased risk of dementia and cardiovascular disease
- Prevalence
  - community-dwelling older people has been reported to vary between 9% and 34%.9
  - In aged care facilities and acute hospital settings→ 50%
- High prevalence in diabetes and Parkinson's disease

Orthostatic Hypotension (OH)

- Definition:
  - Decrease in systolic blood pressure of 20 mm Hg or a decrease in diastolic blood pressure of 10 mm Hg
    - Within three minutes of standing when compared with blood pressure from the sitting or supine position

How to measure a lying and standing blood pressure (BP) as part of a falls assessment



Pathophysiology

- When a healthy person stands, approximately 700 mL blood pools below the diaphragm and results in decreased venous return to the heart
- How is BP maintained: baroreflex-mediated sympathetic activation, along with parasympathetic withdrawal, results in increased heart rate, stroke volume and peripheral vasoconstriction, maintaining BP
- Aging-related changes

Symptoms of OH

- Hypoperfusion:
  - light-headedness
  - dizziness
  - Weakness, fatigue
  - difficulty thinking and feeling faint
- Overcompensation:
  - Palpitations
  - Tremulousness
  - Nausea
  - coldness of extremities and chest pain
- Atypical symptoms
  - Patients with Dementia: fluctuations, confusion, drowsiness and falls
  - dim, blurred or tunnel vision, or a dull pain in the back of the neck and shoulder (coat hanger distribution)

Causes/risk factors

- Normal ageing!
- Neurogenic vs. non-neurogenic

Table 1 Causes of orthostatic hypotension[3,13,14,23,46]

Neurogenic causes
Parkinson's disease
Multisystem atrophy
Pure autonomic failure
Dementia with Lewy bodies
Diabetic autonomic nephropathy
Amyloidosis (familial and primary)
Dopamine β-hydroxylase deficiency
Autoimmune autonomic gangliopathy
Hereditary sensory and autonomic neuropathies
Other peripheral neuropathies (alcohol, paraneoplastic, HIV, Guillain-Barré syndrome)
Spinal cord or brain stem lesions
Sjögren's syndrome
Pernicious anaemia
Chronic renal failure
Non-neurogenic causes
Medications (particularly α-adrenoceptor antagonists, antipsychotics, antihypertensives, diuretics, vasodilators such as nitrates, sympatholytics such as beta-blockers, narcotics, sedatives, tricyclic antidepressants, levodopa and sildenafil)
Sepsis
Dehydration or volume depletion (e.g. secondary to burns, diarrhoea, vomiting, haemorrhage, heat, salt-free diet)
Cardiac causes (e.g. brady- or tachyarrhythmia, myocardial infarction, hypertension, diastolic dysfunction, baroreceptor insensitivity)
Large carbohydrate-rich meals and alcohol
Adrenal insufficiency
Deconditioning (following acute illness and a period of recumbence)
Other metabolic causes (e.g. vitamin B_{12} deficiency, porphyria)

Goals of care

- Aim- ameliorating the symptoms, correcting any underlying cause, improving functional status and reducing the risk of complications
  - As opposed to aiming for an arbitrary BP goal
- Individualised plan
- Relevance of asymptomatic OH??

Management of OH

- Non-Pharmacological interventions

  ??? Should we stop the antihypertensive

  Multidisciplinary approach is essential

Table 2 Non-pharmacological measures for the treatment of orthostatic hypotension[36]

Recommendation	Evidence
Recommended for all patients	
Education and reassurance, including explanation of diagnosis, risk of recurrence and the avoidance of triggers	Expert consensus opinion, small studies, retrospective studies and registries
Adequate hydration and salt intake	Expert consensus opinion, small studies, retrospective studies and registries
Should be considered	
Modification or discontinuation of hypotensive drug regimens	Single randomised clinical trial, large non-randomised studies
Isometric physical counter-pressure manoeuvres	Expert consensus opinion, small studies, retrospective studies and registries
Abdominal binders and/or compression stockings	Single randomised clinical trial, large non-randomised studies
Head-up tilt sleeping (>10°)	Expert consensus opinions, small studies, retrospective studies, and registries

Pharmacological options

- Fludrocortisone
  - increases renal sodium retention and expands plasma volume
  - peak plasma levels are reached within 45 min with a half-life of approximately 7 h
  - 0.1– 0.3 mg fludrocortisone once daily
  - At higher doses, patients may be at an increased risk of hypothalamic–pituitary– adrenal axis suppression
  - Side effects: Headache, peripheral oedema

- Midodrine
  - Midodrine increases BP via vasoconstriction
  - May be preferred over Fludro in patients with CCF or supine hypertension
  - Vasoconstrictors such as midodrine are ineffective when plasma volume is reduced
  - Pro- drug
  - Eliminated in urine but has been used in CRF under specialist supervision
  - 1st dose half an hour before mobilization and last dose 4-5 hrs before bedtime
  - Starting dose 2.5mg mane, up to 10mg TDS
  - Side effects: supine hypertension
  - Conflicting evidence

Pharmacological options

- Pyridostigmine
  - cholinesterase inhibitor
  - For mild to moderate OH of neurogenic nature
  - 30mg BD upto 90mg TDS
  - Side effects: nausea, diarrhoea, urinary urgency, diaphoresis, hyper salivation
  - Needs robust evidence
    - Inferior to Fludro in neurogenic OH in PD

- Droxidopa
  - Droxidopa is a synthetic amino acid precursor that is converted by aromatic L-amino acid decarboxylase into noradrenaline
  - Droxidopa has a short half-life of 2–3 h and should be avoided within 5 h of bedtime to avoid supine hypertension
  - Side effects: hypertension, headache, dizziness, nausea, falls and urinary tract infections

Pharmacological options

- Many other meds trialled!

