CHAPTER 1

INTRODUCTION

Headache is one of the most common complaints encountered by physicians of all specialties. It is a complaint in more than fifty percent of all physician visits and is the seventh leading complaints at medical centres in the United States. Due to headaches five to ten percent of young adults report missing at least a part of a day’s works each month. Consequently, the physician faces a major task in addressing patient's headache complaint. Headache accounts for over ten million outpatient visits per year in the United States. Most of the patients are often quite concerned that their headaches represent serious underlying illness. Headache itself is a painful and often disabling disorder and it has troubled mankind from the dawn of civilization. It is one of the most common symptoms in mankind (Scher, Stewart and Lipton, 1999). For these reason a systematic approach to headache classification and diagnosis is essential both for good clinical management and for useful research. The first edition of the International Classification of Headache Disorders, Headache Classification Committee of the International Headache Society, 1988 (ICHD-1) was accepted as a standard for headache diagnosis. This system was advanced as ICHD-2 in 2004. This system established a uniform terminology and consistent operational diagnostic criteria for the entire range of headache disorders. It was translated into 22 languages. In this system, headaches are classified using principles similar to those developed by the American Psychiatric Association. The criteria broadly divide headache into ‘primary’ and ‘secondary’ headache disorders. The primary headache disorders are those in which the headache condition itself is the problem and no underlying or dangerous cause for it can be identified. The classification is based on symptom profiles. Secondary headaches are those due to an underlying condition such as a tumour, infection or haemorrhage. The secondary headaches are classified according to their causes. Most of the primary and secondary headache disorders are more common in women than in men. Primary headache disorders are much more common than secondary headache disorders. The ‘big three’ primary headache disorders are migraine, tension-type headaches and cluster headache. Tension-type headache is the most common headache disorder, but it is usually mild and self-limiting. It generally prompts medical consultation only when chronic. Migraine is the second most common headache
problem that causes patients to seek medical help. Cluster headache is the most severe of the three conditions, but it is uncommon (Silberstein, Stephen Stiles, Alan, Young and William, 2005). Thus headache can be classified into two categories, i.e. primary headache and secondary headache. These categories are described below.

**PRIMARY HEADACHES**

1. **Tension-Type Headache**: The main pain symptoms of tension type headache are bilateral location, nonpulsating quality, mild-to-moderate intensity and lack of aggravation by routine physical activity. The pain in tension headache is not accompanied by nausea, photophobia or phonophobia. Chronic tension type headache invariably evolves from episodic tension type headache but cannot be diagnosed in patients overusing acute medication. Such patients often meet criteria for medication-overuse headache, although withdrawal of the medication is required to confirm this diagnosis. When a headache fulfills all but one of the criteria for tension type headache and does not fulfill the criteria for migraine without aura, the diagnosis should be probable tension type headache. Tension-Type Headache is the most common type of primary headache. The ICHD-1 distinguished two subtypes of tension type headache- episodic tension type headache (less than 15 attacks per month) and chronic tension type headache (15 or more attacks per month). The ICHD-2 distinguishes three subtypes of tension type headache - infrequent episodic tension type headache (headache episodes on less than 1 day/month), frequent episodic tension type headache (headache episodes on 1–14 days/month) and chronic tension type headache (headache episodes on 15 or more days/month (Stewart, Simon and Lipton, 1998).

2. **Migraine headache**: Migraine is not 'just a headache'. It is very serious problem. It is a neurological condition that is associated with a series of complex changes that occur within the brain and brainstem. These changes are mostly biochemical that, once started, is difficult to stop and they generate all the symptoms that make a migraine. It is an episodic condition and it can occur now and again. Its duration is about 4 to 72 hours. The frequency may be once a week, once a month or even once a year. The frequency will vary from time to time as well as from person to person. Migraine may occur with or without aura. About 10% of people who get migraine get an aura. The most common aura is visual but other aura symptoms include pins
and needles and tingling or numbness. In an attack the person stops doing the things. It is because of that moving about will make the headache worse. Migraine might make feel sick (nauseated) or actually vomit. Light and sound often make the headache feel worse. The person just wants to keep still until the attack has gone (Fontebass, 2007).

3. Cluster Headache: The main pain symptoms of cluster headache are as intermittent, short-lasting, unilateral head pain accompanied by autonomic dysfunction (Kudrow, 1991). The pain of cluster headache is described variously as sharp, boring, drilling, knife-like, piercing or stabbing, in contrast to the pulsating pain of migraine. It usually peaks in 10 to 15 minutes but remains intense for an average of one hour within a duration range of 15 to 180 minutes. During this pain, patients find it difficult to lie still, exhibiting often marked agitation and restlessness and autonomic signs are usually obvious. After an attack, the patient remains exhausted for some time. Cluster headache is classified into two subtypes: - (i) Episodic cluster headache and (ii) Chronic cluster headache. Attacks of episodic cluster headache occur in cluster periods lasting from seven days to one year separated by attack-free intervals of one month or more. Approximately 85% of cluster headache patients have the episodic subtype. In chronic cluster headache, attacks occur for more than one year without remission or with remissions lasting less than one month. Chronic cluster headache can evolve from episodic cluster headache (Dodick, Rozen, Goadsby and Silberstein, 2000).

4. Other types of headaches are as follows:

i. Primary Stabbing Headache: Episodic localized stabs of head pain occurring spontaneously in the absence of any structural cause (formerly referred to as "jabs and jolts") are diagnosed as primary stabbing headache. Pain is exclusively or predominantly in the distribution of the first division of the trigeminal nerve (orbit, temple, and parietal area). It lasts for up to a few seconds and recurs at irregular intervals with a frequency ranging from one to many per day (Pareja, Ruiz, de Isla, al-Sabbab and Espejo, 1996).

ii. Primary Cough Headache: This headache is characterized by coughing and straining (Sjaastad, Pettersen and Bakketeig, 2003).
iii. Primary Exceptional Headache: This disorder is triggered by physical exercise and is distinguished from primary cough headache and headache associated with sexual activity. Primary exertion headache is pulsating and lasts from 5 minutes to 48 hours (Green, 2001).

iv. Primary Headache Associated with Sexual Activity: Headache precipitated by sexual activity usually begins as a dull bilateral ache as sexual excitement increases and suddenly becomes intense at orgasm. Two subtypes are classified: preorgasmic headache, a dull ache in the head and neck and orgasmic headache, explosive and severe, and occurring with orgasm (Lance and 1976).

v. Hyponic Headache: This primary headache disorder is characterized by short-lived attacks (typically 30 minutes) of nocturnal head pain, which awakens the patient at a constant time each night. Hyponic headache is usually bilateral and mild to moderate and very different from the unilateral orbital or periorbital knife-like intense pain of cluster headache (Dodick, Brown, Britton and Huston, 1999).

vi. Hemicrania Continua: This is daily, continuous and strictly unilateral headache. Pain is moderate, with exacerbations of severe pain and autonomic symptoms accompany these exacerbations (Bigal, Sheftell, Rapoport, Lipton and Tepper, 2002).

SECONDARY HEADACHES

1. Headache attributed to head and neck trauma: This category includes headaches that occur for the first time in close temporal relation to a known trauma. If there is remission within three months after the trauma, the headache should be classified as acute post-traumatic headache. Otherwise, chronic post-traumatic headache is the diagnosis. The same rule applies to acute and chronic post-whiplash injury headache. The ICHD-2 also classifies under this group those headaches secondary to intracranial hematoma and postcraniotomy (Packard, 1999).
2. Headache attributed to cranial or cervical vascular disorders: This category encompasses a large group of headaches that fulfill the following criteria: symptoms or signs of a vascular disorder; appropriate investigations indicating the vascular disorder and the headache developing in close relationship with the vascular disorder. This group includes headaches related to (i) ischemic stroke and TIAs; (ii) nontraumatic intracranial hemorrhage; (iii) unruptured vascular malformations; (iv) arteritis (including giant cell arteritis); (v) carotid or vertebral artery pain (including arterial dissection, ostendarterectomy headache, etc.); (vi) cerebral venous thrombosis; and (vii) other intracranial vascular disorders, including CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy), MELAS (mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes), etc. (Gorelick, Hier, Caplan and Langenberg, 1986).

