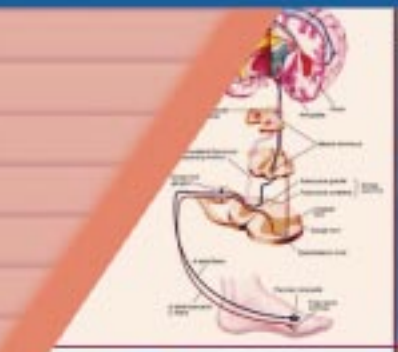
DECEMBER 2005 VOL 13 NO 4 ISSN 1681-5552

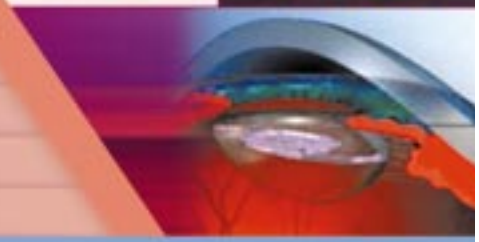
# the SQUARE

## healthcare bulletin









Telemedicine
Neuropathic Pain
Hepatitis C
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*PG Dip. Business Management (India)*

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## From the Desk of Managing Editor

Dear Doctor:

We are very happy to present you the fourth issue of *"the SQUARE"* healthcare bulletin, 2005!.

In this issue we have concentrated on "Telemedicine" which allows health care professionals to use "connected" medical devices in the evaluation, diagnosis and treatment of patients in other locations. Telemedicine is utilized by health providers in a growing number of medical specialties, including, but not limited to: dermatology, oncology, radiology, surgery, cardiology, psychiatry and home health care. We have a special feature on "Neuropathic Pain", which is a complex "chronic pain" state that can be puzzling and frustrating for people who have it and for doctors who treat it. We also bring you all the details on "Hepatitis C", an epidemic for anyone! Without rapid intervention to contain the spread of the disease, the death rate from hepatitis C will surpass that from AIDS by the turn of the century and will only get worse.

Moreover, we have focused on the "Inauguration of SQUARE Cephalosporins Ltd.", the dedicated and state-of-the-art Cephalosporin manufacturing facility at Kaliakoir, Gazipur. We have also highlighted a few "Activities of MSD in 2005" in this issue!

In our regular features, we have one of our "Product Profile" and some fascinating news in the "Medical Breakthrough" section.

We believe you will enjoy reading this publication!

On behalf of the "SQUARE family", we wish you and your family a very joyful, healthy and peaceful life!

Omar Akramur Rab

# Telemedicine

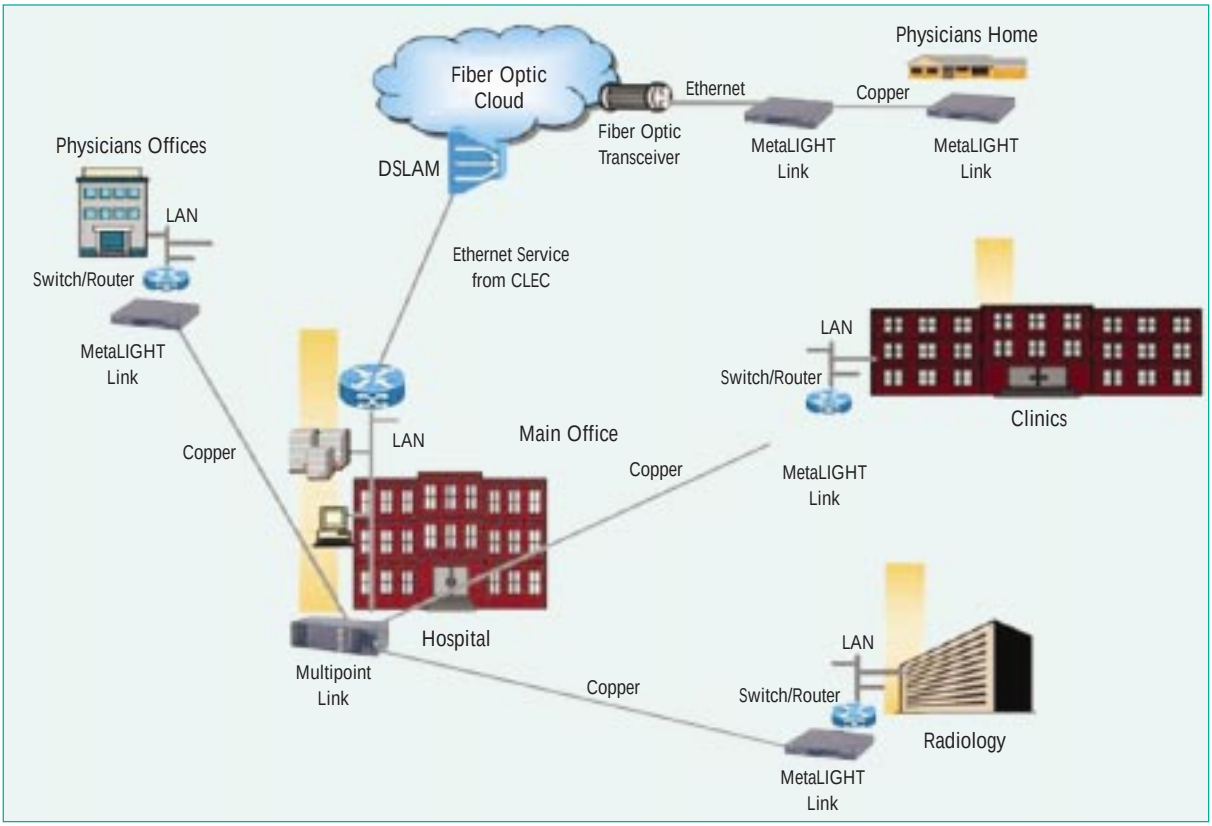


Worldwide, people living in rural and remote areas struggle to access timely, quality specialty medical care. For more than 30 years, clinicians, health services researchers, and others have been investigating the use of advanced telecommunications and computer technologies to improve health care. Because of innovations in computing and telecommunications technology, many elements of medical practice can be accomplished when the patient and health care provider are geographically separated. At the intersection of many of these efforts is telemedicine–a combination of mainstream and innovative information technologies. And so telemedicine could define as the use of electronic information and communications technologies to provide and support health care when distance separates the participants. Telemedicine allows health care professionals to use "connected" medical devices in the evaluation, diagnosis and treatment of patients in other locations. These devices are enhanced through the use of telecommunications technology, network computing, video-conferencing systems and CODECs (Coding and decoding equipment). Specialized application software, data storage devices, database management software, and medical devices capable of electronic data collection, storage and transmission are all key components of the Telemedicine infrastructure.

Types of Technology

Two different kinds of technology make up most of the telemedicine applications in use today. These are:

- Store-and-forward
- Real time




*Telemedicine Application*

*Store-and-forward*

Store-and-forward telemedicine includes captured audio clips, video clips, still images, or data that is transmitted or received at a later time. This is typically used for non-emergent situations, when a diagnosis or consultation ▶

may be made in the next 24 - 48 hours and sent back. Store-and-forward applications enable asynchronous communication, with the advantage of not needing concurrent participant involvement.

Teleradiology, the sending of x-rays, CT scans, or MRIs is the most common application of this technology. Many radiologists are installing appropriate computer technology in their homes, so they can have images sent directly to them for diagnosis, instead of making an off-hours trip to a hospital or clinic.

Telepathology is another common use of this technology. Images of pathology slides may be sent from one location to another for diagnostic consultation. Dermatology is also a natural for store and forward technology (although practitioners are increasingly using interactive technology for dermatological exams). Digital images may be taken of skin conditions, and sent to a dermatologist for diagnosis.

*Real time*

Real time, another widely used technology, is the live presence of both patient and provider in an interactive environment so that the patient is actually seen by the provider and two way communications (both visually and audibly) can take place. Two-way interactive television (IATV), is used when a 'face-to-face' consultation is necessary. The patient and sometimes their provider, or more commonly a nurse practitioner or telemedicine coordinator (or any combination of the three), are at the originating site. The specialist is at the referral site, most often at an urban medical center. Videoconferencing equipment at both locations allow a 'real-time' consultation to take place. The technology has decreased in price and complexity over the past five years, and many programs now use desktop videoconferencing systems. There are many configurations of an interactive consultation, but most typically it is from an urban-to-rural location. It means that the patient does not have to travel to an urban area to see a specialist, and in many cases, provides access to specialty care when none has been available previously. Almost all specialties of medicine have been found to be conducive to this kind of consultation, including psychiatry, internal medicine, rehabilitation, cardiology, pediatrics, obstetrics and gynecology and neurology. There are also many peripheral devices which can be attached to computers which can aid in an interactive examination. For instance, an otoscope allows a physician to 'see' inside a patient's ear; a stethoscope allows the consulting physician to hear the patient's heartbeat.

Many health care professionals involved in telemedicine are becoming increasingly creative with available technology. For instance, it's not unusual to use store-and-forward, interactive, audio, and video still images in a variety of combinations and applications. Use of the Web to transfer clinical information and data is also becoming more prevalent. Wireless technology is being used for instance, in ambulances providing mobile telemedicine services.

Classification of Clinical Applications of Telemedicine

Clinical applications of telemedicine involve care for particular individuals, although any given transaction may also serve educational, administrative, or research purposes.

