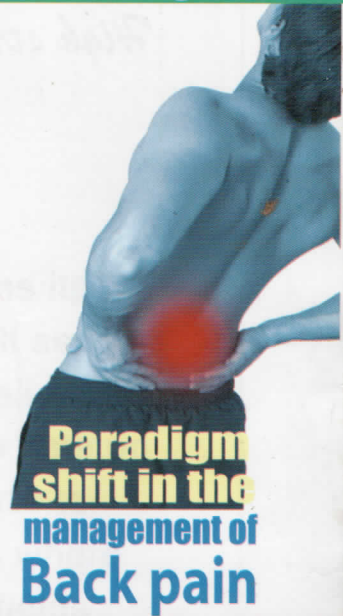




# Health *Management*

Vol. No.1 March'10

An Int'l Standard Medical Journal in Bangladesh



**Paradigm  
shift in the  
management of  
Back pain**

## Hemorrhagic Child Stroke

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Hemorrhagic

## Child Stroke



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### Cilosta®

#### Indications

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The recommended dosage of Cilosta is 100 mg b.i.d. taken at least half an hour before



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#### Description

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*Enterococcus faecium*, *Staphylococcus aureus* (methicillin-susceptible and resistant strains), or *Streptococcus pneumoniae* (penicillin-susceptible strains). *Staphylococcus aureus* (methicillin-susceptible and resistant strains), *Streptococcus pyogenes*, or *Streptococcus agalactiae*. *Staphylococcus aureus* (methicillin-susceptible only) or *Streptococcus pyogenes*. *Streptococcus pneumoniae* (penicillin-susceptible strains only),

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#### Tablet

#### Trimetazidine Dihydrochloride

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Patients should have reversible spasticity so that treatment with Baclofen will aid in restoring residual function.

It may also be of some value in patients with spinal cord injuries and other spinal cord diseases.

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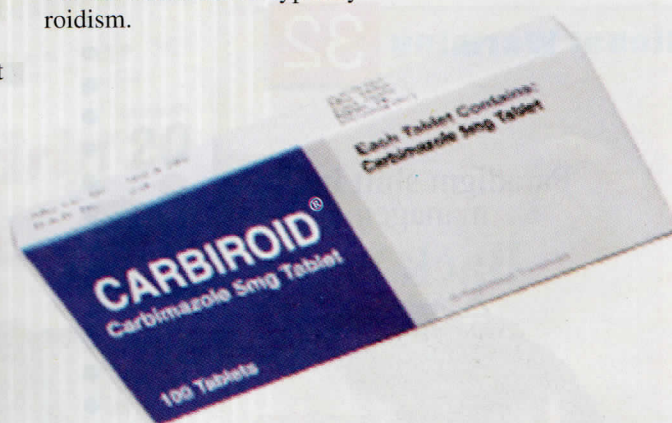
Indication: Acarbose is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

### Carbiroid®

#### Carbimazole BP 5 mg tablet

#### Indication

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Brand: Seclo®

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Brand: Omegut®

Preparations: Cap. 20mg, 40mg, Inj 40mg

■ **Incepta Pharmaceuticals Ltd.**

Brand: Omenix®

Preparations: Cap 20mg, 40mg

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Brand: Omep®

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■ **Beximco Pharmaceuticals Ltd.**

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Preparation: Cap 20mg

■ **ACI Limited**

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Preparations: Cap 10mg, 20mg, 40mg

