CLINICAL PRACTICE GUIDELINES

Diagnosis and Management of Headache

Sep 2007

MINISTRY OF HEALTH
SINGAPORE

MOH Clinical Practice Guidelines 5/2007

Levels of evidence and grades of recommendation

Levels of evidence

Level	Type of Evidence
1^{++}	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias.
1^{+}	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.
1^{-}	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2^{++}	High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2^{+}	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2^{-}	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Grades of recommendation

Grade	Recommendation
A	At least one meta-analysis, systematic review of RCTs, or RCT rated as 1^{++} and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1^{+}, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2^{++}, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1^{++} or 1^{+}
C	A body of evidence including studies rated as 2^{+}, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2^{++}
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2^{+}
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group.

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Diagnosis and Management of Headache

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Published by Ministry of Health, Singapore
16 College Road,
College of Medicine Building
Singapore 169854

Printed by Golden City Colour Printing Co. (Pte.) Ltd.

ISBN 978-981-05-9432-9

Available on the MOH website: http://www.moh.gov.sg/cpg

Statement of Intent

These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient, in the light of the clinical data presented by the patient and the diagnostic and treatment options available.

Foreword

Headache is one of the most common disorders of the nervous system. Although headache disorders are often not life-threatening, its various subtypes cause substantial levels of disability in terms of impaired quality of life, personal suffering and financial cost.

Globally, lifetime prevalence of headache is 66%. WHO ranks migraine 19th in all causes of disability. It is estimated that the Years Lived with Disability for all types of headaches is double that of headache due to migraine alone. This would bring headache into the ten most disabling conditions overall and into the five most disabling for women. In Singapore, the overall lifetime prevalence of headache was found to be 82.7%.

The first national guidelines on headache were published in 2000 to assist doctors in making appropriate choices in the work up and treatment of their patients presenting with headache. To maintain currency of knowledge and to include newer evidence that has emerged in this field, it is timely to update these guidelines. This revised edition not only details diagnosis and treatment of various types of headaches, such as migraine, tension type headaches and medication overuse headache, but also discusses the psychological aspects of headache. Recommendations from the US Headache Consortium have also been integrated into this edition.

I hope that these guidelines will assist doctors in adopting a rational approach in the management of headache disorders.

ASSOC PROFESSOR CHEW SUOK KAI
AG DIRECTOR OF MEDICAL SERVICES

Contents

Executive Summary of Recommendations

Details of recommendations can be found in the main text at the pages indicated.

Tension Type Headaches

Diagnosis and classification

GPP The clinical diagnosis of tension-type headaches should be guided by the International Headache Society criteria (pg 18).

GPP

Treatment

A&B Simple analgesics and nonsteroidal anti-inflammatory drugs are effective and may be used for acute treatment of tension type headaches at the following doses (pg 19):

Drugs	Dosage	Grade and level
Aspirin	500-1000 mg	**Grade A, Level 1+**
Paracetamol	1000 mg	**Grade A, Level 1+**
Ibuprofen	200-400 mg	**Grade A, Level 1+**
Ketoprofen	25-50 mg	**Grade A, Level 1+**
Naproxen	375-550 mg	**Grade B, Level 1+**
Diclofenac	25 mg	**Grade B, Level 1+**

A Caffeine can be used as an analgesic adjuvant for acute treatment of tension-type headache (pg 19).

Grade A, Level 1+

D Medication overuse should be avoided as it increases the risk of developing chronic daily headache (pg 19).

Grade D, Level 4

D Prophylactic treatment should be considered when headaches are frequent (pg 19).

Grade D, Level 4

A Amitriptyline 10-75 mg daily should be considered first for prophylactic treatment of tension-type headache (pg 19).

Grade A, Level 1++

B Other locally available medications with less evidence of efficacy which may be used for prophylactic treatment of tension-type headache include (pg 20):

Drugs	Dosage and frequency	Grade and level
Clomipramine	25-100 mg daily	**Grade B, Level 1+**
Maprotiline	25-75 mg daily	**Grade B, Level 1+**
Mirtazapine	15-30 mg daily	**Grade B, Level 1+**

GPP Medications for prophylactic treatment of tension-type headache should be started at low doses and titrated up to therapeutic doses to minimize adverse effects (pg 20).

GPP

Migraine

Diagnosis

C A validated 3-item questionnaire (ID-Migraine) covering disability, nausea and sensitivity to light should be used by primary care physicians if screening for migraine is required (pg 21).

Grade C, Level 3

Assessment of diability

B Standardized self-assessed questionnaires, e.g. MIDAS, HIT-6 (Appendix 1 & 2 on pages 30 and 31), to determine migraine disability should be administered where practicable (pg 21).

Grade B, Level 2++

Treatment principles

B Stratified care strategies (tailoring drugs to headache severity) should be used in preference to step-care strategies (using drugs in a progressive predetermined way) within or across attacks because the former provides significantly better clinical outcomes (pg 21).

Grade B, Level 1+

C Symptomatic medications should be administered early in an acute attack when pain is only mild to moderate (pg 22).

Grade C, Level 2+

D Over-the-counter paracetamol-based medication should be tried as first-line acute treatment of migraine (pg 22).

Grade D, Level 2+

D If paracetamol is ineffective in an individual patient, non-steroidal anti-inflammatory drugs should be tried. If non-steroidal anti-inflammatory drugs are ineffective or contraindicated, migraine-specific agents (triptans, ergotamine) should be tried (pg 22).

Grade D, Level 4

D A non-oral route of administration should be chosen for patients who present with early nausea or vomiting (pg 22).

Grade D, Level 4

D In some patients, concomitant treatment with an antiemetic and oral migraine medication may be appropriate (pg 22).

Grade D, Level 4

D The danger of medication-overuse headache developing with excessive use of symptomatic migraine medication should be emphasized to the patient (pg 23).

Grade D, Level 4

Pharmacological treatment of acute attacks

A,B&C Recommended dosage and frequency of various drugs used in the treatment of acute migraine episode (pg 23-24):

Drugs	Dosage and frequency	Grade and level
• **Non-steroidal anti-inflammatory drugs**		
Acetylsalicylic	600-800 mg 8 hrly/prn	**Grade B, Level 1+**
Ibuprofen	400-800 mg 8 hrly/prn	**Grade A, Level 1++**
Naproxen sodium	275-550 mg 6 hrly/prn	**Grade A, Level 1++**
Diclofenac	I/M 30 mg 6 hrly, up to 2 doses/day	**Grade B, Level 1+**
Diclofenac-K	50-100 mg stat	**Grade B, Level 1+**

Drugs	Dosage and frequency	Grade and level
• **Antiemetics**		
Metoclopramide	I/V 10 mg stat	**Grade B, Level 1+**
Procholorperazine	I/M 10-12.5 mg stat	**Grade B, Level 1+**
*Domperidone	20-40 mg	**Grade C, Level 2+**
• **Nonselective 5-hydroxytryptamine receptor agonists**		
Ergotamine	1-2 mg 1 hrly (up to total of 3 doses) + Caffeine	**Grade A, Level 1++**
• **Selective 5-hydroxytryptamine receptor agonists**		
Sumatriptan	S/C 6 mg stat Oral 50-100 mg 2 hrly (up to 2 doses/day)	**Grade A, Level 1++**
Zolmitriptan	2.5 mg 2 hrly (up to 2 doses/day)	**Grade A, Level 1++**
Naratriptan	2.5 mg 4 hrly (up to 2 doses/day)	**Grade A, Level 1++**
Eletriptan	40-80 mg 2 hrly (up to 2 doses/day)	**Grade A, Level 1++**

* Domperidone can be used as an adjunct to oral treatment when nausea is prominent.

Prophylaxis

D The following principles will enhance the success of prophylactic treatment (pg 24-25):

1. *Medication use:*

   A. Therapy may need to be started with the lowest effective dose, with a gradual upward titration of the dose until clinical benefits are achieved in the absence of adverse events or until limited by adverse events.
   B. Give each treatment an adequate trial of at least 1 month to establish benefit or lack thereof.
   C. Use of a long-acting formulation may improve compliance.

2. *Patient education:*

   A. Maximize compliance. Discuss with the patient the rationale for a particular treatment, when and how to use it, and what adverse events are likely.
   B. Address patient expectations. Discuss with the patient the expected benefits of therapy and how long it will take to achieve them.
   C. Create a formal management plan.

3. *Evaluation:*

   A. Patients with difficult headaches should be monitored with headache diaries. Diaries should be user-friendly and should measure attack frequency, severity, duration, disability, response to type of treatment, and adverse effects of medication.

Grade D, Level 4

D Daily migraine prophylactic treatment should be considered if 2 or more attacks a month occur (pg 25).

Grade D, Level 4

D The decision to start or withhold pharmacological prophylaxis should be individualized to the patient with migraine. Apart from the frequency of attacks, attack severity, failure or intolerance of acute treatments, concurrent medical conditions and prolonged aura may be relevant considerations (pg 25).

Grade D, Level 4

GPP If benefit is seen with the migraine prophylactic treatment, a course of medication ideally lasting at least 6 months should be given (pg 25).