- To treat or not to treat- supine hypertension!

Table 3 Other medications with potential utility in orthostatic hypotension

Medication	Mechanism of action	Comment	Adverse events and precautions
Atomoxetine	Noradrenaline reuptake inhibitor that exerts a vasopressor effect	Used for management of ADHD, but a proof-of-concept study comparing atomoxetine with midodrine in patients with OH reported that it increased standing SBP more than midodrine;[5] further trials are required before considering this agent for OH treatment	Insomnia, nausea, vomiting, weakness and hepatotoxicity Hypertension may develop in 10% of patients
Domperidone	Dopamine receptor antagonist	Anecdotal evidence for use in treating OH that occurs after initiating the dopamine agonist apomorphine in people with Parkinson's disease[56,57]	Can cause QT prolongation and is associated with an increased risk of ventricular tachyarrythmias and sudden cardiac death in patients with pre-existing cardiac disease
Mirabegron	β_3-Adrenoceptor agonist	Used for treatment of overactive bladder but, given its stimulatory effect on the cardiovascular system, it has been considered for OH[5]	There is a risk of severe hypertension[5]
Octreotide	Synthetic somatostatin analogue that constricts splanchnic circulation and reduces venous pooling	Can be effective when other agents fail, but does not have robust evidence to support its use; its use is limited by side effects and the need for subcutaneous administration	Abdominal pain, nausea, hyperglycaemia Use with caution in patients with T2DM because they are more prone to side effects and rarely tolerate this drug.[4,13,15]
Erythropoietin	Expands red cell mass and increases total blood volume;[2] also appears to have a vasoconstrictor effect because of its effects on NO production[34]	Has been shown to be effective in patients with anaemia and autonomic dysfunction	Supine hypertension, stroke, myocardial infarction[13,18]
NSAIDs	Inhibit the vasodilatory effects of prostaglandins and increase BP in some patients with OH[13]	Lacks a strong evidence base for OH;[2] use with caution in older people due to the risk of adverse effects	Gastrointestinal bleeds, renal impairment[4]
Caffeine	Adenosine receptor blocker that inhibits adenosine-induced vasodilatation	Has been used in doses of 200 mg in the form of brewed coffee or tablets; may attenuate OH symptoms in some patients[18] but evidence for its use is mixed[13]	Insomnia (therefore should be taken in the morning)
Desmopressin	Vasopressin analogue that increases water reabsorption and reduces nocturia	Efficacy is uncertain and clinical utility is limited by side effects[3,13,30]	Hyponatraemia

ADHD = attention deficit hyperactivity disorder; BP = blood pressure; NO = nitric oxide; NSAIDs = non-steroidal anti-inflammatory drugs; OH = orthostatic hypotension; SBP = systolic blood pressure; T2DM = type 2 diabetes mellitus.

Thyroid issues in older people

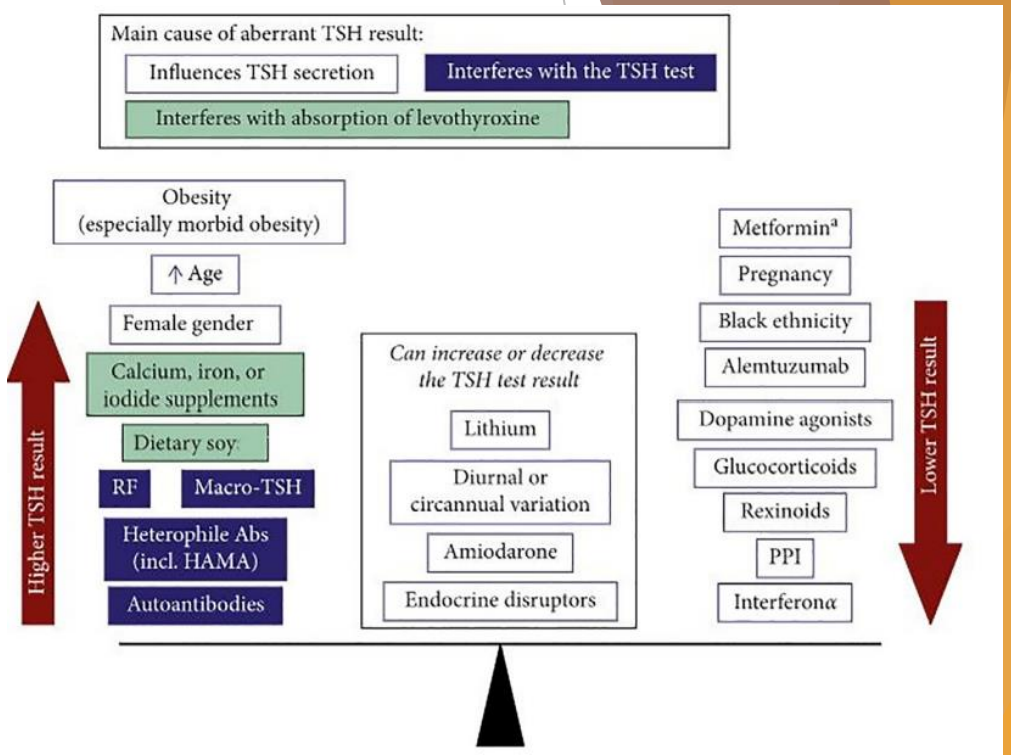
- Age-dependent physiological changes in thyroid function
- Coexistent chronic non-thyroid illnesses
- Polypharmacy
- Clinical presentation is different to younger people
- Untreated conditions
  - significant morbidity due to their concomitant illnesses

