Rare Primary Headache Syndromes

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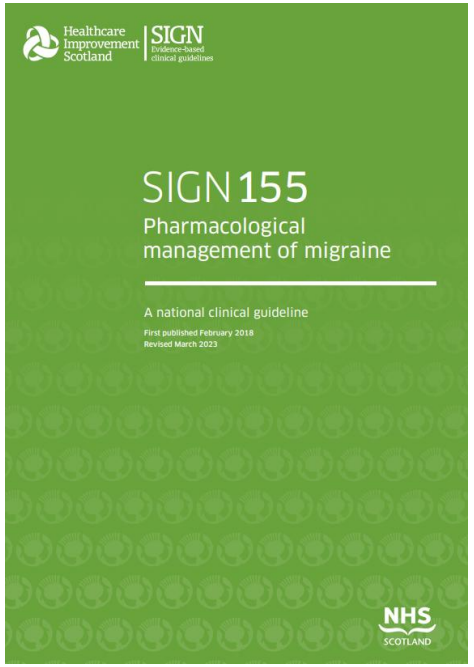

Rare Primary Headaches

4.1	Primary Cough Headache
4.2	Primary Exercise Headache
4.3	Primary Headache Associated with Sexual Activity
4.4	Primary Thunderclap Headache
4.5	Cold stimulus Headache
4.6	External Pressure Headache
4.7	Primary Stabbing Headache
4.8	Nummular Headache
4.9	Hypnic Headache
4.10	New Daily Persistent Headache

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Indometacin responsive

Can be given as:
Pre-emptive treatment
Continuous prophylaxis

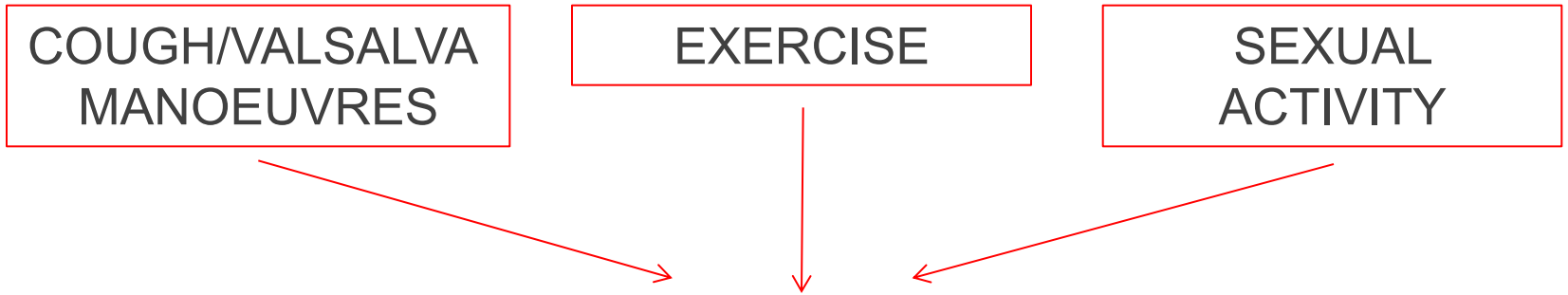
Indometacin

- **Continuous Prophylaxis**
  - Oral trial
    - Start indometacin 25mg tds with PPI
    - Increase to 50mg tds after 3 days to 1 week
    - Then to 75mg tds after 3 days to 1 week
    - If no effect after 10 days negative trial
  - Once effective dose achieved taper down to minimum effective dose
  - **Effect should be absolute for PH and HC (usually within a few days of an adequate dose)**
  - **Not absolute for other indomethacin sensitive headaches**
  - **Partial response may indicate an analgesic effect (Risk of MOH)**

- **Pre-emptive indomethacin**
  - Bioavailability of orally administered indomethacin is virtually 100%, and peak concentrations are reached within 30 mins and 2 hrs.
  - Onset of action is within 30 min and the duration of action is about 4 to 6 hrs.
  - Plasma half-life averages 3 hrs but can range from 3 to 10 hrs.