Clinical applications of telemedicine can be classified into six general categories:

1. Initial urgent evaluation of patients for triage, stabilization, and transfer decisions;
2. Supervision of primary care by nonphysician providers when a physician is not available locally;
3. One-time or continuing provision of specialty care when a specialist is not available locally;
4. Consultation, including second opinions;
5. Monitoring and tracking of patient status as part of follow-up care or management of chronic problems; and
6. Use of remote information and decision analysis resources to support or guide care for specific patients.

Services Provide by Telemedicine

Telemedicine encompasses a broad variety of medical and health services:

- Specialist referral services typically involves of a specialist assisting a general practitioner in rendering a diagnosis. This may involve a patient "seeing" a specialist over a live, remote consult or the transmission of diagnostic images and/or video along with patient data to a specialist for viewing later. Radiology continues to make the greatest use of telemedicine with thousands of images "read" by remote providers each year. Other major specialty ▶

areas include: dermatology, ophthalmology, mental health, cardiology and pathology.

**Categories and Examples of Telemedicine Applications**

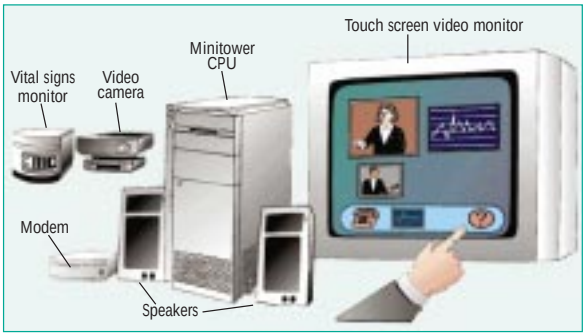
| Category | Examples |
|---|---|
| Patient care | Radiology consultations; postsurgical monitoring; triage of emergency patients. |
| Professional education | Continuing medical education programs; on-line information and education resources; individual mentoring and instruction. |
| Patient education | On-line help services for patients with chronic health problems. |
| Research | Aggregation of data from multiple sites; conducting and coordinating research at multiple sites. |
| Public health | Access to care for disadvantaged groups; poison control centers; disease reporting. |
| Health care administration | Video conferences for managers of integrated health systems; utilization and quality monitoring. |

- Patient consultations such as using audio, video and medical data between a patient and a primary care or specialty physician for use in rendering a diagnosis and treatment plan. This might originate from a remote clinic to a physician's office using a direct transmission link or may include communicating to a physician over the Web.
- Remote patient monitoring uses devices to remotely collect and send data to a monitoring station for interpretation. Such "home telehealth" applications might include a specific vital sign, such as blood glucose or heart ECG or a variety of indicators for homebound patients. Such services can be used to supplement the use of visiting nurses.
- Medical education provides continuing medical education credits for health professionals and special medical education seminars for targeted groups in remote locations.
- Consumer medical and health information includes the use of the Internet for consumers to obtain specialized health information and on-line discussion groups to provide peer-to-peer support.

The Multi-Technology Solution

Telemedicine program requires the melding of a number of different technologies into a seamless telemedicine system. In planning telemedicine system, it is essential to have a completely integrated, fully operational solution set. Often, a single system integrator is selected to install the system and assure its functionality.

The following major areas of technology integration that may be appropriate for review and assessment as part of the planning process.




*Different types of hard ware used in telemedicine*

*Medical Devices:* Ultimately, Medical Devices are the interface between the caregiver and the patient, designed to collect information (whether data, images or sound) and then transmit that information to interested parties, or store that information for use at a later date. Selection of medical devices should be driven first by the intended medical applications and, thereafter, by a series of operational and technological considerations including:

- Compatibility with operating platform- Devices selected must function with the desired operating platform, whether it is a PC (desktop or laptop), or client server or video.
- Integration- If multiple devices with single application software or multiple devices on a single PC platform used, then those devices and related software must be compatible each with the other and interface with the selected operating platform and operating software.
- Power Supply- Most devices require access to a power supply to function. The power supply must be appropriate for the intended use.
- Telecommunications Compatibility- The devices must be compatible with the desired transmission ▶

method (e.g. "live" or "store and forward") and the available telecommunications platforms. For example, if the program desires to transmit "live" IP sound, then analog sound must be converted to a digital format, interfaced with a PC and software application for transmission. Similar procedures must be followed on the receiving end to decode the sound.

*Network Computing:* Network computing relates to the compu-ting devices which drive functionality, permit the storage of data (whether temporary or permanent, and local or on a central server), and facilitate the transfer of the desired data from the medical device to the available communications platform for distribution to other professionals or for storage.

*Video-conferencing:* Parties desiring "live" transmission of video select video-conferencing equipment to display images and to transmit sound and data on a real time basis. Fortunately, newer generation video-conferencing systems operate on a standards basis and connection of users of different video-conferencing systems can be readily achieved. Even with standards based systems, however, there are limited situations in which devices will not easily interfaced with video-conferencing systems.

*Video conference*

*Software Requirements:* Generally, development of an integrated telemedicine system involves a number of software issues.

- Applications Software- Telemedicine programs often use business or clinical applications software to manage program operations.
  This software often associates data with a particular patient, and then manages transmission of data to various parties.
- Device interfaces- Frequently, devices are designed using proprietary software or systems which do not readily interface to applications software. Device interfaces may be required to assure the flow of information.
- Interface to database/other applications- Quite often, the telemedicine system sponsor would like the program applications to interface with the sponsor's database systems or with other specific applications (e.g. finan-cial reporting, billing, physician scheduling). Because the goal is to mainstream telemedicine, operating software must interface to other software systems customarily used in the operation of health care providers.

*Telecommunications Options:* The telecommunications options at the Originating Site often dictate the transmission method (live vs. store and forward). Generally, transmission of live images, data or sound, or the transmission of extremely large data files, requires high bandwidth telecommunication options.

Consideration must also be given to two way data transfer and transfer in synchronous or asynchronous modes. Understanding of available telecommunications options may dramatically affect the selection of devices.

Conclusion

Successful telemedicine program is the result of thoughtful planning, skillful management, adequate funding and the dedication of participating professionals. They reflect a commitment to teamwork to meld technical and operational complexities into a fully integrated and efficiently functioning program.

In the end, the rewards of a successful telemedicine program are many. But few moments are as rewarding as receiving an anxious look from a patient in need, and giving reassurances that access to the best medical care is only a moment away.

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*the SQUARE*

# Neuropathic Pain

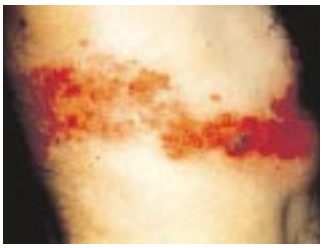
Pain is usually the natural consequence of tissue injury and it is one of the most common reasons for a patient to seek medical care. In general, as the healing process commences, the pain and tenderness associated with the injury will resolve. Unfortunately some individuals experience pain without an obvious injury or suffer protracted pain that persists for months or years after the initial insult. This pain condition is usually neuropathic in nature and accounts for a large number of patients presenting with chronic, non–malignant pain. Rather than the nervous system functioning properly to sound an alarm regarding tissue injury, in neuropathic pain (NP) the peripheral or central nervous systems are malfunctioning and become the cause of the pain. Neuropathic pain, is described as "burning", "electric", "tingling", and "shooting" in nature. It can be continuous or paroxysmal in presentation. The pain is produced by damage to, or pathological changes in the peripheral or central nervous systems.

Epidemiology and Etiology

Neuropathic pain is a world wide chronic disability. It affects the social, economic and health sector of nearly all countries of the world. Disorders of the brain or spinal cord can lead to “central pain,” such as that encountered in multiple sclerosis, after a stroke, and in spondylotic and posttraumatic myelopathy. Peripheral nervous system disorders include diseases of the spinal nerve roots, dorsal root ganglia, and peripheral nerves. Focal lesions of the peripheral nervous system that occur, for example, after amputation and with radiculopathy, carpal tunnel syndrome, and other entrapment neuropathies are usually distinguishable from diffuse disorders such as diabetic polyneuropathy, human immunodeficiency virus (HIV) sensory neuropathy, and idiopathic small-fiber sensory neuropathy.

Diabetic Peripheral Neuropathy (DPN): DPN occurs in persons with diabetes at a rate of 11.6% in those who are insulin dependent and 32.1% in those who are insulin non-dependent. The most common form of painful DPN causes spontaneous burning pain, numbness, and allodynia in the lower extremities. There may be concomitant carpal tunnel syndrome or meralgia paresthetica, pain in the distribution of the lateral femoral cutaneous nerve. Loss of small-fiber sensation in the stocking-glove distribution usually is present in patients with diabetes who have pain. Nocturnally exacerbated symptoms are extremely common; they may prevent restorative sleep and lead to secondary fatigue, irritability, and myofascial dysfunction. Glycemic control currently is emphasized to delay onset and progression of DPN.

Post Herpetic Neuropathy (PHN): Approximately 9% - 24% of patients with herpes zoster infection will develop PHN. After acute herpes zoster infection, PHN develops in 50% of persons older than 70 years and may lead to disability, depression, and social isolation. Frequently, background burning or aching pain is accompanied by paroxysmal stabbing or itching and severe, evoked allodynia and hyperalgesia. Both peripheral and central mechanisms are responsible for the variable manifestations of PHN. Promising strategies for prevention of PHN pain include early treatment with agents specific for NP, antiviral medications, and varicella zoster alloimmunization.