3. Headache attributed to nonvascular intracranial disorders: This category includes an extensive and heterogeneous group of disorders. They are: (i) high cerebrospinal fluid pressure; (ii) low cerebrospinal fluid pressure; (ii) noninfectious inflammatory diseases; (iv) intracranial neoplasm; (v) headache related to intrathecal injections; (vi) postseizure headache; (vii) Chiari malformation type-I (CM1); and (viii) syndrome of transient headache and neurologic deficits with cerebrospinal fluid lymphocytosis (Ramadan, 1996).

4. Headache attributed to a substance or its withdrawal: When new headaches occur in close temporal relation to substance use or withdrawal, they are coded to this group. The ICHD-2 classifies in this group those headaches following acute exposure to (i) nitric oxide donor substances; (ii) phosphodiesterase inhibitors; (iii) carbon monoxide; (iv) alcohol; (v) food components and additives; (vi) monosodium glutamate; (vii) cocaine; (viii) cannabis; and (ix) other acute substance use. In addition, chronic medication overuse is a risk factor for the development of chronic headache disorders (Bartleson, Swanson and Whisnant, 1993).

5. Headache attributed to infection: This is a very straightforward group where headaches secondary to intracranial and extracranial (systemic) infections are
classified. This group also includes headaches related to HIV/AIDS and chronic post infectious headaches (Gomez-Arada, Canadillas and Marti-Masso, 1997).

6. Headache attributed to disorders of homeostasis: This group of headaches was formerly referred as headaches associated with metabolic or systemic diseases. They include the following headaches: (i) headache attributed to hypoxia and/or hypercapnia (high altitude, diving, and sleep apnea); (ii) dialysis; (iii) arterial hypertension; (iv) headache attributed to hypothyroidism; (v) headache attributed to fasting; (vi), cardiac cephalgia; and (vii) headache attributed to other disturbances of homeostasis. (Antoniazzi, Bigal, Bordini, Speciali, 2003).

7. Headache or facial pain attributed to disorders of cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cranial structures: This is a very heteronegenous group classifying headache and facial pain due to disease of the cranium, the neck, and the facial structures. The ICHD-2 includes criteria for cervicogenic headache (Sjaastad, Fredriksen and Stolt-Nielsen, 2002).

8. Headache attributed to psychiatric disorders: This group provides a link to classify those extremely rare headaches that are causally attributable to a psychiatric disorder. The headache may be attributed to a somatization disorder or to a psychotic disorder. This should be distinguished from psychiatric comorbidities where a headache disorder (e.g., migraine) and a psychiatric disorder (e.g., depression) occur together in the same person (Guidetti, Galli, Fabrizi, 1998).

9. Cranial neuralgias and centrals causes of facial pain: Finally, the in last of the ICHD-2 codes the cranial neuralgias and facial pain, including (i) trigeminal neuralgia; (ii) glossopharyngeal neuralgia; (iii) nervus intermedius neuralgia; (iv) superior laryngeal neuralgia; (v) nasociliary neuralgia (Charlin); (vi) supraorbital neuralgia; (vii) other terminal branch neuralgias; (viii) occipital neuralgia; (ix) neck–tongue syndrome; (x) external compression headache;n (xi) cold stimulus headache; (xii) constant pain caused by compression, irritation, or distortion of cranial nerves or upper cervical roots by structural lesions; (xiii) optic neuritis; (xiv) ocular diabetic neuropathy; (xv) herpes zoster; (xvi) Tolosa–
MIGRAINE HEADACHE

Migraine is a medical condition that causes intermittent attacks of headache and is associated with nausea and vomiting and sensitivity to light, sound or smells. Like asthma and epilepsy, migraine is considered a chronic medical disorder. Migraine does not always receive as much attention and respect as other medical conditions. The word migraine is French in origin and comes from the Greek word hemicrania (as does the old English term megrim). Literally, hemicrania means "only half of the head." Although the term migraine derives from the Greek word 'hemicrania' which means half of the head but it is not always strictly unilateral headache; it can be bilateral. And it is important to understand that migraine is a real illness and the condition deserves the same aggressive treatment as any other chronic disorder (Foster and Carol, 2007).

In the 1960s, "The Ad Hoc Committee on Classification of Headache," defines migraine headache as follows: "Recurrent attacks of headache, widely varied in intensity, frequency and duration. The attacks are commonly unilateral in onset and are usually associated with loss of appetite and sometimes with nausea and vomiting. Some patients are preceded by or associated with sensory, motor and mood disturbances. For about 20 years, this was the accepted definition of migraine. Thus headaches that were usually one-sided, that sometimes seemed to cause stomach upset and that were sometimes preceded by warning signals, such as flashes of light, dizziness or changes in mood, were called migraines. Thus it is a painful neurological condition of which the most common symptom is an intense and disabling episodic headache. Migraine is usually characterized by severe pain on one or both sides of the head and is often accompanied by photophobia (hypersensitivity to light), phonophobia (hypersensitivity to sound) and nausea (Young, Silberstein and Sumner, 2004).

Migraine is sub classified into six major categories, the two most important of which are migraine without aura and migraine with aura. This is unchanged from the ICHD-1, but after that there is a restructuring of the criteria for migraine. The ICHD-2 classifies of migraine in two most important types: Migraine without aura and Migraine with aura. These had previously been called common migraine and classic migraine (The International Headache Society (IHS), 1988).
1. Migraine without aura: Migraine without aura is a clinical syndrome characterized by headache features and associated symptoms. According to the ICHD-2 criteria for migraine without aura can be met by various combinations of features and no single feature is required. The features found in a migraine patient are unilateral and throbbing pain but the pain can be bilateral also. Similarly, only one of two possible symptoms is found. Patients show the symptoms of nausea but not photophobia or phonophobia. Attacks usually last from 4 to 72 hours if untreated. If the patient falls asleep during migraine and wakes up without it, the duration of the attack is timed until the time of awakening. In children, attacks may last 1 to 72 hours and in young children, photophobia and phonophobia may be inferred from behavior (Headache Classification Subcommittee of the International Headache Society, 2004).

2. Migraine with aura: The criteria for migraine with aura have been revised substantially. The typical aura of migraine is characterized by focal neurological features that usually precede migrainous headache, but may accompany it or occur in the absence of the headache (Olesen, Friberg and Olsen, 1990). Typical aura symptoms develop over five minutes or more and last no more than 60 minutes and visual aura is overwhelmingly the most common (Jensen, Tfelt-Hansen, Lauritzen and Olesen, 1986). Typical visual aura is homonymous, often having a hemianopic distribution and expanding in the shape of a crescent with a bright, ragged edge, which scintillates. Scotoma, photopsia or phosphenes and other visual manifestations may occur. Visual distortions such as metamorphopsia, micropsia and macropsia are more common in children. Sensory symptoms occur in about one-third of patients who have migraine with aura. Typical sensory aura consists of numbness (negative symptom) and tingling or paresthesia (positive symptoms). The distribution is often cheiro-oral (face and hand). Dysphasia may be part of typical aura, but motor weakness, symptoms of brain stem dysfunction and changes in level of consciousness, all of which may occur during attack (Peres, Siow and Rozen, 2002).

3. Familial hemiplegic migraine (FHM): It is the first migraine syndrome to be linked to a specific set of genetic polymorphisms (Carrera, Stenirri and Ferrari, 2001). Herein, aura includes some degree of motor weakness and may be
prolonged for more than 60 minutes (up to 24 hours). The onset of weakness may be abrupt, but usually lasts less than one hour. A person with FHM may develop migraine with aura when adult and migraine without aura in later ages of life (De Fusco, Marconi and Silvestri, 2003).

