

1. Acute drug-induced headache can be caused by many drugs including

- Nitroglycerin,
- antihypertensives
- (beta-blockers,
- calcium channel blockers,
- angiotensin converting enzyme inhibitors,
- methyl dopa),
- dipyridamole,
- hydralazine,
- sildenafil
- Histamine receptor antagonists (such as
- cimetidine
- and ranitidine)
- NSAIDs especially
- indomethacin
- Cyclosporine,
- amphotericin,
- griseofulvin,
- tetracycline, and
- sulfonamides.

1. Drug-induced aseptic meningitis (see also above)

a. Numerous causes

1. NSAIDs

2. Antibiotics (trimethoprim/sulfamethoxazole, sulfasalazine, cephalosporins, ciprofloxacin, isoniazide, and penicillin)

3. Intrathecal drugs and diagnostics (antineoplastics such as methotrexate and cytarabine; gentamicin; corticosteroids; spinal anesthesia; baclofen; repeated iophendylate for myelography; and radiolabelled albumin)
4. Intraventricular chemotherapy
5. Intravenous immunoglobulin
6. Vaccines (polio; measles, mumps, and rubella; and hepatitis B)
7. Other drugs such as carbamazepine, muromonab CD-3, and ranitidine

Note that the clinical presentation is the same as that of viral meningitis and CSF findings are similar to viral meningitis except for neutrophil predominance in most cases, except Intravenous immunoglobulin where there are eosinophils in the CSF.

Headaches in arachnoiditis patients may be:

- (i) Tension: This type tends to be multifactorial. Sustained contraction of pericranial muscles (muscle contraction headache) is a common feature, although there is no direct correlation between muscle contraction, tenderness, and the presence of headache (migraine sufferers can experience the same or greater muscle contraction).

The tension headache presents often on both sides and may be felt as a tight band across the forehead, and is not aggravated by walking stairs or similar routine physical activity.

It may be referred from upper cervical structures (joints, ligaments, and muscles) and could be due to abnormal neuronal sensitivity and pain facilitation. Central sensitisation due to prolonged pain input from the periphery (e.g. legs in arachnoiditis) can affect the trigeminal nucleus caudalis neurons. Physical or psychological stress, lack of sleep, anxiety and depression can also have this effect.

Tension-type headache in migraineurs may be different than in non-migraineurs in that it may occur due to the typical migraine triggers and light or noise sensitivity often accompany the headache.

(ii) Migraine: possibly due to myofascial trigger points; including vestibular migraines which present as vertigo with or without headache (see below); **Migraine** type headaches often present with auras.

It should be noted that there is an association between photoaversion and anticonvulsant treatment, particularly phenytoin and carbamazepine. ([1](#)) Migraine headaches often involve sensitivity to light and/or noise, and may be accompanied by nausea.

(iii) Neuralgia: neuritic pains tend to be brief but severe: stabbing, lancinating pains; (see under facial pain)

(iv) Cervicogenic headache: Headache arising from the neck: from structures such as joints, ligaments, muscles and cervical discs, all of which have complex nerve endings.

It is typically dull or aching in the occipital (back of the head), temporal (temples) frontal (forehead) or orbital (around the eyes) regions or any combination of these areas; one sided or both sides

There may well be some indication of neck problems such as neck pain, localised neck tenderness, reduced neck movement, aggravation of the headache by neck movement or a history of neck trauma.

In 1987, [Fredriksen, Hovdal, and Sjaastad](#) ([2]), at Trondheim University Hospital in Norway, looked at the clinical manifestations of this headache in 11 typical cases. 6 of the 11 recalled a previous head or neck injury and in 4 the headache had appeared within a month of the trauma.

The typical headache attacks were reported to be of 1-3 days duration separated by intervals of 1-4 weeks. The pain was unilateral, strongest in the orbit or temple but also present in the upper posterior neck, steady in most patients, throbbing at times in some, and often accompanied by nausea/vomiting and light and/or noise sensitivity.

Attacks were often precipitated by such head movements as "washing the ceiling," "polishing the floor" or "turning the head towards someone during conversation." Physical findings were unremarkable, except that in all except one patient, pain, sometimes prolonged, could be induced by firm manual pressure on the neck.

The authors acknowledged that cervicogenic headache could "easily pass for migraine."

In 1998, [Sjaastad, Fredriksen, and Pfaffenrath](#) ([3]) published updated diagnostic criteria on behalf of the Cervicogenic Headache International Study Group:

I. Symptoms and signs of neck involvement:

The presence of Point A by itself signifies neck involvement, but points B and C alone do not. However, B and C together provisionally signify neck involvement.

A. Precipitation of head pain similar to the patient's usual pain:

1. by neck movement and/or sustained awkward head positioning, and/or:
2. By external pressure over the upper cervical or occipital region on the symptomatic side.