- **Indomethacin should be given 30 to 60 minutes before the known trigger, when the trigger cannot be avoided**
  - Start with 25mg and work up as needed (dose range 25-150mg)

Triggered headaches



- *HEADACHE IS* **PRECIPITATED** *BY THESE ACTIVITIES*
  (if aggravated → Migraine)

- **SECONDARY POTENTIALLY LIFE-THREATENING CAUSES NEED TO BE EXCLUDED**
- **PRIMARY FORMS: DIAGNOSIS OF EXCLUSION**

4.1 Cough Headache (Modified from ICHD-3)

Headache **precipitated rather than** aggravated by coughing / straining / lifting /other Valsalva manoeuvres, but not prolonged exercise

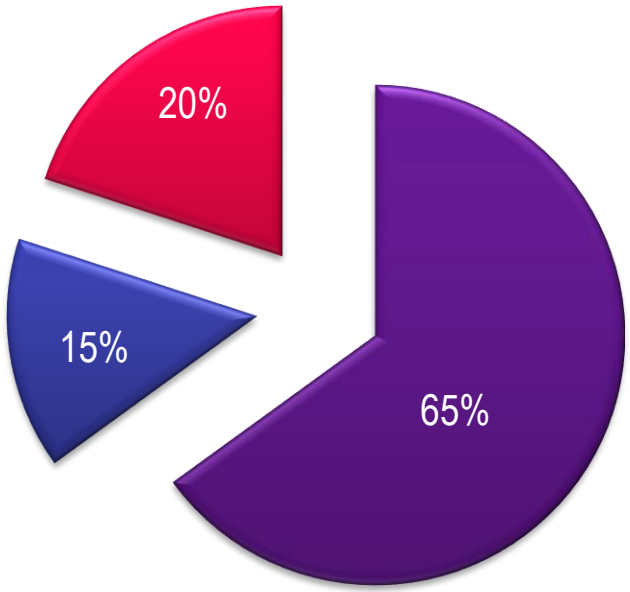
Primary Cough Headache
60%

Secondary Cough Headache
40%

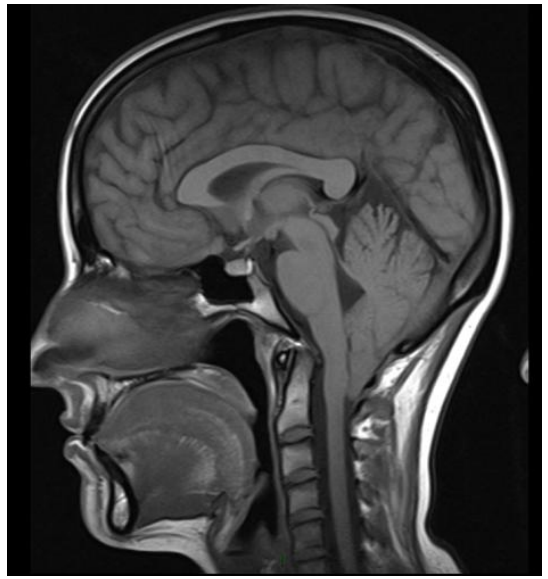
Characteristics:

- Triggered by coughing, straining and/or other Valsalva manoeuver
- Sudden onset; subsides gradually (usually over seconds to a few minutes)
- Duration: 1 sec – 2 hours, but longer durations reported
- Location: Usually bilateral and posterior