4. Basilar-type migraine: It is a new term, replacing “basilar migraine.” The change is intended to remove the implication that the basilar artery or its territory is involved. The distinguishing feature of basilar-type migraine is a symptom profile that suggests posterior fossa involvement. Diagnosis requires at least two of the following aura symptoms: dysarthria, vertigo, tinnitus, decreased hearing, double vision, visual symptoms simultaneously in both temporal and nasal fields of eyes, ataxia, decreased level of consciousness, and simultaneously bilateral paresthesias. Because 60% of patients with FHM have basilar-type symptoms, basilar-type migraine should be diagnosed only when weakness is absent. The headache meets the criteria for migraine without aura (Panayiotopoulos, 1999)

5. Childhood migraine: Childhood Periodic Syndromes commonly precursors of migraine. A number of more or less disorders are classified under this heading are.

i. Cyclical vomiting occurs in up to 2.5% of school children. The hallmark of this disorder is recurrent and stereotyped episodes of intense but otherwise unexplained nausea and vomiting, which last one hour to five days in children. Vomiting occurs at least four times in an hour and no signs of gastrointestinal disease can be found (Fleisher, 1999).

ii. Abdominal migraine afflicts up to 12% of schoolchildren, with recurrent attacks of abdominal pain associated with anorexia, nausea and sometimes vomiting. The abdominal pain has all of the following characteristics: midline location, perilumbilical or poorly localized; dull or “just sore” quality; and moderate or severe intensity. At least two of the following symptoms are present during the episode: anorexia, nausea, vomiting, and/or pallor. Physical examination and investigations exclude other causes of these symptoms (Abu- Arafah and Russel, 1995).
iii. Benign paroxysmal vertigo is a disorder characterized by recurrent (at least five) attacks. Each attack comprising multiple episodes of severe vertigo resolving spontaneously in minutes to hours. Neurological examination and audiometric and vestibular functions are all normal between attacks and the electroencephalogram is also normal (Drigo, Carli, Laverda and 2001).

6. Retinal Migraine: This disorder is rare. Recurrent attacks (at least two) of fully reversible scintillations, scotomata or blindness, affecting one eye only and are accompanied or followed within one hour by migraineous headache. A recent study suggests that many patients with "retinal migraine" experience retinal infarction of migraineous origin (Grosberg, Lipton, 2005).

HISTORY OF MIGRAINE

Headache has troubled mankind from the dawn of civilization. Signs of trepanation, a procedure wherein the skull was perforated with an instrument, are evident on neolithic human skulls dating from 7000–3000 BC (Layons and Petrucelli, 1978). Originally, it was thought that the procedure had been performed to release demons and evil spirits. But recent evidence suggests that it was carried out for medical reasons (Venzmer, 1972). Trepanation continues to be practiced today, without anesthesia, by some African tribes. It is primarily performed for relief of headache or removal of a fracture line after head injury (Rawlings and Rossitch, 1994). Headache prescriptions written on papyrus were already known in ancient Egypt. The Ebers Papyrus, dated circa 1200 BC to 2500 BC described migraine, neuralgia and shooting head pains (Critchley, 1967). It was a practice at that time to firmly bind a clay crocodile holding grain in its mouth to the patient’s head using a strip of linen that bore the names of the gods (Edmeads, 1990 and Lance, 1982). This technique may have produced headache relief by compressing and cooling the scalp (Edmeads, 1990). Hippocrates (470–410 BC), described a shining light, usually in the right eye, followed by violent pain that began in the temples and eventually reached the entire head and neck area (Edmeads, 1990). He believed that headache could be triggered by exercise or intercourse. He also believed that migraine resulted from vapors rising from the stomach to the head and that vomiting could partially relieve the pain of headache (Edmeads, 1990 and Lance, 1982). Celsus (AD 215–300) believed 'drinking wine, or crudity [dyspepsia] or cold, or heat of a fire or the sun' could trigger migraine. Because
of these classic descriptions, Aretaeus of Cappodocia is credited with discovering migraine headache. The term ‘migraine’ is derived from the Greek word ‘hemicrania’, introduced by Galen in approximately AD 200. He believed it was caused by the ascent of vapors, either excessive, too hot or too cold. Thus, migraine was well known in the ancient world (Critchley, 1967).

Migraine over the centuries: In the twelfth century, Abbess Hildegard of Bingen described her vision about migraine aura (Singer, 1958). Migraine was distinguished from common headache by Tissot in 1783, who ascribed it to a supraorbital neuralgia, provoked by reflexes from the stomach, gallbladder or uterus’ (Sacks, 1985). Over the next century, DuBois Reymond, Mollendorf and Eulenburg proposed different vascular theories for migraine. In the late eighteenth century, Erasmus Darwin grandfather of Charles Darwin, suggested treating headache by centrifugation. He believed headaches were caused by vasodilation and suggested placing the patient in a centrifuge to force the blood from the head to the feet (Edmeads, 1990 and Lance, 1982). Fothergill in 1778 introduced the term ‘fortification spectra’ to describe the typical visual aura or disturbance of migraine. Fothergill used the term ‘fortification’ because the visual aura resembled a fortified town surrounded with bastions (Patterson and Silberstein, 1993 and Raskin, 1988). In 1873, Liveing wrote the first monograph on migraine, entitled On Megrim, Sickheadache, and Some Allied Disorders: A Contribution to the Pathology of Nerve-storms and originated the neural theory of migraine. He ascribed the problem as disturbances of the autonomic nervous system’, which he called ‘nerve storms’ (Patterson and Silberstein, 1993). William Gowers, in 1888, published an influential neurology textbook, ‘A Manual of Disease of the Nervous System’ (Raskin, 1988). Gowers emphasized the importance of a healthy lifestyle and advocated using a solution of nitroglycerin (1% in alcohol), combined with other agents, to treat headaches. The remedy later became known as the ‘Gowers mixture’. Gowers was also famous for recommending Indian hemp (marijuana) for headache relief (Edmeads, 1990 and Lance, 1982). Lewis Carroll described migrainous phenomena in Alice in Wonderland and Through the Looking Glass, depicting instances of central scotoma, tunnel vision, phonophobia, vertigo, distortions in body image, dementia and visual hallucination. Greek and Roman ancient writings include references to ‘blighted grains’ and ‘blackened bread’, and to the use of concoctions of powdered barley flower to hasten childbirth. During the Middle Ages, written accounts of ergot poisoning first
appeared. Epidemics were described in which the characteristic symptom was gangrene of the feet, legs, hands and arms, often associated with burning sensations in the extremities. The disease was known as 'Ignis Sacer' or 'Holy Fire' and, later, as 'St. Anthony's Fire', in honor of the saint at whose shrine relief was obtained. This relief probably resulted from the use of a diet free of contaminated grain during the pilgrimage to the shrine (Bove, 1970). The term 'ergot' is derived from the French word 'argot' meaning 'rooster's spur'. It describes the small, banana-shaped sclerotium of the fungus. Louis René Tulasne of Paris in 1853 established that ergot was not a hypertrophied rye seed, but a fungus having three stages in one life cycle, and he named it Claviceps purpurea. Once infected by the fungus, the rye seed was transformed into a spurs-shaped mass of fungal pseudotissue, purple-brown in colour: the resting stage of the fungus, known as the 'sclerotium' (derived from the Greek 'skleros') (Bove, 1970). In 1831, Heinrich Wiggers, a pharmacist of Göttingen, Germany tested ergot extracts in animals. Among his models was the 'rooster comb test': a rooster, when fed ergotin, became ataxic and nauseous, acquired a blanched comb and suffered from severe convulsions, dying days later. The 'rooster comb test' continued to be used into the following century by investigators studying the physiologic properties of ergot (Bove, 1970). Later Woakes, in 1868, reported the use of ergot of rye in the treatment of neuralgia (Woakes, 1868). The earliest reports in the medical literature on the use of ergot in the treatment of migraine were those of Eulenberg in Germany in 1883, Thomson in the United States in 1894 and Campbell in England in 1894. Stevens’ Modern Materia Medica mentioned the use of ergot for the treatment of migraine in 1907 (Silberstein, 1997). The first pure ergot alkaloid, ergotamine, was isolated by Stoll in 1918 and used primarily in obstetrics and gynecology until 1925, when Rothlin successfully treated a case of severe and intractable migraine with a subcutaneous injection of ergotamine tartrate. This indication was pursued vigorously by various researchers over the following decades and was reinforced by the belief in a vascular origin of migraine and the concept that ergotamine tartrate acted as a vasoconstrictor. In 1938, John Graham and Harold Wolff demonstrated that ergotamine worked by constricting blood vessels and used this as proof of the vascular theory of migraine (Graham and Wolff, 1938).