B. Restriction of the range of motion in the neck.

C. Ipsilateral neck, shoulder, or arm pain of a rather vague non-radicular nature or, occasionally, arm pain of a radicular nature.

II. Confirmatory evidence by diagnostic anesthetic blocks.

III. Unilaterality of head pain without sideshift.

(v) Rebound headache due to regular analgesic use, particularly opiates. This type of headache should be suspected if:

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medications seem to be less effective.

- taking more medication (higher dose or more often), but getting less relief.
- headache is worse 3-4 hours after taking medication.
- [preventive](#) medications (for migraines) are not working as well as before.
- need to take medication to avoid severe pain or incapacitation.

Dr Timothy Steiner, reader at Imperial College School of Medicine and honorary consultant at Charing Cross Hospital and The Princess Margaret Migraine Clinic, ([\[4\]](#)) suggests that 4% of the population suffer from chronic daily headache, and that

"analgesic rebound headache" or "drug-abuse headache";

is one cause of this problem. He prefers to use the term

"medication misuse headache (MMH)";,

about which he writes:

"This evolution can occur over as little as four weeks or much longer, depending to a large extent on the medication used, although this is not the sole factor... A key factor is that many MMH sufferers use medication pre-emptively, in anticipation of headache and before its onset."

The MMH headache tends to be oppressive and is often present on waking up in the morning, and increases during and after physical exertion.

Nausea such as experienced in migraines is infrequent and less pronounced. Once well

established, MMH may involve a headache, which persists all day, fluctuating with (and despite) medication use, which tends to be repeated every few hours.

Migraine prophylaxis is ineffective, as is the use of amitriptyline.

Combination analgesics have been suspected of being particularly related to development of MMH, but Dr. Steiner suggests that there is no

"evidence that they promote the condition more readily than simple analgesics alone."

Prophylactic (preventive) drugs for migraines such as ergotamine and triptans are however known causes of MMH. Dr. Steiner also points out a possible link with NSAID or opioid medication, as gastrointestinal symptoms have been reported in nearly 40 per cent of patients with MMH.

(NSAIDs can cause upper gastrointestinal distress and opioids are associated with constipation).

(vi) Frequent sinusitis may cause sinus related headache with sensation of fullness around the face (these headaches tend to be worse on bending forward, also first thing in the morning and on exercising.) Headache is one of the key symptoms in acute or chronic sinusitis.

In addition to a headache, sinusitis patients may experience: pain and pressure around the eyes, across the cheeks and the forehead, an achy feeling in the upper teeth, fever and chills, facial swelling, nasal stuffiness and possibly a yellow or green discharge.

(viii) Myodil-related headaches Wicke et al (in Germany) ([\[5\]](#)), Mamaurian and Briggs ([\[6\]](#)) and Hackney et al. (

[7]

), described retained residuals, whether intracranial or intraspinal, as 'common'.

In 1982, Avrahami and Cohen ([8]) published an article in German concerning post-myelography headaches persisting for more than 6 months. The authors suggested that these were the result of residual Pantopaque causing blood vessel irritation.

In May, 1983: Junck and Marshall ([9]) stated:

'The most important adverse effects observed with myelographic agents include acute and chronic meningeal reactions with iophendylate, and seizures and transient encephalopathy with Metrizamide.'

(viii) Low blood sugar: chronic stress and constant pain may cause increases or fluctuations in circulating levels in hormones such as adrenaline, cortisol and insulin.

The latter may result in fluctuating blood sugar levels. Low levels may induce headache associated with anxiety, sweating, pallor and sometimes aggression or agitation or feeling faint.

Eating a high sugar meal may result in onset of symptoms 3-4 hours later as the body may overcompensate for the rapid increase in blood sugar by releasing high levels of insulin which then cause what is termed 'rebound hypoglycaemia': a low blood sugar.

The shaky feeling and other symptoms would resolve quickly on eating food, especially if it is high in sugar.

(ix) Caffeine-related: a study of short-term caffeine withdrawal looked at adults with a

low-moderate daily caffeine intake of an equivalent of about 2.5 cups of coffee (mean of 235 mg) per day

Upon withdrawal of caffeine, 50% had a headache by the second day, with other symptoms such as nausea, depression, and flu-like symptoms.

In patients with frequent headaches, it can be helpful to obtain a history of caffeine use in over the counter and prescription medications as well as beverages and ice cream.

Some examples of caffeine content include:

- 12 ounces of Coca-Cola contains 45 mg
- 8 ounces of brewed coffee contains 135 mg.

Less commonly:

Occipital radiating from the back of the head, forwards to behind the eyes, with possible feeling of pressure around the temple. : Onset of these is usually after exertion, valsalva manoeuvre (e.g. opening the bowels) or bending forward. These seem similar to headaches due to raised intracranial pressure. One can note a similarity with Chiari-1 malformation.