Secondary Cough Headache



- Chiari malformation type 1
- Posterior fossa lesions
- Others



- Meningioma
- Arachnoid cyst
- Dermoid tumour

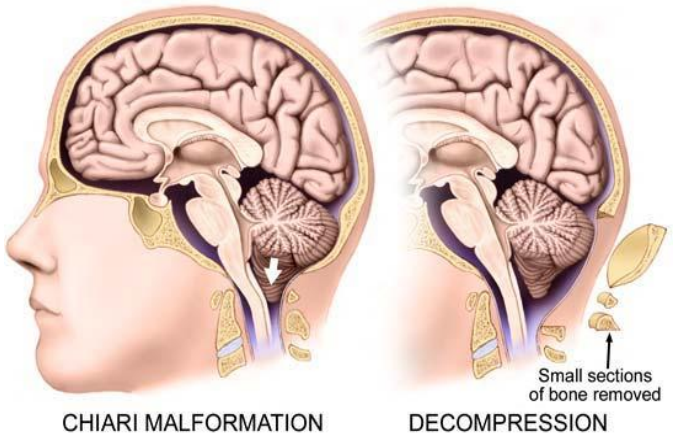
- CSF leak
- Obstructive hydrocephalus
- Subdural haematoma
- Pneumococcal meningitis
- RCVS
- Carotid/vertebrobasilar dissection
- Cerebral aneurysms

Primary cough headache is a diagnosis of exclusion

Treatment of Cough Headache

Primary Cough Headache
*Indomethacin
*Acetazolamide
*Topiramate
Others: naproxen, propranolol, IV DHE, methysergide
*Lumbar Puncture: Removal of 40 ml of CSF Effective: 14/24 patients (58%)

Secondary Cough Headache
Chiari malformation type I Indication: Headache + progressive neurological deterioration Procedure: Foramen magnum decompression



* Postulated to be due to intracranial pressure reduction.

Medical treatment can be effective in secondary cough headache
Avoid pressure lowering treatment if cough headache is part of intracranial hypotension

Cordenier, et al Journal of Headache and Pain. 2013; 14;42

4.2 Primary Exercise Headache

Clinical Features (Modified from ICHD-3)

- Brought on by and occurring only during or after strenuous physical exercise
- Lasting from 5 minutes to 48 hours

- **Treatment**
  - Pre-emptive Indometacin – 25-150mg taken 30-60 mins before planned exercise
  - Other treatments used: Ergotamine (pre-emptive), Naproxen, Propranolol, Flunarizine

- **Exercise is also a fairly common trigger in some migraineurs for their typical migrainous headaches.**

Secondary Exercise Headache

- **Structural intracranial lesions present in 10-40%**
  - Vascular causes - cerebral aneurysm, arteriovenous malformation, intracranial haemorrhage, dissection, RCVS
  - Tumours (both metastatic and primary)
  - Third ventricular colloid cyst
  - Chiari type I malformation

- **Extracranial causes of exertional headache are very rare**
  - Pheochromocytoma
  - **Cardiac cephalalgia** (look for cardiac risk factors and consider ECG)

Upadhayaya, et al Current Neurology and Neuroscience Reports. 2020; 20;9

4.3 Primary Headache Associated with Sexual Acitivity

Clinical Features (Modified from ICHD-3)

- Brought on by and only occurring during sexual activity
- Either or both of
  - Increasing in intensity with increasing sexual excitement
  - Abrupt explosive intensity just before or with orgasm
- Lasting from 1 minute to 24 hours with severe intensity and/or up to 72 hours with mild intensity

- **Treatment**
  - Majority time-limited and period of abstinence may be appropriate
  - Pre-emptive: Indometacin – 25-150mg taken 30-60 mins before planned intercourse; also Triptans / ergots
  - Preventative: Indometacin, Propranolol, Nimodipine

Exclude secondary underlying pathologies (CT-LP/MRI/MRA scan)

- Subarachnoid haemorrhage
- Arteriovenous malformation
- Carotid/vertebral dissection

- RCVS – multiple thunderclap headaches

- Drugs – cannabis, pseudoephredine, COCP
- Phaechromocytoma (investigate when symptoms are present remote from sexual activity)

- CSF leak may develop during sexual activity (followed by orthostatic headache)

Maynard and Pace. Current Pain and Headache Reports. 2024; 28;627-632

4.4 Primary Thunderclap Headache

Clinical Features (Modified from ICHD-3)

- High-intensity headache of abrupt onset, mimicking that of ruptured cerebral aneurysm, in the absence of any intracranial pathology.
  - **Abrupt onset reaching max intensity in <1 min**
  - **Lasting >5 mins**
  - ***In reality most will be instant, but SAH can present with headache escalating over up to 5 mins in 20%***