Modern approaches: The modern approach to treat migraine began with the development of sumatriptan by Pat Humphrey and his colleagues. Based on the concept
that serotonin can relieve headache, they designed a chemical entity that was similar to serotonin, although more stable and with fewer side effects. This development led to the modern clinical trials for acute migraine treatment and to the elucidation of the mechanism of action of what are now called the triptans. We are at the threshold of an explosion in the understanding, diagnosis and treatment of migraine and other headaches. Many new triptans have been developed and many more will soon be, or are already, available, including zolmitriptan, naratriptan, eletriptan, frovatriptan, rizatriptan and almotriptan. Modern preventive treatment began with the belief that migraine was due to excess serotonin. (Humphrey, 1991). Sicuteri helped develop methysergide, a serotonin antagonist, for the prophylactic treatment of migraine and cluster headache. After that new drugs are being tested and developed for the preventive treatment of migraine. The anti-epileptic drugs have been investigated and some have already been proven to be effective for migraine (Sicuteri, 1959).

PREVALENCE OF MIGRAINE

Migraine is one of the most prevalent disorders seen in clinical practice today, affecting nearly 28 million Americans. It is also a major cause of disability at the workplace and it leads to indirect costs to society greater than 13 billion dollars a year. The prevalence of migraine is highest during the years of peak productivity, i.e., between the ages of 25 and 55 years (Nissan and Diamond, 2005). European and American studies have shown that 6-8% of men and 15-18% of women experience migraine each year. Frequency of headaches varies greatly by individual. It is the second most common type of headache syndrome in the United States. Tension headaches are the first most common headache. Migraines most commonly are found in women, with a 3:1 female-to-male ratio. In childhood, however, migraines are more common in boys than in girls. The first attack often occurs in childhood and incidence increases in adolescence. More than 80% of patients who develop migraines will have a first attack by the age of 30. Migraines continue through the patient's 30s and 40s. They may begin or occur at any age but are rare after age 50. With increased age, attacks usually decrease in severity and frequency (Blanda and Wright, 2006).

Researchers in Puerto Rico have found that 6% of men and 17% of women suffering from migraine. A survey conducted in Turkey revealed even greater prevalence in that country 10% in men and 22% in women. The higher rates in women
everywhere (2-3 times those in men) are hormonally driven. Migraine appears somewhat less prevalent, but still common, in Asia (3% of men and 10% of women) and in Africa 3% of women and 7% of men (Scher, 1999). But in India, anecdotal evidence suggests that high temperatures and light levels for more than eight months of the year and the heavy noise pollution, the Indian habit of not having breakfast, frequent fasting and eating rich, spicy and fermented food, are common triggers\(^3\).

Migraine prevalence also varies by race and geography. In the United States, it is highest in Caucasians, intermediate in African Americans and lowest in Asian Americans. Similarly, a meta-analysis of prevalence studies suggested that migraine is most common in North and South America and Europe, but lower in Africa, and often lowest in studies from Asia (Tepper, Dahlof and Dowson, 2004). In a Danish epidemiologic study, lifetime prevalence of migraine was found 16% (8% in men and 25% in women) and one-year prevalence was 10% (6% in men and 15% in women), (Russell, Rasmussen, Thorvaldsen and Olesen, 1995). In the US population, the one-year prevalence of migraine was 12% (6% in men and 18% in women), (Stewart, Lipton, Celentano and Reed, 1992). The same rates were found in France (Henry, Michel and Brochet, 1992). Migraine has been estimated to affect 1.5% of people in Hong Kong, 2.6% in Saudi Arabia, and 3% in Ethiopia. In Japan and Malaysia, prevalence rates were similar to those found in Western countries (8.4 and 9.0%, respectively. A recent epidemiologic study in South America showed one-year prevalence of migraine in women of 17% in Brazil, 6% in Argentina, 14% in Colombia, 12% in Mexico and 12% in Venezuela (Morillo, Sanin and Takeuchi, 2001).

**PHASES OF MIGRAINE**

In relation to migraine four phases of migraine are recognized and these are: Prodrome phase, Aura phase, Headache phase and Postdrome phase. The *prodrome phase* consists of premonitory phenomena generally occurring hours to days before the headache and include mental and mood changes (depression, anger, euphoria), stiff neck, fatigue, yawning, food cravings, fluid retention and increase in urination. The *aura phase* is composed of focal neurologic symptoms that usually precede the headache, lasting in general less than 60 minutes. Visual symptoms are the most common, such as zigzag or scintillating figures (fortification spectrum), scotomata, distortions in shape and size. Motor, sensory or brainstem disturbances can also occur.
The headache phase is typically characterized by unilateral pain, throbbing, moderate to mark in severity and aggravated by physical activity. The pain of migraine is invariably accompanied by other features. Nausea occurs in almost 90% of patients, while vomiting occurs in about one-third of migraineurs. Many patients experience sensory hyperexcitability manifested by photophobia, phonophobia, and osmophobia and seek a dark, quiet room. Other systemic symptoms, including anorexia, blurry vision, diarrhea, abdominal cramps, stiffness and tenderness of the neck and sweating, may be noted during the headache phase. Impairment of concentration is common, often there is some memory impairment also. Depression, fatigue, anxiety, nervousness, and irritability are common. Lightheadedness and a feeling of faintness may occur. In the postdrome phase, the patient may feel tired, washed out, irritable and listless and may have impaired concentration, scalp tenderness, or mood changes. Some people feel unusually refreshed or euphoric after an attack, while others note depression (Young and Silberstein, 2004).

**PATHOPHYSIOLOGY OF MIGRAINE ATTACKS**

1. **Vascular theory:** For many years, two principal hypotheses have been proposed for explaining the pathogenesis of migraine. A vascular hypothesis held that migraine was primarily a disease of cranial blood vessels. Due to this the pain occurred as a result of sensory nerve activation by inappropriate vasodilatation in the cranial circulation. The second view is the neurogenic hypothesis which proposed that neurogenic inflammation in the meninges was responsible for trigeminal sensory nerve activation and the generation of headache (Moskowitz, 1992). More recently, brain imaging studies during migraine has shown that the activation of brain-stem regions involved in the central modulation of head pain (Weiller, May and Limmroth, 1995).

2. **Positron emission tomography (PET) studies:** These studies further supported the involvement of brain-stem regions in migraine pathogenesis. The studies showed regionally specific increases in cerebral blood flow within the reticular formation, during spontaneous migraine attack (Diener, May, Sandler, Ferrari and Harnett 1996).
3. **Serotonin and migraine:** For many years, the principal pharmacological interest in approaching migraine has been directed toward released from platelets. Subsequently, when changes in circulating 5HT levels proved to be pharmacologically small, interest in the humoral role of 5HT in migraine declined. Current theories also found the role of serotonin in migraine. The theories suggest that parasympathetic projections from brain-stem regions innervate intracranial meningeal blood vessels (Goadsby, Uddman and Edvinsson, 1996). The activation of these pathways could trigger headache by releasing nitric oxide (NO), which is a potent vasodilator and activator of perivascular sensory nerves. The existence of other pathways that could cause NO-mediated vasodilatation through 5HT acting at endothelial 5HT receptors has also been proposed. Indeed, anti-migraine prophylactic agents that are 5HT antagonists may act by preventing this initial vasodilator stimulus. These hypotheses provide a potential integrating link between the vascular and the neural theories of migraine (Fozard, 1996).

