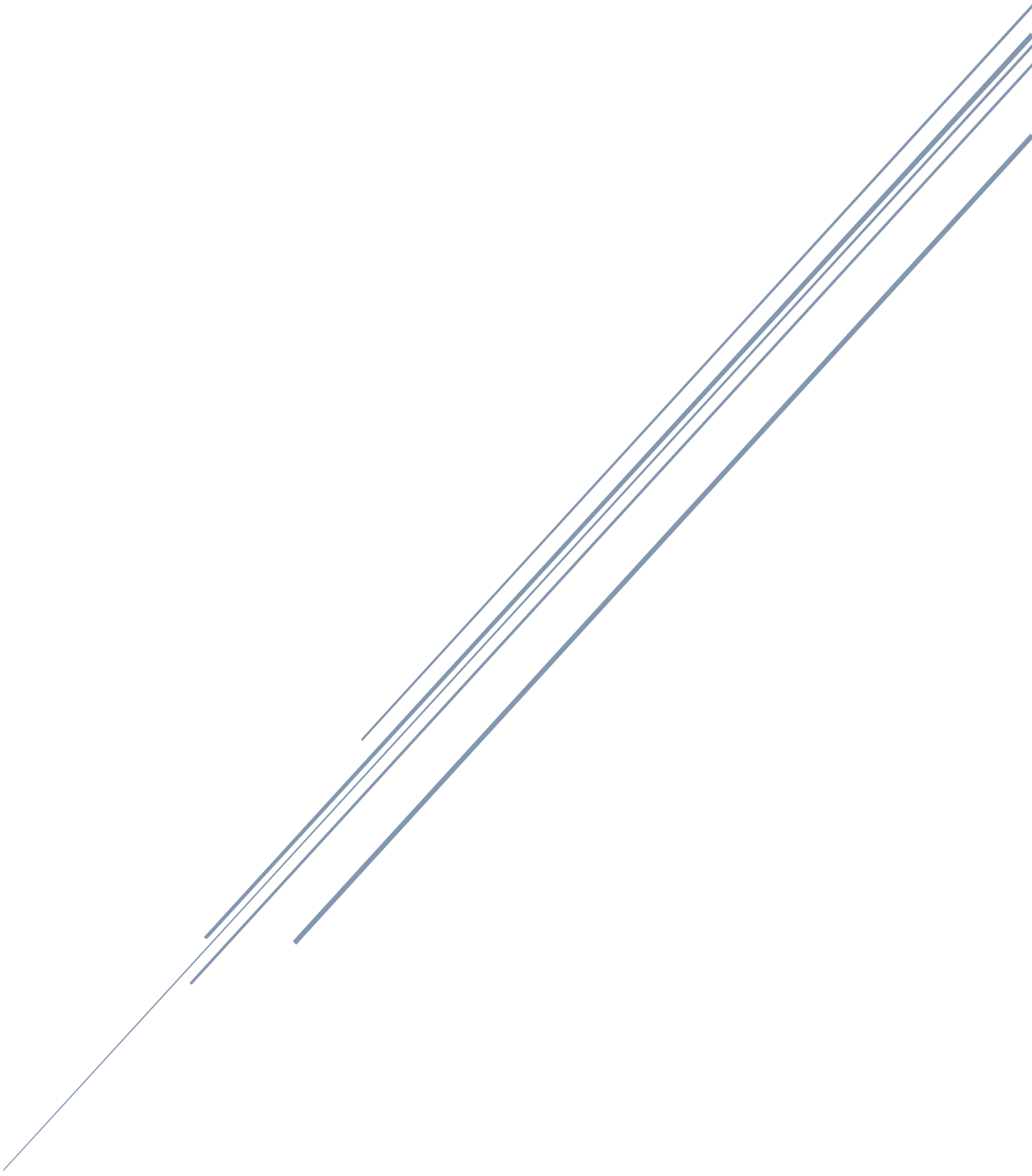

BASH
BRITISH ASSOCIATION FOR THE STUDY OF HEADACHE

NATIONAL HEADACHE MANAGEMENT SYSTEM FOR ADULTS **2019**

CONTENTS

FOREWORD

"The truth is never pure and rarely simple"

Oscar Wilde

Considerable advances have been made in the understanding of headache. To assist in management, various guidelines have been developed by different organisations in the UK and internationally. The primary purpose of guidelines, the stringency of criteria used, and the structure of the healthcare system for which they are written may differ and can result in variation. In addition, it should be acknowledged that different clinical subspecialties may also have different systematic approaches to clinical risk management.

The purpose of the BASH Headache Management System for Adults 2019 is to provide a simple, safe and standardised approach which can be used in real time to help manage the majority of common headache conditions. It has been produced with feedback from national patient charities – the Migraine Trust and the Organisation for the Study of Cluster Headache – and the Royal Pharmaceutical Society.

We hope to increase people's confidence in managing their own condition and hope the system is accessible to both patients and their clinical teams.

For people suffering from headache we are also developing downloadable information sheets for the recommended treatments, a useful and quick to complete headache diary and headache impact measurement tool, and links to useful educational videos made by members of BASH to help with greater understanding of their conditions. These resources will also be helpful to clinicians when guiding care.

The intention is that the BASH Headache Management System will encourage a national consistency in approach to caring for people with common headache disorders. The expectation is that the BASH system will largely replace the multiplicity of different regional headache algorithms and in doing so will reduce variation in care.

Through our relationship with NHS Right Care and engaging with the getting it right first-time programmes (GIRFT) we anticipate the management system will become a nationally commissioned approach to common headache conditions. Over time it will evolve to become an even more comprehensive system encompassing all headache disorders.

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BASH Guideline Writing Committee

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The guideline committee would like to express thanks to the **Migraine Trust**, the **Organisation for the Study of Cluster Headache UK**, the **Royal Pharmaceutical Society** and **BASH council** for their support, particularly in seeking patient/professional feedback on the utility of this guideline and the development of the patient information sheets.

The committee would also like to thank **Thomas Hart** (St George's Hospital, London) for his work in preparing the documents for publication.

RATIONALE

Building on the original BASH guidelines, the BASH national headache management system has been designed as a pragmatic tool to assist busy clinicians across the medical community. The purpose is to provide simple and easy to follow recommendations applicable to the majority of patients with headache.

The guidance is structured in a brief and relatively didactic fashion and reflects a deliberate decision to achieve three important aims: -

1. To create guidance useful to the clinician when seeing a patient in 'real time'
2. To assist allied health professionals in managing patients with common primary headache disorders using a relatively simple and standardised menu of care
3. To support and facilitate patients in self-management, through use of educational videos, patient information sheets and headache diaries and with a view to developing patient electronic self-management tools in collaboration with national organisations and charities

METHODOLOGY

A writing committee was established by consensus through the BASH council.

All treatments included in the guideline are supported by randomised placebo-controlled trials.

As the level of evidence supporting class A recommendations in international guidelines is not consistent, BASH has therefore chosen only to recommend treatments that are consistently considered to have class A evidence and are recommended in two or more of the following guidelines (NICE, SIGN, AHS & EFNS).

Newer treatments for headache with a specific UK license are also recommended if supported by adequately powered clinical trials with accepted IHS end points and done in a randomised placebo-controlled manner.

Other treatment options (with randomised placebo-controlled trial data) are included as appendices.

In recognition of the lack of comparative data, where relevant, treatment options are presented in alphabetical order.

The text does not include a comprehensive overview of side effect profiles, adverse events, contraindications, or drug interactions. When considering therapeutic options, standard resources should be consulted, for example the British National formulary and the product information sheets.

Both prescribers and patients should also note, that while treatment options have placebo control data, not all have a specific licence for a headache condition.

The first draft was sent to BASH council in 2018 (with 4 months for comments). The final draft was circulated in early 2019 for a further month of consultation prior to publication.

SECTION 1:
THE CLINICAL APPROACH

- Clinical assessment of headache
- The role of imaging in headache
- When to consider secondary headaches

CLINICAL ASSESSMENT OF HEADACHE

Classification

Headaches are classified by the International Headache Society as primary or secondary headaches (http://www.ichd-3.org).

The majority of headache is primary (such as migraine). Primary headache is the best validated within this classification system (http://www.ichd-3.org).

Secondary headaches are precipitated by another condition or disorder, local or systemic[1-3]. Serious causes of secondary headache are uncommon.

How to differentiate primary from secondary headache

The most consistent indicators for serious secondary headache are:

- Thunderclap (sudden onset) headache[4-6]
- Associated focal neurological deficit[4,7,8]
- Associated systemic features[4,7,8]
- Patients over the age over 50 years[9,10]

The history is the key to diagnosis in headache. The neurological examination is also helpful in differentiating primary from secondary headache[4,7,8]. For example, patients with migraine (with or without typical aura) or tension-type headache and a normal neurological examination do not have an increased likelihood of a secondary precipitant relative to the background population[11-13].