Neurosurgeon Michael Rosner in USA suggests that Chiari malformation may be seen in Chronic Fatigue Immune Deficiency Syndrome (CFIDS) and Fibromyalgia (FMS), both of which are quite often diagnosed in arachnoiditis patients.

A recent study in USA ([\[10\]](#)) has linked Chiari with FMS:

- of 364 patients with Chiari,
- nearly 60% had a prior diagnosis of Fibromyalgia,
- 12% of CFS,
- 31% migraine/sinus headache,
- 9% MS
- and 63% psychiatric/malingering.

Features of Chiari include: occipital headache* radiating behind eyes (exacerbated by exertion, especially leaning the head backward or coughing); disordered eye movements, vision changes; dizziness, autonomic symptoms (orthostatic hypotension, NMH); muscle weakness; unsteady gait; cold, numbness and paraesthesiae in extremities; chronic fatigue; tinnitus; sleep apnoea; hearing loss; Irritable Bowel Syndrome (IBS); frequent urination; difficulty swallowing.

As we have seen from the survey results, many of these symptoms are seen in arachnoiditis. (* headache occurs in about 50% of Chiari cases and the brief type tend to be caused by transient herniation of the base of the brain, part of the brain stem called the tonsils down through the hole at the base of the skull into the spinal canal)

Sansur et al. ([\[11\]](#)) recently looked at the pathophysiology of headache associated with Chiari 1 malformation. 26 patients had Chiari 1 plus syringomyelia, 4 had only Chiari. They found that headache linked to coughing in patients with Chiari I malformation is associated with sudden increased intrathecal pressure caused by obstruction to the free flow of CSF in the subarachnoid space.

A further possibility is intermittent raised intracranial pressure similar to that seen in a condition called pseudotumour cerebri or benign intracranial hypertension (BIH).

In this condition, there may be severe, frequent headaches, which are worst in the morning (and may indeed waken the patient), visual disturbances (transient blurring or loss of part of the visual field) and sometimes a pulsatile tinnitus (pulsing sound in the ears).

This has not been proven as such in arachnoiditis, but there is a known association between arachnoiditis and a condition called hydrocephalus which leads to enlarged ventricles in the

brain due to raised pressure of the CSF; another similar condition affects the spinal part of the CSF: syringomyelia.

It may well be that the scar tissue of arachnoiditis impairs normal CSF circulation and this affects the pressure gradient in what is a closed system.

[1] Bayer A, Thiel HJ, Zrenner E, Paulus W, Ried S, Schmidt D *Nervenarzt* 1995 Feb; 66(2): 89-96 [Disorders of color perception and increase glare sensitivity in phenytoin and carbamazepine therapy. Ocular side effects of anticonvulsants.

[2] Fredriksen TA, Hovdal H, Sjaastad O. *Cephalalgia* 1987; 7:147-60 Cervicogenic headache"; Clinical manifestation.

[3] Sjaastad O, Fredriksen TA, Pfaffenrath V. *Headache* 1998; 38:442-45. Cervicogenic headache: Diagnostic criteria.

[4] Internet resource: <http://www.dotpharmacy.co.uk/updaily.html>

[5] Wicke L, Fruhwald F, Neuhold A, Schwaighofer B. *ROFO Fortschr Geb Rontgenstr Nuklearmed* 1987 Dec; 147(6): 663-5
[MR effects of x-ray contrast media]

[6] Mamourian AC, Briggs RW. *Radiology* 1986 Feb; 158(2): 457-60 Appearance of Pantopaque on MR images.

[7] Hackney DB, Grossman RI, Zimmerman RA, Joseph PM, Goldberg HI, Bilaniuk LT. *J Comput Assist Tomogr* 1986 May-Jun; 10(3): 401-3 MR characteristics of iophendylate (Pantopaque).

[8] [Avrahami E, Cohn DF](#). *Schweiz Arch Neurol Neurochir Psychiatr*. 1982; 131(2): 157-60.
[The problem of postmyelography headaches]

[9] Junck L, Marshall WH. *Ann Neurol* 1983 May; 13(5): 469-84 Neurotoxicity of radiological contrast agents.

[10] Milhorat TH, Chou MW, Trinidad EM, Kula RW, Mandell M, Wolpert C, Speer MC *Neurosurgery* 1999 May;44(5):1005-17 Chiari I malformation redefined: clinical and radiographic findings for 364 symptomatic patients.

[11] Sansur CA, Heiss JD, DeVroom HL, Eskioglu E, Ennis R, Oldfield EH. *J Neurosurg* 2003 Mar; 98(3):453-8 Pathophysiology of headache associated with cough in patients with Chiari I malformation.