*Shingles*

Low Back Pain and Neck Pain: Low back and neck pain are among the most common reasons for physician visits. Although the percentage of patients with low back and neck pain of solely NP origin is unknown, chronic radicular pain develops in more than 20% of those requiring spinal surgery. In addition to axial pain, patients with chronic radiculopathy usually experience activity-dependent aching, burning, and lancinating or stabbing pain in the sensory distribution of a nerve root. Occasionally, spontaneous burning or lancinating pain predominates, especially in patients with other evidence of neurologic dysfunction such as sensory loss, weakness, and/or loss of deep tendon reflexes. The degree of reported pain intensity or disability may not correlate with the physical examination or radiographic findings. Superimposed myofascial, inflammatory, and skeletal nociceptive pain generators often coexist. Opportunities for prevention of long-term disability may include early mobilization and physical therapy facilitated by aggressive symptomatic management, patient education, ▶

and psychological interventions in high-risk patients. Pharmacotherapy alone is rarely effective, and interdisciplinary management strategies may be required.

Complex Regional Pain Syndrome (CRPS): Formerly known as reflex sympathetic dystrophy, CRPS type I is characterized by the development of neuropathic pain after tissue trauma such as surgery or bone fracture. In CRPS type II, formerly known as causalgia, neuropathic pain results from an injury to a peripheral nerve with pain that extends beyond the distribution of the injured nerve. In both types, hallmark features of CRPS such as asymmetric sweating, changes in skin texture, diminished skin temperature, and fluctuating degrees of swelling may accompany more universal symptoms of neuropathic pain such as burning, allodynia, and motor dysfunction. By definition, these symptoms outlast the period of normal tissue healing. Neuropathic pain in CRPS is considered sympathetically maintained when it is reduced by sympatholytics or sympathetic nerve blocks. Sympathetic-independent pain may emerge in the later stages of the illness.

Trigeminal Neuralgia (TN): An uncommon condition, idiopathic trigeminal neuralgia (TN) is characterized by paroxysmal, lancinating, and evoked pain in the distribution of 1 or more divisions of the trigeminal nerve. Patients who have sensory loss or other neurologic symptoms need to be evaluated for a primary nervous system structural lesion or an inflammatory disorder such as multiple sclerosis. The symptoms of TN can be debilitating. For example, speaking or chewing may become incapacitating.

Carcinoma: Neuropathic pain is a common and important source of morbidity in patients with cancer. Neuropathic symptoms often coexist with nociceptive pain generators such as bone metastases and visceral pain. The most common cancer-related etiologies of NP include tumor-related neural compression, radiation-induced neural injuries, and neuropathies related to paraneoplastic disorders and chemotherapeutic agents. Although the mainstay of pharmacological treatment of cancer-related pain is opioids, referral to a pain management center for neurolytic blocks or other medical management may be required to optimize quality of life.

Human Immunodeficiency Virus (HIV) Infection: In patients with HIV, neuropathic pain may have multiple manifestations. In moderately advanced disease (CD4 cell count, 0.200-0.500 x $10^9$/L), concomitant infection with hepatitis C or human T-lymphotropic virus 1 can lead to painful peripheral neuropathy. In advanced HIV-1 disease (CD4 cell count, <0.200 x $10^9$/L), distal symmetrical sensory polyneuropathy can present with paresthesias, cramps, and disabling burning and lancinating pain in the feet. Cytomegalovirus infection occurs in 2% of patients with advanced HIV-1 disease and may cause debilitating low back pain, radicular pain, and myelopathy. Several antiretroviral agents, including lamivudine and saquinavir, can cause patients to develop acute toxic neuropathy, with 50% of patients presenting with pain as their first symptom.

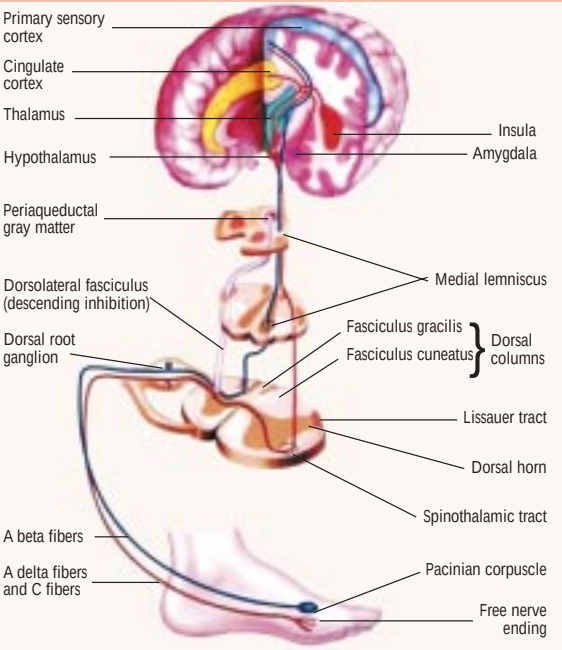
## Clinical Manifestation

The hallmark of neuropathic pain is the experience of both paresthesias (nonpainful abnormal sensations) and dysesthesias (unpleasant abnormal sensations). Spontaneous pain qualities such as burning, tingling, itching, and aching often coexist with evoked pain qualities such as shooting, stabbing, or electric pains. Hyperalgesia is an exaggerated response to a painful stimulus, whereas allodynia, pain after an innocuous stimulus, is common and often disabling. Hypoesthesia or anesthesia (reduction or loss, respectively, of normal sensation) in an area of NP is known as anesthesia dolorosa. Symptoms of neuropathic pain from various etiologies are remarkably similar (e.g. 2 individuals with postherpetic neuralgia [PHN] and diabetic peripheral neuropathy [DPN] may both experience burning pain).

## Transmission of Pain

The spinothalamic tract transmits input encoded for pain and temperature, and the dorsal column transmits input encoded for light touch. The free nerve ending of an A delta fiber or a C fiber senses pain and temperature and has its cell body in the dorsal root ganglion. This synapses in the dorsal horn with a second-order neuron that immediately crosses the midline and ascends on the contralateral side in the spinothalamic tract. The axons of the second-order neuron terminate in the hypothalamus and thalamus. In the thalamus, some projections are made directly to the primary sensory cortex, whereas others go to ▶

the limbic system, which includes the insula, amygdala, and cingulate cortex. The Pacinian corpuscle is a first-order neuron that senses pressure. This neuron's cell body is also in the dorsal horn, and the axon ascends a few levels, crosses the midline, and ascends in the contralateral dorsal column/ medial lemniscus, through the medulla and midbrain, and terminates in the thalamus. There, the neuron synapses with a second-order neuron, which projects to the primary sensory cortex.




*Normal sensory tracts*

Pathophysiology of Neuropathic Pain

The mechanisms involved in neuropathic pain are complex and the underlying dysfunction may involve deafferentation within the peripheral nervous system (e.g. neuropathy), deafferentation within the central nervous system (e.g. post–thalamic stroke) or an imbalance between the two (e.g. phantom limb pain).

Central deafferentation: Overactivity of a second-order neuron in the dorsal horn leads to enhanced pain transmission. In some individuals, central sensitization results after a peripheral nerve injury induces changes in pain processing within the dorsal horn. It is characterized by a lowered threshold for activation and expanded receptive fields, leading to the activation of key excitatory amino acid receptors such as the N-methyl-D-aspartate (NMDA) receptor.

Disinhibition: Reduced activation of key central inhibitory inputs from the dorsolateral fasciculus through endogenous opioid, serotonin, and norepinephrine pathways may result in neuropathic central pain. Disinhibition also may result from loss of local inhibitory pathways from an interneuron.

Sympathetic activation: Sympathetic nerve endings sprout from a nearby blood vessel toward the site of injury and can enhance signal transmission in the dorsal root ganglion. Catecholamine release and up-regulation of adrenergic receptors on free nerve endings and neuromas also contribute to sympathetically mediated pain.

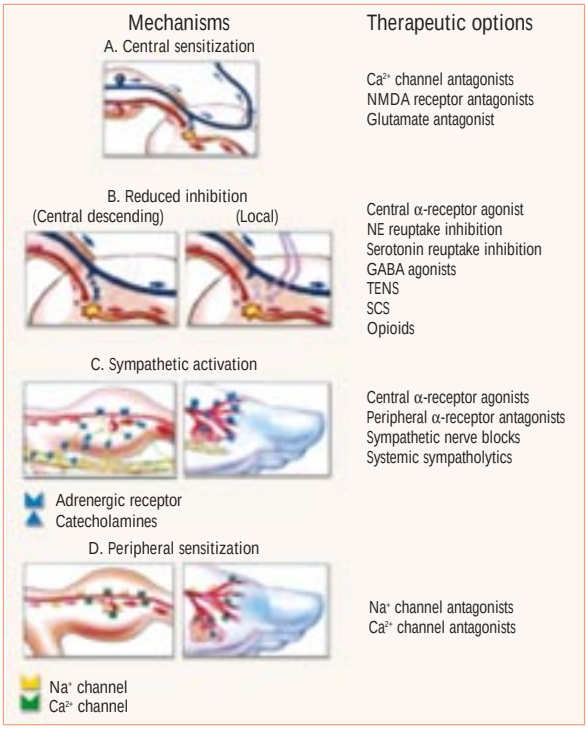
Abnormal electrical connections can occur between adjacent demyelinated axons. These are referred to as ephapses. "Ephaptic cross talk" may result in the transfer of nerve impulses from one axon to another. Cross talk between A and C fibers develops in the dorsal root ganglion. Nerve growth trophic factors may be important in the elaboration of these changes. A similar event referred to as "crossed afterdischarge" has also been described whereby "the sprouts of primary afferents with damaged axons can be made to discharge at high frequencies by the discharge of other afferents. It is also theorized that injured nerves may contain ephapses between sensory and sympathetic fibers, and such cross–connections may play a role in the pathogenesis of sympathetically mediated pain.