For other isolated headache syndromes with normal neurological examination there is insufficient data to enable a definitive conclusion[14].

Using the temporal pattern of headache to help differentiate primary from secondary headache

While we acknowledge that not all the following descriptors have tight definitions, we have tried to consider different temporal clinical patterns that the 'jobbing' clinician might frequently encounter and recognise.

Sudden onset headache

Sudden onset headache reaching maximum intensity within 5 minutes is called thunderclap headache[4-6,15-17]. Thunderclap headache has the greatest probability of a secondary precipitant[4-6].

Recent onset and progressive headache

Evolution of headache over days to weeks. If associated systemic features and/or focal neurological signs there is an increased probability of secondary precipitant[4,7,8].

Recurrent episodic headache

Recurrent episodic headache in isolation is most likely due to a primary headache disorder[13,18].

Headache which occurs on the majority of days in a month

Headache present for at least 15 days per month for over 3 months in isolation is most likely due to a primary headache disorder[18].

Differentiating between common primary headache disorders

Laterality and site of headache

Strictly unilateral (right or left but never bilateral) headache most consistently occurs in the Trigeminal Autonomic Cephalalgias (TACS) (http://www.ichd-3.org). 11.5- 20% of migraine sufferers experience unilateral headache[19,20].

Bilateral headache more commonly occurs in migraine, and is a more consistent defining feature of tension-type headache[21-23].

In most primary headache disorders the pain is experienced in the distribution of the first division of the trigeminal nerve and second cervical root. Neck pain can therefore be a feature of a migraine attack[22,24-31].

Associated symptoms

Prominent features in migraine include nausea, vomiting, photophobia, phonophobia and motion sensitivity (a tendency for the headache to be exacerbated by head movement or mild exertion)[21,23,32-35].

Cranial autonomic features, such as lacrimation, conjunctival injection, rhinorrhoea, and nasal blockage, are characteristic of the TACs, but can occur in up to 25% of migraine sufferers[36,37].

Unlike migraine sufferers who are frequently motion sensitive and generally prefer to remain still during an attack, patients with cluster headache and to a lesser extent TACs tend to be restless during an attack[25-27,38]

Aura can be experienced in all headache disorders, but is by far most common in migraine[39].

Duration and Frequency

The majority of untreated migraine headaches last between 4-72 hours[33,40,41].

Untreated TACS are typically of shorter duration and with higher attack frequency[42-49].

Table 1 shows a comparative table to distinguish between common primary headaches

Table 1. Comparative table to distinguish between common primary headaches (based on http://www.ichd-3.org)

MIGRAINE	TENSION-TYPE HEADACHE	CLUSTER HEADACHE
Episodic		
Unilateral (although often bilateral)	Bilateral	Unilateral (never bilateral)
Pulsating	Pressing, tightening, non-pulsating	
Moderate or severe	Mild or moderate *but not disabling*	Very severe
Aggravated by, or causing avoidance of, routine physical activity	No aggravation by, or avoidance of, routine physical activity	Restlessness No aggravation by physical activity
Nausea and/or vomiting Photophobia Phonophobia	No nausea, vomiting, photophobia, or phonophobia	*Ipsilateral to pain, there may be:* Conjunctival injection Lacrimation Nasal congestion Rhinorrhoea Eyelid swelling/drooping
Attacks last hours to days (usually 4-72 hours)	Attacks last hours to days	Attacks last from 15 mins to 3 hours
Frequency 1-2 attacks per month		Frequency 1-3 attacks per day (up to 8) and usually occur daily for 2-3 months at a time
Chronic		
Chronic migraine or chronic tension-type headache: At least 15 headache days per month for >3 months with the above clinical description, in the absence of medication overuse		Chronic cluster headache: Attacks occurring for more than 1 year without remission, or remission periods lasting <3 months
Medication-overuse headache		
Ergotamine, triptans, or opioids taken on 10 or more days per month, or 15 days for simple analgesics, for >3 months. Chronic migraine is fulfilled 2 months after medication has been withdrawn without improvement		**No medication overuse headache** Medication-overuse headache only reported in patients with a predisposition to migraine and/or tension-type headache; clinical syndrome of the headache exacerbated by the acute-relief medication overuse is of the migraine and/or tension-type headache[50]

Examination

The presence of abnormal neurological signs significantly increases the chance of an intracranial abnormality. Therefore, an appropriate neurological examination including fundoscopy is required when assessing the patient presenting with headache.

Useful and brief ways to perform the neurological examination are found at:

https://www.youtube.com/watch?v=wyBNYB0RLvU
https://www.youtube.com/watch?v=q56WgXvn0iU

(Please see 'Useful Videos' section)

THE ROLE OF IMAGING IN HEADACHE

People suffering from headache can be anxious about the possibility of a brain tumour. Outside of an emergency setting, current data indicates that the risk of finding serious secondary pathology in patients with isolated headache and a normal neurological examination is similar to that in people who do not have headache[8,11,12,51].

Normal imaging can reduce subsequent health care utilisation in the short term (less than one year) presumably because of reassurance. The effect however does not appear to be sustained in patients with anxiety and depression[8,52].

Moreover, there is a significant potential for uncovering incidental findings in 6-15% patients, which may not necessarily require further management but can themselves increase anxiety[1-3], and even potentially affect insurance coverage/premiums for that individual.

An information sheet can be useful to act as an 'aide memoire' when discussing these issues (link to information sheet about brain imaging).

WHEN TO CONSIDER SECONDARY HEADACHE

Identifying headache due to secondary causes

Serious secondary headaches are uncommon[4,7,13]. Very few secondary causes of headache have been reliably shown to have unique headache symptoms.

The most consistent indicators for secondary headache are: -

- Thunderclap (sudden onset) headache[4-6]
- Associated focal neurological deficit[4,7,8]
- Associated systemic features[4,7,8]
- Patients over the age over 50 years[9,10]

There is currently poor evidence that different disease processes associated with headache have unique or specific clinical presentations not covered by the clinical indicators cited above. For example:

- Giant Cell Arteritis – onset age >50 years plus systemic features
- Idiopathic intracranial hypertension – abnormal neurological examination with papilloedema
- CNS infection – systemic features (e.g. pyrexia) +/- focal neurological features

Features that do not help to differentiate primary from secondary headaches are:

- Severity
- Clinical characteristics
- Treatment response

Neither severity[53] nor response to drug treatment differentiates between primary and secondary headache. For example, headaches associated with intracerebral haemorrhage[54], subarachnoid haemorrhage[55,56], venous sinus thrombosis[57], carotid dissection[58,59], and carbon monoxide poisoning[60] have all been reported to respond to simple analgesics or triptans.

There is no specific 'brain tumour' type headache. The most frequent phenotype of headache associated with brain tumours is that of episodic tension-type headache, or migraine without aura[61].

Patients with the clinical syndrome of migraine (with or without typical aura) or tension type headache and a normal neurological examination do not have an increased risk of a secondary precipitant[11-13].

The following may be of reassurance to busy clinicians: data from the Landmark study suggest that a new clinic diagnosis of migraine was almost always correct - 98% of patients with a clinic diagnosis of migraine met international headache society criteria for migraine (87%, or probable migraine 11%)[62].

For other isolated headache syndromes with normal neurological examination there are insufficient data to enable a definitive conclusion.

As the presence of focal or systemic symptoms and/or abnormal neurological signs significantly increases the chance of there being an abnormality, an appropriate neurological examination – including fundoscopy – is required when assessing the patient presenting with headache.

Useful and brief ways to perform the neurological examination are found at:

http://www.youtube.com/watch?v=wyBNYB0RLvU
http://www.youtube.com/watch?v=q56WgXvn0iU

(Please see 'Useful Videos' section)

Thunderclap headache

Thunderclap headache is the most common isolated headache associated with a secondary precipitant[4-6].

The primary concern in thunderclap headache is to exclude a subarachnoid haemorrhage. In prospective studies of thunderclap headache (primary and secondary care), subarachnoid haemorrhage was present in 19.5-25%, and in 12% headache was the only symptom[63,64].

Investigation of Thunderclap Headache

- Refer immediately to hospital
- Urgent CT brain imaging

In patients presenting with isolated thunderclap headache with no other associated general or neurological symptoms, a normal neurological examination and a clear time of onset, the sensitivity of high resolution CT performed within 6 hours of onset is 98.5% - 99.85% for diagnosis of subarachnoid haemorrhage[65-69].

This sensitivity drops to 90% after more than 6 hours[66].

Lumbar puncture

If CT brain is normal, a lumbar puncture for examination of cerebrospinal fluid should be performed.