- Isolated Thunderclap Headache is a common presentation to ED / Acute Medical Units
  - **Can not differentiate Primary from Secondary**
  - **On first presentation investigation for SAH and its differential mandated**
  - **RCVS should be considered in patients with recurring Thunderclap Headache over weeks**
  - **NO "safe number" of Thunderclap Headaches.**
  - **ALL patients should be investigated on first presentation**

Exclude secondary underlying pathologies (CT-LP/MRI/MRA scan)

- **Unenhanced CT Head +/- LP (SAH)**
  - Good quality CT reported by competent radiologist within 6 hours
  - +/- LP (12 + hours from ictus)
  - Important to consider SAH differential

- **RCVS – multiple thunderclap headaches**
  - CTA / MRA

- **CSF leak may present with Thunderclap Headache followed by orthostatic headache**
  - MRI Brain and spine looking for evidence of low pressure and risk factors
  - Remember to consider if "can't get LP"

Thunderclap Headache: Differential Diagnosis

Well recognised

- **Subarachnoid haemorrhage**
- **Arterial dissection**
- **Intracranial Haemorrhage**
- **Cerebral venous sinus thrombosis**
- **RCVS**

Less well recognised

- **Spontaneous intracranial hypotension**
- **Ischaemic stroke**
- **Pituitary apoplexy**
- **Giant Cell Arteritis**
- **Meningitis**
- **Acute hypertensive crisis**
- **Third ventricle colloid cyst**

Primary Headache

- Thunderclap headache
- Headache associated with sexual activity
- Exertional Headache

Warning!

The triggered headaches (cough, exertional, sexual activity) and thunderclap are benign mimics of potentially life-threatening secondary headaches

Diagnosis is one of exclusion

All patients require investigation on first presentation

4.5 Cold Stimulus Headache

- **Headache brought on by a cold stimulus applied externally to the head or ingested or inhaled.**
- **Most don't require treatment**
  - Not associated with underlying disease
  - More common in migraineurs
  - Conservative measures including wearing a hat
  - An interesting case:

34 year old keen cyclist

Develops unpleasant burning frontal headache when outside in cold weather

Wooly hat unhelpful and has to drive to work

50mg Indometacin taken 30 mins before cycling to work in cold weather prevents headache

- **External**
  - Brought on by and occurring only during application of an external cold stimulus to the head
  - Resolving within 30 minutes after removal of the cold stimulus
- **Internal**
  - Brought on by and occurring immediately after a cold stimulus to the palate and/or posterior pharyngeal wall from ingestion of cold food or drink or inhalation of cold air
  - Resolving within 10 minutes after removal of the cold stimulus

Chebini and Dilli. Current Neurology and Neuroscience Reports. 2019; 19:46

4.6 External Pressure Headache

- **External Compression Headache**

Headache resulting from sustained compression of peri-cranial soft tissues, for example by a tight band around the head, hat or helmet, or goggles worn during swimming or diving, without damage to the scalp

  - **Brought on by and occurring within 1 hour during sustained external compression of the forehead or scalp sustained external compression of the forehead or scalp**
  - **Maximal at the site of external compression**
  - **Resolving within 1 hour after external compression is relieved**

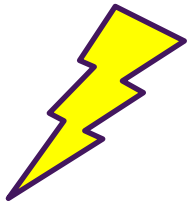
- **External Traction Headache**

Headache resulting from sustained traction on peri-cranial soft tissues, without damage to the scalp.