Peripheral defferentation: Injury to peripheral nerves may lead to the hyperexcitability of peripheral nerve terminals, or nociceptors, normally responsible for the transduction of painful stimuli. Formation of ectopic neuronal pacemakers can occur at various sites along the length of the nerve. This may be a result of altered expression of sodium channels, calcium channels, and adrenergic receptors in peripheral nerves and dorsal root ganglia.

Neurogenic inflammation may cause pain and hyperalgesia. Inflammatory neuropeptides (substance P) and prostaglandins (PGE2) are released from primary afferent nociceptors and sympathetic postganglionic neurons respectively, activating nearby receptors and triggering a process of spreading activation. These ▶

mechanisms may explain the clinical response of some neuropathic pain patients to topical nonsteroidal anti–inflammatory drugs, lidocaine, and capsaicin.

The connective tissue sheath around peripheral nerves is innervated by the nervi nervorum. Injury, compression, and inflammation of the sheath may cause pain. In cancer patients, pain associated with tumor compression of neural structures is clinically indistinguishable from non–malignant neuropathic pain. This nervi nervorum related pain may resolve following tumor resection or treatment of tumor induced inflammation.




*Pathophysiology (left column) and therapeutic options of neuropathic pain.*

## Management of Neuropathic Pain

Initial evaluation of the patients entails detailed review of the diagnosis and previous treatments. Patients need reassurance that disease-based treatments are optimized. Educating patients about pain mechanisms diminishes their fears of undiagnosed disease.

Assessment and evaluation: A detailed history of the onset and nature of pain is important. Individual pain assessment remains primarily subjective. The visual analog scale and numeric rating scales allow pain to be rated from “no pain” to “worst pain imaginable.” Pain diaries reviewed periodically by the physician encourage patient involvement and are useful for outcome assessments.

Neurological and musculoskeletal examination: a detailed neurologic and musculoskeletal examination should be performed.

Electromyography and nerve conduction test: Electromyography and nerve conduction studies are useful in assessing large-fiber involvement and the presence of axonal loss and reinnervation. Assessments of small-fiber pathology with dermal biopsies or quantitative sensory testing remain principally research tools. Referrals to appropriate specialists for help in pinpointing a diagnosis allow for use of disease-based therapies, when available.

Psychological screening: Finally, for patients in whom concomitant psychological dysfunction is suspected, psychological screening for depression and anxiety should be performed.

### Pharmacotherapy

Neuropathic pain clearly can impact a patient’s ability to carry out his or her activities of daily living (ADLs). Increased pain during the night interferes with sleep. The patient may have difficulty ambulating without feeling pain. Handling eating utensils or tools may cause pain. The patient may guard an affected painful limb, limit social activities, or develop depression. Pain relief is important to improve the patient’s quality of life.

Complete pain relief may not be achieved with treatment. Despite improvements with pharmacotherapy, up to 30% of patients may have intractable pain. Previous medical regimens, including dosing, escalation, and reasons for failure, should be reviewed. A more realistic goal is to decrease pain to a tolerable level. Effective treatment usually combines nonpharmacologic methods with medication. Patients should understand the goals of each step and need to know that effects are not immediate. Serum levels are generally unpredictive of response and should be monitored if maximal doses are achieved without toxicity or benefit. Medications are not necessarily lifelong therapy, and tapering should be considered after a period of sustained relief and improved function. ▶

Many patients, especially those with localized symptoms, may respond to initial therapy with topical lidocaine. In diffuse syndromes, pharmacotherapy begins at the lowest available dose of a single drug, followed by gradual titration to efficacy and tolerability. Initial systemic therapy may begin with gabapentin or nortriptyline. Tricyclic antidepressants (TCA) should be used with caution in patients with a history of cardiac conduction disturbances. The tertiary amines, such as amitriptyline, should be avoided in elderly persons because of their increased risk of falling. To best evaluate efficacy and possible adverse effects, it is advisable to avoid simultaneous adjustments of an existing regimen and the addition of new agents. Incomplete or partial responses to drugs with minimal risk such as topical lidocaine often can be augmented by the addition of a drug with a different mechanism of action (such as gabapentin). Although many patients respond favorably to 2 or 3 drugs with synergistic profiles, careful attention must be given to the use of more than 3 drugs when incremental benefit does not occur. Improving the activities of daily living is an important goal from the outset of therapy but is also important when a ceiling of analgesic efficacy has been reached with a pharmacological regimen.

Tramadol can be considered a treatment option for patients in whom a TCA or gabapentin fails or is only partially effective, especially when nociceptive pain (eg, from osteoarthritis or cancer) coexists. Many of these individuals will require more potent opioids, and individual tolerability varies widely. Rotation to a different opioid may be useful in patients with poor tolerability to an initial agent. Patients who may benefit from opioid use can be identified with a trial of a short-acting agent such as hydrocodone, oxycodone, or morphine, depending on the severity of the problem. If the trial is effective, long-term therapy with a sustained-release or long-acting preparation is advisable. A dosing schedule at regular intervals is preferable to use of “breakthrough” medications for patients with chronic pain. Use of nonpharmacological options, such as psychological techniques, TENS (Transcutaneous Electric Nerve Stimulation), and local modalities (heat, ice, massage) should be encouraged instead of “as needed” or “breakthrough” medications when a stable dose of opioid has been achieved.

Non Pharmacological Management

Refractory pain leads to depression, anxiety, impaired productivity, declining social functioning, and diminished quality of life. Characterized by the escalating use of health care, affective disorders, and physical deconditioning, the chronic pain syndrome requires a comprehensive treatment strategy incorporating interdisciplinary management. Nonpharmacological management plays an important role in restoring function and reducing disability. Every effort should be made to normalize the patient’s sleep schedule. Reviewing good sleep hygiene, limiting caffeine intake, and encouraging exercise can prevent dependence on a nightly sedative. Psychological referral for biofeedback, cognitive-behavioral techniques, group therapy, and counseling is warranted early in patients with psychosocial impairment. Physical therapy referral should be made for neuromuscular rehabilitation, gait and prosthetic device assessment, therapeutic exercise instruction, desensitization (especially in patients with severe allodynia and hyperalgesia), and TENS trials. A structured program with stepwise advancement is imperative in many disorders, especially CRPS and chronic radiculopathy. Occupational therapy and vocational rehabilitation may help the patient transition to functional independence. The network of care completed by mental health providers and physical and occupational therapists often helps sustain patient optimism and participation.

*Interventional Therapy*

Interventional therapy (diagnostic or therapeutic nerve blocks or implantable technologies) may be considered in patients with continuing pain and dysfunction who are unresponsive to conservative approaches. Techniques such as local anesthetic and corticosteroidal nerve blocks generally are used to hasten return of function while long-term strategies are identified. Although evidence for the efficacy of epidural injections is limited, in some cases success rates are higher than with conservative therapy. Patients with acute neck or back pain with a radicular pattern may derive the greatest benefit from epidural corticosteroid injection. Interventional strategies such as epidural corticosteroid injections may be considered in acute radiculopathy if symptoms persist despite physical therapy and use of oral analgesics. ▶

In CRPS, early physical rehabilitation of the affected limb is crucial for recovery. If the patient is unable to undergo physical therapy despite adequate medication trials, referral to a pain clinic is appropriate. Nerve blocks such as a lumbar sympathetic block (lower extremity), stellate ganglion block (upper extremity), or somatic nerve block may provide sufficient analgesia for participation in physical therapy and remobilization. The duration and extent of analgesia should be considered when determining the need for subsequent nerve blocks and escalation of physical therapy.

After multiple medication trials have been ineffective, referral to a pain clinic is warranted for additional medical management and appropriate interventions by the pain specialist. A trial of spinal cord stimulation (SCS) may be indicated for certain NP diagnoses. The positive results of SCS for patients in whom other therapies have failed for low back pain syndrome and CRPS have led to the use of SCS in other neuropathic disorders. Intrathecal opioids, clonidine, baclofen, and local anesthetics (alone or in various combinations) have been used long term in selected patients with refractory pain. For example, intrathecal morphine has been used successfully in patients who respond to oral opioids but have unmanageable adverse effects. Intrathecal drug delivery should be considered early in patients with NP and cancer in whom systemic analgesics are poorly tolerated.

Steps for contemporary neuropathic pain evaluation and management

| | Step 1 | Step 2 | Step 3 |
|---|---|---|---|
| Diagnostic evaluation | Detailed medical history and physical examination<br>Neuroimaging and electrodiagnostic studies when necessary | Neurological consultation<br>Neurosurgical consultation<br>Pain clinic referral* | Disease-specific tests by subspecialist |
| Nonpharmacological management | Patient education<br>Functional assessment<br>Psychological assessment<br>Sleep assessment† | Patient support groups<br>Physical therapy<br>Cognitive behavioral therapy<br>Sleep hygiene optimization<br>Exploration of complementary therapies (eg, acupuncture) | Vocational rehabilitation<br>Pain rehabilitation program |
| Pharmacological management | First-line agents‡ | Second-line agents or adjuvant medications§ | Determined by pain medicine specialist |
| Interventional management | None; pursue nonpharmacological and pharmacological management first | Diagnostic somatic or sympathetic nerve blocks | Advanced pain management techniques by pain medicine specialist |

*Include early referral to a pain clinic if diagnostic somatic or sympathetic nerve blocks are warranted.