The current consensus is based on the guidelines for the analysis of CSF for bilirubin in suspected SAH[70]:

- Measure CSF pressure when performing the LP
- Send the CSF for standard constituents – protein, glucose, microbiology, and bilirubin/xanthochromia

- Send a simultaneous blood sample for glucose, bilirubin and total protein
- The specimen for spectrophotometry should be the least blood-stained fraction of CSF to be taken. The reason is that oxyhaemoglobin may interfere with the detection of bilirubin, and is a confounding element in analysis
- Protect the CSF sample for spectrophotometry from light to reduce the degradation of bilirubin, in order to minimise false-negative results
- Current consensus is that CSF should not be examined for bilirubin earlier than 12 hours after the ictus. Bilirubin in CSF forms 9-15 hours after a bleed[70-72]

If negative results are obtained from both CT brain and CSF analysis from 12 hours to within 2 weeks of the onset of thunderclap headache, it can be considered that SAH is excluded as a diagnosis[70,73].

Other pathologies associated with thunderclap headache

Thunderclap headache has been associated with other secondary pathologies, including infective causes, cerebrovascular causes such as intracranial haemorrhage[74], cerebral venous sinus thrombosis[75-77], malignant hypertension[78,79] and arterial dissection[17,80-85], non-vascular neurological causes (such as pituitary apoplexy)[86-92] and spontaneous intracranial hypertension[93-101]. Spontaneous intracranial hypotension classically presents as an orthostatic headache[102,103].

If CT and CSF are normal, additional investigations may be indicated if warranted by the clinical presentation. There are a significant number of guidelines for thunderclap headache from different countries and different subspecialty organisations but there is no universal consensus as to when additional investigations are indicated. If CT or MR angiography is considered, the fact that this may identify incidental intracranial aneurysms or other abnormalities should be borne in mind[104].

SECTION 2:
PRIMARY HEADACHES

- Migraine
- Medication overuse headache
- Tension-type headache
- The trigeminal autonomic cephalalgias:
  - v. Cluster headache
  - vi. Paroxysmal hemicrania
  - vii. SUNCT/SUNA
  - viii. Hemicrania continua

MIGRAINE

Epidemiology

Migraine is the most common disabling headache disorder, ranked as 7th highest among specific causes of disability globally and is responsible for 2.9% of all years of life lost to disability[105].

The global lifetime prevalence is 10% in men and 22% in women[106].

Peak prevalence increases to the age of 40 years and declines thereafter in both women and men, though can present de novo later in life [107-109].

Chronic migraine is a highly disabling primary headache disorder that affects 2% of the population[110,111], with reduced quality of life[112], increased risk of anxiety, depression and chronic pain and greater use of healthcare resource[113].

Around two-thirds of patient with chronic migraine have medication overuse[114].

Clinical features

Migraine is characterised by recurrent episodes of moderate to severe headaches, unilateral or bilateral and frequently throbbing. There may be associated nausea/vomiting, and light, noise and/or motion sensitivity[21,23,32-35]. (http://www.ichd-3.org).

Attacks can last 4-72 hours with freedom from symptoms in between, and vary in frequency from one per year to a few times per month[33,40,41,115].

The median frequency is one to two attacks per month[116].

Headache on 15 or more days per month for 3 consecutive months, of which at least 8 days have features of migraine, is termed chronic migraine (http://www.ichd-3.org).

The most sensitive and specific features of migraine are[117]:

- Nausea
- Disability (limitation of activity
- Photophobia

Prior to the onset of headache, patients can frequently experience premonitory symptoms, the most common of which are feeling tired (72%), difficulty concentrating (51%), and a stiff neck (50%)[118].

After the headache has ended patients often experience postdrome symptoms of a similar nature. In most attacks (93%), there was return to normal within 24 hours[119].

Aura affects around a third of migraine sufferers[120,121].

A typical aura comprises of fully reversible visual and/or sensory/ and/or speech symptoms, evolving over minutes with a total duration of up to 60 minutes (http://www.ichd-3.org).

Aura may occur without headache particularly in older patients[122].

Aura usually precedes, but may occur during, or after the headache.

Aura is not unique to migraine. It may occur in other forms of primary headaches[39].

The current classification of migraine with or without aura is well validated[19-21,23,33-35,40,41] (see table 2), though these classification systems are used primarily as a research tool rather than in everyday clinical practice.

Table 2: International headache classification definitions of migraine

MIGRAINE WITHOUT AURA

A. At least 5 attacks fulfilling criteria B-D
B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)
C. Headache has ≥2 of the following characteristics:
    a. Unilateral location
    b. Pulsating quality
    c. Moderate or severe pain intensity
    d. Aggravation by or causing avoidance of routine physical activity (e.g. walking climbing stairs)
D. During headache ≥1 of the following:
    a. Nausea and/or vomiting
    b. Photophobia and phonophobia
E. Not better accounted for by another ICHD-3 diagnosis

MIGRAINE WITH AURA

A. At least 2 attacks fulfilling criteria B and C
B. >1 of the following fully reversible aura symptoms: 1. Visual 2. Sensory 3. Speech and/or language 4. Motor 5. Brainstem 6. Retinal
C. >2 of the following 4 characteristics:
    a. 1 aura symptom spreads gradually over > 5 minutes, and/or > 2 symptoms occur in succession.
    b. each individual aura symptom lasts 5-60 minutes
    c. 1 aura symptoms are unilateral
    d. aura accompanied or followed in < 60 minutes by headache
D. Not better accounted for by another ICHD-3 diagnosis, and TIA excluded

CHRONIC MIGRAINE

Headache occurring on 15 or more days/month for more than 3 months, which, on at last 8 days/month, has the feature of migraine headache.

A. Headache (migraine-like or tension type like) on 8 ≥ days/month for > 3 months, and fulfilling criteria B and C
B. Occurring in a patient who has had at least five attacks fulfilling criteria B-D for 1.1 Migraine without aura and/or criteria B and C for 1.2 Migraine with aura.
C. On ≥ 8 days/month for > 3 months, fulfilling any of the following:
    a. Criteria C and D for 1.1 Migraine without aura
    b. Criteria B and C for 1.2 Migraine with aura
    c. Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative.
D. Not better accounted for by another ICHD-3 diagnosis.

Management

General principles

Validate the impact the condition has on the individual and family.

Manage expectations: Patients may have low or unrealistic expectations of what is achievable. Explain that migraine cannot be cured but can be effectively managed in most cases[123,124].

Reassurance: Patients often worry about an underlying serious disorder. Explaining the nature of the condition to the patient can be of therapeutic value[125].

Empower the patient to help promote self-management[126].

Prescribing decisions should be made with reference to the patient's current clinical situation and their future plans (e.g. pregnancy or contraception). Potential issues of medication overuse, both with respect to the impact on headache and side effects should be discussed.

Cognitive behavioural therapy has shown a greater reduction in migraine associated disability compared to drug therapy alone[127].

Acute Treatments

When prescribing acute treatments there are two broad strategies[128]:

1. **Stepped approach**: start with simple analgesics and if ineffective step-up e.g. to a triptan
2. **Stratified approach**: target treatment based on attack severity

The stratified approach is associated with better health related outcomes and lower indirect costs (e.g. GP and hospital visits)[128,129].

Adding an anti-emetic to an acute treatment improves efficacy unrelated to nausea and/or vomiting[130] and can improve gastric motility and hence drug absorption[131-133].

The end point of an effective treatment is a significant response at two hours, because the natural history for most attacks is to spontaneously improve in 4 hours[134].

If a treatment is not effective at 2 hours, then it is unlikely to work in that attack at that dose and considering an alternative acute treatment or combination treatment would be reasonable[135].

Lack of response to one triptan does not predict response to other triptans[135].

Triptans are most effective when taken early in the headache phase of the attack[136].

Triptans are less likely to be effective at treating the headache if taken during the preceding aura[137-139].

After 2 treatment failures with a particular triptan a trial with an alternative triptan is recommended. This rationale is based on the finding that in patients who experienced treatment failure in two attacks, 70% failed to respond in the third attack. Around 30% patients do not respond to any triptan[140].

Acute treatments can be associated with the development of medication overuse headache[141].

Opioids are not recommended for the treatment of acute headache because of the significant risk of medication overuse and the most protracted withdrawal[141].

For patients attending the emergency department parenteral NSAIDs or subcutaneous sumatriptan should be considered, and evidence also supports the use

of antiemetics[142]. Opioids have not been shown to be significantly effective and should not be used[143].

Recommended acute treatments are included in tables 3 and 4.