4. **Nitric oxide and magnesium:** Several findings demonstrate that monoamine and peptides involved in neural inflammation are not able to cause migraine pain. Experimental studies using two different human headache models, based on glyceryl trinitrate administration (an exogenous NO donor) and histamine (which is able to liberate NO from vascular endothelium), have suggested a key role of NO in migraine (Thomsen and Olesen, 1998). Several physiological effects of NO theoretically implicated in the pathophysiology of migraine: several neurotransmitters in brain tissue, peripheral cerebral nerves and blood, stimulate the formation of NO in brain neurons and arterial endothelium and possibly interact with NOS-containing nerve terminals. NO is a potent vasodilator for intra and extracranial arteries: it has been postulated that NO is also able to activate periphery vascular sensory nerve fibres and initiate perivascular neurogenic inflammation. NO is considered as neurotransmitter activated in the cascade of biochemical events leading to a migraine attack (Olesen, Thomsen, Lassen and Jansen, Olesen, 1995). This theory has considerable experimental support and drugs are being developed that can block NOS, which are helpful in treatment of migraine (Thomsen and Olesen, 1998).
5. Magnesium deficiency and migraine: Magnesium deficiency has also been suspected of playing a role in the pathogenesis of migraine. Magnesium concentration modulates 5HT receptors, NO synthesis and release, N-methyl-D-aspartate (NMDA) receptors and a variety of other migraine-related receptors and neurotransmitters (Mauskop and Altura, 1998). Available evidence suggests that up to 50% of patients have lowered levels of ionized magnesium during a migraine attack (Soriani, Arnaldi and De Carlo, 1995). In these patients, infusion of magnesium results in a rapid and sustained relief of the acute attack of migraine (Mauskop, Altura, Cracco and Altura, 1995).

6. Dopamine and migraine: Together with 5HT, dopamine also appears to play a crucial role in the mechanism of the migraine attack. Dopaminergic hypersensitivity is found in migraine patients (Sicuteri, 1997). It was also found that as nausea often precedes headache, changes in the brain-stem dopaminergic neurotransmission must be present in migraine. In fact, a variety of prodromal symptoms, including yawning, drowsiness, irritability and hyperactivity, is reported by a significant percentage of migraine patients hours or days before the attack onset. Interestingly, in migraine patients yawning can be induced by doses of the dopamine agonist apomorphine (5 μg/kg) that are ineffective in control individuals (Blin, Azulay, Masson, Aubrespey and Serratrice, 1991). Higher doses of dopaminergic agonists induce hyperactivity and stereotypes in rodents, mood fluctuations, irritability, hypotension, nausea and vomiting in humans, as well as involuntary movements in predisposed subjects. In migraine patients, all these symptoms can be blocked by dopamine agonists such as haloperidol, chlorpromazine, prochlorperazine, domperidone and metoclopramide. Although the D2-related antiemetic effect of these drugs is well known, in migraine patients they are also able to block the migraine attack (Peroutka, 1997).

Thus all these pathophysiological theories described the biological or biochemical causes for migraine attack. These are the physiological causes of migraine which emerged from time to time and these theories explained that there can be any of this biological reason for the occurrence of migraine. Along
with these biochemical factors several other factors play an important role in the causation of migraine.

OTHER MIGRAINE TRIGGERS

It is important to realize the difference between a headache cause and a headache trigger. Among other things, stress and weather changes can trigger a headache. A brain tumor, a high fever or head trauma can cause a headache. Many people are convinced that their headaches are caused by certain foods. However, although many foods are recognized headache triggers very few can directly cause a headache. One exception, of course, is the dreaded “ice-cream headache,” in which ice cream or another cold stimulus to the back of the mouth produces a brief, severe headache. Thus headaches often have triggers and many people confuse triggers with causes. The neck pain would be the trigger of the migraine. There may be other migraine triggers, but when the neck problem is serious, the migraine will be much more severe. Removing the trigger is important, but it is also important not to get confused and say that the problem is strictly in the neck. Persons with trigeminal neuralgia have trigger points on the face and the mucous membranes of the mouth. Slight stimulation of these trigger points by eating, speaking, exposure to cold air, brushing the teeth or stroking, shaving or washing the face may provoke an attack. Menstruation is a regular trigger of migraine in many women. Wine can be a migraine triggers. Strangely white wine triggers migraine in France and red wine is a trigger in England. Sleep problems may be a cause or a trigger of headaches. Sleep apnea, a condition in which an individual stops breathing while asleep and then partially awakens, is a common problem, especially in the overweight individual. It may cause morning headache. With these some psychological triggers may cause headaches, such as depression, stress, anxiety and anger. Life is full of stress and stressors which may lead to migraine. These include marital and family status, education, occupation, outside interests, friendships and major life changes, such as marriage, divorce, separation, a new job, retirement, or a birth or death in the family. Employment provides many stressors. Thus migraine triggers can be of two types: Internal triggers like hormonal changes (such as menstruation), missing meals, illness, hypoglycemia (low blood sugar) and dehydration. External triggers like stressful events, anxiety, food/drink like alcohol, food additives, schedule or time changes, sleep disruption,
changes in eating habits, weather change, head or neck pain, physical exertion, exercise, sex, intense heat or cold, intense light, sound, or odors, overuse of certain medication, drugs, perfume, allergic reaction, bright lights, loud noises, smoking, prolonged muscle tension. So, in many of migraine triggers the most common trigger for migraine attack is emotional stress. An emotionally stressful event or situation brings a situation which is called the “fight-or-flight” response. During such a response, epinephrine is released, which can hyper excite brain cells and bring a migraine attack (Young and Silberstein, 2004).

STRESS

Everybody talks about stress and everybody says they have stress and everybody knows stress is bad for health. Job stress, teen stress and stress at workplace, stress related to daily hassles are causing thousands of stress related illnesses every day. All of our senses are involved in gathering information about our environment and delivering this information to brain 24 hours a day, 365 days a year. Thus stress is one of the many ways the body responds to the environment. It is, how our body reacts to the things we see, hear, taste smell and feel every day. It has been found that stress and disease can actually change the shape of our blood cells. Normal healthy cells are round, smooth and sharp. These happy blood cells do their job well and can help us to stay healthy. While the stressed cells are somewhat distorted in shape and look curled up and don’t function as well as the happy round cells. Stress can be of two types: (i) Acute or short-term stress. It leads to rapid changes throughout the body. Almost all body systems the heart and blood vessels, the immune system, the lungs, the digestive system, the sensory organs, and brain gear up to meet perceived danger. These stresses could prove beneficial in a critical or life-or-death situation, (ii) Chronic or long-term stress: It may have real health consequences. It leads to several psychological and physiological problems. Stressors can also be of two types: External and Internal Stressors. People can experience stress from external or internal factors. External stressors include adverse physical conditions such as pain or hot or cold temperatures or stressful psychological environments such as poor working conditions or abusive relationships. Internal stressors can also be of physical infections and other illnesses, inflammation or psychological stressors such as intense worry about a harmful event that may or may not occur. Stressors can also be defined in terms of time as short-term.
(acute) or long-term (chronic). Short term or acute stress is the reaction to an immediate threat, commonly known as the fight or flight response. The threat can be any situation that is perceived, even subconsciously or falsely, as a danger. Common acute stressors include: noise, crowding, isolation, hunger, danger, infection, high technology effects like playing video games, frequently ringing mobile phones, imagining a threat or remembering a dangerous event. Long term stress or chronic stress is a stressful situation that is not short-lived. It is a situation of fight or flee. In this situation stress, then, becomes more chronic. Common chronic stressors include: ongoing highly pressured work, long-term relationship problems, loneliness, and persistent financial worries. With all these views we can say that technically, stress is a normal physical response that most of us recognize. Stressors are the events that trigger a stress response. Sometimes stress responses develop spontaneously, without the need for outside triggers. At vulnerable times minor life hassles may trigger a stress response. At less vulnerable times, the same event may be no more than a small irritant. Thus major or minor life events lead to stress which in turn triggers headaches. It may be tension type or migraine headache. The anecdotal relationship between stress and the onset, persistence, and severity of head pain is a venerable one. This ancient association achieved academic credibility through the seminal work of Wolff. He suggested that migraine is experienced in genetically susceptible individuals due to cephalic vasomotor changes occurring in response to stress. Wolff also suggested certain characteristics to be typical of the migraine sufferer. He described the sufferer as rigid, ambitious and perfectionist (Wolff, 1948). Emotional stress is one of the most common causes of migraine. Migraine sufferers are generally found to be more emotional and highly affected by stressful events. The headache itself is perhaps the most difficult stressor that confronts all headache sufferers and their families. Fear of getting headache plus fear of being unable to work and to complete required tasks or take care of children can be a significant stressor. Unfortunately, headache-related fear (cephalgia-phobia) can further increase headache vulnerability and aggravate a developing headache or lead to overuse of pain medication even before the severe headache hits. Thus most of the headaches are symptoms of stress. Both female and male headache sufferers report that headaches are more likely to occur during or after periods of stress. Major life-changing events like marriage, birth of a child or career changes all are the sources of stress. However, research has found that it is actually the day-to-day stress or chronic "hassles" that are important in triggering headache.
Compared to men, women often experience more types of stress that provoke headache.