†Patient's sleep hygiene should be reviewed, and complementary medicine may be considered.

‡When instituting pharmacological agents, primary care physician should administer adequate trials (usually 6-8 weeks) of first-line agents. Dose should be escalated until intolerable adverse effects occur or until efficacious.

§Considered, if first-line agents have been ineffective. Adjuvant medications include sleeping agents, muscle relaxants, antidepressants, and anxiolytics.

## Conclusion

Neuropathic pain remains a clinical challenge for treatment. Any medication used to treat neuropathy must be weighed for benefits and risks before using. It may take several trials to find an effective medication or combination of medications. Patients may need support throughout the process. Neuropathic pain often requires a combination of medication and nonpharmacologic modalities in order to achieve adequate pain relief.

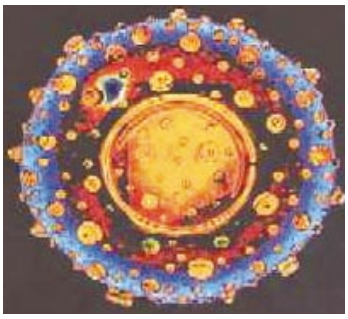
References:


- Review: Contemporary Management of Neuropathic Pain for the Primary Care Physician. Mayo Clinic Proceedings, 2004; 79(12): 1533-45.
- Steven Richeimer, MD. Understanding Neuropathic Pain. Obtained from: USC Pain Management, USC Medical Center at www.helpforpain.com on November 10, 2005.
- Jacintha S. Cauffield, Pharm.D., BCPS. Treatment Options in Neuropathic Pain. US Pharmacist, 25:6.

# Hepatitis C



Hepatitis C is a viral infection of the liver which had been referred to as parenterally transmitted "non A, non B hepatitis" until identification of the causative agent in 1989 by molecular cloning. The discovery and characterization of the hepatitis C virus (HCV) led to the understanding of its primary role in post-transfusion hepatitis and its tendency to induce persistent infection. HCV is a major cause of acute hepatitis and chronic liver disease, including cirrhosis and liver cancer. Globally, an estimated 170 million persons are chronically infected with HCV and 3 to 4 million persons are newly infected each year. HCV is spread primarily by direct contact with human blood. Most HCV-infected persons might not be aware of their infection because they are not clinically ill. Infected persons serve as a source of transmission to others and are at risk for chronic liver disease or other HCV-related chronic disease.



*Hepatitis C virus*

The major causes of HCV infection worldwide are use of unscreened blood transfusions, and re-use of needles and syringes that have not been adequately sterilized. Although its means of transmission are well documented, the hepatitis C virus itself still remains an enigma.

No vaccine is currently available to prevent hepatitis C and treatment for chronic hepatitis C is too costly for most persons in developing countries to afford. Thus, from a global perspective, the greatest impact on hepatitis C disease burden will likely be achieved by focusing efforts on reducing the risk of HCV transmission from nosocomial exposures (e.g. blood transfusions, unsafe injection practices) and high-risk behaviors (e.g. injection drug use).

## Pathogen

The hepatitis C virus is an enveloped RNA virus with a diameter of about 50 nm, classified as a separate genus (Hepacivirus) within the Flaviviridae family which appears to have a narrow host range. Humans and chimpanzees are the only known species susceptible to infection, with both species developing similar disease. An important feature of the virus is the relative mutability of its genome, which in turn is probably related to the high propensity (80%) of inducing chronic infection. HCV is highly heterogeneous. HCV is clustered into several distinct genotype, eleven HCV genotypes with several distinct subtypes have been identified throughout the world, which may be important in determining the severity of the disease and the response to treatment. Moreover, such heterogeneity hinders the development of vaccines, since vaccine antigens from multiple serotypes will probably be necessary for global protection. The virus is inactivated by-

- Exposure to lipid solvents or detergents
- Heating at 60˚C for 10 hours or 100˚C for 2 minutes in aqueous solution
- Formaldehyde (1:2000) at 37˚C for 72 hours
- β-propriolactone
- Ultra violet irradiation

HCV is relatively unstable to storage at room temperature or repeated freezing and thawing.

## Epidemiology

HCV infection occurs throughout the world, and up until the introduction of anti-HCV screening test for blood donors, introduced in 1990/1991 in Europe and the United States, it has represented the major cause transfusion associated hepatitis.

**Hepatitis C global infection rates**

| Country | Population | Residents with HCV infections | Percent of population infected with HCV |
|---|---|---|---|
| Bangladesh | 150,589,000 | 3,614,136 | 2.4% |
| India | 1,041,543,000 | 18,747,774 | 1.8% |
| Pakistan | 162,409,000 | 3,897,816 | 2.4% |
| Nepal | 24,409,000 | 144,504 | 0.6% |
| Sweden | 8,560,000 | 257 | 0.003% |
| United Kingdom | 58,393,000 | 11,679 | 0.02% |
| United States | 266,096,000 | 4,789,728 | 1.8% |
| Egypt | 64,210,000 | 11,622,010 | 18.1% |

*Source: World Health Organization c. 1999.*

The incidence of HCV on a global scale is not well known, because acute infection is generally asymptomatic. About 150,000 new cases occur annually in the US and in Western Europe, and about 350,000 in Japan. Of these, about 25% are asymptomatic, but 60 to ▶

80% may progress to chronic liver disease, and 20% of these develop cirrhosis. About 5-7% of patients may ultimately die of the consequences of the infection.

WHO estimates that about 170 million people, 3% of the world's population, are infected with HCV and are at risk of developing liver cirrhosis and/or liver cancer. The prevalence of HCV infection in some countries in Africa, the Eastern Mediterranean, South-East Asia and the Western Pacific (when prevalence data are available) is high compared to some countries in North America and Europe.

Endemicity

Egypt has a very high prevalence of HCV and a high morbidity and mortality from chronic liver disease, cirrhosis, and hepatocellular carcinoma. Approximately 20% of Egyptian blood donors are anti-HCV positive. Egypt has higher rates of HCV than neighboring countries as well as other countries of the world with comparable socio-economic conditions and hygienic standards for invasive medical, dental, or paramedical procedures. The strong homogenecity of HCV subtypes found in Egypt suggests an epidemic spread of HCV. Since a history of injection treatment has been implicated as a risk factor for HCV, a prime candidate to explain the high prevalence of HCV in Egypt is the past practice of parenteral therapy for schistosomiasis. The large reservoir of chronic HCV infection established in the course of these campaigns remains likely to be responsible for the high prevalence of HCV morbidity and may be largely responsible for the continued endemic transmission of HCV in Egypt today.

In Italy the prevalence of anti-HCV is >5% in some communities. In one region the prevalence was 12.6% overall, the rate among persons younger than 30 years of age was only 1.3% compared with 33.1% in those above 60. The use of glass syringes for medical treatment, a common practice before 1970 in Italy, or a history of dental therapy were found to be associated with anti-HCV positivity. A similar risk from the immunizations in the 1950s using non-disposable syringes was reported from Japan.

Hepatitis C is a serious threat for South East Asia region. HCV is not tested for in this region, not least because it would add to the costs. In the unscreened blood in this region the seroprevalence of hepatitis B is 0.06-8.5% and of hepatitis C is 1.2–3%, according to WHO. The South East Asia accounts for 25% of the world's population and faces severe shortage of safe blood. The problem is further compounded by inappropriate use of blood without separation into its components, with 80-85% of blood being used as whole blood. If the blood was used more appropriately, number of transfusions could be brought down by 30% according to International Red Cross. Private commercial blood banks, often offering unscreened blood, are allowed to flourish in both Bangladesh and Pakistan because they do not have any national blood policy. The quality of screening is also not always to the desired level in the entire region. In Islamabad, Pakistan testing results in 1998 showed that 8.1% of blood was infected with hepatitis C. 5 to 10% of HIV infections in South East Asia are transfusion induced.

Mode of transmission

HCV is spread primarily by direct contact with the contaminated blood or plasma derivates. Contaminated needles and syringes are most important vehicles of spread especially among the injecting drug users. Transmission by household contact and sexual activity appears to be low.

Only a small portion of HCV infection is transmitted at birth from mother to child. About 5 out of every 100 infants born to HCV infected women become infected at ▶

Hepatitis C estimated prevalence and number infected by WHO Region

| WHO Region | Total Population (Millions) | Hepatitis C prevalence Rate % | Infected Population (Millions) | Number-of countries by WHO Region where data are not available |
|---|---|---|---|---|
| Africa | 602 | 5.3 | 31.9 | 12 |
| Americas | 785 | 1.7 | 13.1 | 7 |
| Eastern Mediterranean | 466 | 4.6 | 21.3 | 7 |
| Europe | 858 | 1.03 | 8.9 | 19 |
| South-East Asia | 1 500 | 2.15 | 32.3 | 3 |
| Western Pacific | 1 600 | 3.9 | 62.2 | 11 |
| Total | 5 811 | 3.1 | 169.7 | 57 |

*Source: Weekly Epidemiological Record. N° 49, 10 December 1999, WHO*

the time of birth. Unfortunately, no treatment can prevent this from happening. The risk of mother to infant transmission of HCV increases dramatically if the mother is co-infected with HIV possibly due to an increase in HCV titer as a result of immunosuppression. The risk of mother-baby transmission correlates with the titer of maternal HCV viremia. For women found to be HCV positive, there are no recommendations against pregnancy or breast-feeding, nor is a special method recommended to deliver the baby. However, invasive fetal monitoring (e.g. using scalp electrodes) should be avoided. HCV-positive mothers should consider abstaining from breast-feeding if their nipples are cracked or bleeding.