Inj 40mg

■ **Radiant Pharmaceuticals Limited**

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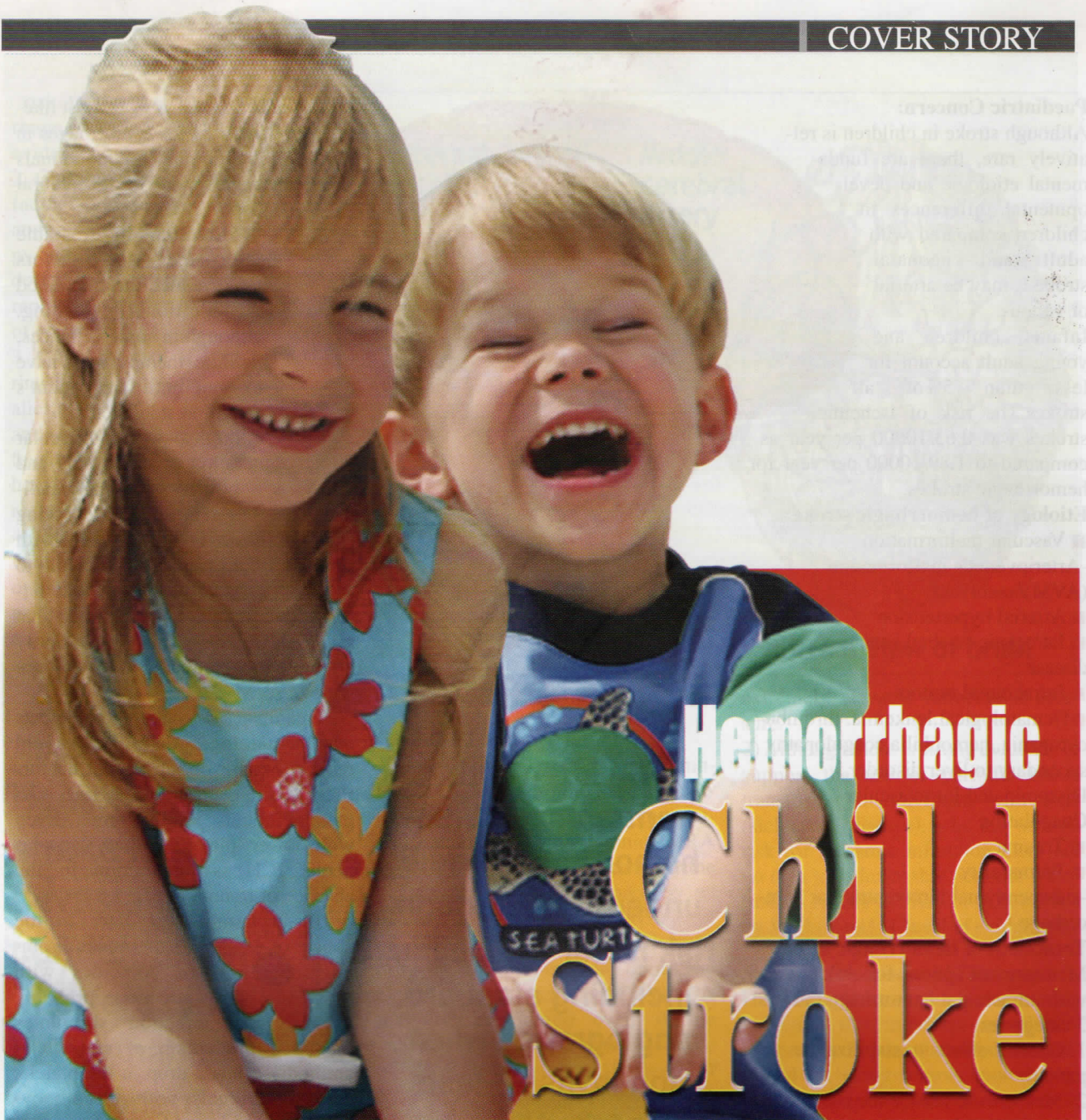
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# Hemorrhagic Child Stroke



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**M**iss Nasreen Akhtar, 12 years old, right handed person, non diabetic, non hypertensive hailing from Aligonj, Narayongonj with the complains of weakness of left side of body for 2 months and deviation of angle of mouth to the right side of body for 2 months. According to patient's statement she was relatively alright 2 months back. Then she noticed weakness of left side of body which was sudden on onset. She complains headache, vomiting for several times during the onset of weakness. She complains deviation of angle of mouth to the right side of body which occurred simultaneously. No complains in bowel, bladder involvement. No history of fever or altered consciousness.

Other systemic examination reveals nothing contributory. On examination of the nervous system, hemiplegic gait is found. Muscle power on left side of body is reduced. CT scan of brain reveals right sided intracerebral haemorrhage with intraventricular extension. MRI of brain shows subacute hematoma in right thalamus.



### Paediatric Concern:

Although stroke in children is relatively rare, there are fundamental etiologic and developmental differences in children compared with adult and neonatal stroke. It may be arterial or venous.

Infants, children and young adult account for less than 5% of all strokes. The risk of ischemic strokes was 0.63/10000 per year as compared to 1.89/10000 per year for hemorrhagic strokes.

