1 Morrell DC. Symptom interpretation in general practice. *Journal of the Royal College of General Practitioners* 1972;22:295-309.
2 Jerrett WA. Lethargy in general practice. *Practitioner* 1981;4:731-7.
3 David A, Pelosi A, McDonald E, Stephens D, Ledger D, Rathbone R, *et al.* Tired, weak, or in need of rest: fatigue among general practice attenders. *BMJ* 1990;301:1199-202.
4 Cox B, Blaxter M, Buckle A, Fenner NP, Golding JF, Gore M, *et al. The health and lifestyle survey.* London: Health Promotion Research Trust, 1987.
5 Banks MH, Beresford SAA, Morrell DC, Waller JJ, Watkins CJ. Factors influencing demand for primary medical care in women aged 20-44 years: a preliminary report. *Int J Epidemiol* 1975;4:189-95.
6 Morrison JD. Fatigue as a presenting complaint in family practice. *J Fam Pract* 1980;10: 795-801.
7 Sugarman JR, Berg AO. Evaluation of fatigue in a family practice. *J Fam Pract* 1984;19:643-7.
8 Oakley A. *The sociology of housework.* London: Pitman, 1974.
9 Goldberg D, Bridges K. Screening for psychiatric illness in general practice: the general practitioner versus the screening questionnaire. *Journal of the Royal College of General Practitioners* 1987;37:15-8.
10 Johnstone A, Goldberg D. Psychiatric screening in general practice. *Lancet* 1976;ii:605-8.
11 American Psychiatric Association Committee of Nomenclature and Statistics. *Diagnostic and statistical manual of mental disorder.* 3rd edn. Washington DC: American Psychiatric Association, 1980. (DSM-3.)
12 Brown G, Harris T. *Social origins of depression.* London, Tavistock. 1978.
13 Hollyman JA, Freeling P, Paykel ES, Bhat A, Sedgwick P. Double-blind placebo-controlled trial of amitriptyline among depressed patients in general practice. *Journal of the Royal College of General Practitioners* 1988;38:393-7.
14 Royal College of General Practitioners, Office of Population Censuses and Surveys, and Department of Health and Social Security. *Morbidity statistics from general practice. Third national study, 1981-82.* London: HMSO, 1986.
15 Sharpe MC, Archard LC, Banatvala JE, Borysiewicz LK, Clare AW, David A, *et al.* A report—chronic fatigue syndrome: guidelines for research. *J R Soc Med* 1991;84:118-21.
16 Miller NA, Carmichael HA, Calder BD, Behan PO, Bell EJ, McCartney RA, *et al.* Antibody to Coxsackie B virus in diagnosing postviral fatigue syndrome. *BMJ* 1991;302:140-3.
17 Yousef G, Bell E, Mann G, Murugesan V, Smith DG, McCartney RA, *et al.* Chronic enterovirus infection in patients with postviral syndrome. *Lancet* 1988;ii:146-50.
18 Jamal GA, Hansen S. Electrophysiological studies in the post-viral fatigue syndrome. *J Neurol Neurosurg Psychiatry* 1985;48:691-4.
19 Stokes MJ, Cooper RG, Edwards RHT. Normal muscle strength and fatigability in patients with effort syndromes. *BMJ* 1988;297:1014-7.
20 Hamblin TJ, Hussain J, Akbar AN, Tang YC, Smith JL, Jones DB. Immunological reason for chronic ill health after infectious mononucleosis. *BMJ* 1983;287:85-8.
21 Wessely S, Powell R. Fatigue syndromes: a comparison of chronic "postviral" fatigue with neuromuscular and affective disorders. *J Neurol Neurosurg Psychiatry* 1989;52:940-8.
22 Butler S, Chalder T, Ron M, Wessely S. Cognitive behaviour therapy in chronic fatigue syndrome. *J Neurol Neurosurg Psychiatry* 1991;54:153-8.

Sumatriptan in migraine

May be better than aspirin and metoclopramide

Migraine disables. Conventional treatment provides only moderate relief of symptoms, and many patients cannot work for 12 to 48 hours. The principal aims of treating acute attacks are to control pain, nausea and vomiting, and other concomitant symptoms of migraine, thereby achieving the prompt return of the patient to normal activities. Rest, simple analgesics, ergotamine, or non-steroidal anti-inflammatory drugs combined with antiemetics such as metoclopramide or domperidone are the mainstays of traditional treatment. The introduction of sumatriptan, a serotonin-1 ($5HT_1$) agonist, for acute attacks heralds a new pharmacological approach to treatment, derived from fundamental studies on receptor mechanisms that shed light on the pathogenesis of headaches.