Thus stress is one of the most common triggers of migraine. In fact, in one recently-published study, up to 80 percent of people listed stress and anxiety as triggers of their migraine headaches. Events like getting married, having a baby, or moving to a new home are all sources of stress. But migraine research studies have found that it is the day-to-day stresses, not these major life changes that are most often linked to migraines. Juggling our many roles such as taking care of children, having a career, and handling financial pressures can be daily stresses for men and women.

Different kind of scientific approaches were found which concerned mainly to the external stimuli lead to physiological and psychological problems in humans. At first, the focus was on severe intrusions in life the so-called ‘life events’. Major life events were, for example, the loss of a partner or child and a marital separation are also stressful (Holmes and Rahe, 1967). It has been found that individuals in the normal population who experience more major life events have a higher risk ratio for headache than those who do not (Passchier, Schouten, van der Donk and van Romunde, 1991). Later researchers also found that less intense but more frequent stressful moments were associated with more physical complaints like head pain (Kanner and Feldman, 1991). Daily stress has clearly been found to be a provoking factor for headache attacks in adult patients. Research studies, in which patients with chronic headache were asked which factors, were most likely to elicit headaches, showed ‘mental stresses as the most commonly mentioned factor (Passchier and Andrasik, 1993). Sorbi, Maassen and Spierings, (1996) using a computer device and reported that migraine patients experienced more hassles and psychological arousal in the days before an attack. In fact, research has shown that it is the frequency of minor hassles that appears to have the greatest impact on migraine, while patients may rise to the occasion and cope effectively with severe stressors (such as a heart attack in a family member) while maintaining good headache control. Our thoughts and actions have a major impact on the extent to which difficult events lead to a stress response or trigger headache. Catastrophic thinking like this is terrible, things will never change, my life is ruined, is a very powerful amplifier of our physical stress responses. In contrast, realistic but less catastrophic coping thoughts can turn down the physiological gain like this is difficult but I will get through it, one step at a time, I can do it. Recent research has revealed that
patients who believe that they can successfully manage stressors and take actions to do so with relaxation, supportive self-talk, assertively dealing with conflict, are significantly less likely to develop stress-related headaches than those who believe they are helpless victims of events outside their control, and do nothing other than perhaps take medication (Lake, 2001).

Psychological stress arises from three sources: frustration, conflict, pressure. Frustration arises from a failure to meet our needs and desires. Conflict arises when there are two incompatible needs or valued goals; Pressure is the demand made on the individual from without or from within. This demand forces us to intensify our efforts. However, added to this equation are social, cultural or family beliefs which the individual may have subsumed into her or his belief system. Thus, if a person believes that he or she ‘must’ ‘absolutely’ ‘always’ perform ‘perfectly’ at work and at home too, it brings undue pressure on the person. In reality, the ‘must’ is an internal and not an external pressure, as the individual does not have to hold on rigidly to this belief. Many clients receiving stress counseling cognitively appraise experiences as ‘very stressful’ as a result of their own beliefs which distort the importance of an actual or feared event. Stress if not handled adequately may trigger biological changes in neurochemical pathways that in turn influence the headache process. A migraineur may learn that stressful situations tend to precipitate headache and a consequent expectation of headache is then set and actually may increase its probability of occurring. Our reactions to stress also will influence how we perceive pain, and this perception is integral to setting what commonly is referred to as the “pain threshold.” Unmastered stress also increases anxiety and this leads to worsening of the anxiety syndromes that commonly are associated with migraine. Once again, stress should be viewed as a headache trigger but not as the “cause” of headache. As with other triggers, identification of stress and its proper management may lessen headache frequency and intensity. Efforts to improve problem solving, a search for emotional support, the fostering of new coping skills and efforts to smooth out the peaks of stress that may occur over the day are all helpful in decreasing the number and severity of headache attacks. Some research has indicated that headache tends to occur about an hour following a peak stress and stress experienced during a migraine attack may increase pain intensity. Continuous stress influences the clinical expression of migraine less than shifting levels of stress. The former requires fewer changes in coping skills and less
need for problem solving. Major life events, whether positive or negative, increase stress and can trigger a migraine attack or a more prolonged period of migraine worsening. During a time of ongoing stress, migraineurs may find they are relatively protected from headaches as soon as the stress is relieved, however, the headache arrives. For example, college students who worry that their headaches will escalate during the time of final examinations often feel well until that stressful period is over and at that point they often suffer what is termed a “let down headache. Some of the authors have also talked about “migraine personality.” The classic descriptions of that migraine personality emphasize the presence of anxiety, depression, hypochondria (i.e., excessive preoccupation with illness), rigidity, hostility and resentment. In the literature, migraineurs are represented as perfectionists who are prone to neuroticism, a general over activity of emotion that may lead to the development of psychological decomposition when the individual is under stress. But the concept of a specific migraine personality probably is flawed and results from studies that examined clinic-based patients, a self-selected population of people who obviously are inclined to seek treatment. Prospective studies have also shown that mood disorders are more prevalent in migraineurs than in individuals without migraine and it seems likely that migraine and certain types of psychiatric disorders share specific genetic and environmental risk factors. There are 16-18 million migraine headache sufferers in which 70% are women. Most of these headaches are a symptom of stress.

AGGRESSION, ANGER, HOSTILITY AND IMPULSIVITY

Traditionally, aggression has been defined as the intention to harm another living being and not simply the delivery of harm (Baron & Richardson, 1994). It is a manifest response "aimed at the injury of a target" (Berkowitz, 1989; Dollard et al., 1939; Feshbach, 1964). This intention seems clear in some kinds of aggression, but in others the perpetrators of the harm might be able to deny any intent to cause harm; for example, aggression would simply be the infliction of harm on others. These different definitions distinguish between proximate and ultimate goals. Intention to harm is viewed as a necessary feature in any kind of aggression, but only as a proximate goal. At the level of ultimate goal, though, there is a clear difference between different types of aggression. Thus, both robbery and physical assault are acts of aggression because both include intention to harm the victim at a proximate level. However, they typically
differ in ultimate goals, with robbery serving primarily profit-based goals and assault
serving primarily harm-based goals (Anderson & Bushman, 2002). Arnold Buss
(1961), distinguished three dimensions of aggression. The **physical verbal** dimension
distinguishes between whether one uses physical means or words to harm another
person (Berkowitz, 1994 and Björkqvist, 1994). The **active-passive** dimension refers to
the extent to which the aggressor actively engages in a behavior aimed at harming
someone, with passive aggression referring to causing harm by not doing something
(Björkqvist, 1994, Björkqvist 1992, Buss, 1961). **Direct** aggression involves face-to-
face confrontation between the aggressor and the target. It is defined as any behavior
aimed at the goal of harming another living being (Baron & Richardson, 1994). This
form of aggression may be either verbal or physical, for example, direct aggression
might involve screaming at another person or hitting that person. **Indirect** aggression is
defined as any behavior aimed at the goal of harming another living being that is
delivered circuitously through another person or object, even if it must nevertheless be
intended to harm someone (Richardson & Green, 2003). **Undirected** aggression is that
wherein there is a discharge of negative affects against no one in particular (Buss,
through purposeful manipulation and damage of their peer relationships", including
behaviors such as exclusion and telling the target they won't be friends anymore. These
forms of relationally oriented aggression include both direct and indirect behaviors. For
example, telling a target they won't be friends is a direct, verbal approach and denying a
request is similarly direct. This form of aggression also involves primarily verbal
aggression that causes harm by disrupting relationships.