GPP

A&B Recommended dosage and frequency of various drugs used in the prevention of recurrent migraine episodes (pg 26):

Drugs	Dosage and frequency	Grade and level
• **Beta blockers**		
Atenolol	50-100 mg om	**Grade A, Level 1++**
Propranolol	40-240 mg/day	**Grade A, Level 1++**
Metoprolol	50-300 mg daily	**Grade A, Level 1++**
Bisoprolol	5 mg/day	**Grade B, Level 1+**
• **Calcium channel blockers**		
Flunarizine	5-10 mg on	**Grade A, Level 1++**
Verapamil	240 mg om	**Grade A, Level 1++**
• **Serotonin receptor antagonists**		
Pizotifen	0.5-2 mg tds	**Grade A, Level 1++**
• **Antidepressants**		
Amitriptyline	10-150 mg on	**Grade A, Level 1++**
Fluoxetine	10-40 mg om	**Grade B, Level 1+**
Venlafaxine	75-150 mg/day	**Grade B, Level 1+**
• **Anticonvulsants**		
Sodium Valproate/ Valproic acid	500-1500 mg/day	**Grade A, Level 1++**
Topiramate	50-200 mg/day	**Grade A, Level 1++**
Gabapentin	1200 mg/day	**Grade B, Level 1+**
• **Non-steroidal anti-inflammatory**		
Naproxen sodium	550 mg bd	**Grade A, Level 1++**
• **Angiotensin blockers**		
Candesartan	16 mg/day	**Grade B, Level 1+**
Lisinopril	10-20 mg/day	**Grade B, Level 1+**
• **Others**		
Feverfew	50-82 mg/day	**Grade B, Level 1+**
Magnesium	400-600 mg/day	**Grade B, Level 1+**
Riboflavin	200 mg bd	**Grade B, Level 1+**
Coenzyme Q10	300 mg/day	**Grade B, Level 1+**
Botulinum toxin A	Botox 25U	**Grade A, Level 1+**
Butterbur (Petadolex)	50 mg-150/day	**Grade B, Level 1+**

A Homeopathic treatment should not be used for migraine prophylaxis (pg 27).

Grade A, Level 1+

Migraine in pregnancy and lactation

D Non-pharmacological management of migraine is preferred in pregnancy (pg 27).

Grade D, Level 2

D Biofeedback, relaxation training, and physical therapy may be tried in the treatment of migraine in pregnancy (pg 27).

Grade D, Level 3

The U.S. Food and Drug Administration classify drugs according to the foetal risk associated with their use.

Category A	-	safety established using human studies
Category B	-	presumed safety based on animal studies
Category C	-	adverse effects in animal studies, human effects unknown
Category D	-	known foetal risks
Category X	-	high foetal risks

GPP Drugs with a Category A or Category B rating should be used to manage migraine in pregnancy. Category C drugs should be considered after careful consideration of potential risks and benefits. Category D or Category X drugs should be avoided (pg 27).

GPP

GPP Therapy for migraine in women who are pregnant or lactating should be approached cautiously and initiated only with the consent of the patient after informed evaluation of the risks (pg 27).

GPP

D Paracetamol (Category B) is the drug of choice for treatment of acute migraine in pregnancy. Codeine which is catagory B drug becomes category D in 3rd trimester. Therefore, codeine is not recommended in the 3rd trimester (pg 27).

Grade D, Level 4

B Naproxen, ibuprofen and aspirin which are category B drugs becomes category D after 32 weeks of gestation. Hence, their use should be avoided after 32 weeks of gestation because of the risk of maternal or foetal bleeding and premature closure of the foetal ductus arteriosis (pg 28).

Grade B, Level 2+

D Intravenous magnesium sulphate 1g over one to three minutes up do a maximum of three IV injections given a week apart may be given to patients who experience frequent disabling headaches during pregnancy (pg 28).

Grade D, Level 3

D Intravenous prochlorperazine may be considered if extreme nausea and vomiting are present during migraine in pregnancy (pg 28).

Grade D, Level 3

D Fluoxetine, metoprolol and magnesium (category B) can be used as prophylactic treatment of migraine (pg 28).

Grade D, Level 4

B Valproic acid and its derivatives can be teratogenic and should be avoided. Lisinopril and candesartan should not be used during pregnancy (pg 28).

Grade B, Level 2+

D Acetaminophen, narcotics, diclofenac, ibuprofen, prochlorperazine, ß-blockers, and moderate caffeine may be considered for treating migraine in lactating women (pg 29).

Grade D, Level 4

Menstrual migraine

A&B Recommended dosage and frequency of various drugs used in the prophylaxis of menstrual migraine (where 90% of the headaches occur within the 48 hours prior to menses) (pg 29).

Drugs	Dosage and frequency	Grade and level
Oestrogen patches/gel*	50 ug - 1.5 mg/day	**Grade A, Level 1++**
Naproxen	275-550 mg bd	**Grade B, Level 1+**
Naratriptan	2.5 mg bd	**Grade B, Level 1+**
Magnesium	360 mg of magnesium pyrrolidone carboxylic acid	**Grade B, Level 1+**

*Migraine without aura is not an established contraindication to contraceptive use.

D Estrogen-containing oral contraceptives should be avoided in women with migraine with focal neurologic signs (pg 29).

Grade D, Level 4

Migraine in children less than 18 years old

A Acute migraine attacks in a child should be treated with paracetamol or ibuprofen. Oral triptans are not superior to placebo in paediatric migraine (pg 29).

Grade A, Level 1++

A Propanolol (60-120 mg/day) or flunarizine (5-10 mg/day) should be considered if migraine prophylaxis is required in a child (pg 30).

Grade A, Level 1+

B Amitriptyline or cyproheptadine may also be used for childhood migraine prophylaxis (pg 30).

Grade B, Level 2++

D Valproate, topiramate and levetiracetam may also be considered for childhood migraine prophylaxis on the basis of limited data (pg 30).

Grade D, Level 3

Headaches - Psychiatric and Psychological Aspects

Psychological management

D Patients with migraines and tension headaches should be evaluated for psychiatric co-morbidities such as anxiety or depression (pg 32).

Grade D, Level 4

D If hyperventilation accompanies tension headache and migraines, specific explanation and advice regarding anxiety disorder should be provided (pg 32).

Grade D, Level 3

Biofeedback

C Adjunctive psychological interventions should be considered in patients with headaches that are difficult to manage (pg 33).

Grade C, Level 2+

Secondary Headaches

Referral of patients with suspected secondary headaches

GPP All patients with suspected secondary headaches should be referred to a specialist (pg 34).

A referral is indicated if the following features are present:

1. Systemic symptoms such as fever or change in mental state
2. Neurological deficits
3. Sudden onset or maximum severity at onset
4. The first severe or worst headache in an individual's life
5. New persistent or progressively worsening headaches
6. Changed character in the normal established headache pattern
7. A new headache in middle age or later
8. Headache precipitated by coughing, sneezing, standing, bending forwards or recumbency

GPP

Headache attributed to chronic subdural haematoma

D Chronic subdural haematoma should always be considered in an elderly patient with a progressive headache, particularly if there is some cognitive impairment or focal signs (pg 36).

Grade D, Level 3

Investigations for Headaches

Neuroimaging

C Neuroimaging should be considered in patients with nonacute headache and an unexplained abnormal finding on neurological examination (pg 42).

Grade C, Level 2+

C Neuroimaging is not warranted for patients diagnosed with migraines and having a normal neurological examination (pg 43).

Grade C, Level 2+

Skull X-rays

D Skull X-rays are not recommended in the evaluation of headaches (pg 43).

Grade D, Level 3

Lumbar punctures

D Lumbar punctures are not recommended in the routine evaluation of headaches (pg 44).

Grade D, Level 3

GPP Neuroimaging is mandatory before lumbar puncture if a neurological deficit is present or increased intracranial pressure is suspected (pg 44).

GPP

Medication Overuse Headaches

Management

C For ergotamine-induced medication overuse headache**,** naproxen 500 mg twice daily may be used for pain reduction during the withdrawal period (pg 47).

Grade C, Level 2+

GPP During withdrawal, prophylactic treatment of the primary headache should be started concurrently (pg 47).

GPP

GPP Strictly limited doses of anti-emetic medication and analgesics may be used to treat break-through attacks (pg 47).

GPP

C Prednisolone 60 mg/day for 2 days, 40 mg/day for next 2 days and 20 mg/day for last 2 days and ranitidine 200 mg/day during the 6 days should be taken to alleviate headache intensity (pg 47).

Grade C, Level 2+

D Highly motivated patients who are not using barbiturates and tranquilizers (benzodiazepines) may be treated as outpatients. Patients who overuse drugs containing codeine, barbiturates or tranquilizers, those who are depressed or who have failed previously to withdraw as outpatients, would be candidates for hospitalized management (pg 47).

Grade D, Level 4

Prevention

GPP The best strategy to reduce the prevalence of medication overuse headache is to prevent the development of medication overuse headache in the first place. Doctors should set maximal monthly dosages for headache abortive drugs. Maximum doses and frequencies of types of medications that cause medication overuse headache: (pg 48).

Medication	Maximum Dose
Simple analgesics (aspirin and paracetamol)	Intake < 10 days per month
Combination analgesics (caffeine or barbiturate-containing drugs)	≤ 3 tablets/day
Opioids	≤ 1 tablet /day
Ergotamine (oral)	Max 4 mg/attack and ≤ 20 mg/month
Serotonin 5-$HT_{1B/1D}$ receptor agonists ("triptans")	< 2 doses/attack and < 6 doses per month

GPP

D Patients should be educated on the risk of medication overuse headache (pg 49).