Changes in thyroid anatomy with ageing

- Thyroid volume decreases due to progressive fibrosis and atrophy with advancing age
  - secondary to organ-specific autoimmune disease resulting in atrophic thyroiditis in absence of goiter
  - Prevalence of thyroid antibodies increase with age
  - Iodine status is often low due to dietary restrictions of salt intake prompted by comorbid conditions such as hypertension, heart disease and renal disease.

Changes in thyroid function with age

- TSH- conflicting studies?
- Role of polypharmacy
  - E.g Metformin
- T4 and T3
  - Role of poly pharmacy!
- Thyroperoxidase (TPO) and thyroglobulin antibodies
  - increased prevalence of TPO and thyroglobulin antibodies



2. Polypharmacy and other factors altering TSH levels.

Brief classification of thyroid issues

Thyroid disorders are classified as:

- primary—caused by a disorder within the thyroid gland, affecting the production or secretion of thyroid hormones (triiodothyronine [T_3] and thyroxine [T_4])
  - subclinical—serum T_3 and T_4 concentrations are within the normal range, but serum thyroid stimulating hormone (TSH) concentration is outside the normal range. Subclinical disease is usually asymptomatic
  - overt—serum T_3, T_4 and TSH concentrations are outside the normal range. Overt disease is usually symptomatic
- secondary—caused by a disorder within the anterior pituitary gland, affecting the production or secretion of TSH, which in turn affects the production of thyroid hormones
- tertiary—caused by a disorder within the hypothalamus, affecting the production or secretion of thyroid releasing hormone, which in turn affects the production of TSH and thyroid hormones.

Hypothyroidism

- Hypothyroidism in adults over 65 years
  - Overall increase in mortality and an increased incidence of cardiovascular events
  - Subclinical vs. overt
  - Hashimoto thyroiditis
  - Polypharmacy again!!

- Clinical presentation
  - Often non-specific!
  - Fatigue, drowsiness, memory loss or a decrease in cognitive functioning and constipation

Management of hypothyroidism

- Levothyroxine
- Elderly patients absorb L-thyroxine less efficiently than younger patients; however they often require 20-25% less dose per kilogram body weight, due to decrease in lean body mass
- Over-replacement of thyroxine might result in adverse effects
- Start low go slow may be the mantra
- For patients 60 years and older, a reasonable serum TSH target range is 1 to 5 milliunits/L.
- For patients older than 80 years, consider an even higher serum TSH target range (eg 4 to 6 milliunits/L).
- For frail elderly patients and patients with biochemically severe hypothyroidism at baseline, base initial dose adjustments on clinical response rather than serum TSH concentration

Subclinical Picture!

- Subclinical hypothyroidism occurs in around 5% of the Australian population
- Subclinical hypothyroidism who has a positive thyroid peroxidase antibody is more likely to progress to overt disease than a patient a with negative thyroid peroxidase antibody
- Initial partial replacement is recommended for patients with only mildly elevated serum thyroid stimulating hormone (TSH) concentration or subclinical disease
- levothyroxine 25 to 50 micrograms orally, daily. Adjust the dose every 4 to 8 weeks as required

Therapeutic Guidelines

Interpretation of serum TSH and free T_4 concentrations

High serum TSH concentration	
Serum free T_4 concentration	**Possible interpretations**
high serum free T_4 concentration	possible laboratory error secondary hyperthyroidism (TSH-secreting pituitary adenoma) [NB1] thyroid hormone resistance [NB1] intermittent poor adherence to levothyroxine
normal serum free T_4 concentration	subclinical primary hypothyroidism (also called mild thyroid failure) recent severe nonthyroidal illness
low serum free T_4 concentration	overt primary hypothyroidism recent severe nonthyroidal illness antithyroid overtreatment

Normal serum TSH concentration	
Serum free T_4 concentration	**Possible interpretations**
high serum free T_4 concentration	possible laboratory error secondary hyperthyroidism (TSH-secreting pituitary adenoma) [NB1] thyroid hormone resistance [NB1] sampling within 6 hours of levothyroxine dose
normal serum free T_4 concentration	normal thyroid function
low serum free T_4 concentration	secondary hypothyroidism (pituitary cause) or tertiary hypothyroidism (hypothalamic cause) severe nonthyroidal illness use of drugs that affect serum free T_4 concentration antithyroid overtreatment

Low serum TSH concentration	
Serum free T_4 concentration	**Possible interpretations**
high serum free T_4 concentration	overt primary hyperthyroidism [NB2] [NB3] levothyroxine overtreatment
normal serum free T_4 concentration	subclinical primary hyperthyroidism [NB3] levothyroxine overtreatment nonthyroidal illness treated secondary hypothyroidism (pituitary cause) or tertiary hypothyroidism (hypothalamic cause) recently started antithyroid drug
low serum free T_4 concentration	secondary hypothyroidism (pituitary cause) or tertiary hypothyroidism (hypothalamic cause) severe nonthyroidal illness

Hyperthyroidism

- Diagnostic challenge in older people
- Atrial fibrillation in hyperthyroidism
- Osteoporosis in hyperthyroidism

Atypical presentation of hyperthyroidism in elderly.
Apathy
Depression
Restlessness
Generalized weakness.
Anorexia with weight loss
Absence of tachycardia and palpitations
New or recurrent atrial fibrillation
Heart failure
Angina
Absence of eye and skin changes
Absence of heat intolerance
Constipation
Failure to thrive.