Other modes of transmission such as social, cultural, and behavioral practices using percutaneous procedures (e.g. ear and body piercing, circumcision, tattooing) can occur if inadequately sterilized equipment is used. HCV is not spread by sneezing, hugging, coughing, food or water, sharing eating utensils, or casual contact.

Risk groups

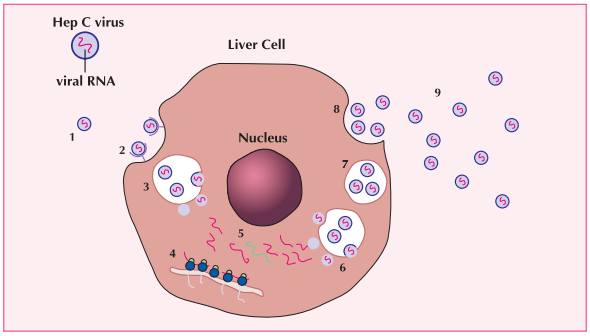
Groups at risk of contracting an HCV infection:

- Recipients of previously unscreened blood, blood products and organs (blood transfusion or solid organ transplant before 1992, coagulation factor concentrates before 1987)
- Patients and employees in hemodialysis centers (nosocomial infections)
- Hemophiliacs
- Injecting drug users sharing contaminated needles and/or injection materials
- People exposed to unsterile medical or dental equipment
- Occupational exposure to blood
- People administrating or receiving acupuncture and/or tattooing with unsterile medical devices
- Health care workers
- Sexual, household and perinatal transmission is possible.
- Infants born to infected mothers

A number of cases, 10% to 40%, have no identifiable risk factor.

Pathogenesis

HCV infects hepatocytes. It is still unclear whether the liver damage associated with HCV infection is the result of a direct cytopathic effect or is caused by a host immune-mediated cytolytic response. Both processes are probably involved in causing hepatic damage. Chronic hepatitis C is characterized by portal inflammation, typically periportal hepatocellular necrosis, and fibrosis.




*Hepatitis C Virus Life-cycle*

Factors that may affect the natural history of HCV infection:

- Patients with co-infection with hepatitis B virus (HBV) and HCV have a higher risk of hepatocellular carcinoma than those who are only infected with one virus. Chronic HBV / HCV co-infection is uncommon globally, although it may be emerging in China.
- The serological profile of anti-HBc alone / anti HCV positive is common. Some evidence suggests that presence of anti-HBc alone might increase the risk of hepatocellular carcinoma (HCC) among patients with chronic HCV infection.
- Intake of more than 50 g alcohol / day accelerates progression to cirrhosis with a threefold risk increase.
- Consistently normal ALT levels are associated with slower fibrosis progression.
- Steatohepatitis, rather than obesity, seems to be the important co-factor.
- The influence of HIV infection depends upon CD4 count with a confounding effect of immune reconstitution following successful antiretroviral treatment (HAART). The relative risk for the

development of cirrhosis among HIV and HCV co-infected patients is around two.

- ❑ Preliminary evidence suggests that smoking may influence the development of HCC.

Viral load or genotypes do not influence disease severity or progression. The size of the viral inoculum received may determine the course of disease: post-transfusion cases may proceed more aggressively than infections associated with injecting drug use (IDU). Disease expression is related to viral expression: low levels of circulating HCV RNA are generally found in asymptomatic patients with normal ALT levels. Experiments carried out with chimpanzees have shown that the administration of powerful immunosuppressants before and after virus inoculation prevents the development of acute hepatitis despite viremia in the animal and viral expression in the liver. Removal of the immunosuppressant triggered an immune response which resulted in the onset of acute hepatitis followed by virus elimination

### Clinical features of acute infection

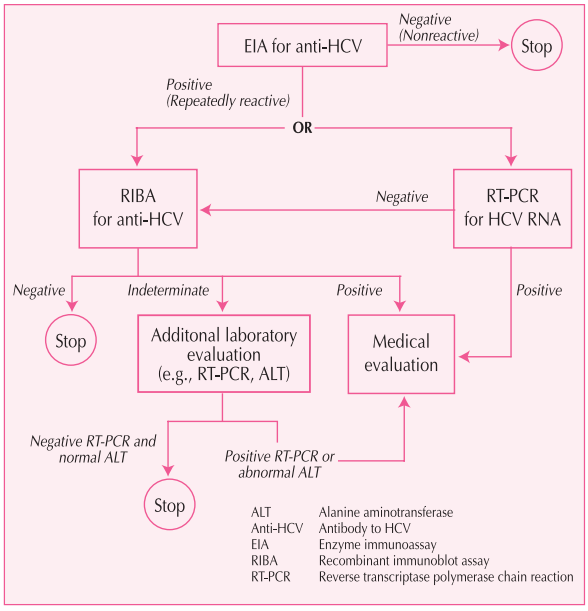
The incubation period for acute hepatitis C averages 6 to 10 weeks. Most persons who develop acute hepatitis C have no symptoms. The onset of disease is usually insidious, with anorexia, vague abdominal discomfort, nausea and vomiting, fever and fatigue, progressing to jaundice in about 25% of patients, less frequently than hepatitis B. Rapid, fulminant liver failure associated with HCV infection is a rare event. Probably as many as 70%-90% of infected people fail to clear the virus during the acute phase of the disease and become chronic carriers.

### Chronic infection and consequences

An important clinical feature of infection with HCV is the high rate of chronic hepatitis and slowly progressive lifelong infection, which may lead to cirrhosis and liver failure in about 10%-20% of persons with chronic hepatitis C. HCV-associated cirrhosis leads to liver failure and death in about 20%-25% of cirrhotic cases. HCV-associated cirrhosis now represents a leading indication for liver transplantation. Chronic HCV infection appears to be associated with the development of hepatocellular carcinoma (HCC) in 1%-5% of persons with chronic hepatitis C. Development of HCC is rare in patients with chronic hepatitis C who do not have cirrhosis. Chronic infection is often not symptomatic, until evidence of liver failure becomes clinically apparent. The rate of progression to cirrhosis is usually slow, with 20 or more years elapsing between infection and the development of serious complications. The period of communicability spans from one or more weeks before onset of the first symptoms and may persist in most persons indefinitely. HCV infection does not cause fulminant hepatic failure, but, occurring in the setting of another chronic liver disease such as chronic HBV infection, may precipitate liver failure. Persons who have chronic liver disease are at increased risk for fulminant hepatitis A. Most of the serious liver disease associated with HCV is a consequence of the chronic, persistent nature of the infection. Even in the asymptomatic carrier, a decrease in quality of life has been reported. Histopathology grade and stage of liver damage is not reflected by serum ALT/AST levels or serological status.

### Diagnosis

Diagnostic tests for HCV are used to prevent infection through screening of donor blood and plasma, to establish




*Hepatitis C virus (HCV ) infection-testing algorithm for asymptomatic persons.*

the clinical diagnosis and to make better decisions regarding medical management of a patient. Diagnostic ▶

tests commercially available are based on Enzyme immunosorbant assays (EIA) for the detection of HCV specific antibodies. EIAs can detect more than 95% of chronically infected patients but can detect only 50% to 70% of acute infections. A recombinant immunoblot assay (RIBA) that identifies antibodies which react with individual HCV antigens is often used as a supplemental test for confirmation of a positive EIA result. Testing for HCV circulating by amplification tests RNA (e.g. polymerase chain reaction or PCR, branched DNA assay) is also being utilized for confirmation of serological results as well as for assessing the effectiveness of antiviral therapy. A positive result indicates the presence of active infection and a potential for spread of the infection and or/the development of chronic liver disease.

Treatment

Antiviral drugs such as interferon taken alone or in combination with ribavirin, can be used for the treatment of persons with chronic hepatitis C, but the cost of treatment is very high. Treatment with interferon alone is effective in about 10% to 20% of patients. Interferon combined with ribavirin is effective in about 30% to 50% of patients. Ribavirin does not appear to be effective when used alone.

Prevention

There is no vaccine against HCV. Research is in progress but the high mutability of the HCV genome complicates vaccine development. Lack of knowledge of any protective immune response following HCV infection also impedes vaccine research. It is not known whether the immune system is able to eliminate the virus. Some studies, however, have shown the presence of virus--neutralizing antibodies in patients with HCV infection.

*In the absence of a vaccine, all precautions to prevent infection must be taken including:*

- ❏ Screening and testing of blood, plasma, organ, tissue, and semen donors;
- ❏ Virus inactivation of plasma derived products;
- ❏ Implementation and maintenance of infection control practices in health care settings, including appropriate sterilization of medical and dental equipment;
- ❏ Promotion of behavior change among the general public and health care workers to reduce overuse of injections and to use safe injection practices; and Risk reduction counseling for persons with high-risk drug and sexual practices.

*Routine precautions for the care of all hemodialysis patients-*

- ◆ Patients should have specific dialysis stations assigned to them, and chairs and beds should be cleaned after each use.
- ◆ Sharing among patients of ancillary supplies such as trays, blood pressure cuffs, clamps, scissors, and other nondisposable items should be avoided.
- ◆ Nondisposable items should be cleaned or disinfected appropriately between uses.
- ◆ Medications and supplies should not be shared among patients, and medication carts should not be used.
- ◆ Medication should be prepared and distributed from a centralized area.
- ◆ Clean and contaminated areas should be separated.