Grade D, Level 4

D A headache diary is a useful tool for patients and their doctors to monitor the frequency of headaches and medication usage (pg 49).

Grade D, Level 4

Use of Acupuncture in the Management of Migraine and Tension Headache

Evidence for efficacy

A Acupuncture may be considered for headache prophylactic treatment (pg 51).

Grade A, Level 1++

Cautions

GPP Caution should be exercised in using acupuncture in the following conditions (pg 51):

- Patients with severe bleeding disorders or on anti-coagulant treatment – a contraindication for needle acupuncture
- Pregnancy
- Presence of a cardiac pacemaker – a contraindication for electrical stimulation
- Indwelling needles should not be used in patients at risk from bacteremia, such as asplenic patients or those who may become neutropenic

GPP

1 Introduction

1.1 Headaches in Singapore

Headaches are one of life's most common medical afflictions. Studies have shown that up to 90% of the general population suffer from headaches at some point in life. Here in Singapore, a large-scale epidemiological study[1] found that the overall lifetime prevalence of headache here was 82.7%, which did not vary between racial groups. Of these, migraines afflicts up to 9.3% of people, 39.9% suffer from episodic tension type headache and 2.4% from chronic tension type headache. Headaches could not be classified in 31.2% of the respondents.

The modal age of headache onset in all races was in the second decade and was similar in all races. Headache morbidity was independent of age, sex, income level, marital status, shift duties, and educational level, and correlated only with race and a positive family history of severe headache. Non-Chinese compared with Chinese were more likely to suffer from severe headaches, seek medical attention and to require medical leave for their symptoms. Non-Chinese also had more migrainous headaches than Chinese did.

The study also found that elevated blood pressure, poor visual acuity, and decreased hours of sleep did not correlate with increased frequency, intensity, or duration of headaches. Individuals who performed shift work had more frequent, although not more intense or long-lasting, headaches. High or low income had no effect on headache prevalence or severity. In another early study done on National University of Singapore undergraduates,[2] 10.9% had migraine without aura, 29.8% had tension-type headaches, 1.1% had migraine with aura, and in 56.3% the headache could not be classified. The lifetime prevalence of headache in this population was 98.1%.

1.2 Aim and scope of guidelines

These guidelines were developed to raise awareness of the different forms of headaches and the importance of making a correct diagnosis. A correct diagnosis will lead to appropriate management and speedy control of the patients' headaches which will in turn reduce disability caused by headaches. We discuss here the mainstay treatment for the various headaches as well as alternative treatments such as acupuncture. The dangers of medication overuse headaches are also highlighted.

1.3 Target group

These guidelines will benefit all health care professionals, especially primary care physicians, who care for the majority of headache sufferers. More intractable headaches which require specialized care would not be discussed in these guidelines and should be left to the appropriate specialist care.

1.4 Guideline development

These guidelines have been produced by a committee of neurologists, psychiatrists and family practitioners appointed by the Ministry of Health. This allows a multi-disciplinary approach to this disorder. They were developed using the best available current evidence and expert opinion.

1.5 What's new in the revised guidelines

The following is a list of major changes or additions to the guidelines:

- Recommendations from the US Headache Consortium have been integrated into these guidelines
- A section on migraine has been added detailing the various forms of migraine and its treatment modalities.
- Psychological aspects of headaches have also been added to provide a psychological viewpoint
- The section on secondary headaches has been expanded

- Investigations for headaches have been streamlined for clarity
- A new section has been added on tension type headaches
- The dangers of medication overuse headaches are deemed important enough to warrant a section on their own
- Alternative headache treatments, specifically acupuncture, have been added

1.6 Review of guidelines

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supercede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review five years after publication, or if new evidence appears that requires substantive changes to the recommendations.

2 Tension Type Headaches

2.1 Diagnosis and classification

GPP The clinical diagnosis of tension-type headaches should be guided by the International Headache Society criteria.[3]

GPP

The clinical characteristics of tension-type headaches as defined by the International Headache Society include (a) bilateral location (b) pressing/tightening (non-pulsating) quality (c) mild or moderate in intensity (d) not aggravated by routine physical activity such as walking or climbing stairs. There is no associated nausea or vomiting and no more than one symptom of photophobia or phonophobia. A diagnosis of tension type headache should be made only when secondary headaches are considered unlikely.

Classifying tension-type headaches into the subtypes helps guide management. They can be classified according to the number of headache days a month, as episodic (≤ 14 day/month) and chronic headaches (> 14 day/month on average and > 3 months).[3]

2.2 Treatment

Tension-type headaches respond to pharmacological as well as non-pharmacological treatment alone or in combination.[4] The non-pharmacological treatment will be discussed in a separate section.

Pharmacological treatment can be divided into acute and prophylactic. Acute treatment aims at aborting the headache symptoms while prophylactic treatment aims to decrease the frequency and intensity of headaches.

2.2.1 Pharmacological treatment of acute attacks

A&B Simple analgesics and nonsteroidal anti-inflammatory drugs are effective and may be used for acute treatment of tension type headaches at the following doses:[5-26]

Drugs	Dosage	Grade and level
Aspirin	500-1000 mg	**Grade A, Level 1+**
Paracetamol	1000 mg	**Grade A, Level 1+**
Ibuprofen	200-400 mg	**Grade A, Level 1+**
Ketoprofen	25-50 mg	**Grade A, Level 1+**
Naproxen	375-550 mg	**Grade B, Level 1+**
Diclofenac	25 mg	**Grade B, Level 1+**

There is, at present, limited data on the efficacy of selective cyclooxygenase-2 inhibitors for treatment of tension type headaches.[27]

A Caffeine can be used as an analgesic adjuvant for acute treatment of tension-type headache.[15,18,23,28]

Grade A, Level 1+

D Medication overuse should be avoided as it increases the risk of developing chronic daily headache.[29]

Grade D, Level 4

2.2.2 Prophylaxis

D Prophylactic treatment should be considered when headaches are frequent.[3]

Grade D, Level 4

A Amitriptyline 10-75 mg daily should be considered first for prophylactic treatment of tension-type headache.[24,30-34]

Grade A, Level 1++

The use of prophylactic amitriptyline is supported by evidence from randomised controlled trials.

B Other locally available medications with less evidence of efficacy which may be used for prophylactic treatment of tension-type headache include:

Drugs	Dosage and frequency	Grade and level
Clomipramine	25-100 mg daily	**Grade B, Level 1+**
Maprotiline	25-75 mg daily	**Grade B, Level 1+**
Mirtazapine	15-30 mg daily	**Grade B, Level 1+**

Currently, only evidence from case series exists for efficacy of venlafaxine in prophylactic treatment of tension-type headache. [38]

GPP Medications for prophylactic treatment of tension-type headache should be started at low doses and titrated up to therapeutic doses to minimize adverse effects.

GPP

Presently, there is conflicting evidence for the efficacy of selective serotonin reuptake inhibitors in prophylactic treatment of tension type headaches.[34,39-42]

Although earlier open label studies reported a beneficial effect of botulinum toxin on tension-type headache, recent randomised control studies did not find evidence of efficacy.[43-47]

3 Migraine

3.1 Diagnosis

C A validated 3-item questionnaire (ID-Migraine) covering disability, nausea and sensitivity to light should be used by primary care physicians if screening for migraine is required.[48-50]

Grade C, Level 3

3.2 Assessment of disability

B Standardized self-assessed questionnaires, e.g. MIDAS, HIT-6 (Appendix 1 & 2 on pages 30 and 31), to determine migraine disability should be administered where practicable.

Grade B, Level 2++

Disability assessments assist in migraine management by allowing stratified care based on headache disability and are useful ways to help physicians determine and monitor the impact of migraine on their patients. Both MIDAS and HIT-6 scores are only available in English for the Singaporean population.[51-60]

3.3 Treatment principles

Acute attacks of migraine should be effectively treated to reduce use of healthcare resources and disability, increase productivity and improve health-related quality of life.[61-63]

B Stratified care strategies (tailoring drugs to headache severity) should be used in preference to step-care strategies (using drugs in a progressive predetermined way) within or across attacks because the former provides significantly better clinical outcomes.[64]

Grade B, Level 1+

Patients and doctors should be free to use different medications (as below) that effectively treat the acute symptoms of migraine.

C Symptomatic medications should be administered early in an acute attack when pain is only mild to moderate.[65-68]

Grade C, Level 2+

D Over-the-counter paracetamol-based medication should be tried as first-line acute treatment of migraine.