Table 3. Recommended acute treatments – simple analgesics and antiemetics

DRUG	DOSE	MAXIMUM DAILY DOSE	INFORMATION
Simple analgesics			
ASPIRIN[144-148]	600-1000 mg (UK doses are 300-900 mg)	4000 mg (for oral dosing)	
DICLOFENAC[149-152]	25 mg	150 mg	
IBUPROFEN[153-155]	400-600 mg	2400 mg	
KETOPROFEN[156,157]	75-150 mg	150 mg	
NAPROXEN[158-160]	250 mg	1000 mg	
PARACETAMOL[133,161]	1000 mg	4000 mg	
TOLFENAMIC ACID[162]	200 mg	400 mg	
Antiemetics			
DOMPERIDONE[133]	10 mg	30 mg	Safety alert: https://www.gov.uk/drug-safety-update/domperidone-risks-of-cardiac-side-effects
PROCHLORPERAZINE[163-165]	10 mg	30 mg	
METOCLOPRAMIDE[132,166,167]	10 mg	30 mg	Safety alert: https://www.gov.uk/drug-safety-update/metoclopramide-risk-of-neurological-adverse-effects

Table 4. Recommended acute treatments – triptans

DRUG	FORMULATION	STRENGTH	SINGLE DOSE	MAX/24 HOURS
ALMOTRIPTAN[168,169]	TABLET	12.5 mg	12.5 mg	25 mg
ELETRIPTAN[170]	TABLET	40 mg	40 mg	80 mg
FROVATRIPTAN[171]	TABLET	2.5 mg	2.5 mg	5 mg
NARATRIPTAN[172]	TABLET	2.5 mg	2.5 mg	5 mg
RIZATRIPTAN[173]	TABLET ORODISPERS LYPOPHILLISATE	5 mg/10 mg 10 mg 10 mg	10 mg 10 mg 10 mg	20 mg 20 mg 20 mg
SUMATRIPTAN[137,174]	TABLET SPRAY SUBCUT INJ	50 mg/100 mg 100 mg/ml or 200 mg/ml 6 mg	50-100 mg 10 - 20 mg 6 mg	300 mg 12 mg
ZOLMITRIPTAN[175-177]	TABLET ORODISPERS SPRAY	2.5 mg/5 mg 2.5 mg/ 5 mg 50 mg/ml	5 mg 5 mg 5 mg	10 mg 10 mg 10 mg

Choosing a triptan

Sumatriptan 6 mg subcutaneous remains the most rapid and effective treatment for pain relief but has a higher risk of adverse events than other formulations.

Combination of a triptan and an NSAID with a long half-life, such as naproxen, is better than monotherapy[178].

In comparison to sumatriptan 100 mg[171,179-181]:

- **Lower adverse events:** naratriptan 2.5 mg, almotriptan 12.5 mg and frovatriptan 2.5 mg
- **Better 2-hour pain response:** eletriptan 80 mg and rizatriptan 10 mg, almotriptan 12.5 mg
- **Lower recurrence rate**: frovatriptan 2.5 mg, and eletriptan 40 mg

Contraindications to triptans include ischaemic heart disease, cerebrovascular disease, previous myocardial infarction, and uncontrolled or severe hypertension. The cardiovascular risk of triptans is very low in the absence of these contra-indications[182].

The NNTs for therapies to achieve the outcome of pain freedom at two hours from a baseline of moderate to severe pain can be accessed by the SIGN guideline (www.sign.ac.uk/assets/sign155.pdf).

Preventive Treatments

General Principles

Prescribing decisions should be made with reference to the patient's current clinical situation and their future plans (e.g. pregnancy or contraception).

Preventive treatment should be offered as an option to patients with 4 or more migraine days a month as this frequency is associated with significant disability. Such

an approach will also mitigate the risk of escalation of acute treatment and consequent development of medication overuse headache.

Acute treatment on more than 2 days per week is associated with medication overuse, which renders preventive treatment less effective[183].

As there are relatively few head to head comparative studies, the choice of preventive depends primarily upon the side-effect profile of the drug and co-existing morbidities.

Preventive medications must be titrated slowly to an effective or maximum tolerable dose and continued for at least 6-8 weeks to adequately assess effect[184,185].

A headache diary may help evaluate response to treatment.

Consider gradual withdrawal after 6-12 months of effective preventive[184].

Monitor quality of life through validated tools such as HIT-6[186]. The HIT-6 score can be downloaded at http://www.bash.org.uk/wp-content/uploads/2012/07/English.pdf, or can be found in the information sheet section of these guidelines (Patient reported outcome measure HIT-6).

Treatment options

In selecting a preventative treatment, a reasonable strategy would be to consider which options might be most suitable for the individual patient, given their previous treatment, medical and other co-morbidities, personal preferences, and side effect profiles of the various treatments.

Table 5 shows the dose and titration regimen for recommended preventive treatments in both episodic and chronic migraine.

Table 6 shows dose and treatment regimen for recommended preventive treatments in chronic migraine only.

All preventive treatments with randomised placebo-controlled trial data are listed as an appendix.

Table 5. Recommended preventive treatments in episodic and chronic migraine

DRUG	START DOSE	TITRATION	TRIAL STUDIED DAILY DOSES
Amitriptyline[187-191]	10-25 mg OD	10 -25 mg	25-150 mg
Candesartan[192,193]	2 mg OD	2 mg	8-16 mg total/day
Propranolol[187,194,195]	10 mg BD	10-20 mg BD	120-240 mg total/day
Topiramate[196-205]	25 mg daily	25 mg od	25-200 mg total/day
CGRP monoclonal antibodies			
Erenumab[206-209]	70-140 mg monthly	Max dose as per licensed indication	
Fremanezumab[210]	225 mg monthly 675 mg three-monthly	Max dose as per licensed indication	
Galcanezumab[211-213]	120-240 mg monthly	Max dose as per licensed indication	

Table 6. Recommended preventive treatments for chronic migraine only

Onabotulinumtoxin A[214-218]	155-195 IU intramuscularly, as per PREEMPT protocol	Every 12 weeks

Onabotulinumtoxin A

The efficacy and safety of Onabotulinumtoxin A for prophylaxis of Chronic Migraine has been shown through in the Phase III Research Evaluating Migraine Prophylaxis Therapy (PREEMPT) clinical programme.

Patient selection: Treatment is licensed for adult patients with chronic migraine. Treatment is not effective in episodic migraine (< 15 days a month).

BASH considers it good practice to address medication overuse prior to commencing Botox treatment. Patients are advised to restrict their acute headache medication to no more than two days a week on a regular basis.

As 60% of patients failed two oral preventive treatments in the PREEMPT trial, BASH recommends considering use of 2-3 oral preventive treatments prior to Botox therapy.

Treatment response should be monitored using quality of life measures, for example HIT-6.

Appendix 1. All preventive treatments for migraine

DRUG	START DOSE	INCREMENT	MAX DOSE	COMMENTS
Acupuncture[219]	10 sessions			
Angiotensin Receptor Blockers/ACE inhibitors				
Candesartan[192,193]	2 mg/day	2 mg	8 mg BD	
Lisinopril[220]	10 mg/day	10 mg	20 mg/day	
Anticonvulsants				
Topiramate[196-205]	25 mg/day	25 mg	100 mg BD	
Sodium Valproate[221-227]	200 mg BD	100 mg	1000 mg BD	MHRA and NHS safety alerts*
Beta Blockers				
Propranolol[187,194,195]	10-20 mg BD	10-20 mg	120-240 mg/day	
Metoprolol[228-230]	25-50 mg/day	50mg BD	200 mg total daily in BD or TDS regimen	
Nadolol[231]	40 mg/day	40 mg	160 mg/day	
Timolol[232]	10 mg BD	10 mg	30 mg BD	
Atenolol[233]	50 mg/day	50 mg	200 mg/day	
Calcium Channel Blockers				
Flunarizine[234-236]	5 mg/day	5 mg	10 mg/day	Not marketed in the UK
CGRP monoclonal antibodies				
Erenumab[206-209]	70-140 mg monthly		Max dose as per licensed indication	
Fremanezumab[210]	225 mg monthly 675 mg three-monthly		Max dose as per licensed indication	
Galcanezumab[211-213]	120-240 mg monthly		Max dose as per licensed indication	
Greater Occipital Nerve Block[237-240]	Local anaesthetic +/- steroids SC		Not applicable if using local anaesthetic only	4 small RCT - 3 showing reduced headaches frequency over 1-4 weeks
Onabotulinumtoxin A[214-218]	155 IU		195 IU	IM every 3 months
Neuromodulation				
External Trigeminal Nerve Stimulation[241]	As per specialist recommendations			
Single Transcranial Magnetic Stimulation[242]	As per specialist recommendations			During aura or start of headache
Transcutaneous Vagal Nerve Stimulation[243]	As per specialist recommendations			

Supplements				
Co-enzyme Q10[244]	150 mg/day			
Magnesium[245]	400 mg/day	200 mg	600 mg/day	
Riboflavin[246]	400 mg/day			
Tricyclic Antidepressants				
Amitriptyline[187-191]	10 - 25 mg/day	10 - 25 mg	150 mg ON	

***Valproate Patient Safety Alert**

In girls and women of childbearing potential, valproate should be initiated and supervised by a specialist and only prescribed when other medications have not been tolerated or have found to be ineffective. This is because of 30-40% risk of neurodevelopmental disability in unborn babies exposed to valproate (MHRA April 2017). Valproate should only be prescribed by following the MHRA guidance, including a signed contraceptive plan and signed consent form documenting discussion of the risks (see MHRA website)

https://www.gov.uk/drug-safety-update/valproate-and-developmental-disorders-new-alert-asking-for-patient-review-and-further-consideration-of-risk-minimisation-measures

https://improvement.nhs.uk/documents/911/Patient_Safety_Alert_-_Resources_to_support_safe_use_of_valproate.pdf

Menstrual Migraine

A proportion of women suffer from migraine attacks in association with the menstrual cycle, termed menstrual related migraine (MRM). MRM occurs between days -2 and +3 of the first day of menstruation (which is +1) in at least 2 out of 3 menstrual cycles.