The innervation of pain sensitive dura and vessels is through the trigeminal nerve and the upper three cervical nerve roots. On the afferent side there is a "centre" in the upper cervical cord. Pain fibres descend in the spinal root of the trigeminal nerve to C2, where they converge with afferents from C1-C3 on second order neurones. This provides a pain pathway from the head to the neck and vice versa.[1] The raphe nuclei and locus coeruleus project rostrally to the cortex and caudally as part of the "endogenous pain control circuit." Stimulation of these brain stem nuclei and of the trigeminal complex increases extracranial blood flow by reflex connection with the parasympathetic part of the facial nerve through the greater superficial petrosal nerve and sphenopalatine and otic ganglia. This constitutes a link between neural[2,3] and vascular mechanisms: the "trigeminovascular reflex." Activation of this pathway probably foments a variety of headaches.

Serotonin-1 agonists (such as ergotamine and sumatriptan) bind to receptors and constrict dural and pial vessels. They block the extravasation of plasma in the dura and venous sinuses, which is stimulated by perivascular trigeminal fibres that release neurokinin A, calcitonin G related peptide, and substance P. This important pain mechanism may provide the final common pathway for migraine and other cephalgias, explaining the similarities and overlap between different headache syndromes. Sumatriptan is a specific and selective agonist of serotonin type 1 receptors in cranial blood vessels that causes vasoconstriction. It does not penetrate the blood-brain barrier and has no effects on the central nervous system. The drug has high bioavailability—96% subcutaneously and 14% orally—with peak plasma concentrations at 5-20 minutes.

It is currently available only by subcutaneous injection. Early clinical trials showed relief of headache in 77% of patients at 60 minutes and 83% at two hours, with corresponding improvements in nausea, vomiting, and photophobia.[4] It is also effective in cluster headaches, relieving symptoms at 15 minutes in 74% of patients compared with 26% given placebo.[5] To date, no serious cardiovascular or neurological adverse effects have been reported, though 38% of patients have reported mild transient nausea, vomiting, an odd taste, and flushing and tingling in the head and chest. The subcutaneous preparation will almost certainly be superseded by an oral form, which provides relief in about half to two thirds of attacks within two hours. Second and third attacks respond as well as the first. Comparative trials have shown that sumatriptan is slightly but significantly better than aspirin 900 mg and metoclopramide 10 mg (Legg N, 8th Migraine Trust international symposium, London, 1990).

Goadsby *et al* recently reported a favourable response at two hours in 51% of the patients given oral sumatriptan compared with 9% of those given placebo; rescue medication was needed by 41% of patients taking sumatriptan, but 88% of patients taking placebo.[6] Of 28 patients free of headache at two hours, 11 experienced recurrent headache within 24 hours—a substantial "rebound effect," which may owe more to the natural course of migraine than to a true pharmacological effect.

Sumatriptan seems an effective, safe, and prompt remedy for acute attacks of migraine, suppressing all the symptoms—not just headache—but it does not work in every patient. The present high cost (£41 for two injections) may limit its use to patients prone to unusually refractory, severe, or inconveniently timed attacks. Wider clinical experience is needed before its final place in the treatment of migraine can be defined.

J M S PEARCE

Consultant Neurologist, Hull Royal Infirmary, Hull HU3 2JZ.

1 Lance JW. The pathophysiology of migraine. In: Dalessio DJ, ed. *Wolff's headache and other head pain.* New York: Oxford University Press, 1988:58-87.
2 Pearce JMS. Neural aspects of migraine. In: Blau JN, ed. *Migraine.* London: Chapman and Hall, 1987:247-65.
3 Pearce JMS. Is migraine explained by Leão's spreading depression? *Lancet* 1985;ii:763-6.
4 The Sumatriptan Auto-injector Study Group. Self-treatment of acute migraine with subcutaneous sumatriptan. *Eur Neurol* 1991;31:323-31.
5 The Sumatriptan Cluster Headache Study Group. Treatment of acute cluster headache with sumatriptan. *N Engl J Med* 1991;325:322-6.
6 Goadsby PJ, Zagami AS, Donnan GA, Symington G, Anthony M, Bladin PF, *et al.* Oral sumatriptan in acute migraine. *Lancet* 1991;338:782-3.