Grade D, Level 2+

Many migraine sufferers in Singapore are satisfied with over-the-counter medication for treatment of their migraine.[69]

D If paracetamol is ineffective in an individual patient, non-steroidal anti-inflammatory drugs should be tried. If non-steroidal anti-inflammatory drugs are ineffective or contraindicated, migraine-specific agents (triptans, ergotamine) should be tried.[70]

Grade D, Level 4

D A non-oral route of administration should be chosen for patients who present with early nausea or vomiting.[70]

Grade D, Level 4

D In some patients, concomitant treatment with an antiemetic and oral migraine medication may be appropriate.[70]

Grade D, Level 4

Triptans are ineffective in treating aura or preventing headache when given in the aura phase of migraine with aura.[71,72]

Despite their high cost, triptans may be cost-effective, but formal cost-effectiveness evaluations have not been done in Singapore.[73,74]

Patients who fail to obtain adequate relief of symptoms with one triptan may be successfully treated with a different triptan.[75,76]

D The danger of medication-overuse headache developing with excessive use of symptomatic migraine medication should be emphasized to the patient.[77-79]

Grade D, Level 4

3.4 Pharmacological treatment of acute attacks

A,B&C Recommended dosage and frequency of various drugs used in the treatment of acute migraine episode:

Drugs	Dosage and frequency	Grade and level
• **Non-steroidal anti-inflammatory drugs**		
Acetylsalicylic acid[80,81]	600-800 mg 8 hrly/prn	**Grade B, Level 1+**
Ibuprofen[82,83]	400-800 mg 8 hrly/prn	**Grade A, Level 1++**
Naproxen sodium[84,85]	275-550 mg 6 hrly/prn	**Grade A, Level 1++**
Diclofenac[86]	I/M 30 mg 6 hrly, up to 2 doses/day	**Grade B, Level 1+**
Diclofenac-K[87]	50-100 mg stat	**Grade B, Level 1+**
• **Antiemetics**		
Metoclopramide[88-91]	I/V 10 mg stat	**Grade B, Level 1+**
Procholorperazine[92,93]	I/M 10-12.5 mg stat	**Grade B, Level 1+**
*Domperidone[94,95]	20-40 mg	**Grade C, Level 2+**
• **Nonselective 5-hydroxytryptamine receptor agonists**		
Ergotamine[96-101]	1-2 mg 1 hrly (up to total of 3 doses) + Caffeine	**Grade A, Level 1++**

* Domperidone can be used as an adjunct to oral treatment when nausea is prominent.

Drugs	Dosage and frequency	Grade and level
• **Selective 5-hydroxytryptamine receptor agonists**		
Sumatriptan[102-115]	S/C 6 mg stat Oral 50-100 mg 2 hrly (up to 2 doses/day)[116-126]	**Grade A, Level 1++**
Zolmitriptan[127-129]	2.5 mg 2 hrly (up to 2 doses/day)	**Grade A, Level 1++**
Naratriptan[130,131]	2.5 mg 4 hrly (up to 2 doses/day)	**Grade A, Level 1++**
Eletriptan[132-135]	40-80 mg 2 hrly (up to 2 doses/day)	**Grade A, Level 1++**

3.5 Prophylaxis

The goals of migraine preventive therapy are to:

(1) reduce attack frequency, severity, and duration
(2) improve function and reduce disability.
(3) improve responsiveness to treatment of acute attacks

D The following principles will enhance the success of prophylactic treatment:[136]

1. *Medication use:*

   A. Therapy may need to be started with the lowest effective dose, with a gradual upward titration of the dose until clinical benefits are achieved in the absence of adverse events or until limited by adverse events.
   B. Give each treatment an adequate trial of at least 1 month to establish benefit or lack thereof.
   C. Use of a long-acting formulation may improve compliance.

2. *Patient education:*

   A. Maximize compliance. Discuss with the patient the rationale for a particular treatment, when and how to use it, and what adverse events are likely.
   B. Address patient expectations. Discuss with the patient the expected benefits of therapy and how long it will take to achieve them.
   C. Create a formal management plan.

3. *Evaluation:*

   A. Patients with difficult headaches should be monitored with headache diaries. Diaries should be user-friendly and should measure attack frequency, severity, duration, disability, response to type of treatment, and adverse effects of medication.

Grade D, Level 4

D Daily migraine prophylactic treatment should be considered if 2 or more attacks a month occur.[137]

Grade D, Level 4

D The decision to start or withhold pharmacological prophylaxis should be individualized to the patient with migraine. Apart from the frequency of attacks, attack severity, failure or intolerance of acute treatments, concurrent medical conditions and prolonged aura may be relevant considerations.[138]

Grade D, Level 4

GPP If benefit is seen with the migraine prophylactic therapy, a course of medication ideally lasting at least 6 months should be given.

GPP

A&B Recommended dosage and frequency of various drugs used in the prevention of recurrent migraine episodes:

Drugs	Dosage and frequency	Grade and level
• **Beta blockers**		
Atenolol[139,140]	50-100 mg om	**Grade A, Level 1++**
Propranolol[141-152]	40-240 mg/day	**Grade A, Level 1++**
Metoprolol[153-158]	50-300 mg daily	**Grade A, Level 1++**
Bisoprolol[159]	5 mg/day	**Grade B, Level 1+**
• **Calcium channel blockers**		
Flunarizine[160-167]	5-10 mg on	**Grade A, Level 1++**
Verapamil[168-170]	240 mg om	**Grade A, Level 1++**
• **Serotonin receptor antagonists**		
Pizotifen[171-182]	0.5-2 mg tds	**Grade A, Level 1++**
• **Antidepressants**		
Amitriptyline[183-186]	10-150 mg on	**Grade A, Level 1++**
Fluoxetine[187,188]	10-40 mg om	**Grade B, Level 1+**
Venlafaxine[189,190]	75-150 mg/day	**Grade B, Level 1+**
• **Anticonvulsants**		
Sodium Valproate/ Valproic acid[191-194]	500-1500 mg/day	**Grade A, Level 1++**
Topiramate[195-201]	50-200 mg/day	**Grade A, Level 1++**
Gabapentin.[202,203]	1200 mg/day	**Grade B, Level 1+**
• **Non-steroidal anti-inflammatory**		
Naproxen sodium[204-209]	550 mg bd	**Grade A, Level 1++**
• **Angiotensin blockers**		
Candesartan[210]	16 mg/day	**Grade B, Level 1+**
Lisinopril[211]	10-20 mg/day	**Grade B, Level 1+**
• **Others**		
Feverfew[212-215]	50-82 mg/day	**Grade B, Level 1+**
Magnesium[216-218]	400-600 mg/day	**Grade B, Level 1+**
Riboflavin[219-221]	200 mg bd	**Grade B, Level 1+**
Coenzyme Q10[222]	300 mg/day	**Grade B, Level 1+**
Botulinum toxin A[223-226]	Botox 25U	**Grade A, Level 1+**
Butterbur (Petadolex) [227-229]	50 mg-150/day	**Grade B, Level 1+**

A Homeopathic treatment should not be used for migraine prophylaxis.[230,231]

Grade A, Level 1+

3.6 Migraine in pregnancy and lactation

D Non-pharmacological management of migraine is preferred in pregnancy.[232]

Grade D, Level 2

D Biofeedback, relaxation training, and physical therapy may be tried in the treatment of migraine in pregnancy.[233,234]

Grade D, Level 3

The U.S. Food and Drug Administration classify drugs according to the foetal risk associated with their use.

Category A - safety established using human studies
Category B - presumed safety based on animal studies
Category C - adverse effects in animal studies, human effects unknown
Category D - known foetal risks
Category X - high foetal risks

GPP Drugs with a Category A or Category B rating should be used to manage migraine in pregnancy. Category C drugs should be considered after careful consideration of potential risks and benefits. Category D or Category X drugs should be avoided.

GPP

GPP Therapy for migraine in women who are pregnant or lactating should be approached cautiously and initiated only with the consent of the patient after informed evaluation of the risks.

GPP

3.6.1 Acute treatment of migraine in pregnancy and lactation

D Paracetamol (Category B) is the drug of choice for treatment of acute migraine in pregnancy. Codeine which is catagory B drug becomes category D in 3rd trimester.

Therefore, codeine is not recommended in the 3rd trimester.[235]

Grade D, Level 4

B Naproxen, ibuprofen and aspirin which are category B drugs becomes category D after 32 weeks of gestation. Hence, their use should be avoided after 32 weeks of gestation because of the risk of maternal or foetal bleeding and premature closure of the foetal ductus arteriosis.

Grade B, Level 2+

The teratogenic effects of triptans are unknown. Available data from an international registry do not show any increase of birth defects with the inadvertent use of Sumatriptan in the first trimester.[236]

D Intravenous magnesium sulphate 1g over one to three minutes up do a maximum of three IV injections given a week apart may be given to patients who experience frequent disabling headaches during pregnancy.[237]

Grade D, Level 3

D Intravenous prochlorperazine may be considered if extreme nausea and vomiting are present during migraine in pregnancy.[238]

Grade D, Level 3

3.6.2 Prophylactic treatment of migraine in pregnancy

D Fluoxetine, metoprolol and magnesium (category B) can be used as prophylactic treatment of migraine.[239-241]

Grade D, Level 4

B Valproic acid and its derivatives can be teratogenic and should be avoided. Lisinopril and candesartan should not be used during pregnancy.[242,243]

Grade B, Level 2+

3.6.3 Treatment of migraine in lactation

D Acetaminophen, narcotics, diclofenac, ibuprofen, prochlorperazine, ß-blockers, and moderate caffeine may be considered for treating migraine in lactating women.[244]

Grade D, Level 4

3.7 Menstrual migraine

A&B Recommended dosage and frequency of various drugs used in the prophylaxis of menstrual migraine (where 90% of the headaches occur within the 48 hours prior to menses).

Drugs	Dosage and frequency	Grade and level
Oestrogen patches/gel*[245-247]	50 ug - 1.5 mg/day	**Grade A, Level 1++**
Naproxen[248]	275-550 mg bd	**Grade B, Level 1+**
Naratriptan[249]	2.5 mg bd	**Grade B, Level 1+**
Magnesium[250]	360 mg of magnesium pyrrolidone carboxylic acid	**Grade B, Level 1+**

* Migraine without aura is not an established contraindication to contraceptive use.