  - **Brought on by and occurring only during sustained external traction on the scalp**
  - **Maximal at the traction site**
  - **Resolving within 1 hour after traction is relieved**

Hensel and Kraya. Brain and Behaviour. 2025; 15:e70202

4.7 Primary Stabbing Headache



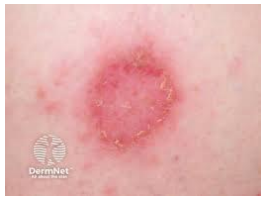
- **Often under-recognised, but not especially rare**
  - 3% of general population
  - 42% of migraineurs, also commoner in CH, PH, HC
- **Spontaneous, usually without other features**
  - Single stab or series of stabs, rarely occurs repeatedly over a few days, 1 report of status lasting 1 week
- **Duration: 3 secs or less in 80%, rarely can last 10 - 120 secs**
- **Frequency: generally low with 1 or a few / day, can be frequent and disabling**
- **May be unifocal (1/3) or move around the head**
  - Commonly V_1, but any part of the head / face may be affected
- **Case reports of secondary aetiologies**
  - Consider imaging CT/MRI
  - Consider investigation for GCA / Herpetic neuralgia
- **Classified as one of the Indomethacin responsive headaches**
  - As stabs very brief and often infrequent treatment may not be required
  - Same dosage schedule as PH/HC, but response more variable
  - Other treatments much less effective: Celecoxib and Melatonin
  - If associated with migraine watch for development of MOH
  - If associated with migraine can respond to migraine preventatives

Murray and Dilli. Current Neurology and Neuroscience Reports. 2019; 19:47

Primary Stabbing Headache: Differential diagnosis

SUNCT/SUNA	• Longer lasting attacks • Prominent cranial autonomic features • Side-locked
Trigeminal neuralgia	• V2-V3 • Subcutaneous triggers • Side-locked

4.8 Nummular Headache



Nummular eczema

- **Coin shaped (*Latin for "resembling coins" – nummus = coin)***
  - Pain of highly variable duration, but often chronic, in a small circumscribed area of the scalp in the absence of any underlying structural lesion.
  - Mainly mild-moderate (can be severe), pressure-like, sharp, stabbing
  - Any part of scalp – usually strictly unilateral, most commonly parietal, rarely multifocal
  - Variable combinations of hypoesthesia, hyperesthesia, dysesthesia, paresthesia, allodynia, and tenderness
  - Associated migrainous / cranial autonomic features uncommon
  - Co-existing migraine common
- **Investigation**
  - History to ensure not part of systemic autoimmune process
  - Physical examination, including inspection and palpation of the affected scalp
  - Imaging (CT/MRI) to exclude underlying structural cause
- **ICHD III**
  - Continuous or intermittent head pain felt exclusively in an area of the scalp, with all of the following four characteristics:
    - **1. sharply contoured**
    - **2. fixed in size and shape**
    - **3. round (80%) or elliptical (20%)**
    - **4. 1–6 cm in diameter**
- **Treatment options**
  - May not be required for mild pain
  - Tricyclic antidepressants
  - Gabapentin / Pregabalin
  - Indometacin
  - Botox – over the affected area

Wilhour et al. Current Neurology and Neuroscience Reports. 2019; 19:26

4.9 Hypnic Headache

Clinical Features (Modified from ICHD-3)

- Developing only during sleep and causing wakening
- May be bilateral or unilateral
- Lasting from 15 minutes to 4 hours
- No cranial autonomic symptoms or restlessness

- Treatment
  - Acute – caffeine on wakening with headache
  - Preventative
    - Caffeine at bed time e.g. “a strong cup of coffee”
    - Indometacin – 25-150mg nocte
    - Lithium – 150-600mg nocte
    - Melatonin – 3-5mg nocte

Differential Diagnosis

- Other primary headache
  - Nocturnal onset migraine
  - Cluster headache

- Secondary hypnic headache
  - Medication withdrawal (MOH)
  - Obstructive sleep apnoea
  - Nocturnal hypertension
  - Nocturnal hypoglycaemia
  - Structural lesion

Linder et al. Hypnic Headache – what do we know in 2022? Cephalalgia. 2023; 43:1-7

Hypnic Headache: Clinical Characteristics

- **Rare – 250 adult patients and 5 children (case reports and case series)**
- **Majority (92%) > 50 years old**
- **Nearly all patients reported headache occurring at consistent times**
  - 2-4 am most common
  - Most patients had single attack, a few reported multiple attacks
- **Pain intensity 64% mild-moderate**
- **Dull 68%, Throbbing 25%**
- **Majority bilateral (67%)**
- **Migrainous features may be present**
- **Majority leave bed for a purposeful activity (cf migraine), but not do not reach the degree of restless, which is typically seen in cluster headache**
  - ICHD 3 specifically excludes TAC
    - **No cranial autonomic features or restlessness**

Table 2. Clinical characteristics in adult hypnic headache.