Aggressive behavior has traditionally been classified into two distinct subtypes:
hostile and instrumental aggression (Bushman and Anderson, 2001). **Hostile** aggression
has historically been conceived as being impulsive, thoughtless or thought confusion
emotionally charged, driven by anger and characterized by loss of behavioral control
and occurring as a reaction to some perceived provocation (Barratt, Stanford, Kent and
Felthous, 1997). Psychologically, it is associated with disruptive behavior, hostile
attributional biases, intention-cue detection deficits in interpretation, internalizing
problems, such as depression or somatization and victimization Physiologically, it is
characterized by a marked sympathetic over-arousal (Dodge & Coie, 1987). On the
other hand, the **instrumental** aggression is a tool for solving problems or for obtaining
a variety of objectives other than harming the victim, such as some reward, profit or advantage for the aggressor such as power, money, control and domination. It is purposeful and goal-oriented, thus, requiring neither provocation nor anger. Psychologically, it is associated with a 'positive' evaluation of aggression (Berkowitz, 1993).

HOSTILITY

Hostility is a negative evaluation of persons and things (Buss, 1961). It is accompanied by a clear desire to do harm or to aggrieve others (Kaufmann, 1970). It is considered as a negative attitude that mixes anger and disgust and it is accompanied by feelings of indignation, disgust, contempt and resentment towards others; in occasions it can even become bitterness and violence (Plutchik, 1980). This cluster of negative feelings towards others is known as 'hostile attribution', (Barefoot, 1992). According to him, hostility is expressed when we say we don’t like somebody, especially if we wish him ill. A hostile person is somebody that usually does negative evaluations of and towards others, showing an overall dislike and contempt for others (Spielberger, Jacobs, Rusell and Crane, 1983). The term hostility is also described as a broad construct involving affect, cognition and behavior, but this term has a more specific meaning involving cognitive factors (Miller, Smith and Turner, 1996). The cognitive phenomenon of hostility consists of negative beliefs and attitudes toward others, including cynicism, mistrust, and denigration. Cynicism refers to the belief that others are motivated by selfish concerns and mistrust is the often co-occurring expectation that others are likely to be provoking and hurtful. When these cognitive factors are considered together, hostility can be seen as a general trait connoting “a devaluation of the worth and motives of others, an expectation that others are likely sources of wrongdoing, a relational view of being in opposition toward others, and a desire to inflict harm or see others harmed” (Smith, 1994). Three types of hostility have been suggested—covert, overt and experiential. Bendig (1962) reported a factor called covert hostility, consisting mainly of irritable acts and overt hostility, consisting mainly of assault and verbal aggression. Another distinction is between the experience and expression of hostility. Experiential hostility primarily refers to subjective factors, notably the affective processes of anger and related emotions and the cognitive processes comprising hostility (e.g., suspicion and cynicism). In contrast, expressive or
behavioral hostility refers to overt verbal or physical aggressiveness, or both. Psychologically, hostility has a close relationship with irritability and aggression (Miller et al., 1996)

**IMPULSIVITY**

Impulsivity is a multidimensional concept that involves the tendency to act quickly and without reflection, having something to do with restraining one's behavior, handling of different emotions and rapid processing of information, novelty seeking and ability to delay gratification. The balance of countervailing forces determines the resulting behavior. It does not seem to depend on an impaired critical judgment, but on the loss of control over one's cravings and has been described as a process over and above particular drives. Psychologists view it as a tendency to act on the spur of the moment, neither thinking, nor planning, nor considering potential risks and alternative modes of action (Plutchik & van Praag, 1995). Murray (1938) described it as the tendency to respond quickly to a given stimulus and without enough reflection about consequences (Buss and Plomling 1975). The impulsive is a do-er, not a thinker (Barratt, 1972). Douglas (1972) related it to inability to sustain attention. Lorr and Wunderlich (1985), stresses two major bipolar components: a) resisting urges vs. giving in to urges; and b) responding immediately to a stimulus vs. planning before making a move. Psychiatrists consider impulsivity in a broader way, as a tendency to perform acts that are harmful to self or others. From this perspective, it would be an aspect of behavioral disorders of various kinds: kleptomania, pyromania, addictions, perversions, some sexual disorders, bulimia, suicidal threats, self-mutilating behavior. It has been recognized as a general process that underlies some socially important problems such as drug abuse, aggressive behavior, and suicide (Horesh, Rolnick, Iancu, Dannon, Lepkifker, Apter and Kotler, 1997; Ripke, 2005).

**ANGER**

Anger seems to be the dominant fact of modern life. Not merely the black statistics of murder, suicide, alcoholism and divorce betray anger, but almost any innocent, everyday act: the limp or over hearty handshake, the second pack of the cigarettes, the forgotten appointment, the stammer in midsentence, the wasted hour before the T.V. set; all display the shade of anger as it introduces itself in daily life.
Time and again psychologists and philosophers have emphasized the role of anger in our day to day life (Sarson, 1960). Anger refers to feelings and attitudes. It represents the emotional or affective component of aggressive behavior. Spielberger (1983) has classified anger as state and trait anger. *State anger* is defined as an emotional state that involves displeasure and consists of subjective feelings that vary in intensity, from mild irritation or annoyance to intense fury and rage (Spielberger, 1983; Van Goozen, Fridja, Kindt and Van de Poll, 1994). This internal state is embedded in a specific situational context, assuming that it would fluctuate over time as a function of perceived injustice or frustration (Ramírez, Santisteban, Fujihara and Van Goozen, 2002). Anger would escalate if the source is seen as being intentional, preventable, unjustified, blamed and when values are compromised, promises and expectations are broken, rules violated personal freedom and rights abridged. It is typically accompanied by autonomic nervous system arousal such as increases in heart rate and respiration, cognitive distortions and deficiencies and socially constructed and reinforced scripts (Ramírez, 2002 and Sukhodolsky, 1995). *Trait anger* may be considered to be a general temperament of low threshold reactivity in which angry feelings are experienced in response to a very wide variety of relatively mild triggers such as a short delay on a cashier's line, a slightly late mail delivery by the postal letter carrier or noticing that a student has made unexpected spelling errors. Anger proneness may be seen as a personality trait or characteristic conceived in terms of individual differences in the frequency over time to appraising emotional situations in an angry way (Deffenbacher, 1992; Ramírez, 2002, Van Goozen et al., 1994). The expression of anger must be distinguished conceptually and empirically from the experience of anger as an emotional state (S-anger) and individual differences in anger as personality trait (T-anger). The conceptual distinction between "anger-in" and "anger-out" was introduced by Funkenstein, King and Dralette, (1954) in their classic studies of the effects of anger expression on the cardiovascular system. In research on anger expression, individuals are typically classified as "Anger-in" if they tend to suppress their anger or direct it inward toward the ego or self (Averill, 1982; Funkenstein, King and Drallte, 1954 and Tavris, 1982). They are classified as "anger-out" if they express anger toward other persons or the environment. Thus, "anger-out" generally involves both the experience of S-anger and manifestations of aggressive behavior. The psychoanalytic conception of anger turned inward toward the ego or the self implies that feelings of guilt and depression will be experienced though thoughts and memories relating to the anger
provoking situation and the feelings of anger themselves may be repressed and, thus, not directly experienced (Alexander & French, 1948). Anger and anger expression are different between persons with and without headache after controlling for depression and anxiety. Persons with headache may experience more problems with anger and its expression when compared with persons without headache. Some studies assess the relationship between trait anger, anger-in, hostility, anxiety, and depression among persons with and without headache and evaluated whether trait anger and anger-in differentiated groups independent of depression and anxiety. In a study participants were 422 adults recruited from a larger study within a university setting. Of those, 171 suffered from headache (mean age, 21 years; 81% were female; 69% were white; mean years with pain. Another 251 sex-matched individuals (mean age, 21 years; 81% female; 62% white) met criteria for the headache-free group. Participants provided information regarding their headache characteristics and were administered affective trait measures (Trait version of the State-Trait Anxiety Inventory, Brief Symptom Inventory-Depression), trait anger measures (Trait Anger Scale, Cook-Medley Hostility Scale), and a measure of the extent to which individuals hold their anger in. The current findings indicate that persons with headache hold their anger in more than those without headache even after controlling for levels of trait anger, depression, and anxiety. However, after controlling for depression and anxiety, individuals no longer differed on trait anger. Also, anger-in was the strongest predictor of headache. The current findings suggest that holding anger in is more common among headache sufferers (Robert, Nicholson, Gramling, Ong and Luis Buenevar, 2003).