D Estrogen-containing oral contraceptives should be avoided in women with migraine with focal neurologic signs.[251]

Grade D, Level 4

3.8 Migraine in children less than 18 years old

A Acute migraine attacks in a child should be treated with paracetamol or ibuprofen. Oral triptans are not superior to placebo in paediatric migraine.[252-254]

Grade A, Level 1++

A Propanolol (60-120 mg/day) or flunarizine (5-10 mg/day) should be considered if migraine prophylaxis is required in a child.[255,256]

Grade A, Level 1+

B Amitriptyline or cyproheptadine may also be used for childhood migraine prophylaxis.[255,256]

Grade B, Level 2++

D Valproate, topiramate and levetiracetam may also be considered for childhood migraine prophylaxis on the basis of limited data.[257-261]

Grade D, Level 3

Appendix 1 The Migraine Disability Assessment (MIDAS) questionnaire to determine migraine disability

Items

1. On how many days in the last 3 months did you miss work or school because of your headaches?
2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches? *(Do not include days you counted in question 1 where you missed work or school)*
3. On how many days in the last 3 months did you not do household work because of your headaches?
4. How many days in the last 3 months was your productivity in household work reduced by half or more because of your headaches? *(Do not include days you counted in question 3 where you did not do household work)*
5. On how many days in the last three months did you miss family, social or leisure activities because of your headaches?

Total score: add answers to the questions above

Interpretation

Grade	Definition	Score
I	Minimal or infrequent disability	0-5
II	Mild or infrequent disability	6-10
III	Moderate disability	11-20
IV	Severe disability	21+

Source: Lipton R. Migraine Disability Assessment Questionnaire (cited 19 Sep 07). Available from: http://www.midas-migraine.net/edu/question/Default.asp.

Appendix 2 Headache Impact Test Questionnaire (HIT-6) to determine migraine disability

Rated on 5-point scale of :
"Never", "rarely", "sometimes", "very often", "always"

- "Never" scores are worth 6 points each
- "Rarely" scores are worth 8 points each
- "Sometimes" scores are worth 10 points each
- "Very often" scores are worth 11 points each
- "Always" scores are worth 13 points each

The range of scores = 36-78 points.

Items

1. When you have headaches, how often is the pain severe?
2. How often do headaches limit your ability to do usual daily activities including household work, work, school, or social activities?
3. When you have a headache, how often do you wish you could lie down?
4. In the past 4 weeks, how often have you felt too tired to do work or daily activities because of your headaches?
5. In the past 4 weeks, how often have you felt fed up or irritated because of your headaches?
6. In the past 4 weeks, how often did headaches limit your ability to concentrate on work or daily activities?

Interpretation:
< 48 points : Little/no headache impact
50-54 points: Some impact
56-58 points: Substantial impact
≥ 60 points : Very severe impact

Source: Headache Inpact Test Questionnaire (cited 19 Sep 07). Available from: http://www.headtalk.com/Hit6Quiz/Hit6QuizIntro.jsp

4 Headaches - Psychiatric and Psychological Aspects

4.1 Psychiatric and psychological aspects

Psychiatric comorbidity such as depression and anxiety is common in chronic daily headache.[262]

4.2 Psychological management

D Patients with migraines and tension headaches should be evaluated for psychiatric co-morbidities such as anxiety or depression.[263]

Grade D, Level 4

The doctor and patient must invest time and patience in the initial discussion. The goals of this initial discussion are to provide patients with a chance to unburden themselves, the opportunity to gain objective advice, and the knowledge that their problem is not unique and has been overcome by many others.

Although physicians generally agree that psychological factors are important in triggering headache, few carefully controlled trials demonstrate the effectiveness of psychological management in general and the comparative merits of the various forms of treatment used.

D If hyperventilation accompanies tension headache and migraines, specific explanation and advice regarding anxiety disorder should be provided.[264]

Grade D, Level 3

4.3 Combined pharmacotherapy and psychological intervention

Evidence from mostly uncontrolled studies indicates that combination pharmacotherapy with cognitive behavioural therapy or stress management therapy is more effective than pharmacotherapy alone.[262,265,266]

4.4 Hypnosis

Hypnosis results in reduced frequency, duration, and intensity of chronic tension headache compared with a control group.[267]

4.5 Biofeedback

Biofeedback is beneficial in adult and child migraine patients. In general, meta-analysis of clinical trials show that biofeedback, relaxation training and hypnosis treatment yield effects comparable to prophylactic medication, i.e., average reduction of attacks around 45%, as compared to 14% placebo effects.[268]

C Adjunctive psychological interventions should be considered in patients with headaches that are difficult to manage.

Grade C, Level 2+

5 Secondary Headaches

5.1 Secondary headaches

This section highlights the relatively common, potentially treatable, and sinister secondary headaches. It is adapted from the International Headache Society's *The International Classification of Headache Disorders (second edition)*.[269]

Secondary headaches refer to headaches associated with a known organic cause. The characteristics of most secondary headaches are either poorly described or lacking in specific features. It is diagnosed by its close temporal relation to a disorder that is known to cause headache. The headache usually improves or resolves within 3 month following successful treatment or spontaneous remission of the causative disorder.

5.2 Referral of patients with suspected secondary headaches

GPP All patients with suspected secondary headaches should be referred to a specialist.

A referral is indicated if the following features are present:

1. Systemic symptoms such as fever or change in mental state
2. Neurological deficits
3. Sudden onset or maximum severity at onset
4. The first severe or worst headache in an individual's life
5. New persistent or progressively worsening headaches
6. Changed character in the normal established headache pattern
7. A new headache in middle age or later
8. Headache precipitated by coughing, sneezing, standing, bending forwards or recumbency

GPP

5.3 Chronic post-traumatic headache

Chronic post-traumatic headache is associated with any of the following features: loss of consciousness, drowsiness, post-traumatic amnesia, or imaging evidence of a traumatic brain lesion. The non-descript headache develops within 7 days after head trauma or after regaining consciousness following head trauma and persists for more than 3 months after head trauma. Post-traumatic headache is often part of the post-traumatic syndrome which includes symptoms such as disequilibrium, poor concentration, decreased work ability, irritability, depressive mood, and sleep disturbances.[269-273]

5.4 Chronic headache attributed to whiplash injury

Following a whiplash injury caused by sudden acceleration and deceleration movement of the neck, headache develops within 7 days after the injury and lasts for more than 3 months. Chronic headache secondary to whiplash injury does not have special characteristics and is often part of the post-traumatic syndrome associated with cognitive, behavioural, and affective disorders.[269,274-276]

5.5 Headache attributed to epidural haematoma

Epidural hematoma occurs within hours of moderately severe head trauma. The associated headache occurs within 24 hours of the hematoma. It is always associated with focal signs and impairment of consciousness. The headache usually resolves within 3 months after evacuation of the hematoma.[269,277]

5.6 Headache attributed to subdural haematoma

The headache following a subdural hematoma has an acute onset and may be progressive. It develops within 24 to 72 hours after the development of the hematoma and resolves within 3 months of evacuation of the hematoma.

Sometimes the causative head trauma is trivial and forgotten by the patient.[269,278]

D Chronic subdural haematoma should always be considered in an elderly patient with a progressive headache, particularly if there is some cognitive impairment or focal signs.

Grade D, Level 3

5.7 Headache attributed to intracerebral hemorrhage

Headache caused by intracerebral hemorrhage occurs acutely. It is associated with focal deficits or coma.[269]

5.8 Headache attributed to subarachnoid hemorrhage

The headache of subarachnoid hemorrhage is a thunderclap headache – one in which the maximum intensity of the pain is present at its onset. It is often unilateral at onset and associated with nausea, vomiting, impaired consciousness, and neck stiffness. The headache usually resolves within 1 month. Diagnosis is confirmed by CT scan or MRI with fluid-attenuated inversion recovery sequences. If neuroimaging is equivocal, lumbar puncture is advised.[269,279,280]

5.9 Headache attributed to cerebral venous thrombosis

Severe headache occurs in about 90% cases of CVT. It is usually diffuse and progressive. It can also be unilateral and abrupt in onset. Over 90% of cases of cerebral venous thrombosis are associated with focal neurological deficits, seizures, or signs of intracranial hypertension. Diagnosis is made by MRI plus MR venography or CT scan plus CT venography. In equivocal cases, intra-arterial angiography is undertaken.[269,281]

5.10 Headache attributed to giant cell arteritis

Giant cell arteritis usually occurs in a patient over 60 years of age. It causes a persistent headache. It is normally associated with a swollen, tender superficial temporal artery with elevated ESR or CRP. It is confirmed by temporal artery biopsy demonstrating giant cell arteritis. The major complication is blindness secondary to anterior ischemic optic neuropathy, sometimes preceded by amaurosis fugax. This is usually followed by blindness of the other eye within 1 week. The headache resolves or improved with 3 days of high-dose steroid treatment.[269,282]