Drugs interfering with thyroid function

Drugs interfering with thyroid function.

	Hypothyroidism	Hyperthyroidism
Drugs Affecting Hypothalamic–Pituitary Control of the Thyroid	Synthetic retinoid bexarotene Mitotane Immune checkpoint inhibitors *Suppress TSH without clinical hypothyroidism:* Glucocorticoids Dopamine agonists Somatostatin Metformin	
Drugs Affecting Thyroid Hormone Synthesis or Release	Amiodarone Lithium	Iodine excess (Jod–Basedow phenomenon) Radioactive Iodine contrast Amiodarone Topical povidone–iodine Over-the-counter preparations expectorants, vaginal douches, and kelp, Lithium
Drugs That Enhance Thyroid Autoimmunity	Immune check point inhibitors	Immune check point inhibitors *(Initially causes painless thyroiditis with hyperthyroidism followed by hypothyroidism)*
Drugs Causing Direct Thyroid Damage	Amiodarone Tyrosine kinase inhibitors (Sunitinib)	Amiodarone
Drugs Affecting Protein Binding of Thyroid Hormone	Oral estrogen and selective estrogen-receptor modulators Methadone Heroin Mitotane Fluorouracil	Antiepileptic agents (phenytoin and carbamazepine) Nonsteroidal anti-inflammatory drugs High-dose furosemide Heparin
Drugs Affecting Thyroid Hormone Activation, Metabolism, and Excretion	Amiodarone Dexamethasone (and other glucocorticoids) Propranolol Phenobarbital, phenytoin, carbamazepine Rifampin Sorafenib Bile acid sequestrants (Cholestyramine, colestipol, and colesevelam)	
Drugs Affecting Absorption of Thyroid Hormone Preparations	Proton-pump inhibitors Ferrous sulfate Calcium carbonate Aluminum hydroxide Sucralfate Bile acid sequestrants Raloxifene Biotin	Biotin

Subclinical hyperthyroidism

- 5% to 10% of older people

- Potential risks of untreated subclinical hyperthyroidism
  - progression to overt hyperthyroidism
  - progression to overt hyperthyroidism
  - bone effects (osteoporosis)

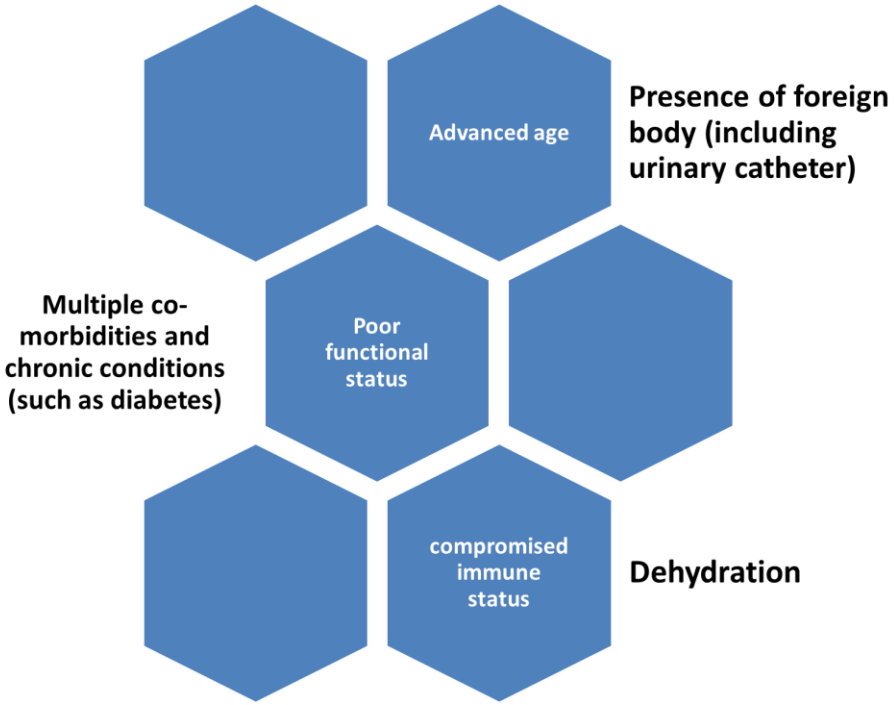
- Refer to the Therapeutic Guidelines!

UTI in Older people

- How common is UTI in older people?

- Older the age more the UTIs?

