NEUROPATHIC PAIN
Pain is an unpleasant sensation that originates from ongoing or impending tissue damage. Management of different types of pain (acute, postoperative, inflammatory, neuropathic or cancer) is the most frequent issue encountered by clinicians and pharmacological therapy is the first line of approach for the treatment of pain.1

Neuropathic pain is result of damage or dysfunction of periphery or central nervous system. Peripheral mechanisms of neuropathic pain include hyperexcitability of cell membrane and periphery sensibilization. Central mechanism includes central sensibilization, central reorganization of alpha-beta fibers and loss of inhibition mechanisms.

The main symptoms of neuropathic pain are described as lancinating, stabbing, or shooting pain. Hyperalgesia and allodynia are special kind of neuropathic pain that is provoked by mechanic or thermal stimuli. Mononeuropathy, plexopathy, radiculopathy, and myelopathy, lesions of thymus, cortex or brain stem are real cause of neuropathic pain.

The aim of treatment of patients with neuropathic pain is soothing of pain and suffering and prevention of further development of the pathological process. In the treatment of neuropathic pain drugs such as opioid, nonsteroid antirheumatics, analgesics, tricyclic antidepressants and antiepileptic agents are used. The most successful treatment is with antiepileptic drugs of second generation. Carbamazepine was the drug of choice till ten years ago. Since then the leader position in treatment has belonged to gabapentin.2

GABAPENTIN IS A NOVEL MODULATOR OF NEUROTRANSMISSION
The term ‘Ca++ channel alpha2delta ligands’ has recently been applied to an evolving drug class that includes gabapentin, and reflects significant progress over the past decade in elucidating the mechanism of action of these drugs: a novel, specific action at one of the subunits constituting voltage-sensitive Ca++ channels.

Binding of these ligands to the alpha2delta subunit is considered to explain their usefulness in treating several clinical disorders, including epilepsy, pain from diabetic neuropathy, post-herpetic neuralgia and fibromyalgia, and generalized anxiety disorder.3

GABAPENTIN VERSUS “THE OTHERS” IN DIABETIC PAINFUL NEUROPATHY
Diabetic painful neuropathy (DPN) is one of the most common causes of neuropathic pain. The management of DPN consists of excluding other causes of painful peripheral neuropathy, maximising diabetic control and using medications to alleviate pain.

Evidence from placebo-controlled studies has shown that opioids, antiepileptic and antidepressant drugs together with capsaicin are effective for alleviating DPN. Tramadol and oxycodone have been shown to be effective in studies of limited duration but their adverse effects, such as constipation and physical dependency, may limit their usefulness as a first-line treatment for DPN. Of the antidepressant drugs, the tricyclic antidepressants have been shown to be effective for alleviating DPN. These medications are widely used but their anticholinergic and sedative properties may not be well tolerated by patients.

There is also good evidence that the serotonin-noradrenaline reuptake inhibitor antidepressant drugs venlafaxine and duloxetine are effective for treating DPN. However, venlafaxine may cause cardiac dysrhythmias, and patients using this medication require careful cardiac monitoring. Duloxetine appears to be less cardiotoxic and is licensed in the US and EU for alleviating DPN.

The gabapentinoid group of drugs, gabapentin and pregabalin,
appear to be the most evidence-based of the antiepileptic drugs for treating DPN. Large placebo-controlled studies have been performed with both of these agents. For many patients, it is still unclear what advantages pregabalin has over gabapentin for DPN. Topiramate, lamotrigine, sodium valproate and oxcarbazepine have been shown to be effective in smaller studies but do not have the same evidence base as the gabapentinoid group of drugs.

**Gabapentin for the Treatment of Post-Herpetic Neuralgia**

Herpes zoster episodes commence with a prodromal period of about 4 days with symptoms including pain and malaise. This is followed by a rash lasting approximately 2-4 weeks, with possible subacute herpetic neuralgia for up to 3 months, followed, in some patients, by a period of post-herpetic neuralgia (PHN) lasting months or possibly years. Severe acute pain is more likely in older females and those with a prodrome or severe rash. Patients with herpes zoster experience severe pain and potential lasting complications such as post-herpetic neuralgia, opthalmic disease/damage, and, rarely, skin complications (e.g., infection of rash area).

Two separate mechanisms of PHN have been proposed: the first is that the excitability of primary afferent neurons is increased after nerve damage, causing irritable nociceptors and central sensitization, resulting in pain and allodynia; the second involves the degeneration of nociceptive neurons, which leads to deafferentation with central hyperactivity, causing pain but without allodynia. Both mechanisms may co-exist in an individual patient.

PHN occurs mainly in HZ patients 60 years of age and older, in particular in those suffering from more severe acute pain and rash. Administration of antiviral drugs reduces the duration of pain associated with HZ. The pathophysiology of PHN may be distinctly different between patients with either reduced or increased skin sensitivity.

Therapy is with tricyclic drugs (e.g., nortriptyline), alpha 2 delta-ligands (e.g., gabapentin) or opiates with adjunctive topical lidocaine or capsaicin.