### Etiology of hemorrhagic stroke:

- Vascular malformation
  - Arteriovenous malformation (AVM)/aneurysm
- Arterial hypertension
- Iatrogenic cerebral venous occlusive disease
- Intracranial tumors
- Hematological: leukemia, thrombocytopenia, hemophilia, coagulopathy secondary to liver disorder, Disseminated Intravascular Coagulation
- Trauma
- Prematurity
  - subependymal intraventricular hemorrhage

### Treatment of hemorrhagic stroke

Management options for children with intracranial hemorrhage fall into 3 categories.

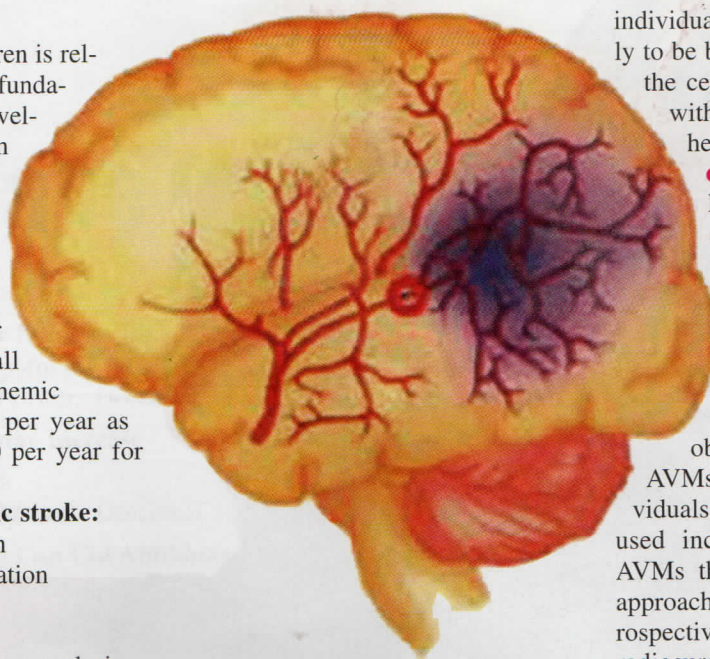
1. General efforts to stabilize the patient
2. Measures to reduce the risk of rebleeding and
3. Attempts to treat the hemorrhage itself.

### Stabilizing measure include.

- Optimizing the respiratory effort,
- Controlling systemic hypertension,
- Preventing epileptic seizures and
- Medically managing increased intracranial pressure.

Additionally, individuals with SAH may benefit from control of vasospasm. There is no compelling evidence that surgical evacuation of supratentorial intraparenchymal hematoma is beneficial at any age.

- There is anecdotal evidence that hematoma evacuation may alleviate impending brain herniation in selected



■ ■ ■ ■ ■

**Children with nontraumatic brain hemorrhage should undergo a thorough risk factor evaluation, including standard angiography when non invasive tests have failed to establish an origin, in an effort to identify treatable risk factors before another hemorrhage occurs.(class1, level of evidenceC)**

■ ■ ■ ■ ■

individuals. Such surgery is most likely to be beneficial for hemorrhages in the cerebellum and for individuals with large lesions in the cerebral hemisphere.

- Correction of treatable hemorrhage risk factors should reduce the likelihood of additional bleeding, although in some instances, definite therapy may have to wait until the patient's condition stabilizes.

- Surgical or endovascular obliteration of aneurysms and AVMs is effective for many individuals, but radiosurgery is being used increasingly in children with AVMs that are small or difficult to approach surgically. Several large retrospective studies have reported that radiosurgery is safe and evidently effective for the treatment of children with an AVM.

- Treatment of coagulation defects and hematologic disorders should reduce the risk of subsequent hemorrhage. Brain hemorrhage is rare with platelet counts  $>20000/\text{mm}^3$ . Even with lower platelet counts, spontaneous ICH is uncommon in the absence of trauma.

- Brain hemorrhage later in the course of acquired isoimmune thrombocytopenia often coincides with asystemic viral infection, probably because the infection stimulates increased production of antiplatelet antibodies, thus a drop in the platelet count. Individuals with thrombocytopenia should avoid aspirin or other antiplatelet drugs, as well as situations that seem likely to produce head trauma. Likewise, factor V111 administration can prevent or minimize intracranial traumatic hemorrhage in children with factor V111 deficiency.