Women with MRM will also have attacks at other times.

Less than 10% of women report migraine exclusively with menstruation and at no other time ('pure' menstrual migraine)[247-253]

Acute Treatment

The acute treatment of menstrual related attacks is no different to non-menstrual attacks.

Head-to-head studies do not show clear superiority of one triptan over any other[254].

Recommended short term preventive treatments for menstrual related migraine, or pure menstrual migraine.

Table 7. Recommended triptans for short term prevention of menstrual related migraine or pure menstrual migraine

DRUG	FORMULATION	STRENGTH
FROVATRIPTAN[255,256]	TABLET	2.5 mg twice daily on the days migraine is expected (generally from two days before until three days after bleeding starts).
ZOLMITRIPTAN[257]	TABLET	2.5 mg twice or three times a day on the days migraine is expected (generally from two days before until three days after bleeding starts).

Appendix 2. All treatments for short term prevention of menstrual related migraine or pure menstrual migraine

DRUG	FORMULATION	STRENGTH
FROVATRIPTAN[255,256]	TABLET	2.5 mg twice daily on the days migraine is expected (generally from two days before until three days after bleeding starts)
NARATRIPTAN[258,259]	TABLET	2.5 mg twice daily on the days migraine is expected (generally from two days before until three days after bleeding starts)
ZOLMITRIPTAN[257]	TABLET	2.5 mg twice or three times a day on the days migraine is expected (generally from two days before until three days after bleeding starts)

Targeted oestrogen supplementation

Menstrually targeted oestrogen supplementation (assuming no contraindications) has been found in some studies to offer benefit in menstrual related migraine[260-262].

However, a rebound increase in migraine attack frequency has been found when the effect of this strategy has been considered over the whole menstrual cycle[263].

The risk of stroke in migraine with aura, when taking oestrogen-containing contraceptives

Females suffering migraine with aura have an inherent increased risk of stroke[264].

Use of the oestrogen contraceptive pill is also associated with increased risk of stroke in all individuals. The incidence of stroke in females with migraine with aura, who are also taking the oestrogen-containing contraceptive pill is additionally increased.

Consequently, contraceptive methods other than oestrogen containing contraception are advised for women with migraine with aura. There is no established additional risk in migraine without aura.

Treatment in pregnancy & breast feeding

- In the majority of women, migraines improve during pregnancy[265,266]

- Caution is advised and checking with British National formulary data and pregnancy register is recommended especially when prescribing in pregnancy, breast feeding, and considering contraception. The resource Best Use of Medicine in Pregnancy (BUMPS) may also be of help to patients (http://www.medicinesinpregnancy.org/)

- Paracetamol is not generally considered to be associated with a significantly elevated risk throughout pregnancy and lactation[267]

- The Sumatriptan & Naratriptan Pregnancy Registry found no evidence of teratogenicity associated with major birth defects for sumatriptan[268-271]

MEDICATION OVERUSE HEADACHE

Epidemiology & diagnosis

In patients with migraine or tension-type headache, regular frequent use of acute treatment can result in exacerbation of the pre-existing primary headache[272].

Medication overuse headache (MOH) is classified as a chronic headache disorder. The headache occurs on more than 15 days a month for at least 3 months, affecting between 1-2% of the general population and, up to 20-50% of the chronic headache population[105,106,273-276].

MOH has been recognized since the 1940s and is a worldwide issue resulting from an interaction between frequently used acute headache medication in a susceptible patient[277,278].

Majority of patients improve on withdrawal of the overused medication[279-283].

All medications used to treat an acute headache can result in medication overuse headaches. Triptans, opioids and combination analgesics are likely to result in development of MOH more rapidly (treatment taken on 10 days or more per month) as compared to simple analgesics such as paracetamol (treatment taken on 15 days or more per month)[141,272,284-286].

MOH occurs primarily in individuals with migraine or tension type headache and is generally of the same phenotype[141].

Overuse of triptans has been shown to cause MOH faster and with fewer doses compared with analgesics. The average interval between the first intake and daily MOH was 1.7 years for triptans, 2.7 years for ergots and 4.8 years for analgesics[141].

Patients must provide details of their usage of both prescription medications and of treatments taken over the counter.

Clinicians must specifically ask how many days in a month the patient takes medication for treating the acute headache and preferably correlate this with a headache diary.

In patients with a history of migraine or tension type headaches pain killer medication taken regularly for non-headache pain, such as joint or back pain, can result in medication overuse headaches[278,287].

The association between analgesic overuse and chronic pain is strongest for chronic migraine (odds ratio of 10.3)[288].

Clinical features

Triptan overuse may result in daily migraine like headache or an increase in migraine frequency, whereas overuse of other analgesics may lead to daily headache with features of both migraine and tension type headache[141].

Many patients continue to take their acute medications despite the apparent lack of effect, while also reporting significant rebound in headache when acute medications are not taken[279-283].

The prevalence of comorbid psychiatric disorders, including depression and anxiety, is greatly increased in patients with MOH. In patients with medication overuse headache with pre-existing episodic tension type headache 67.7% have comorbid psychiatric disorders while in those with pre-existing migraine these were present in 53.7%. Depression and anxiety themselves also be risk factor[289].

Migraine is comorbid with depression and anxiety and these may be risk factors for developing MOH[290,291].

Dependence related behaviour is noted in 60–70% patients and relapses are common[290].

Management

Patient education

An important aspect in the management of MOH is to increase awareness of the condition amongst health care providers as well as the general population.

Patients must be advised that restricting their acute headache medications to no more than 2 days in a week minimizes the potential of developing MOH[292].

Educational intervention is crucial and results in improvement in headache[293].

Comparison of advice alone with a structured detoxification program in patients with MOH is similarly effective[294].

The use of rescue medications, including steroids, does not improve outcomes[294-297].

Patients should be encouraged to seek preventive treatments for migraine as this can prevent the conversion from episodic to chronic migraine thereby reducing the risk of development of MOH[298].

Medication withdrawal

The MOH is unlikely to resolve unless the offending medication is stopped[299].

There is no difference in outcome with either abrupt or gradual withdrawal of the causative drug[300].

Outpatient medication withdrawal is as effective as inpatient detoxification[294,301,302].

Withdrawal headache usually lasts for 2-10 days from the time of complete cessation of the overused medication[114,303,304].

After medication withdrawal patient's headaches gradually improve. This improvement can take up to 12 weeks[286].

The average duration of withdrawal headache appears to be shortest in patients overusing triptans (4 days)[305].

Response to acute and preventive medications improves following withdrawal of the overused medication[299,306].

Prognosis

At 8 weeks following medication withdrawal 45% of patients report improvement in headaches while in 48 % the headaches remain unchanged[299] (though it must be noted that this data is from a single trial).

Between 22 – 45% patients relapse back into MOH within 1 year, and 40 – 60% within 4 years of withdrawing from their overused medications[307,308].

The relapse rate is lower for patients with migraine and for individuals overusing triptans rather than analgesics (21% vs 71%)[308].

Comorbid anxiety and depression can be associated with difficulty in medication withdrawal and a high risk of relapse following withdrawal of medication[290].
Response to migraine preventive medications improves following withdrawal of the overused acute headache medication[299,309].

There is no difference in outcome if preventive medication is started during or after withdrawal, as long as the acute medication is withdrawn. Preventive treatment is more effective once the overused medication is withdrawn[183,201,306,310].

The most important step in MOH management is to identify the diagnosis and inform the patient of the importance of reducing or stopping the offending medication, and no further measures may then be required[311-313].

TENSION-TYPE HEADACHE

Epidemiology

Tension-Type Headache (TTH) is the most common primary headache disorder with a mean global lifetime prevalence of 42% (Range 19-83%)[314]. Chronic tension-type headache affects 0.5 - 4.8 % of the worldwide population[315].

Clinical features

TTH is characterised by mild-moderate and *not severe*, headache. It is bilateral and often described as pressing or tightening like a vice or tight band.

It **typically** lacks the specific features that characterise migraine such as nausea, light and noise sensitivity.