*Postexposure follow-up of health-care, emergency medical, and public safety workers for HCV infection*

- ❏ For the source, baseline testing for anti-HCV.
- ❏ For the person exposed to an HCV-positive source, baseline and follow-up testing including-
  - ◆ Baseline testing for anti-HCV and ALT activity; and
  - ◆ Follow-up testing for anti-HCV (at 4-6 months) and ALT activity.
- ❏ Confirmation by supplemental anti-HCV testing of all anti-HCV results reported as positive by enzyme immunoassay (EIA).

Reference:

- ❍ World Health Organization, 2002
- ❍ Centers for Disease Control & Prevention, December 17, 2004
- ❍ National Center for Complementary and Alternative Medicine, 2003
- ❍ Mayo Foundation for Medical Education and Research, February 18, 2004.
- ❍ News. BMJ; Volume 320; 15 April 2000.

*the SQUARE*

# Inauguration of SQUARE Cephalosporins Ltd.



Yet another milestone in Pharmaceutical manufacturing was set by Square on September 27, 2005 when the company launched its dedicated and state of the art Cephalosporin Manufacturing facility at Kaliakor, Gazipur.

Dr. Khandaker Mosharraf Hossain, MP, Hon'ble Minister for Health and Family Welfare inaugurated the facility built as per US, FDA and UK, MHRA cGMP specifications. Mr. Mizanur Rahman Sinha, MP Hon'ble State Minister for Health and family Welfare also graced the occasion.

This world class facility is housed in a 95,000 sq. feet of covered area and will manufacture Cephalosporin antibiotics in tablets, Capsules, Dry Syrup and Injectable preparations. The annual capacity per shift of the plant is 64 million tablets, 47 million capsules, 3.32 million bottle of dry syrps and 10.58 million of injectables. The facility was built by Telstar S.A. of Spain, a world renowned pharmaceutical manufacturing facility, on a turn key basis.

The facility will add new era in Pharmaceutical export from Bangladesh. Patients in the country will also now get developed country standard Cephalosporins from the facility.

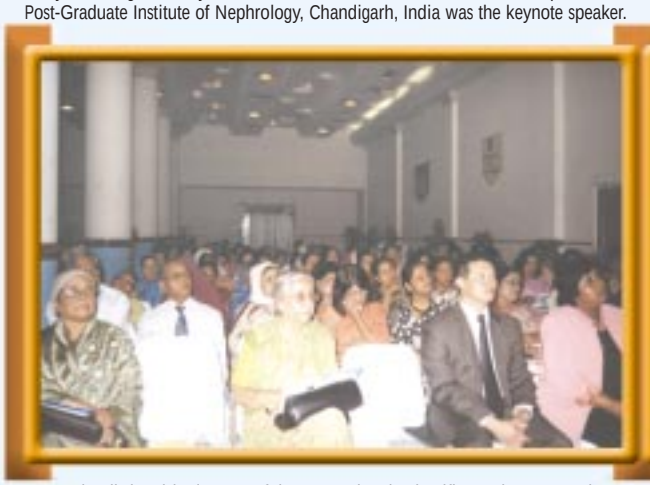
Presidents and Secretary Generals of Bangladesh Medical Association (BMA) and Bangladesh Pharmaceutical Manufacturers Association (BAPI) along with many dignitaries from Home and Abroad attended the inauguration.

# MSD Activities 2005- Few Highlights


Medical Services Dept. (MSD) of *SQUARE* Pharmaceuticals Ltd. organized the scientific seminar on "Osteoporosis and Its Management" at the Gynae & Obstetrics Dept. of BSMMU, Dhaka.

MSD of *SQUARE* Pharmaceuticals Ltd. sponsored a scientific seminar on "Renal Mycosis" organized by Teachers' Association of RMCH. Prof. K. L. Gupta from Post-Graduate Institute of Nephrology, Chandigarh, India was the keynote speaker.

MSD of *SQUARE* sponsored the "Annual Scientific Seminar" of Chittagong Medical College Teachers Association at Chittagong.



The distinguished guests of the International Scientific Seminar at Hotel Agrabad, Chittagong. The program was organized by OGSB and sponsored by MSD, *SQUARE* Pharmaceuticals Ltd.


*SQUARE* Pharmaceuticals Ltd. sponsored the scientific seminar on "Post Stroke Rehabilitation" organized by Rotary Health Care and Physiotherapy Centre in Association of CRP Savar, Dhaka at Khulna.

## Correct answers of the 'Test Yourself - 20'

1. b & c  2. a & c  3. a & d  4. a & d  5. b & c  6. a & c

The following are the 10 winners of the "Test Yourself -20"; they have been selected through lottery.

### Congratulations from "the SQUARE" Editorial Board

Dr. A. E. M. Mazharul Islam
Asst. Professor, Cardiology
NICVD, Dhaka

Dr. Debasish Ghose, *MBBS*
Medical Officer
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Lohagara, Chittagong

Dr. Md. Anwar Hussain
*MBBS, MCPS (ENT), DLO*
Consultant, ENT
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Brahmanbaria

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Internee Doctor, Surgery Unit – III
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General Hospital
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Dr. Md. Maruful Islam
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A/R, Surgery Unit-II
Rangpur Medical College Hospital

Dr. Md. Najmul Karim (Robin), *MBBS*
House No. 471, Road No. 1/5
G. L. Roy Road
Rangpur

Dr. Sayeed Ahmed, *MBBS*
Room No. 309
Dr. Milon Internee Hostel
Bakshi Bazar, Dhaka

Dr. Syed Amanul Islam, *MBBS*
EMO
Khulna Medical College Hospital
Khulna

Dr. Tangina, *MBBS*
Room No. 107, Rumana Smriti Hostel
Sir Salimullah Medical College &
Mitford Hospital
Dhaka

*Soon our officials will be visiting you with a token of our appreciation*

## Test Yourself – 21

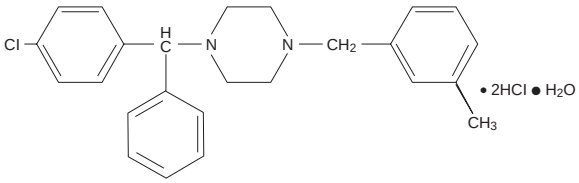
1. All the following regarding "Neuropathic Pain" is correct except:
   a. It is described as 'burning', 'electric', 'tingling' and 'shooting' in nature.
   b. It is "continuous" in presentation.
   c. It is a worldwide acute disability.
   d. Multiple sclerosis, post-traumatic myopathy can lead to 'central pain'.
2. The following points are true for "Telemedicine" except:
   a. It helps in remote patients monitoring.
   b. Patient transfer is possible through this.
   c. Consumers' medical and health information can be transferred.
   d. Specialist referral services can be achieved.
3. The below mentioned points are true for "Neuropathic Pain" except:
   a. DPN occurs in diabetic persons at a rate of 11% in those who are insulin dependent.
   b. About 9% - 24% of the patients with herpes zoster infection will develop PHN.
   c. Complete pain relieve may not be achieved with treatment.
   d. TCA should be used with caution in persons with a history of cardiac conduction disturbances.
4. All the following points are true except:
   a. Vertina® has CNS depressant, antiemetic, anticholinergic, antispasmodic and antihistaminic properties.
   b. Vertina® is only indicated for the prevention and treatment of nausea and vomiting.
   c. Vertina® is chewable tablet.
   d. Use of Vertina® is not recommended for the children under 12 years of age.
5. All the following are correct regarding clinical applications of "Telemedicine" except:
   a. Consultation, including second opinion.
   b. Monitoring and tracking the patients status.
   c. Supervision of primary care by the physician only.
   d. Continuous provisions of specialty care by a local specialist.
6. All the following points are true for "Hepatitis C" except:
   a. Globally, an estimated 170 million persons are chronically infested with HCV.
   b. Sneezing, coughing, food or water spreads HCV.
   c. The incubation period for acute hepatitis C averages 6-10 weeks.
   d. HCV is spread primarily by contaminated blood or plasma derivatives.

## Vertina®

### Composition

Vertina® Tablet : Each chewable tablet contains Meclizine HCl USP 50 mg.

### Chemical Structure




### Pharmacology

Vertina® (Meclizine hydrochloride) is an antihistamine which shows marked protective activity against nebulized histamine and lethal doses of intravenously injected histamine in guinea pigs. It has a marked effect in blocking the vasodepressor response to histamine, but only a slight blocking action against acetylcholine. Its activity is relatively weak in inhibiting the spasmogenic action of histamine on isolated guinea pig ileum.

### Mechanism of Action

Meclizine has CNS depressant, antiemetic, anticholinergic, antispasmodic and antihistaminic properties. Meclizine depress labyrinth excitability and conduction in vestibular-cerebellar pathways. The antiemetic and antimotion sickness action of meclizine result from its central anticholinergic and CNS depressant properties.

### Indication

Vertina® (Meclizine hydrochloride) is indicated for the prevention and treatment of nausea and vomiting, and dizziness associated with motion sickness. It is also indicated in the management of vertigo associated with diseases affecting the vestibular system.

### Dosage and Administration

*Vertigo*

For the control of vertigo associated with diseases affecting the vestibular system, the recommended dose of Vertina® (Meclizine hydrochloride) is 25 to 100 mg daily, in divided dosage, depending upon clinical response.

*Motion Sickness*

The initial dose of 25 to 50 mg of Vertina® (Meclizine hydrochloride) should be taken one hour prior to embarkation for protection against motion sickness. Thereafter, the dose may be repeated every 24 hours for the duration of the journey.