### Recommendations for Evaluation and Treatment of hemorrhage in children:

#### Class 1 Recommendations

1. Children with nontraumatic brain hemorrhage should undergo a thorough risk factor evaluation, including standard angiography when non invasive tests have failed to establish an origin, in an effort to identify treatable



risk factors before another hemorrhage occurs.(class1, level of evidenceC).

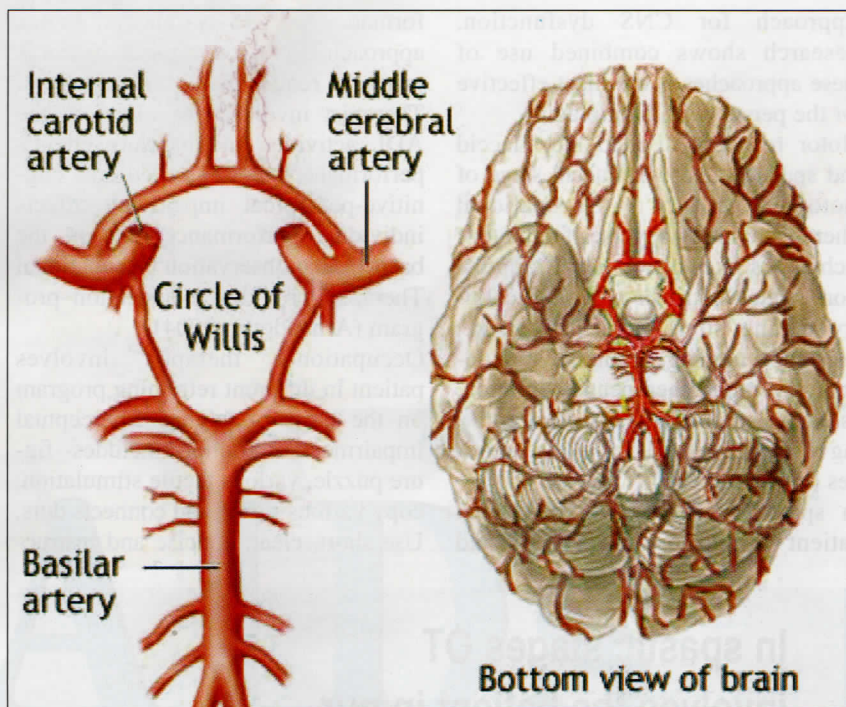
2. Children with a severe coagulation factor deficiency should receive appropriate factor replacement therapy and children with less severe factor deficiency should receive factor replacement after trauma(class1,level of evidence A).

3. Given the risk of repeated hemorrhage from congenital vascular anomalies,these lesions should be identified and corrected whenever it is clinically feasible.Similarly, other treatable hemorrhage risk factors should be corrected(class1,level of evidenceC).

4. Stabilizing measures in patients with brain hemorrhage should include optimizing the respiratory effort, controlling systemic hypertension,controlling epileptic seizures and managing increased intracranial pressure



**Hemorrhagic stroke is a devastating condition that interferes in all performance component areas of an individual including-sensory-motor, cognitive-perceptual, psychosocial & functional independence.**



(class1,level of evidence C)

#### Class11 Recommendations

1) It is reasonable to follow up asymptomatic individuals who have a condition that predisposes them to intracranial aneurysms with a cranial MRA every 1 to 5 years, depending on the perceived level of risk posed by an underlying condition (class11a,level of evidenceC) . If the individual develop symptoms that could be explained by an aneurysm, CTA or CA may be considered even if the patient's MRA fails to show evidence of an aneurysm (class11b, level of evidenceC).Given the possible need for repeated studies over a period of years, CTA may be preferable to CA for screening individuals at risk of aneurysm (class11b, level of evidence C).

2)Individuals with SAH may benefit from measures to control cerebral vasospasm(class11b, level of evidence C)

#### Class 111 recommendations

1) Surgical evacuation of a supratentorial intracerebral hematoma is not recommended for most patients (class111, level of evidence C).

However, information from small numbers of patients suggests that surgery may help selected individuals with developing brain herniation or

extremely elevated intracranial pressure.

2) Although there is strong evidence to support the use of periodic blood transfusion in individuals with SCD (sickle cell disease), who are at high risk for ischemic infarction there are no data to indicate that periodic transfusions reduce the risk of ICH caused by SCD (class111,level of evidenceB).