The headache is *not* aggravated by routine physical activity and this is a key criterion for diagnosis[21,316-318].

Duration of pain can be variable with a range from half an hour to several days. TTH on 15 or more days per month for at least 3 months is termed chronic TTH.

Disabling TTH is rare. Most patients diagnosed with disabling TTH have migraine, and respond to triptans[319,320].

Management

Reassurance may suffice in the majority of patients.

Individual attacks can be treated with simple analgesics (see table 8).

Table 8. Recommended acute treatments in tension-type headache

ANALGESIC	SINGLE DOSE	MAXIMUM DAILY DOSE
Paracetamol[321-323]	1000 mg	4000 mg
Aspirin[324,325]	500-1000 mg (UK doses are 300-900 mg)	4000 mg (for oral dosing)

Preventive treatment is rarely necessary, though can be considered if symptoms are causing significant disability (see table 9).

Table 9. Recommended preventive treatment in tension-type headache

DRUG	STARTING DOSE	TITRATION	MAXIMUM DOSE
Amitriptyline[326-330]	10 mg	10-25 mg	150 mg

Appendix 3. All acute treatments in tension-type headache

TREATMENT	SINGLE DOSE	MAX DAILY DOSE
Aspirin[324,325,331]	500-1000 mg (UK doses are 300-900 mg)	4000 mg (for oral dosing)
Diclofenac[332]	25-75 mg	150 mg
Ibuprofen[331,333,334]	400 mg	2400 mg
Ketoprofen[334-338]	50 mg	300 mg
Naproxen[339]	250-500 mg	1000 mg
Paracetamol[321-323]	1000 mg	4000 mg

Appendix 4. All preventive treatments in tension-type headache

TREATMENT	STARTING DOSE	TITRATION	MAXIMUM DAILY DOSE
Acupuncture[340-347]	6 treatment sessions		
Amitriptyline[326-329]	10 mg	10-25 mg	150 mg

THE TRIGEMINAL AUTONOMIC CEPHALAGIAS

The trigeminal autonomic cephalalgias are a group of headache disorders with prominent autonomic features and a shared pathophysiology[348,349].

There are four trigeminal autonomic cephalalgias. Each disorder can be either episodic or chronic.

The trigeminal autonomic cephalalgias are uncommon headache disorders. Therefore, there is a high misdiagnosis rate[350,351] and few randomised-controlled treatment trials.

The clinical characteristics of the trigeminal autonomic cephalalgias as defined by the International Classification of Headache Disorders are based upon the published cases reports and series apart from cluster headache which has population-based data.

The trigeminal autonomic cephalalgias are:

i. **Cluster headache**
ii. **Paroxysmal hemicrania**
iii. **SUNCT/SUNA** (Short-lasting neuralgiform attacks with conjunctival injection and tearing/Short-lasting neuralgiform attacks with cranial autonomic features)
iv. **Hemicrania continua**

CLUSTER HEADACHE

Epidemiology

- Cluster headache has a prevalence of about 0.1%[352]
- The peak age of onset is between the 3rd and 4th decades[25,42,353-356]
- The disorder is four times more common in men[352]
- Cluster headache sufferers are often smokers[25,43,348]

Clinical features

The current classification of cluster headache is well validated (http://www.ichd-3.org).

Attacks are characterised by excruciating strictly unilateral and strictly unilateral headache. However, attacks can change side, across different bouts, within the same bout and rarely within an acute attack[26,27,37,38,42,353,355,357].

Bilateral pain in cluster headache is rare[25,42,358-360].

The attacks are accompanied by ipsilateral cranial autonomic features which are primarily parasympathetic and can most commonly include lacrimation, conjunctival injection, rhinorrhoea, nasal congestion, drooping or swelling of the eyelid. The presence of cranial autonomic features in headache does not necessarily indicate cluster headache or another TAC. For example, these features can also occur in migraine.

One of the most distinguishing features during the cluster attack is restlessness. Patients typically walk up and down, or rock to and fro, clutching the affected side, unlike migraineurs who are motion-sensitive and prefer to remain still[25-27,38].

Attack duration is usually between 15 minutes to 3 hours and attack frequency 1-2 a day. Cluster headache can be episodic or chronic. Episodic cluster bouts usually last between 2 weeks and 3 months and most often occur once every 1-2 years. Ten to 20% of sufferers experience chronic cluster headache, which is currently defined as attacks occurring without a remission period, or with remissions lasting < 3 month, for at least 1 year[38,42,44,353-355,357].

Active bouts of cluster headache can be seasonal and at the same time each year. During an active bout, sufferers can experience attacks at set times during the day for weeks or months. The pattern can change or become less predictable[25,45,353,355,361,362].

Cluster attacks often wake patients *from* sleep, usually about 1.5-2 hours after they have fallen asleep[25,27,37,363,364].

Some individuals can exclusively have nocturnal attacks[37].

In between attacks of pain patients can experience a background dull ache in the same distribution of the cluster attacks. The interparoxysmal pain tends to settle when the cluster bout resolves[365].

During an active cluster bout some patients can be exquisitely sensitive to alcohol triggering an attack, usually within an hour. The propensity does not occur out of the bout[366].

Clinically relevant commonalities and differences between migraine and cluster headache include:

- Cluster sufferers can have nausea and vomiting, photophobia and phonophobia[25-27,38]

- Up to 25% of migraine sufferers can experience autonomic features during an attack[37]

- Aura can be experienced in up to 23% of cluster headache sufferers[27,38,360,367] (though in practice is rare)

- 20-40% of migraine sufferers experience strictly unilateral headache[19,24]

- The duration of untreated migraine attacks in adults is invariably longer than 4 hours[35,41]

- A key feature in cluster headache is restlessness and lack of motion sensitivity, while migraine sufferers prefer to be still[25-27,38]

Management

Acute Treatment

The most effective acute treatment is the sumatriptan 6mg subcutaneous injection with significant relief within 15 minutes[368].

The maximum limit is two 6mg injections a day[369].

The treatment is generally well tolerated, without tachyphylaxis[370,371].

Patients who have cluster headache rarely develop medication overuse headache[370,371].

Patients who also have migraine may develop exacerbation of their migraine disorder whilst using a triptan effectively for their cluster attacks[50,372].

High flow oxygen 100% at 7-15 litres/minute for 15-20 minutes, using a non-rebreathable mask, is effective in aborting acute attacks of cluster headache[373,374].

There is no limit to the use of high flow oxygen, though obvious cautions around smoking/flames/fire hazards near oxygen need to be considered/addressed. Oxygen is often used together with triptans in patients with multiple attacks. Table 10 shows recommended acute cluster attack treatments.

Table 10. Recommended Acute Cluster attack treatments

Treatment	Formulation	Strength	Maximum Daily Dose
Oxygen[373,374]	Inhalation through non-rebreathable mask	7-15 L/min	No limit
Sumatriptan[368]	Subcutaneous injection	6 mg	12 mg
Sumatriptan[375]	Nasal spray	20 mg	40 mg
Zolmitriptan[376-378]	Nasal spray	5 mg	15 mg
Non-invasive vagal nerve stimulation[379]	Transcutaneous	As per specialist recommendation	

Appendix 5: All acute cluster attack treatments

Name	Formulation	Strength	Maximum Daily Dose	Comment
Lidocaine[380]	Nasal spray	4%	Not specified	Self – administered using a nasal dropper
Octreotide[381]	Subcutaneous injection	100 mcg	Not specified	
Oxygen[373,374]	Inhalation through non-rebreathable mask	7-15 L/min	No limit	
Sphenopalatine Ganglion Stimulation (SPG)[382,383]	Implantable device	As per specialist recommendation		
Sumatriptan[368]	Subcutaneous injection	6 mg	12 mg	
Sumatriptan[375]	Nasal spray	20 mg	40 mg	
Zolmitriptan[376-378]	Nasal spray	5 mg	15 mg	

Preventive treatments

Verapamil is an effective preventive treatment in cluster headache[384].

The doses required to suppress cluster headache attacks can be higher than those used to treat cardiac disorders. Clinically significant cardiac rhythm disturbances can occur and are neither dose nor time dependent[385,386]. It is possible for patients to develop cardiac conduction abnormalities even after they have been on a stable dose for a long period.

BASH recommends an ECG done at baseline and following each increase in dose. At a stable dose ECG should be done once every six months. Any cardiac rhythm disturbance may require dose reduction or drug withdrawal[385].

In episodic cluster headache, once control has been achieved, towards the end of the expected bout, the preventive can be slowly withdrawn. If attacks recur the preventive should be re-established.

Oral corticosteroids have been shown to be effective in the prevention of cluster headache attacks[387].

The response should be seen within 48 hours. Given the high adverse effect profile corticosteroid use is best restricted as a short-term measure in patients with multiple daily attacks, which cannot be treated effectively acutely, whilst an alternative preventive is being introduced.