Why are older people at increased risk of UTI



Risk factor	Proposed mechanism
Diabetes, cancer, autoimmune disorders	• Impaired cellular function • Treatment with the sodium-glucose co-transporter two inhibitors (e.g. canagliflozin and dapagliflozin)
Co morbidities such as dementia, stroke, Parkinson's disease	• Bladder and bowel incontinence and functional decline
Oestrogen deficiency	• Vaginal prolapse, atrophy and urinary incontinence resulting in an ascending flow of bacteria to sterile urinary tract • Impaired protective action of intravaginal microflora against bacterial over-colonisation of the vagina
Prostatic hypertrophy	• Urinary retention (i.e. increased postvoid residual volume) and turbulent urine flow may predispose patients to chronic prostatitis
Presence of foreign body (including urinary catheter, stone, suture, surgical material)	• Disruption of defence mechanisms, granting bacteria easier access to the bladder • Pathogens may colonise catheters by binding to host receptors that attach to the surface of the catheter; they are more virulent and can create a biofilm by producing exopolysaccharides that entrap and protect replicating bacteria • Catheter encrustations may obstruct urine flow, promoting urine stagnation and bacterial replication
Sexual activity	• A risk factor for both men and women, and most critically in the older population

Definitions

- Urinary Tract Infection: Infection of the urinary system including the lower urinary tract (bladder, prostate, epididymis) and/or upper urinary tract (kidneys).

- Asymptomatic Bacteriuria (ASB): The established definition of significant bacteriuria is $\geq 10^8$ colony-forming units/mL[26] from a midstream urine sample or detection of bacteriuria using bedside dipstick testing (which can detect nitrites and leukocyte esterase).

There are some other terms that may be used to differentiate UTI from a suspected UTI

- Suspected UTI: Criteria for suspected UTI include all three of:
  - localising urinary tract symptoms and signs or localising urinary tract symptoms and signs plus systemic symptoms and signs.
  - symptoms and signs that are new or changed/worse.
  - no alternative better reason identified for symptoms and signs.
- Proven UTI: Criteria for proven UTI include both of:
  - symptoms and signs as for suspected UTI.
  - confirmation by urine culture result with significant growth of bacteria recognised to be a uropathogen.

Symptomatology of UTI

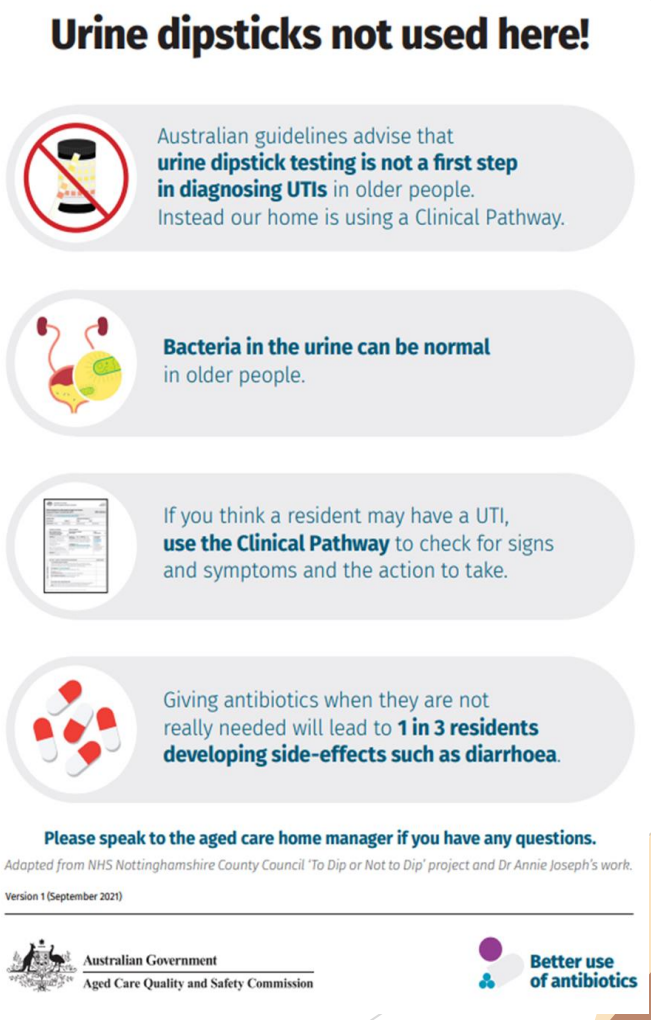
- Dysuria, urinary frequency and urgency (cystitis)
- Back/flank pain, and costovertebral angle tenderness (pyelonephritis) +/- fever
- Atypical symptoms: confusion (not an absolute marker of UTI)
- Challenges in diagnosis: chronic urinary symptoms such as incontinence, nocturia, and urgency that are unrelated to a UTI

Prevention is better than cure!

- Non-pharmacological approaches.
- Antibiotics should not be used for continuous prophylaxis.
- Discuss with consumers (residents, families) the effectiveness, or lack of effectiveness, of methenamine hippurate (in most situations) and cranberry products (not recommended by Therapeutic Guidelines for prevention or treatment of UTI).
  - Caution with drug interactions with herbal products and some medications
- Intravaginal estrogen (with ongoing review) in postmenopausal women with recurrent UTIs has beneficial effects on vaginal flora and reduces the incidence of UTIs.

To dipstick or not to dipstick- that is the question!

- Dipstick testing of urine is often used as a fast method for ruling out UTI as the cause of symptoms.
- This test detects the presence of leucocyte esterase (surrogate marker for pyuria) and nitrites (a marker for gram-negative bacteriuria).
- However, Gram-positive bacteria and other organisms such as Enterococci and Pseudomonas species account for larger proportion of UTI in older adults and these microorganisms do not reduce urinary nitrates to nitrites.
- This may mean that urine dipstick nitrite test will not test positive for these organisms.
- Dipstick testing results cannot be interpreted in isolation without taking into consideration the resident's clinical symptoms and signs.