#### Scope of Occupational Therapy:

Hemorrhagic stroke is a devastating condition that interferes in all performance component areas of an individual including-sensory-motor, cognitive-perceptual, psychosocial & functional independence.

Occupational Therapists use holistic approaches to work in all affected areas for a person suffering hemorrhagic stroke. Turner *et al* (1996) describes purposeful activity, therapeutic exercise, special equipments, skills training and environmental modifications are used to maximize the person's ability to attain independence in everyday living and to improve their quality of life.

In Hemorrhagic stroke rehabilitation, Occupational Therapists use different sensory-motor & neuro-developmental treatment approaches like-Brunnstrom's Movement Therapy, Bobath Approach and Rood's



Approach for CNS dysfunction. Research shows combined use of these approaches is the most effective for the person with hemiplegia.

Motor recovery divided into flaccid and spastic stages. In flaccid stage of motor recovery Occupational Therapist collectively uses facilitatory techniques like- heavy joint compression, stretch, intrinsic stretch, secondary ending stress, stretch pressure, resistance, tapping, vestibular stimulation, inversion, therapeutic vibration, osteopressure patterns and incorporating with different daily living activities (Pedretti, 1990).

In spastic stages OT involves the patient in purposeful activity and

performance for CNS dysfunction. In this approach client active participation is primary requirement. Occupational Therapist involved the client in the ADL activities and measure client's performances and observed how cognitive-perceptual impairment affects individual performance and on the basis of that observation Occupational Therapist provides re-education program (Arnadottir, 2004).

Occupational therapist involves patient in different retraining program on the basis of cognitive-perceptual impairment. Retraining includes- figure puzzle, various tactile stimulation, copy various figure and connects dots. Use short, clear, concise and instruc-

sing to the family members. Educate the patients and their family member about disease process. Encourage the family member to continue individual role (like schooling) and encourage in social interaction (like religious program). Maximize patient activities of daily living such as dressing, washing, eating etc. Resettle the client within the family friends, productive and leisure roles. Environmental modification includes house modification, ramps or rails that may be required. Need to provide assistive device (splints, wheelchair, modified spoon, modified pen) and vocational training (Turner, 1996).

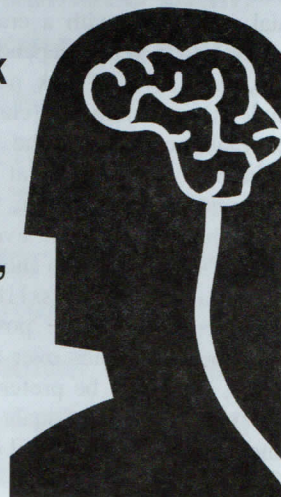
Rehabilitation is a lengthy process for CNS dysfunction. Recovery from CNS dysfunction continues up to two years though maximum recovery occurs within first six months (Davies, 1985). Occupational therapy treatment need to starts from early stages of recovery. As it is said early treatment better prognosis.

#### **Role of Rehabilitation:**

The most important part of the management of the stroke patient is its rehabilitation. The goal of rehabilitation is to make the patient fit again by identifying disability, improving functional independence above all improving quality of life(QOL).

Rehabilitation should start early to prevent complication and for quick recovery simultaneously along the medical treatment. There are some preventable complication such as intellectual deterioration, depression, bed-sore, respiratory tract infection etc should be managed efficiently. Bed modification, air filled mattresses are very effective to prevent Achilles contracture and bed sore. Proper measure should be taken to prevent subluxation of the hemiplegic shoulder. A pillow under the axilla may help to prevent fixed adduction of the shoulder. Physiotherapy such as IRR, EST etc are very effective for early recovery and exercise such as ROM, strengthening exercise, gait retraining are the corner stone of rehabilitation. ■

**In spastic stages OT involves the patient in purposeful activity and combined uses inhibitory techniques with activities includes- positioning, trunk rotation, weight bearing, scapular mobility, reflex inhibiting patterns, rocking, slow rolling and involved the patient in fine & gross motor activities.**



combined uses inhibitory techniques with activities includes- positioning, trunk rotation, weight bearing, scapular mobility, reflex inhibiting patterns, rocking, slow rolling and involved the patient in fine & gross motor activities (Trombly, 2002).