Suboccipital nerve block (i.e. suboccipital depot steroid and local anaesthetic injection) has shown a significant reduction or resolution of attacks compared to placebo and despite a high placebo response rate[388,389].

Table 11 shows recommended preventive treatments for cluster headache.

Table 11: Recommended preventive treatments for cluster headaches

Name	Start dose	Titration	Max daily dose	Comments
Greater occipital nerve block[388,389]	Depot steroid + local anaesthetic	Not applicable	Not applicable	Different formulations of steroid & anaesthetic used*
Verapamil[384]	80 mg TDS	Increase 80 mg every 2 weeks	960 mg	ECG monitoring recommended

*There does not seem to be a difference between different local anaesthetics

Appendix 6: All preventive treatments for cluster headaches

Name	Start dose	Increment	Max daily dose	Comments
Greater occipital nerve block[388,389]	Depot steroid + local anaesthetic	Not applicable	Not applicable	Different formulations of steroid & anaesthetic used*
Lithium[390]	200 mg/day	200 mg/week	According to serum lithium levels. Note preparations vary widely in bioavailability	Monitor levels as per BNF
Melatonin[391]	10 mg		10 mg	
Non-Invasive Vagal Nerve Stimulation[379]	As per specialist recommendation			
Prednisolone/prednisone[387,392]	40mg for 10-14 days	Taper thereafter	Short term interim use only	
Sphenopalatine Ganglion Stimulation[383,393]	As per specialist recommendation			
Verapamil[384]	80 mg TDS	Increase 80 mg every 2 weeks	960 mg	ECG monitoring recommended

*There does not seem to be a difference between different local anaesthetics

Appendix 7: Classification of cluster headache (http://www.ichd-3.org)

CLUSTER HEADACHE DIAGNOSTIC CRITERIA

A. Severe/very severe unilateral orbital, supraorbital and/or temporal pain lasting 15–180 minutes (untreated)
B. Either or both of the following:
    1. At least one of the following symptoms or signs, ipsilateral to the headache:
        a. Conjunctival injection and/or lacrimation
        b. Nasal congestion and/or rhinorrhoea
        c. Eyelid oedema
        d. Forehead and facial sweating
        e. Forehead and facial flushing
        f. Sensation of fullness in the ear
        g. Miosis and/or ptosis
    2. A sense of restlessness or agitation

C. Attack frequency between one every other day up to 8/day for > half the time the disorder is active

EPISODIC CLUSTER HEADACHE

A. Attacks fulfilling criteria for Cluster headache and occurring in bouts (cluster periods)
B. At least two cluster periods lasting from 7 days to one year (when untreated) and separated by pain-free remission periods of three months

CHRONIC CLUSTER HEADACHE

Attacks fulfilling criteria for Cluster headache and occurring without a remission period, or with remissions lasting < 3 months, for at least 1 year

PAROXYSMAL HEMICRANIA

Epidemiology

Population-based data on the prevalence of paroxysmal hemicrania is sparse and has been cited as 0.05% in the 18-65-year age group[394].

Total published cases remain less than 200.

There may be a slight female preponderance with ratios ranging between 1.1to 2.36.

Mean age of onset is between the 4thand 5th decades[46,395,396].

Clinical features

The pain is strictly unilateral with associated ipsilateral autonomic features (http://www.ichd-3.org).

The classification of paroxysmal hemicranias is shown as an appendix.

Attack duration ranges between 2-30 minutes and frequency of attacks is reported up to 50 a day. The mean lies between seven and 13 attacks per day[46,395].

A greater proportion present with chronic paroxysmal hemicrania. The disorder has an absolute response to indomethacin[46,47,395-397].

The attacks are shorter and more frequent than in cluster headaches and longer and less frequent than in SUNCT/SUNA. The typical circadian characteristics seen in cluster headache are less prominent in paroxysmal hemicrania. All attacks are spontaneous unlike SUNCT/SUNA, in which attacks are often triggered immediately by various sensory stimuli. The key distinction is the clear therapeutic response to Indomethacin. The main differential diagnoses are shown are shown as an appendix.

Management

There are no RCTs for preventive treatment in paroxysmal hemicranias.

Acute treatment

The attacks of paroxysmal hemicrania are usually too short to respond to any oral acute treatment. Open label observation suggests that sumatriptan 6mg subcutaneous injection and high flow oxygen are generally not effective[398,399].

Preventive treatment

By definition paroxysmal hemicrania is an indomethacin-responsive disorder.

The effective dose range is between 25-300mg daily dose[46,397].

Although most patients show a rapid response to indomethacin, some patients can take up to a week to demonstrate a response to an effective dose. Based upon this BASH recommends indomethacin 25mg PO TDS for 7 days, 50mg TDS 7 days, up to 75mg TDS. We recognise and emphasise the higher dose is above the BNF quoted maximum of 200mg per day, and should only be considered if clinically required, after appropriate counselling with the patient, and with clear criteria for dose reduction.

Dose requirements can change over time and some patients may go into remission[400].

Therefore, once symptoms are well controlled for a period of time gradual dose reduction should be tried to maintain the lowest effective dose or, if there is no recurrence on each dose reduction, withdrawal during remission periods.

Gastrointestinal side effects with indomethacin are common and may preclude use of the drug. A concomitant proton-pump blocker or H2-antagonist can be used.

SHORT-LASTING UNILATERAL NEURALGIFORM HEADACHE ATTACKS WITH CRANIAL AUTONOMIC FEATURES (SUNA)

The original description of this disorder was termed SUNCT, short-lasting unilateral neuralgiform attacks with conjunctival injection and tearing[48].

Conjunctival injection and tearing (lacrimation) are the most common autonomic symptoms in all the TACs[26,27,30,38,42,395,396].

The terminology SUNA was proposed based on the fact that a number of patients were noted to lack one or both of these symptoms[49,401]. The distinction remains within the ICHD classification. From a clinical perspective, management remains the same.

The distinction remains within the ICHD classification. BASH recommends this as a research tool and for current clinical purposes will adopt the terminology of SUNA to encompass both groups[49].

Epidemiology

SUNCT/SUNA is rare[401,402].

The mean age of onset is 48 years with a slight male preponderance 1.5[403].

Clinical features

The attacks are the shortest and most frequent of all the TACs. Attacks can be either spontaneous or induced by cutaneous triggers. Mean duration is about one minute (range 1-600 seconds) with frequency up to 30 attacks in an hour[31].

The character of the attacks can vary: attacks can occur in single stabs, a group of stabs or a long attack with a 'saw-tooth' pattern of stabs between which the pain does not return to baseline. Other features of TACs may be present, such as agitation. SUNCT/SUNA can be misdiagnosed as Trigeminal Neuralgia. However, the location of the pain, autonomic features, duration of attacks and spontaneity of attacks in SUNCT/SUNA, differentiate between the two (See appendix Table. Differential diagnosis of The Trigeminal Autonomic Cephalalgias).

Management

There are no RCTs for preventive treatment in SUNCT/SUNA.

Acute treatment

Because of the short attack duration there are no effective acute treatments in SUNCT/SUNA[49].

Preventive treatment

The most effective reported treatment is lamotrigine with dose range up to 400 mg. Topiramate may be effective in SUNCT[385]. Carbamazepine and gabapentin may also be effective[31,49,404].

Appendix 8. Classification of paroxysmal hemicranias (http://www.ichd-3.org)

PAROXYSMAL HEMICRANIA

A. At least 20 attacks fulfilling criteria B-E
B. Severe unilateral orbital, supraorbital and/or temporal pain lasting 2-30 minutes
C. Either or both of the following:
    1. At least one of the following symptoms or signs, ipsilateral to the headache:
        a. conjunctival injection and/or lacrimation
        b. nasal congestion and/or rhinorrhoea
        c. eyelid oedema
        d. forehead and facial sweating
        e. miosis and/or ptosis
    2. A sense of restlessness or agitation
D. Occurring with a frequency of >5 per day
E. Prevented absolutely by therapeutic doses of indomethacin
F. Not better accounted for by another ICHD-3 diagnosis.

EPISODIC PAROXYSMAL HEMICRANIA

A. Attacks fulfilling criteria for 3.2 *Paroxysmal hemicrania* and occurring in bouts
B. At least two bouts lasting from 7 days to 1 year (when untreated) and separated by pain-free remission periods of ≥3 months.

CHRONIC PAROXYSMAL HEMICRANIA

A. Attacks fulfilling criteria for 3.2 *Paroxysmal hemicrania*, and criterion B below
B. Occurring without a remission period, or with remissions lasting <3 months, for at least 1 year

HEMICRANIA CONTINUA

A. Unilateral headache fulfilling criteria B-D
B. Present for >3 months, with exacerbations of moderate or greater intensity
C. Either or both of the following:
    1. at least one of the following symptoms or signs, ipsilateral to the headache:
        a. conjunctival injection and/or lacrimation
        b. nasal congestion and/or rhinorrhoea
        c. eyelid oedema
        d. forehead and facial sweating
        e. miosis and/or ptosis
    2. a sense of restlessness or agitation, or aggravation of the pain by movement
D. Responds absolutely to therapeutic doses of indomethacin
E. Not better accounted for by another ICHD-3 diagnosis.