Characteristic		
Age at onset (years)[a]	60.9 ± 10.6	
Duration of attacks (min)[b]	162 ± 74.1 (15–600)	
Frequency (days/months)[b]	20.8 ± 9.9 (5–31)	
	n	%
Gender	250	
Male	88	35.2
Female	162	64.8
Timing of attacks	250	
Before 0:00	3	1.2
0:00–2:00	64	25.6
2:00–4:00	131	52.4
After 4:00	52	20.8
Intensity of pain	250	
Mild	16	6.4
Moderate	150	60.0
Severe	84	33.6
Character of pain	250	
Dull	172	68.8
Throbbing/pulsating	64	25.6
Sharp/stabbing/burning	14	5.6
Laterality	250	
Unilateral	81	32.4
Bilateral	169	67.6
Migrainous features	250	
Nausea	52	20.8
Vomiting	1	0.4
Phono-/photophobia	18	7.2
Trigemino-autonomic features[c]	208	
Lacrimation	13	6.3
Ptosis	5	2.4
Rhinorrhoea/nasal congestion	16	7.7

[a]Number of patients = 250.
[b]Number of patients = 225.
[c]After excluding two studies that excluded patients with trigeminal autonomic symptoms from further study.

Laing and Wang. Hypnic Headache: A review of clinical features, therapeutic options and outcomes. Cephalalgia. 2014; 34:795-805

4.10 New Daily Persistent Headache

Persistent headache with distinct and clearly remembered onset,

with pain becoming <u>continuous and unremitting within 24 hours.</u>

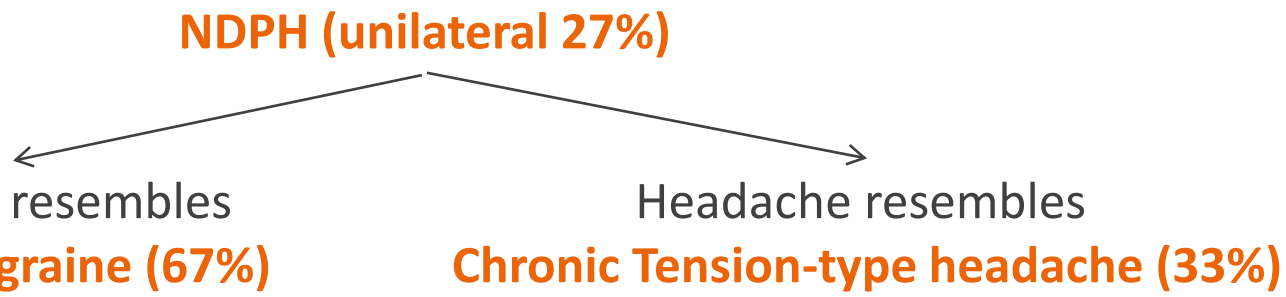
- **NOT ESPESIALLY RARE! – 18% Chronic Daily Headache in children; 4% in adults**
- **Patients often remember the exact day (and circumstances) of onset**
- **Medication overuse is a common complication (19% children/adolescents; 31% adults)**
- **If side locked must exclude Hemicrania Continua**

Diagnosis of exclusion, and secondary causes must be actively excluded

- Spontaneous Intracranial Hypotension (NDPH with initial orthostatic quality)
- IIH and other raised intracranial pressure
- Post traumatic headache
- SAH (3.6-14.8% onset following Thunderclap Headache)

Cheema et al. NDPH: A systematic review and meta-analysis. Cephalalgia. 2023; 43:1-13