5.11 Headache attributed to idiopathic intracranial hypertension

Idiopathic intracranial hypertension commonly occurs in young obese women. It causes a diffuse and non-pulsating daily headache that is aggravated by coughing or straining. Neurological examination shows papilledema, an enlarged blind spot, visual field defect, or abducens nerve palsy. Examination is sometimes normal. Suspicious symptoms include tinnitus, transient visual obscurations and diplopia. The diagnosis is confirmed by lumbar puncture showing increased CSF pressure of more than 200 mmH_2O in the supine position in the non-obese and more than 250 mmH_2O in the obese. Headache improves after withdrawal of CSF to reduce pressure to 120-170 mm H_2O and resolves within 72 hours of persistent normalisation of intracranial pressure. It is important to exclude venous sinus thrombosis, metabolic, toxic, or hormonal causes before diagnosing idiopathic intracranial hypertension.[269,283-285]

5.12 Headache attributed to intracranial hypertension secondary to hydrocephalus

Headache secondary to hydrocephalus presents in much the same way as in idiopathic intracranial hypertension. Neuroimaging shows ventricular enlargement. Headache resolves within 72 hours of normalisation of CSF pressure.[269]

5.13 Headache attributed to spontaneous (or idiopathic) low cerebrospinal fluid pressure

Low cerebrospinal fluid pressure causes a distinct headache. The headache worsens within 15 minutes after sitting or standing and improves within 15 minutes of recumbency. It is associated with neck stiffness, tinnitus, hyperacusis, photophobia, or nausea. There is usually a history of trauma to the back or of recent lumbar puncture. Sometimes, there is history of vigorous coughing or exposure to sudden drop in atmospheric pressure. CSF pressure is less than 60 mmH_2O in sitting position. MRI may show pachymeningeal enhancement. CSF leakage can be seen on conventional myelography, CT myelography or cisternography. The headache resolves within 72 hours after successful epidural blood patching.[269,286-289]

5.14 Headache attributed directly to neoplasm

The headache associated with intracranial neoplasm is usually progressive, localised, worse in the morning, and aggravated by coughing or bending forward. The headache resolves within 7 days after treatment of the neoplasm with surgery or corticosteroids.[269,290]

5.15 Nitric oxide (NO) donor-induced headache

The headache induced by nitric oxide donors (e.g. amyl nitrate, glyceryl trinitrate, and isosorbibe mono- or dinitrate) has a pulsating quality, is located over bilateral frontotemporal region, and is aggravated by physical activity. It occurs immediately within 10 minutes after absorption of an NO donor and resolves within 1 hour after release of NO has ended. With chronic drug use tolerance develops within a week. With intermittent use the headache continues. An NO donor may also induce a delayed headache that occurs after NO is cleared from the blood and resolves within 72 hours after single exposure.[269,291]

5.16 Phosphodiesterase (PDE) inhibitor-induced headache

PDE inhibitors induce a pulsating headache located over the bilateral frontotemporal region and is aggravated by physical activity. The headache develops within 5 hours of PDE inhibitor intake and resolves within 72 hours. Examples of PDE inhibitors are dipyridamole and sildenafil.[269,292]

5.17 Headache attributed to bacterial meningitis

Headache is the commonest symptom of bacterial meningitis. The pain is diffuse and progressive and is associated with fever, nausea, photophobia and/or phonophobia, or neck stiffness. The diagnosis is confirmed by characteristic CSF examination and culture. The headache resolves within 3 months of treatment.[269,293]

5.18 Headache attributed to lymphocytic meningitis

Lymphocytic meningitis is associated with an acute-onset severe headache accompanied by nuchal rigidity, fever, nausea, photophobia and/or phonophobia. Infection is suspected from the CSF picture. Headache resolves within 3 months after successful treatment or spontaneous remission of the infection.[269,294]

5.19 Headache attributed to encephalitis

The headache is diffuse with increasing severity and associated with neurological symptoms and signs of acute encephalitis, fever, nausea, photophobia or phonophobia. The diagnosis is confirmed by EEG, neuroimaging, and laboratory investigations. The headache resolves within 3 months after successful treatment or spontaneous remission of the infection.[269,295,296]

5.20 Sleep apnoea headache

Patients with sleep apnoea (respiratory disturbance index ≥5) may develop a bilateral, pressing headache that occurs on more than 15 days per month. The headache is present upon wakening and resolves within 30 minutes. Lasting relief is achieved after effective treatment of sleep apnoea. It is unclear whether the headache is related to hypoxia, hypercapnia or disturbance of sleep.[269,297,298]

5.21 Headache attributed to phaeochromocytoma

The headache develops concomitantly with an abrupt rise in blood pressure and resolves or markedly improves within 1 hour of normalisation of blood pressure. It is associated with sweating, palpitations, anxiety, or pallor. The diagnosis of phaeochromocytoma is confirmed by analysing 24-hour urine sample for elevation of catecholamines or catecholamine metabolites.[269,299,300]

5.22 Headache attributed to hypertensive crisis

A paroxysmal rise in systolic pressure (>160 mmHg) or diastolic pressure (>120 mmHg) can induce a severe bilateral, pulsating headache without clinical features of hypertensive encephalopathy. The headache resolves within 1 hour after normalisation of blood pressure.[269,301,302]

5.23 Cardiac cephalgia

A severe headache and nausea may be precipitated by exertion in patients with acute myocardial ischemia. Diagnosis requires documentation of headache and simultaneous cardiac ischemia during treadmill or nuclear cardiac stress testing.[269,303,304]

5.24 Headache attributed to acute glaucoma

Acute glaucoma can produce pain in and behind or above the eye. It is associated with conjunctival injection, clouding of the cornea, or visual disturbances. The pain

resolves within 72 hours of effective treatment of glaucoma.[269,305,306]

5.25 Headache attributed to rhinosinusitis

Rhinosinusitis causes frontal headache accompanied by pain in one or more regions of the face, ears or teeth. Diagnosis requires clinical, nasal endoscopic, CT and/or MRI imaging and/or laboratory evidence of acute or acute-on-chronic rhinosinusitis. The clinical features include purulent discharge from the nasal cavity, nasal obstruction, hyposmia, and fever. The headache and facial pain resolve within 7 days after remission or successful treatment of the rhinosinusitis. Chronic sinusitis is not a cause of headache or facial pain.[269,307,308]

5.26 Headache or facial pain attributed to temporomandibular joint (TMJ) disorder

TMJ disorder presents with recurrent pain in one or more regions of the head or face. The pain is precipitated by jaw movements or chewing of hard or tough food. There is reduced range of or irregular jaw opening. There may be noise from one or both TMJs during jaw movements. The joint capsule(s) of one or both TMJs may be tender. The headache resolves within 3 months after successful treatment of the TMJ disorder.[269,309,310]

6 Investigations for Headaches

6.1 Neuroimaging

In making decisions about neuroimaging in headaches, certain principles apply:

1. Testing should be avoided if it will not lead to a change in management
2. Testing is not recommended if the individual is not significantly more likely than anyone else in the general population to have an abnormality
3. Testing that normally may not be recommended as a population policy may make sense at an individual level if resources are available. For example, exceptions can be considered for patients who are disabled by their fear of serious pathology, or for whom the provider is suspicious even in the absence of known predictors of abnormalities on neuroimaging studies (red flags).

C Neuroimaging should be considered in patients with nonacute headache and an unexplained abnormal finding on neurological examination.

Grade C, Level 2+

An abnormal neurological examination increases the likelihood of finding significant intracranial pathology (e.g. brain tumor, arteriovenous malformation, hydrocephalus) on neuroimaging. The absence of any abnormalities on neurological examination reduces the odds of finding a significant abnormality on imaging.[311-315]

There is insufficient evidence to make specific recommendations regarding neuroimaging in the presence of focal neurological symptoms (e.g. hemisensory disturbance) without clinical deficits.[316]

Symptoms such as headache causing wakening from sleep, headache worsened by Valsalva maneuver, headache causing wakening from sleep, onset of new headache in an older population or progressively worsening headache may point to significant intracranial pathology. In general, the

absence of signs and symptoms is less informative than their presence.[313]

C Neuroimaging is not warranted for patients diagnosed with migraines and having a normal neurological examination.[317-325]

Grade C, Level 2+

A meta-analysis of patients with migraine and a normal neurological examination found a rate of significant intracranial lesions of 0.18%.[326]

There is insufficient evidence to make an evidence-based recommendation for the use of neuroimaging in tension-type headache with a normal neurological examination.[320,325]

There is insufficient evidence to make an evidence-based recommendation for the relative sensitivity of MRI compared with CT in the evaluation of migraine or other nonacute headaches.[320,322,327]

MRI is more sensitive than CT at detecting white matter lesions and developmental venous abnormalities, but the greater resolution and discrimination of MRI appeared to be of little clinical importance in patients with nonacute headache.[322]

6.2 Skull X-rays

D Skull X-rays are not recommended in the evaluation of headaches.

Grade D, Level 3

Skull X-rays play no role in the evaluation of non-traumatic headaches except for the identification of chronic sinus disease.[328,329]

6.3 Lumbar punctures

D Lumbar punctures are not recommended in the routine evaluation of headaches.

Grade D, Level 3

Lumbar punctures should be restricted to headaches believed to be due to CNS infections, subarachnoid haemorrhages and idiopathic intracranial hypertension.[330]

GPP Neuroimaging is mandatory before lumbar puncture if a neurological deficit is present or increased intracranial pressure is suspected.