**Gabapentin for the Treatment of Fibromyalgia**

To assess the efficacy and safety of gabapentin in patients with fibromyalgia, a 12-week, randomized, double-blind study was designed to compare gabapentin (1,200-2,400 mg/day) (n=75 patients) with placebo (n=75 patients) for efficacy and safety in treating pain associated with fibromyalgia.

Gabapentin-treated patients displayed a significantly greater improvement in the Brief Pain Inventory (BPI) average pain severity score. A significantly greater proportion of gabapentin-treated patients compared with placebo-treated patients achieved response at end point (51% versus 31%; P=0.014). Gabapentin compared with placebo also significantly improved the BPI average pain interference score, the Fibromyalgia Impact Questionnaire total score, the Clinical Global Impression of Severity, the Patient Global Impression of Improvement, the Medical Outcomes Study (MOS) Sleep Problems Index, and the MOS Short Form 36 vitality score, but not the mean tender point pain threshold or the Montgomery Asberg Depression Rating Scale. Gabapentin was generally well tolerated. This study showed that gabapentin (1,200-2,400 mg/day) is safe and efficacious for the treatment of pain and other symptoms associated with fibromyalgia.

**Gabapentin for the Treatment of Trigeminal Neuralgia**

Trigeminal neuralgia (TN) is reputed to be one of the most painful conditions in human experience. Thus, many treatments, both medical and surgical, have been developed for this relapsing and remitting, paroxysmal stabbing or electrical, facial pain syndrome. The likely etiology in many cases is vascular compression of the trigeminal nerve root entry zone, leading to focal demyelination and aberrant neural discharges. MRI may disclose neurovascular contact, although not with sufficient sensitivity or specificity to substitute for careful clinical diagnosis.

In treating TN, antiepileptic drugs are superior to traditional

---

**Table: Drug Composition and Administration**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Composition</th>
<th>Packing</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>GABAFINE</td>
<td>Gabapentin 300 mg</td>
<td>10 x 10 Capsule</td>
<td>1 TDS</td>
</tr>
</tbody>
</table>
analgesics. Carbamazepine is the first choice drug. Additional drugs for which there is evidence of efficacy include oxcarbazepine, baclofen, gabapentin, lamotrigine and phenytoin. The choice of drug, whether or when to operate, and which procedure to choose should be individualized to the particular needs and conditions of the patient.8

GABAPENTIN AS A PERIOPERATIVE DRUG
Gabapentin was not, until recently, thought to be useful in acute perioperative conditions. However, a growing body of evidence suggests that perioperative administration is efficacious for postoperative analgesia, preoperative anxiolysis, attenuation of the haemodynamic response to laryngoscopy and intubation, and preventing chronic post-surgical pain, postoperative nausea and vomiting, and delirium.9

Meta-analysis of gabapentin for perioperative pain control
Gabapentin, an anticonvulsant, has recently been suggested as an effective postoperative ‘analgesic’ agent. Following the Quality of Reporting of Meta-analyses recommendations, nine electronic databases until February 2006 were searched, without language restriction, for randomized controlled trials comparing gabapentin with control for postoperative pain control.

Gabapentin caused a 35% reduction in total opioid consumption over the first 24 h following surgery (ratio of means 0.65, 95% CI 0.59 to 0.72), a significant reduction in postoperative pain at rest (in the first 24 h) and with movement (at 2 h, 4 h and 12 h), regardless of whether treatment effects were expressed as ratios of means or weighted mean differences, and a reduction of vomiting (relative risk [RR] 0.73, 95% CI 0.56 to 0.95) and pruritus (RR 0.30, 95% CI 0.13 to 0.70).10

GABAPENTIN/OPIOID COMBINATION VERSUS OPIOID ALONE FOR NEUROPATHIC CANCER PAIN
Neuropathic cancer pain represents a major challenge. Treatment often requires adjuvant analgesics, including gabapentin, to complement the effects of opioids. This study aimed to compare the effectiveness and safety of gabapentin combined with an opioid versus opioid monotherapy for the management of neuropathic cancer pain. Data obtained suggested that gabapentin added to an opioid provides better relief of neuropathic pain in cancer patients than opioid monotherapy; this combination of gabapentin and an opioid may represent a potential first-line regimen for the management of pain in these patients.11

REFERENCES
Life is a continual feast... Gabafine
Gabapentine Capsule

- Differs from other mood stabilizing drugs
- Effective where other anti-depressants & mood stabilizers fail
- Relatively benign side-effect
- Safer for children & elderly
- Management of post herpetic neuralgia
- As an adjunctive therapy in the treatment of partial seizures and without secondary generalization in patients over 12 years of age with epilepsy
- Novel modulator of neurotransmission, useful as perioperative drug, efficacious for postoperative analgesia, preoperative anxiolysis, attenuation of the haemodynamic response to laryngoscopy and intubation

**Indication**
- Epilepsy
- Depression
- Social Anxiety Disorder
- Post-Operative Chronic Pain
- Insomnia
- Migraine Headaches
- Neuropathic Pain
- Post Herpetic Neuralgia
- Trigeminal Neuralgia
- Fibromyalgia