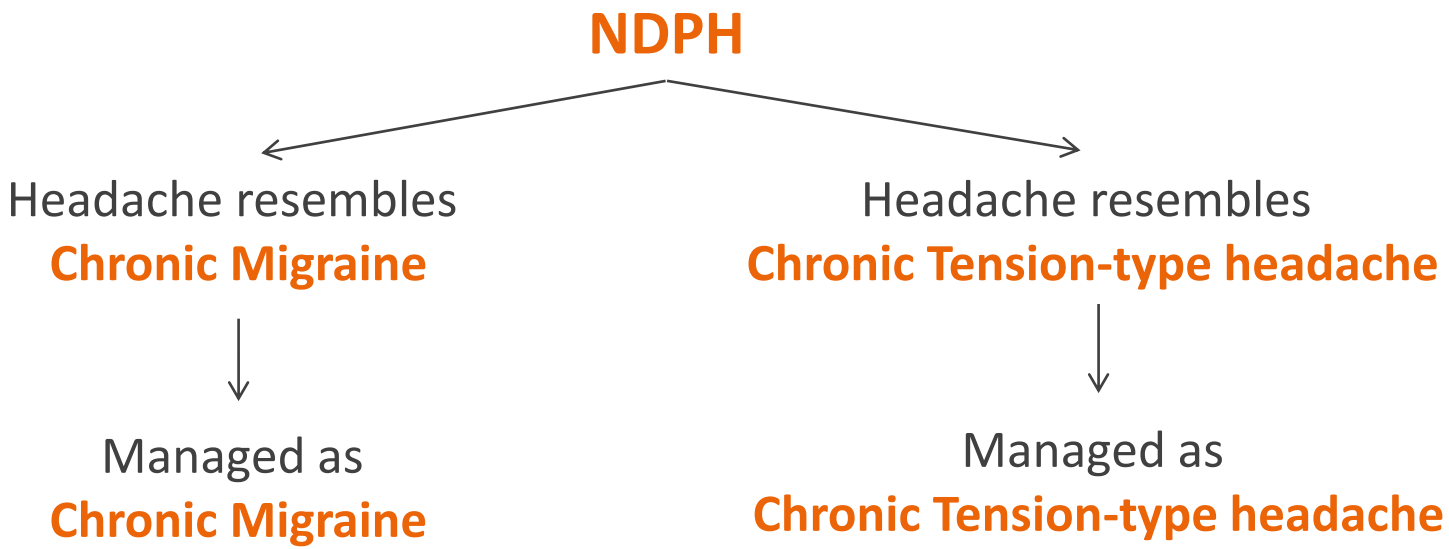
Primary New Daily Persistent Headache



- **2 subtypes:**
  - Self-limiting - usually resolves within several months even without therapy (based on expert opinion)
  - Persistent – long-lasting and often treatment refractory (93% of largest case series)

- **Precipitants and co-morbidities**
  - Precipitants (40%)
    - **Infectious illness – most commonly flu-like illness**
    - **Stressful life event**
    - **Extra-cranial surgery**
  - Co-morbitities
    - **78% children/adolescents and 49% adults episodic headache disorder prior to onset**
    - **40% adults family history of headache disorder**
    - **Hypermobility**
    - **Depression and anxiety**

Primary New Daily Persistent Headache



- **Treatment**
  - Migraine prophylaxis used, but evidence base limited
  - GON blocks (similar efficacy to Chronic migraine)
  - Botox (50% response in 19 patients; 2 out of 9 patients)
- **Prognosis**
  - No long term studies
  - Original description was of a self limiting syndrome
  - Considered to be persistent and highly refractory to treatment

- **SIGN (Scottish Intercollegiate Guidelines Network) guideline 155**
  - **Pharmacological Management of Migraine**
  - https://www.sign.ac.uk/media/2077/sign-155-migraine-2023-update-v3.pdf
  - **Update in progress**

- **Scottish National Headache Pathway**
  - https://www.nhscfsd.co.uk/our-work/modernising-patient-pathways/specialty-delivery-groups/neurology/national-headache-pathway/
  - https://rightdecisions.scot.nhs.uk/neurology-pathways/

- **Scottish National Facial Pain Pathway – in development**