### Contraindication and Precaution

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Patients should avoid alcoholic beverages while taking this drug. Due to its potential anticholinergic action, this drug should be used with caution in patients with asthma, glaucoma, or enlargement of the prostate gland.

### Side Effect

Drowsiness, dry mouth and on rare occasions, blurred vision have been reported.

### Use in Pregnancy and Lactation

Pregnancy Category B. Epidemiological studies in pregnant women, do not indicate that Meclizine increases the risk of developmental anomalies or any abnormalities on fetus when administered during pregnancy. Nevertheless, Meclizine, or any other medication, should be used during pregnancy only if clearly necessary.

### Usage in Children

Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in children under 12 years of age.

### Storage Condition

Store in a cool and dry place, protect from light and moisture. Keep all medication out of reach of children.

### How Supplied

Vertina® Tablet : Each box contains 5x10 chewable tablets in blister pack.

## New Revolutionary CT Scanner!

A new generation of imaging technology is wowing doctors and patients alike. This speedy, pinpoint-accurate machine is changing how doctors view the body.

Like older models, this CT scanner takes cross-sectional pictures of the body using X-rays and detectors. What's different is its speed. In the 70s, it used to take five minutes to take one rotation. In the early 90s, it went down to one second per one rotation, and towards the late 1990s, it went to about half a second for four slices in one rotation.

*New CT Scanner*

With this new scanner, doctors can now take 64 slices every half second. The new scanner is so fast that it can basically freeze the motion of the heart. The other advantage for them is the diagnosis is much more accurate. Doctors say the speed of the scanner will help them unravel more medical mysteries-one scan at a time.

*SOURCE: Ivanhoe Broadcast News*

## Blood Test Predicts Heart Disease Deaths

A simple blood test may help determine who is more at risk of dying from cardiovascular disease. The test measures gamma-glutamyl transferase (GGT), an enzyme produced primarily by the liver. The enzyme is elevated in some forms of liver disease. Now, researchers in Austria found the higher the blood level of GGT, the greater the risk of cardiovascular death. Researchers say that people with high GGT have 1.5-fold more risk of dying from cardiovascular diseases in comparison to people with normal low levels of GGT.

The study also shows the risk of cardiovascular death is 28-percent higher for men with moderately high GGT compared to those with normal levels of the enzyme. It went up to 64-percent for men with highly elevated GGT. In women, the increase in risk ranged from 35 percent to 51 percent.

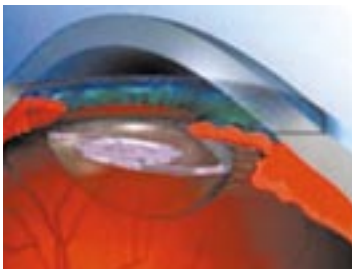
Researchers cite two reasons GGT can predict the risk of cardiovascular death: High levels of GGT show the presence of atherosclerosis, and the enzyme is related to the harmful effects of heavy drinking on blood vessels.

Researchers analyzed data on more than 160,000 Austrian adults. They were age 19 or older when the study began. Researchers followed them for an average of 11 years to 12 years.

*SOURCE: Circulation, 2005; 11 2.*

## "Good Bye" to Cataracts and Glasses!

A cataract clouds the eye's natural lens, making it hard to see clearly. Now, some patients can get rid of cataracts and their glasses or contacts at the same time.



*New Lens for Cataract*

A new lens does double duty. The "new lens" is a lens that has different zones of focus built into the plastic of the lens. When this lens is placed into the eye, it allows the patient to focus distant, intermediate and close-up. Once it is unfolded, It has pretty much the consistency of a stick of gum. In clinical trials, 80 percent of patients who got the "new lens" no longer needed glasses.

*SOURCE: Ivanhoe Broadcast News*

## Implanted Device for Depression!

The FDA has approved a first-of-its-kind implantable electrical nerve stimulator device to treat severe depression. The device, called the Vagus Nerve Stimulation (VNS) System, was approved for adult patients with long-term or recurrent major depression that has not responded adequately to four or more antidepressant treatments.

VNS consists of a stopwatch-sized device that's surgically implanted in the upper chest. Tiny wires attach the device to the vagus nerve, which runs from the neck to the brain The eiectrical stimulation is thought to alter the chemical transmitters that carry messages between nerve cells involved in regulating mood.

More than 32,000 patients worldwide have used the VNS Therapy System.

*SOURCE: WebMD Medical News*

# Clear Key to Success...

... from bacterial infectious diseases.

## Vanprox®

Cefpodoxime proxetil

- USFDA approved
- Broad spectrum
- Highly effective against typhoid fever in children
- Effective option for switch therapy
- Covers most patient groups (15 days to geriatric patients)

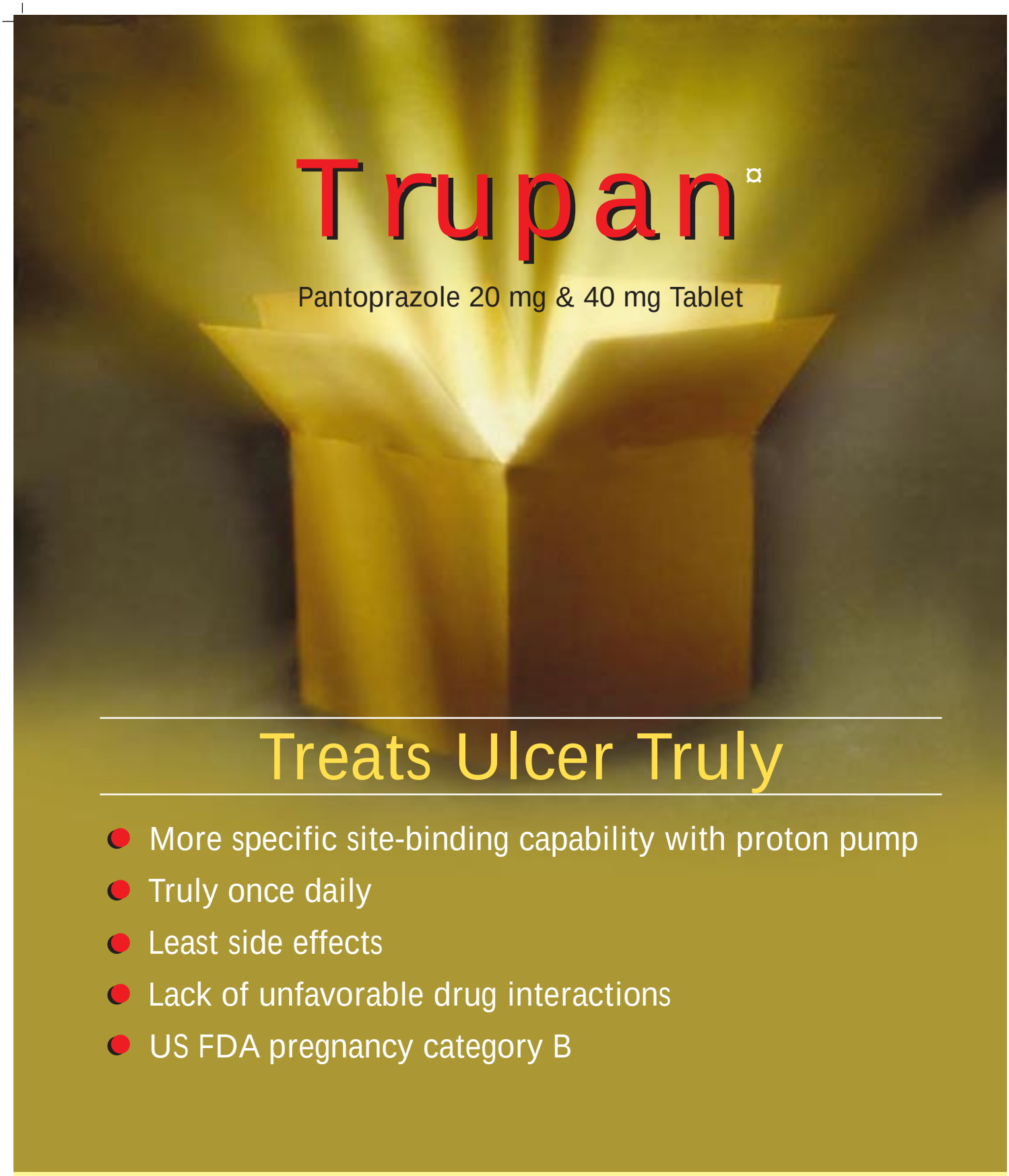
100 & 200 mg capsule
Dry powder for suspension
Paediatric drops

## Erian® ointment

Cinchocaine HCl BP 0.5% + Hydrocortisone BP 0.5% +
Framycetin Sulphate BP 1% + Esculin 1%

Ensures ideal coverage in anorectal disorders

- Relieves
  all symptoms of anorectal disorders
- Ensures
  synergistic activity
- Ensures
  comfort & compliance
- Well
  tolerated




# Treats Ulcer Truly

- More specific site-binding capability with proton pump
- Truly once daily
- Least side effects
- Lack of unfavorable drug interactions
- US FDA pregnancy category B

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Medical Services Department, ***SQUARE PHARMACEUTICALS LTD.*** Corporate Headquarters, SQUARE CENTRE
48, Mohakhali Commercial Area, Dhaka-1212, Tel : 8827729 - 38, 8817729 - 38, Fax : 880 -2-882 8608 / 882 8609
E-mail : info@squaregroup.com, Web Page : http://www.squarepharma.com.bd, Omar Akramur Rab <omar@squaregroup.com>

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