PSYCHOLOGICAL INTERVENTION

Some headache sufferers may prefer non pharmacological treatment in the primary management of their problem before medication is employed. While all have at one time or another used medications to treat their headaches but some do not always respond to traditional drug therapies. In addition, some pharmacological treatments may not be suitable for patients who have particular coexisting conditions. So many patients seek additional types of treatment in addition to medicine to manage migraine and other types of headache. Over the past two decades, several behavioral treatments for migraine prevention have been used widely as independent therapies or combined
with pharmacological therapy, for example relaxation training, biofeedback therapy and
cognitive-behavioral training, rational emotive therapy and stress-management training.

PROGRESSIVE MUSCULAR RELAXATION TRAINING

Progressive muscle relaxation is a systematic technique for achieving a deep
state of relaxation. It was developed by Dr. Edmund Jacobson more than fifty years
ago. Dr. Jacobson discovered that a muscle could be relaxed by first tensing it for a few
seconds and then releasing it. Tensing and releasing various muscle groups throughout
the body produces a deep state of relaxation. In his original book, 'Progressive
Relaxation', Dr. Jacobson developed a series of 200 different muscle relaxation
exercises and a training program that took months to complete. More recently the
system has been abbreviated to 15-20 basic exercises, which have been found to be just
as effective, if practiced regularly as the original more elaborate system. Progressive
muscle relaxation is especially helpful for people whose anxiety is strongly associated
with muscle tension. Relaxation training is the most widely used behavioral
intervention for the treatment of recurrent headache disorders. Relaxation training is a
systematic procedure for teaching individuals to gain awareness of and exert control
over physiological responses. The two most frequently used methods are (a)
abbreviated progressive muscle relaxation (PMR) – the systematic tensing and relaxing
of specific muscle groups throughout the body (Jacobsen, 1938, Bernstein and
Borkovec, 1973), and (b) autogenic training – the use of self-statements of feelings of
warmth and heaviness to achieve a state of deep relaxation (Schulz and Luthe, 1969).
Relaxation may be a useful way of coping with various circumstances that either
precedes or are exaggerated by stress, tension, anxiety, anger, sleeplessness, etc.
Relaxation can be highly beneficial if practiced in routine life and everyday life.
Technique involving relaxation is widely used by people to reduce anxiety and coping
with stress related problems. In the clinical setting, relaxation procedures are active and
educational forms of therapy to reduce stress. In clinical intervention, the client and
therapist work collaboratively to understand the source of the problem and try to
resolve it. There are countless methods used to achieve relaxation but the procedures
that are most commonly practiced in the clinical setting are Jacobson’s (1938)
progressive Muscular Relaxation, Schultz and Luthe’s (1969) Autogenic Training and
Benson’s (1975) Relaxation response. Progressive relaxation is a process of training to
relax the skeletal musculature consciously. This is a technique in which a person learns to relax the entire body by become aware of tensions in various muscle groups, and then relaxes them one at a time (Jacobson, 1929). Benson (1975, 1983) in his observation of the relaxation effects argued that all the relaxation technique produces a single "relaxation response" characterized by diminished sympathetic arousal. Relaxation training is used to assist people to reduce their overall level of physiological arousal to reduce the craving to drink to sleep more easily and to deal effectively with particular environmental factors that result anxiety and headache (Eliany and Rush, 1992). Relaxation techniques are useful in treating adult's recurrent headaches (Primavera & Kaiser, 1992) and children's headaches (Mehta, 1992 and Sartory, Mueller, Metsch and Pothmann, 1998). Relaxation or biofeedback training helps between 40% to 80% of recurrent headache sufferers. Greater improvements are reported at follow-up than immediately after treatment (Blanchard, Ahles and Shaw, 1979). Autonomically focused techniques like autogenic training are used effectively for migraine headaches (Lisspers & Ost, 1990). Somatic techniques like progressive muscle relaxation are used for the treatment of migraine headache (Blanchard, Appelbaum, Radnitz, Morrill, Kirsch, Hillhouse, Evans, Guarnieri, Attanasio, Andrasik, Jaccard and Dentineer, 1990). Cognitive therapy appears to be a particularly potent method for treating tension headaches (Murphy, Lehrer, & Jurish, 1990). A combination of cognitive and relaxation therapy has been shown to be more effective than relaxation alone (Tobin, Holroyd, Baker, Reynolds and Holm, 1988). No systematic differences have been found between cognitive therapy and relaxation for migraine headache (Sorbi, Tellegen and du Long, 1989). Use of progressive muscle relaxation and restricted environmental stimulation therapy showed a significant decrease in headache reports (Wallbaum, Rzewnicki, Steele and Suedfeld, 1991).

**EMG BIOFEEDBACK**

Biofeedback is a non-pharmacological, non-invasive treatment in which individuals learn neuro-musculoskeletal self-regulation. Biofeedback therapies emerged in the 1970s when advances in psychological and medical research converged with developments in biomedical technology (Goleman & Gurin, 1993). This therapy is a non-pharmacological approach in which clients learn self-regulation through the use of monitoring instruments that detect and amplify physiological information, clients are
trained to perceive and alter parasympathetic responses that are often related to pain
and disease (Stern and Ray, 1977). After becoming aware of heart rate, blood pressure,
skin temperature, muscle tension, and other involuntary body functions, conscious
mental effort is used to control these functions. It was found that multiple component
behavioral medicine treatment packages that include biofeedback therapy can lead to
reductions in medication use (Kabela, Blanchard and Applebaum, 1989; O’Grady, 1987
and Young, Bradley and Turner, 1995), as well as reduced physician visits, medical
costs and hospital stays (Shellenberger 1989 and Wauquier, McGrady, Louise, Klassner
and Collins, 1995). When biofeedback information is used to make changes that can
help reduce or stop symptoms, feelings of helplessness are replaced with knowledge
and the feeling that self-regulation is possible. It is a treatment technique in which
people are trained to improve their health by using signals from their own bodies.
Physical therapists use biofeedback to help stroke victims regain movement in
paralyzed muscles. Psychologists use it to help tense and anxious clients learn to relax.
Specialists in many different fields use biofeedback to help their patients cope with
pain. Just as the thermometer tells us about the fever and the scale tells us about the
gaining of weight. Both devices "feed back" information about your body's condition.
And armed with this information we take steps to improve the condition. We go to bed
and drink plenty of fluids for fever and eat less to control weight. Clinicians reply on
complicated biofeedback machines in somewhat the same way of scale or thermometer.
Their machines can detect a person's internal bodily functions with far greater
sensitivity and precision than a person can alone. This information may be valuable.
Both patients and therapists use it to gauge and direct the progress of treatment. For
patients, the biofeedback machine acts as a kind of sixth sense which allows them to
"see" or "hear" activity inside their bodies. One commonly used type of machine, for
example, picks up electrical signals in the muscles. It translates these signals into a
form that patients can detect: It triggers a flashing light bulb, perhaps, or activates a
beeper every time muscles grow more tense. If patients want to relax tense muscles,
they try to slow down the flashing or beeping. Biofeedback is very effective in
headache treatment. Biofeedback has been successfully used in the treatment of
migraine and tension type headaches, fetal and urinary incontinence, epilepsy, irritable
bowel syndrome, asthma, stroke, hypertension, chronic pain, muscle spasms, pain
associated with Reynaud’s disease, and other vascular or muscular disorders (Goleman
and Gurin, 1993).
Headache frequency, intensity, duration and analgesic intake decrease when biofeedback is used as a form of treatment. Kabela in 1989 studied 18 headache patients aged 60 years and older who received either thermal biofeedback (TBF) or electromyographic (EMG) biofeedback. There was a significant overall group improvement in medication intake over a 28-day interval. The reduction in medication intake from 63% to 50% is especially encouraging given the greater likelihood of multiple medication use and ensuing complications, in this population. Moreover, of those patients who initially consumed headache medication, five patients essentially eliminated all medication. Published research strongly supports the effectiveness of biofeedback therapy as a non-pharmacological treatment of headaches (Kabela, 1989). Thus we can say that relaxation therapy and biofeedback are effective in treating migraine.