GPP

7 Medication Overuse Headaches

7.1 Definition

Based on the International Classification of Headache Disorders (ICHDII) 2nd Edition (2004)[331], headache can be associated with substances or their withdrawal (code 8). It is divided into headache induced by acute (code 8.1) or chronic substance abuse (code 8.2). The term "medication overuse headache" refers to headache associated with chronic medication abuse and satisfies the following criteria:

1. headache on 15 or more days per month
2. pain characteristics are bilateral, dull and of light to moderate severity
3. drug intake includes ergots, triptans and opioids for 10 or more days per month, or analgesics for 15 or more days per month, for a minimum of 3 months, and
4. the headache disappears after withdrawal of the drugs

Almost all abortive drugs used to treat headaches can cause medication overuse headache, including analgesics, ergots, serotonin 5-$HT_{1B/1D}$ receptor agonists ("triptans"), opioids or combination medications.[332]

Medication overuse headache is confirmed if the headache resolves or reverts to its previous episodic pattern within 2 months of discontinuation of the medication.

7.2 Clinical characteristics that may suggest medicine overuse headache[333,334]

- The headaches are refractory, daily or near daily.
- The headaches occur in patients with primary headache disorders who use abortive medications very frequently and often in excessive quantities.
- The headaches can vary in severity, type and location.
- The headache is accompanied by other symptoms: asthenia, nausea and gastrointestinal symptoms,

irritability, anxiety, restlessness, depression and difficulty in concentration.

- Headaches may initially worsen if abortive medications are abruptly stopped although eventually headache may improve if the patient continues to abstain from these medications.
- Withdrawal symptoms may be observed if patients are taken off opioid medications abruptly.
- Prophylactic medications are ineffective while the patients are consuming excess amounts of abortive medications.

Overuse of abortive drugs may increase the occurence of other complications, such as gastrointestinal bleeding with non-steroidal anti-inflammatory drugs.

7.3 Epidemiology

The prevalence of medication overuse headache is approximately 1-3% based on cross-sectional, population based and epidemiological studies.[335-340]

There is growing evidence that medication overuse headache can also affect adolescents and children as young as 6 years of age.[341,342]

7.4 Management

There have been no prospective, randomised studies investigating the effectiveness of medication withdrawal or other treatments for medication overuse headache. Current information was derived from clinic-based and non-controlled studies.

Most treatment strategies use a three-pronged approach:

(1) Withdrawal of the drug

Successful therapy of medication overuse headache is defined as no headache at all or an improvement of more than 50% in terms of headache days.[343]

Withdrawal symptoms may last from 2 to 10 days (average 3.5 days) and include headache, nausea, vomiting, tachycardia, sleep disturbances, restlessness, anxiety and nervousness.[344]

C For ergotamine-induced medication overuse headache**,** naproxen 500 mg twice daily may be used for pain reduction during the withdrawal period.[345]

Grade C, Level 2+

(2) Introduction of headache prophylactic drugs

GPP During withdrawal, prophylactic treatment of the primary headache should be started concurrently.

GPP

Please refer to the section on prophylactic medication for migraine and tension-type headache (pgs 19-20, 25-26).

Prophylactic treatment for medication overuse headache is less likely to be effective if patients continue to overuse headache abortive drugs.[348]

(3) Anti-emetic medication

GPP Strictly limited doses of anti-emetic medication and analgesics may be used to treat break-through attacks.

GPP

Please refer to the section on prophylactic medication for migraine and tension-type headache (pgs 19-20, 25-26).

C Prednisolone 60 mg/day for 2 days, 40 mg/day for next 2 days and 20 mg/day for last 2 days and ranitidine 200 mg/day during the 6 days should be taken to alleviate headache intensity.[349]

Grade C, Level 2+

D Highly motivated patients who are not using barbiturates and tranquilizers (benzodiazepines) may be treated as outpatients. Patients who overuse drugs containing codeine,

barbiturates or tranquilizers, those who are depressed or who have failed previously to withdraw as outpatients, would be candidates for hospitalized management.[348]

Grade D, Level 4

7.5 Prognosis of medication overuse headache

After successful treatment, up to 20% of patients may relapse within 1 year and up to 50% after 5 years.

Predictors for relapse include patients with tension type headache or combination type headache, overuse of combination analgesic drugs and a long history of chronic headache. Migraine as the primary headache, 5-$HT_{1B/1D}$ receptor agonists as the medication overused and a short chronic headache history predict good response.[349-352]

7.6 Prevention

GPP The best strategy to reduce the prevalence of medication overuse headache is to prevent the development of medication overuse headache in the first place. Doctors should set maximal monthly dosages for headache abortive drugs. Maximum doses and frequencies of types of medications that cause medication overuse headache:

Medication	**Maximum Dose**
Simple analgesics (aspirin and paracetamol)	Intake < 10 days per month
Combination analgesics (caffeine or barbiturate-containing drugs)	≤ 3 tablets/day
Opioids	≤ 1 tablet /day
Ergotamine (oral)	Max 4 mg/attack and ≤ 20 mg/month
Serotonin 5-$HT_{1B/1D}$ receptor agonists (“triptans”)	< 2 doses/attack and < 6 doses per month

GPP

D Patients should be educated on the risk of medication overuse headache.[348]

Grade D, Level 4

D A headache diary is a useful tool for patients and their doctors to monitor the frequency of headaches and medication usage.[348]

Grade D, Level 4

8 Use of Acupuncture in the Management of Migraine and Tension Headache

8.1 Introduction to acupunture

Acupuncture can be defined as the insertion of one or more dry needles into the skin and underlying tissues at acupuncture points. These points may also be stimulated by pressure (acupressure), laser, ultrasound, heat (moxibustion), or electricity (electroacupuncture).

Acupuncture is primarily used to relieve pain. Scientifically, acupuncture points are sites at which nerves can be stimulated. Thus, acupuncture is considered a method of stimulating nerves. Evidence in support of this hypothesis includes the following:

- Acupuncture releases various neurotransmitters, including opioid peptides and serotonin.[353,354]
- The administration of naloxone, an opioid antagonist, prevents acupuncture-associated analgesia.[355]
- Acupuncture stimulates large, myelinated, rapidly conducting A-delta nerve fibers that may serve to decrease transmission of painful sensations via slower, unmyelinated C fibers.[356]

8.2 Evidence for efficacy

Existing evidence supports the value of acupuncture as prophylactic treatment for migraine and tension-type headache.

A Cochrane database review published in 2001 analyzed 26 clinical trials that compared acupuncture with any type of control intervention for treatment of idiopathic headaches. Acupuncture was superior when compared with placebo in 8 of the 16 trials that compared true acupuncture with sham (placebo) treatment; contradictory results were noted in 10 trials that compared acupuncture with other forms of treatment. The overall conclusion was that existing evidence

supported the value of acupuncture as headache prophylactic treatment.[359]

However, four recent trials suggest that there is no difference between true acupuncture, sham acupuncture and standard treatment for prophylaxis of migraine and tension-type headaches.[358-362]

A Acupuncture may be considered for headache prophylactic treatment.[357]

Grade A, Level 1++

8.3 Evidence of safety

Systematic review of case reports of life-threatening complications of acupuncture has found that such events fall into two main categories: infections (e.g., hepatitis B) and trauma (e.g., pneumothorax). Both are extremely rare and avoidable with adequate training and care.[363-365]

By comparison, mild and transient adverse events occur much more frequently. The reported incidence varies widely. Based upon a review that included nearly a quarter of a million treatments, mild bleeding and aggravation of symptoms were noted in 0.03% to 38%, and pain in 1% to 45%.[363,366]

8.4 Cautions

GPP Caution should be exercised when using acupunture in the following conditions:

- Patients with severe bleeding disorders or on anti-coagulant treatment – a contraindication for needle acupuncture
- Pregnancy
- Presence of a cardiac pacemaker – a contraindication for electrical stimulation
- Indwelling needles should not be used in patients at risk from bacteremia, such as asplenic patients or those who may become neutropenic

GPP

9 Cost-effectiveness of Headaches Treatment

Headache is an extraordinarily common disorder. To evaluate the cost effectiveness of headache treatment, we must first understand its impact, both tangible and intangible not only on the sufferer but also on society in general. In developed countries, tension type headache (TTH) alone affects two-thirds of adult males and over 80% of females. Extrapolation from figures for migraine prevalence and attack incidence suggests that 3000 migraine attacks occur every day for each million of the general population. Less well recognized is the toll of chronic daily headache: up to one adult in 20 has headache every or nearly every day.

Not only is headache distressing, it also causes much disability. Worldwide, according to the World Health Organization (WHO), migraine alone is 19th among all causes of years lived with disability (YLDs). Headache disorders impose recognizable burden on sufferers including sometimes substantial personal suffering, impaired quality of life and financial cost. Repeated headache attacks, and often the constant fear of the next one, damage family life, social life and employment. The long-term effort of coping with a chronic headache disorder may also predispose the individual to other illnesses. For example, depression is three times more common in people with migraine or severe headaches than in healthy individuals.