Urine and blood culture

- Urine culture helps to identify bacteriuria and determine sensitivity to antibiotics
- Requests for urine culture in older people should be limited to eliminate sepsis
- Positive blood culture in absence of other sources of infection is consistent with UTI

Management of UTI

Considerations prior to initiation of treatment:

- Establish whether an advance care plan is in place and if antibiotic treatment is consistent with the expressed goals of the patient. Antibiotic therapy may not be inconsistent with a declared palliative treatment plan.

- Before starting antibiotic therapy, correct dehydration. Delaying antibiotic therapy to assess for symptomatic urinary tract infection (UTI) does not generally lead to adverse outcomes in aged-care facility residents.

- ASB should not be treated with antimicrobial therapy, for either treatment or prophylaxis, as antibiotic therapy does not reduce the rate of complications associated with this condition and has been shown to paradoxically increase the risk of subsequent UTI.

Treatment for established UTI as per Therapeutic Guidelines

Uncomplicated Acute Cystitis empirical therapy in Women

For empirical therapy of acute uncomplicated cystitis in nonpregnant women, use:

1. trimethoprim 300 mg orally, daily for 3 days [Note 1]

OR

2. nitrofurantoin 100 mg orally, 6-hourly for 5 days [Note 2].

See Antibiotic choice for urinary tract infection in adults for a discussion of drug choice.

If trimethoprim and nitrofurantoin cannot be used, for empirical therapy of acute uncomplicated cystitis in nonpregnant women, use:

cefalexin 500 mg orally, 12-hourly for 5 days.

Empirical therapy of non-severe pyelonephritis in adults while awaiting the results of investigations

For empirical therapy of nonsevere pyelonephritis in adults while awaiting the results of investigations, use:

amoxicillin+clavulanate 875+125 mg orally, 12-hourly for 14 days. If clinical response is rapid, stop therapy after 10 days.