REMITTING HEMICRANIA CONTINUA

A. Headache fulfilling criteria for 3.4 *Hemicrania continua*, and criterion B below
B. Headache is not daily or continuous but interrupted (without treatment) by remission periods of ≥24 hours.

UNREMITTING HEMICRANIA CONTINUA

A. Headache fulfilling criteria for 3.4 *Hemicrania continua*, and criterion B below
B. Headache is daily and continuous for at least 1 year, without remission periods of ≥24 hours.

SHORT-LASTING UNILATERAL NEURALGIFORM HEADACHE ATTACKS (SUNCT)

A. At least 20 attacks fulfilling criteria B–D
B. Moderate or severe unilateral head pain, with orbital, supraorbital, temporal and/or other trigeminal distribution, lasting for 1–600 seconds and occurring as single stabs, series of stabs or in a saw-tooth pattern
C. At least one of the following five cranial autonomic symptoms or signs, ipsilateral to the pain:
    a. conjunctival injection and/or lacrimation
    b. nasal congestion and/or rhinorrhoea
    c. eyelid oedema
    d. forehead and facial sweating
    e. miosis and/or ptosis
D. Occurring with a frequency of at least one a day
E. Not better accounted for by another ICHD-3 diagnosis

SUNCT (SHORT LASTING UNILATERAL NEURALGIFORM HEADACHES WITH CONJUNCTIVAL INJECTION AND TEARING)

A. Attacks fulfilling criteria for 3.3 *Short-lasting unilateral neuralgiform headache attacks*, and criterion B below
B. Both of the following, ipsilateral to the pain:
    a. conjunctival injection
    b. lacrimation (tearing)

EPISODIC SUNCT

A. Attacks fulfilling criteria for 3.3.1 *Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing* and occurring in bouts
B. At least two bouts lasting from 7 days to 1 year (when untreated) and separated by pain-free remission periods of ≥3 months

CHRONIC SUNCT

A. Attacks fulfilling criteria for 3.3.1 *Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing*, and criterion B below
B. Occurring without a remission period, or with remissions lasting <3 months, for at least 1 year

SUNA (Short lasting unilateral neuralgiform headaches with cranial autonomic symptoms)

A. Attacks fulfilling criteria for 3.3 Short-lasting unilateral neuralgiform headache attacks, and criterion B below
B. Only one or neither of conjunctival injection and lacrimation (tearing)

EPISODIC SUNA

A. Attacks fulfilling criteria for 3.3.2 *Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms* and occurring in bouts
B. At least two bouts lasting from 7 days to 1 year (when untreated) and separated by pain-free remission periods of ≥3 months

CHRONIC SUNA

A. Attacks fulfilling criteria for 3.3.2 *Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms*, and criterion B below
B. Occurring without a remission period, or with remissions lasting <3 months, for at least 1 year

Appendix 9. Differential diagnosis of The Trigeminal Autonomic Cephalalgias and Trigeminal Neuralgia

TAC	Hemicrania Continua	Cluster Headache	Paroxysmal Hemicrania	SUNA	Trigeminal neuralgia
Male / Female ratio	Female	2.5: 1	Female	Male	Female
Attack duration	Constant	15 minutes – 3 hours	5 – 30 minutes	1-600 seconds	Few seconds - 2 minutes
Attack frequency	Not applicable	Up to 8 / day	Up to 5 / hour	Up to 30 / hour	1-50 / day
Circadian features	-	++	+	-	-
Restlessness	±	++	±	±	-
Interparoxysmal pain*	NA	Yes	Yes	Yes	Yes
Other differentiating features	Typically more migrainous features than other TACs Can be potentiated by acute-relief medication overuse	Strongest association with circadian rhythm, restlessness, attacks from sleep, alcohol triggering	Spontaneous, shorter and more frequent attacks than cluster.	Attacks of pain can be spontaneous and triggered e.g. eating, brushing teeth, cold wind, neck movements. All attacks can be spontaneous. Pain is always primarily in the distribution of the ophthalmic division of the trigeminal nerve with radiation to affect	Attacks of pain can be spontaneous *and* always triggered e.g. eating, brushing teeth, cold wind, neck movements. Pain is always primarily in the distribution of the 2nd and 3rd division of the trigeminal nerve - should rarely affect V1 and should not affect C2 (back of head and neck) No autonomic features
Episodic or chronic tendency	Chronic	Episodic	Chronic	Chronic	Currently undefined.
	Continuous pain, without remission	Attacks occurring in periods lasting from 7 days to a year, separated by pain-free periods lasting at least three months*	Attacks occurring for more than one year without remission (remission is arbitrarily defined as three months pain free)		
Acute attack treatment	None – prone to development of	Sumatriptan 6mg subcutaneous High flow oxygen	None	None – too short	None - too short

	medication-overuse				
Preventive treatment	Indomethacin	Verapamil Prednisolone	Indomethacin	Lamotrigine	Carbamazepine

*The paroxysmal trigeminal autonomic cephalalgias can have pain between acute attacks. In most cases the interparoxysmal pain is part of the same disorder. In some cases, hemicrania continua may be co-exist. Therefore, a trial of Indomethacin could be considered[405-407]

HEMICRANIA CONTINUA

Epidemiology

Hemicrania continua is an uncommon disorder with estimated prevalence of 0.8-1.5% however it is acknowledged that this is compounded by diagnostic inaccuracy[408,409].

The disorder seems to be more common in women. Mean age of onset is between the 3rdand 4thdecade[410,411].

Clinical features

Hemicrania continua is characterized by strictly unilateral pain of moderate severity with ipsilateral autonomic features which may be more prominent during exacerbations.

Hemicrania continua has both clinical and pathophysiological overlap with migraine[412].

Thus, although more than half of cases can be restless during the attacks, others experience motion sensitivity[30,410,411,413,414].

Although the disorder is defined by chronicity it can present in a relapsing and remitting (thus episodic) form[415-420].

Management

There are no RCTs for preventive treatment in hemicrania continua.

Acute treatment

Medication overuse can occur in hemicrania continua. Thus, analgesics should be withdrawn prior to assessing response to indomethacin[421,422].

Preventive treatment

Hemicrania continua is an indomethacin-sensitive disorder. The effective dose range is between 25-300mg daily dose[46,395-397].

Although most patients show a rapid response to Indomethacin, some patients can take up to a week to demonstrate a response to an effective dose. Based upon this BASH recommends Indomethacin 25mg TDS for 7 days, 50mg TDS 7 days, up to 75mg TDS.

Dose requirements can change over time and some patients may go into remission[400].

Therefore, once symptoms are well controlled for a period of time gradual dose reduction should be tried to maintain the lowest effective dose or, if there is no recurrence on each dose reduction, withdrawal during remission periods.

Gastrointestinal side effects with Indomethacin are common and may preclude use of the drug. A concomitant proton-pump blocker or H2-antagonist can be used.

LIST OF ABBREVIATIONS

ACE	Angiotensin converting enzyme
AHS	American Headache Society
ARB	Angiotensin receptor blocker
BASH	British Association for the Study of Headache
BD	Bis in die (*lat.* Twice daily)
CGRP	Calcitonin gene related peptide
CNS	Central nervous system
CSF	Cerebrospinal fluid
CT	Computer tomography
ECG	Electrocardiogram
EFNS	European Federation of Neurological Societies
GCA	Giant cell arteritis
GON	Greater occipital nerve
GP	General practitioner
HIT-6	Headache Impact Test 6
HIS	International Headache Society
ICHD	International Classification of Headache Disorders
IIH	Idiopathic intracranial hypertension
LP	Lumbar puncture
MG	Milligrams
MHRA	Medicines and Healthcare products Regulatory Agency
MOH	Medication overuse headache
MRI	Magnetic resonance imaging
NICE	National Institute for Health and Care Excellence
NNT	Number needed to treat
NSAID	Non-steroidal anti-inflammatory
OD	Omne in die (*lat.* Once daily)
QDS	Quater die sumendum (*lat.* Four times daily)
RCT	Randomised controlled trial
SAH	Subarachnoid haemorrhage
SIGN	Scottish Intercollegiate Guidelines Network
SPGS	Sphenopalatine ganglion stimulation
SUNA	Short lasting unilateral neuralgiform headaches with cranial autonomic symptoms
SUNCT	Short lasting unilateral neuralgiform headaches with conjunctival injection and tearing
TAC	Trigeminal autonomic cephalagia
TDS	Ter die sumendum (*lat.* Three times daily)
TTH	Tension-type headache

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