In a European study, it was calculated that in 29% of headache patients who continued working over a 4 week study period, there was an average loss of labor productivity of 20.7%. 2.5% of these patients lost an average of 3.8 work days and the economic cost was US$8996 for migraine patients and US$4318 for tension headache patients.[368] In all, the economic cost to the European Union is US$17 billion a year and US$ 28.7 billion annually for the United States.[369,370] Another study looking at direct and indirect medical costs for migraine patients vs. non-migraineurs show that migraineurs had higher direct medical costs over the prior six months (US$522 versus US$415), primarily

due to a greater frequency of physician and emergency department visits. The cost of lost productivity for the migraine group was also higher, by more than US$200. The combined total for direct and indirect costs was US$1,242 for migraineurs and US$929 for the comparison group. Additional analyses comparing those with moderate versus severe migraine demonstrated that more severe migraineurs had higher costs for lost productivity (US$1,021 versus US$251) and higher costs when direct and indirect costs were combined (US$1,656 versus US$685).[371] Co-morbid conditions, e.g. anxiety and depression, are also more prevalent in patients with tension and migraine headaches compared to matched controls, with a resultant increase in direct and indirect costs. In a recent study, migraineurs had a direct medical cost of US$5590 versus US$10,223 if associated with anxiety and US$10,582 if associated with depression. This however, is still cheap compared to US$13,442 if these migraine patient had both anxiety and depression. In children outpatient costs were five times higher (US$5045 versus US$945). They were also more likely to be hospitalised.[372]

As for testing in primary headache patients, a study looking at 592 neurologically normal patients complaining of headaches and having cranial computed tomography testing showed that the vast majority or 546 had a normal study compared to 46 which had an incidental finding of ischemic or atrophic changes not related to their headaches. None of these patients had gross intracranial pathology like space-occupying lesions or bleeding. Assuming a cost of US$117 per CT scan, the cost of finding an important pathology would be US$23,400 per case.[373]

Alternative treatments, e.g. acupuncture, are not used infrequently to treat headaches especially in our eastern society where it is well accepted. A British study looked at the cost of acupuncture and its effect on quality adjusted life years (QALY) compared to traditional medical treatment. They found that acupuncture led to a mean health gain of 0.021 QALYs, equivalent to 8 quality adjusted days. This more than made up for the fact that health service costs were higher for these migraine patients.[374]

Headache ought to be a public-health concern. Yet there is good evidence that very large numbers of people troubled by headache do not receive effective care. For example, in representative samples of the general populations of the United States only half of those identified with migraine had seen a doctor for headache-related reasons in the previous 12 months, and only about half had been correctly diagnosed. Most were solely reliant on over-the-counter medications.[375]

Many governments, seeking to constrain health-care costs, do not acknowledge the substantial burden of headache on society. They might not recognize that the direct costs of treating headache are small in comparison with the huge indirect-cost savings that might be made (e.g., by reducing lost working days) if resources were allocated to treat headache disorders appropriately.

10 Clinical Quality Improvement

The following clinical quality improvement parameters, based on recommendations in these guidelines, are proposed:

1. Proportion of patients with tension headaches diagnosed using The International Classification of Headache Disorders criteria (page 18).

2. Proportion of patients with tension headaches treated with aspirin, paracetamol and NSAIDS alone or in combination (page 19).

3. Proportion of patients with tension-type headaches given amitriptyline, mirtazapine or venlafaxine as prophylactic treatment (page 20).

4. Proportion of migraine patients (in primary care setting), who had their diagnosis made using the validated 3-item questionnaire (ID-Migraine) covering disability, nausea and sensitivity to light (page 21).

5. Proportion of migraine patients with migraine receiving instructions from their doctor regarding the following (page 25):

   a. the rationale for a particular treatment
   b. when to take the medication
   c. how to take the medication
   d. advice on the likely types of adverse events
   e. expected benefits of therapy
   f. how long will the process of therapy be in order to achieve these benefits
   g. what course of actions to take if the headache is not improved

6. Proportion of patients who had 2 or more attacks of migraine a month receiving daily migraine prophylactic treatment (page 25).

7. Proportion of patients with migraines and tension headaches evaluated for psychiatric co-morbidities such as anxiety or depression (page 32).

8. Proportion of patients, with following symptoms suspicious of secondary headaches, referred to a neurological specialist (page 34).

- Systemic symptoms such as fever or change in mental state
- Neurological deficits
- Sudden onset or maximum severity at onset
- The first severe or worst headache in an individual's life
- New persistent or progressively worsening headaches
- Changed character in the normal established headache pattern
- A new headache in middle age or later
- Headache precipitated by coughing, sneezing, standing, bending forwards or recumbency

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Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CME point under Category III (Self-Study) of the SMC Online CME System. Before you login to claim the CME point, we encourage you to evaluate whether you have mastered the key points in the Guidelines by completing this set of MCQs. This is an extension of the learning process and is not intended to "judge" your knowledge and is not compulsory. The answers can be found at the end of the questionnaire.

Instruction: Choose "True" or "False.

		True	False
1.	The following are characteristic of tension headaches:		
	A) Bilateral location	☐	☐
	B) A pressing/tightening (non-pulsating) quality	☐	☐
	C) Usually aggravated by routine physical activity such as walking or climbing stairs	☐	☐
	D) Usually accompanied by photophobia and phonophobia	☐	☐
2.	Effective medications used in prophylactic treatment of tension headaches are:		
	A) Amitriptyline	☐	☐
	B) Mirtazapine	☐	☐
	C) Maprotiline	☐	☐
	D) Cafegot	☐	☐
3.	Drugs used for the treatment of migraine attacks are:		
	A) Propranolol	☐	☐
	B) Eletriptan	☐	☐
	C) Naproxen	☐	☐
	D) Prochlorperazine	☐	☐
4.	Migraine prophylactic drugs used safely in pregnancy are:		
	A) Fluoxetine	☐	☐
	B) Valproate	☐	☐
	C) Magnesium	☐	☐
	D) Topiramate	☐	☐

		True	False
5.	Regarding psychological and psychiatric aspects in the management of headaches.		
	A) Patients with migraines and tension headaches should be evaluated for psychiatric co-morbidities.	☐	☐
	B) Many carefully controlled trials have demonstrated the effectiveness of psychological interventions in the management of chronic headaches.	☐	☐
	C) If hyperventilation accompanies tension headaches and migraines, the clinician should entertain the possibility of anxiety disorder.	☐	☐
	D) Adjunctive psychological intervention should be considered in patients with difficult-to-manage headaches.	☐	☐
6.	Regarding secondary headache:		
	A) It is associated with a known organic cause.	☐	☐
	B) It does not have specific clinical features.	☐	☐
	C) It is diagnosed by its close temporal relation to a disorder that is known to cause headache.	☐	☐
	D) The headache usually improves within 3 month following successful treatment.	☐	☐
7.	Indication for referral to the hospital for further management of headache:		
	A) Headache associated with neurological deficits.	☐	☐
	B) Sudden onset or maximum severity at onset.	☐	☐
	C) New persistent or progressively worsening headaches.	☐	☐
	D) Changed character in the normal established headache pattern.	☐	☐

	True	False
8. Neuro-imaging		
A) should be performed on all patients complaining of headaches	☐	☐
B) should be avoided if it will not lead to a change in management	☐	☐
C) may be ordered if the treating physician feels that it is medically indicated	☐	☐
D) should be done if a tension-type headache is diagnosed and an abnormal neurological exam is obtained on testing.	☐	☐
9. Useful investigations for headaches:		
A) Skull X-ray	☐	☐
B) EEG	☐	☐
C) CT scan before a lumbar puncture	☐	☐
D) MRI	☐	☐
10. Medication overuse headache:		
A) can develop if analgesic drug intake occurs for 15 or more days per month, for a minimum of 3 months.	☐	☐
B) disappears after withdrawal of the drugs.	☐	☐
C) can only be caused by NSAID, ergots and opiod medications.	☐	☐
D) can be bilateral and dull.	☐	☐
11. In medication-induced headache, withdrawal symptoms		
A) may last from 2 to 10 days	☐	☐
B) include recurrence of headache, nausea, tachycardia, sleep disturbance, restlessness and anxiety.	☐	☐
C) can be reduced if prophylactic treatment of the primary headache commences as soon as possible.	☐	☐
D) can be relieved by naproxen if it is ergotamine-induced.	☐	☐

		True	False
12.	Needle acupuncture		
	A) can be used as a prophylactic treatment for migraine.	☐	☐
	B) can be used as a prophylactic treatment for tension-type headache.	☐	☐
	C) always cause skin infection.	☐	☐
	D) can be safely used in patients with bleeding tendency.	☐	☐

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Answers

1 A)	T	Pg 18
1 B)	T	
1 C)	F	
1 D)	F	
2 A)	T	Pg 20
2 B)	T	
2 C)	T	
2 D)	F	
3 A)	F	Pgs 23-24
3 B)	T	
3 C)	T	
3 D)	T	
4 A)	T	Pg 28
4 B)	F	
4 C)	T	
4 D)	F	
5 A)	T	Pgs 32,33
5 B)	F	
5 C)	T	
5 D)	T	
6 A)	T	Pg 34
6 B)	T	
6 C)	T	
6 D)	T	
7 A)	T	Pg 34
7 B)	T	
7 C)	T	
7 D)	T	
8 A)	F	Pg 42
8 B)	T	
8 C)	T	
8 D)	T	
9 A)	F	Pgs 43,44
9 B)	F	
9 C)	T	
9 D)	T	
10 A)	T	Pg 45
10 B)	T	
10 C)	F	
10 D)	T	
11 A)	T	Pg 47
11 B)	T	
11 C)	T	
11 D)	T	
12 A)	T	Pg 51
12 B)	T	
12 C)	F	
12 D)	F	

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ISBN 978-981-05-9432-9