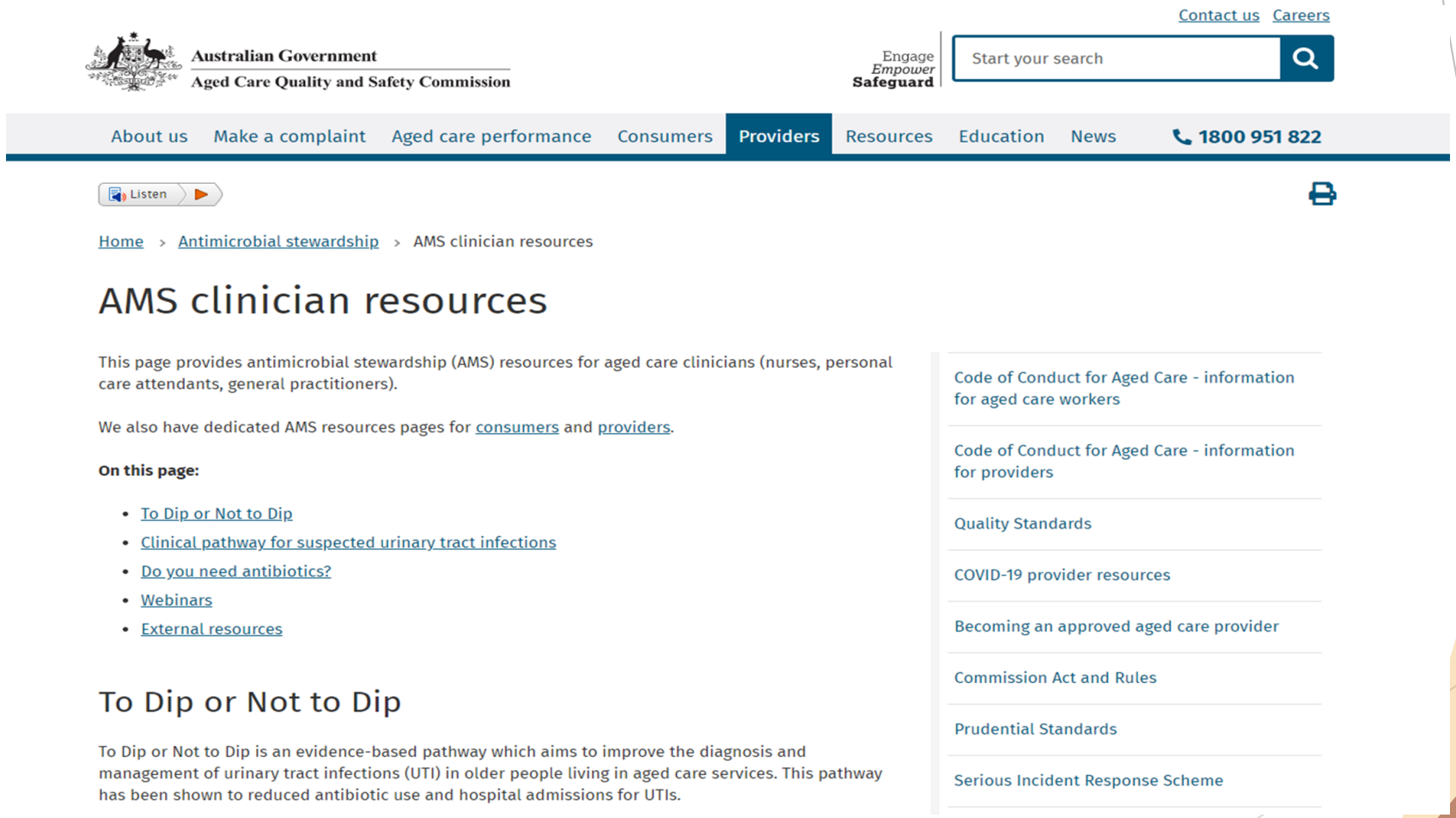
Recurrent UTI

- Recurrent UTI is defined as more than four episodes of UTI in a 12-month period.
- Recurrent UTI differs from recurrent ASB, and warrant further investigation, particularly in men, as this may be indicative of recurrent bacterial prostatitis.
- Whilst routine use of antibiotic prophylaxis is not recommended, the Australian Therapeutic Guidelines recommend either intermittent post-coital or continuous prophylaxis for up to 6 months with a single agent.
- There is currently no published evidence available to support the use of prolonged continuous prophylaxis (>6 months duration) with ‘cycling’ of antimicrobials.

Management of Catheter- associated UTI (CA-UTI)

- For CA-UTI, consideration should be given to removing or changing the catheter as soon as possible, particularly if it has been in place for more than 7 days.
- It is important to note that catheter removal or exchange should not delay antibiotic treatment (Please refer to the treatment flowchart- Therapeutic guidelines).
- Do not collect a urine sample from the drainage bag for culture.
- Some evidence suggests empirical treatment for CAUTI does not improve either short or long term outcomes, which supports avoidance of empirical antimicrobial therapy.
- Empirical therapy is not recommended by the Australian Therapeutic Guidelines.
- Antibiotic prophylaxis is not indicated at the time of catheter placement, removal or replacement.

Useful resources!



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Home > Antimicrobial stewardship > AMS clinician resources

AMS clinician resources

This page provides antimicrobial stewardship (AMS) resources for aged care clinicians (nurses, personal care attendants, general practitioners).

We also have dedicated AMS resources pages for consumers and providers.

On this page:

- To Dip or Not to Dip
- Clinical pathway for suspected urinary tract infections
- Do you need antibiotics?
- Webinars
- External resources

To Dip or Not to Dip

To Dip or Not to Dip is an evidence-based pathway which aims to improve the diagnosis and management of urinary tract infections (UTI) in older people living in aged care services. This pathway has been shown to reduced antibiotic use and hospital admissions for UTIs.

Code of Conduct for Aged Care - information for aged care workers

Code of Conduct for Aged Care - information for providers

Quality Standards

COVID-19 provider resources

Becoming an approved aged care provider

Commission Act and Rules

Prudential Standards

Serious Incident Response Scheme

Polymyalgia Rheumatica in older people

- >50 y.olds
- Unclear aetiology
- Women > men
- Incidence increases with age

Clinical presentation

- Pain and stiffness involving the shoulder and hip girdle
  - symptoms commonly also described in the neck, lower back and thighs
  - Involvement of hands and wrists is possible
  - seronegative symmetrical synovitis
  - Peak in the morning
- European League Against Rheumatism

(EULAR)/American College of Rheumatology (ACR)

classification criteria for polymyalgia rheumatica

Required criteria:

- Age ≥ 50 years
- Bilateral shoulder pain
- Abnormal erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP)

PLUS

- Score of ≥ 4 (or ≥ 5 if ultrasound criteria is used) from the following:

Clinical criteria	
Morning stiffness lasting >45 min	2 points
Hip pain or restricted range of motion	1 point
Negative rheumatoid factor and anti-citrullinated protein antibody	2 points
Absence of other joint involvement	1 point
Ultrasound criteria	
≥1 shoulder with subdeltoid bursitis, biceps tenosynovitis, or glenohumeral synovitis AND ≥1 hip with synovitis or trochanteric bursitis	1 point
Both shoulders with subdeltoid bursitis, biceps tenosynovitis, or glenohumeral synovitis	1 point

Differential diagnoses of polymyalgia rheumatica to consider

Giant Cell Arteritis vs PMR

Inflammatory rheumatic diseases

- Late-onset rheumatoid arthritis
- Late-onset spondyloarthritis
- Connective tissue diseases (e.g. vasculitis)
- Calcium pyrophosphate deposition disease

Non-inflammatory rheumatic diseases

- Rotator cuff pathology
- Shoulder osteoarthritis
- Adhesive capsulitis
- Fibromyalgia

Other

- Viral or bacterial infections
- Malignancy
- Parkinson's disease

ONG-TERM CORTICOSTEROID MONOTHERAPY REMAINS THE STANDARD OF CARE IN PMR

- commenced at a low to moderate dose
- Slow weaning recommended
- Median duration of treatment is 1.93 yrs
- Relapses necessitate return to the last dose of steroids at which symptoms were controlled, followed by a repeat weaning attempt after 1–2 months
- 1 in 4 patients would need >4 years of corticosteroid therapy

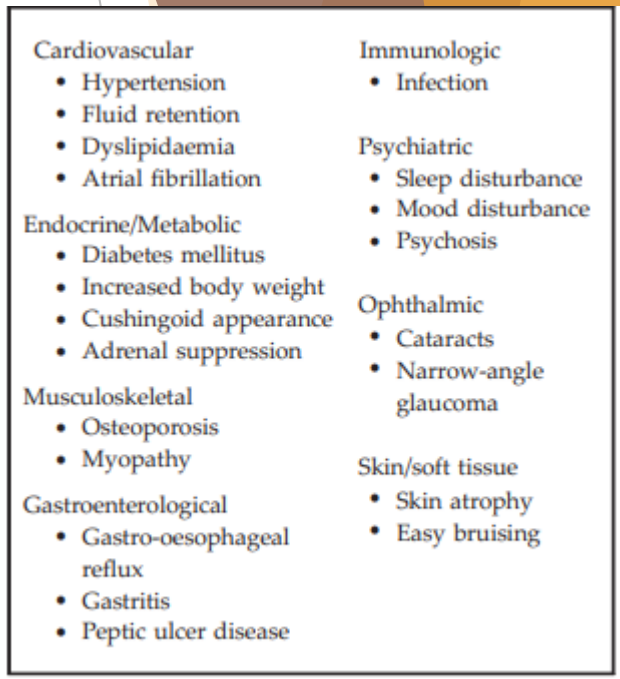
Box 3 British Society for Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR) guidelines for the management of polymyalgia rheumatica[10]

- Daily prednisolone 15 mg for 3 weeks
- Then 12.5 mg for 3 weeks
- Then 10 mg for 4–6 weeks
- Then reduction by 1 mg every 4–8 weeks

CORTICOSTEROID-RELATED ADVERSE EFFECTS

- Clinical dilemma as <5mg steroid doses may have an acceptably low level of harm to justify their use
  - Older people already have reduced muscle and bone mass

- Patient education is the key!



Cardiovascular
- Hypertension
- Fluid retention
- Dyslipidaemia
- Atrial fibrillation

Endocrine/Metabolic
- Diabetes mellitus
- Increased body weight
- Cushingoid appearance
- Adrenal suppression

Musculoskeletal
- Osteoporosis
- Myopathy

Gastroenterological
- Gastro-oesophageal reflux
- Gastritis
- Peptic ulcer disease

Immunologic
- Infection

Psychiatric
- Sleep disturbance
- Mood disturbance
- Psychosis

Ophthalmic
- Cataracts
- Narrow-angle glaucoma

Skin/soft tissue
- Skin atrophy
- Easy bruising

Musculoskeletal effects of longterm steroids

- Ptients with PMR are 1.5- to 5-fold more likely to sustain a fracture than age- and sex-matched individuals without PMR
- Increased excretion of calcium
- Vit D
- BMD
- Anti resorptive therapy
- Cease corticosteroids asap

Steroid sparing agents

- Considered when steroid dose >10mg/d
- Steroid sparing agents are initiated concurrent with a stable prednisolone dose and weaning of prednisolone is attempted again after 1–2 months
- Specialist care recommended
- Most data for methotrexate, leflunomide and tocilizumab

Brief overview of steroid sparing agents

- Low-dose **Methotrexate**
- High risk drug!
  - Once a week dosing
  - Renally cleared
  - Caution with pre-existing liver disease
  - patients with memory impairment may require strategies to reduce the risk of overdosing
  - concurrent use of methotrexate with other folic acid antimetabolites, such as trimethoprim, is best avoided
  - Regular blood tests (e.g every month for the first three months, then every three months thereafter for myelotoxicity and hepatotoxicity)
  - Contrary to common belief, low-dose methotrexate used in rheumatic diseases does not necessitate the same precautions for exposure to the patient's bodily fluids as high doses require, and concurrent use with proton pump inhibitors or non-steroidal anti-inflammatory drugs is not contraindicated

Tocilizumab

- Tocilizumab is a humanised monoclonal antibody that inhibits the action of interleukin (IL)-6 by binding to the IL-6 receptor
- Use in PMR stems from the central role that IL-6 is thought to play in PMR pathogenesis, as well as the successful use of tocilizumab in giant cell arteritis
- Tocilizumab is available in both subcutaneous and intravenous forms, typically used at doses of 162 mg/ week and 8 mg/kg every 4 weeks, respectively
- EXPENSIVE!!
  - At present the use of tocilizumab for patients with PMR is not covered by the Australian Pharmaceutical Benefits Scheme and comes at a considerable cost of approximately A$20 000 per annum
- Possible adverse effects include abnormal liver enzymes (usually asymptomatic and reversible), neutropenia, hyperlipidaemia, hypertension and increased risk of infection, including reactivation of latent infections.
  - In addition, lower gastrointestinal perforation is slightly more frequent in patients receiving tocilizumab, and may present atypically without severe abdominal pain or raised inflammatory markers
- Screening for infections such as hepatitis B and C and tuberculosis prior to commencement of tocilizumab
  - While receiving tocilizumab, regular monitoring of liver function tests, neutrophil counts and lipid profiles is warranted.

Leflunomide

- Disease-modifying antirheumatic drug
- Leflunomide doses of 10–20 mg/day are typically used
- adverse effects of leflunomide include diarrhoea (dose dependent), nausea and vomiting, alopecia, reversible asymptomatic elevations of liver enzymes and increased risk of infections
- Less commonly, leflunomide can result in severe liver injury, bone marrow suppression, hypertension, peripheral neuropathy and leflunomide-induced lung injury (including interstitial pneumonitis and pulmonary fibrosis)
- Regular blood tests to monitor for myelotoxicity and hepatotoxicity should be performed in patients receiving leflunomide

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