**Cognitive-Perceptual Retraining:** Arnadottir OT-ADL Neurobehavioural Evaluation used to evaluate cognitive perceptual impairments and functional assessment of ADL per-

formance for set pattern for dressing (Pedretti, 1990). Provide external cues in relation to person, place, and time. eg calendar, diary with names, photos etc. Involve patient in specific memory training games. Use table top activities that require problem solving skills. Involve patient in simple task planning, sequencing and time management strategies (Zoltan, 1996). Psychosocial and Functional consideration includes - education and coun-





# NSAIDs

## Some critical considerations



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**Renal effects of NSAIDs are based on their pharmacologic mechanism of action. Even with the advent of selective COX-2 inhibitors, nephrotoxicity still remains a concern.**

Pain medications are one of the most widely used medications, with both prescription and over-the-counter medications available. The class of non-steroidal anti-inflammatory drugs (NSAIDs) encompasses the largest class of medications used for common maladies such as arthralgias or headache. Over-the-counter analgesics (OTCAs), principally acetaminophen-containing compounds and NSAIDs are commonly used medications.

### Hepatic events

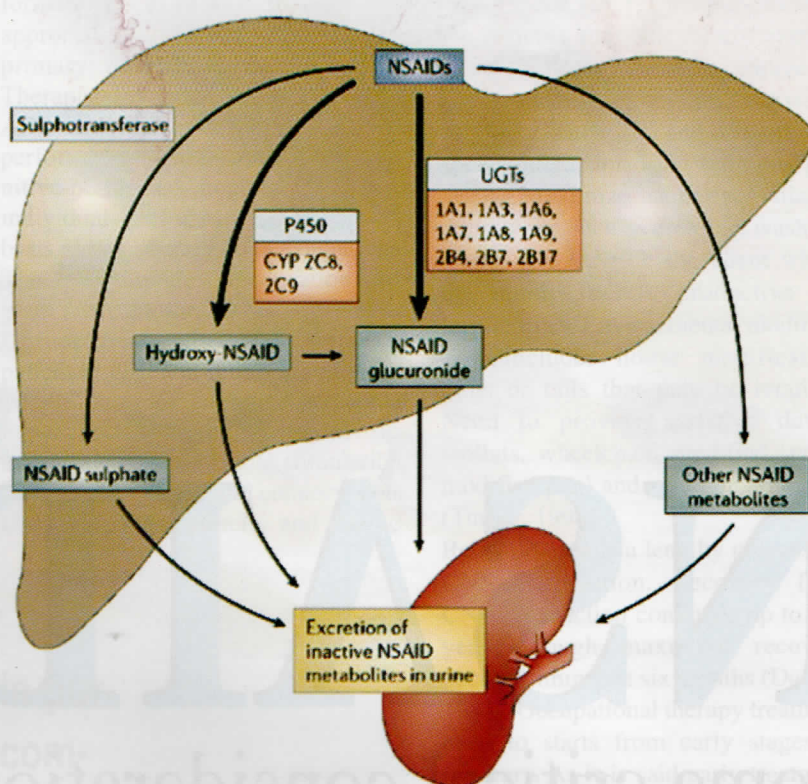
NSAIDs can cause idiosyncratic (unpredictable) liver toxicity. A recent report described three cases of over-the-counter ibuprofen use in patients with hepatitis C which resulted in a greater than 10 fold rise in the

transaminases (liver enzymes). In one of the cases a rechallenge occurred leading to a repeated equal rise in the transaminases. By nature of these unpredictable reactions (idiosyncratic), a risk is taken with each use of NSAIDs in the setting of chronic liver disease. NSAIDs are known to increase the tendency for bleeding by inhibiting platelet function in the setting of cirrhosis where there already is impaired coagulation. NSAIDs also decrease renal prostaglandins (hormones) in cirrhotic patients decreasing kidney blood flow, and thus filtration rates which can lead to renal failure. Guidelines for the use of these agents in patients with chronic liver disease (CLD) are not available, despite the possibility that such patients may be more susceptible to



the effects of an adverse reaction. Notwithstanding the lack of guidelines for healthcare providers, patients are often counseled to modify their use of these drugs.

In EU countries, it has been observed in different studies that recommendations against the use of NSAIDs were significantly less common than recommendations against paracetamol use, in cases of both compensated and decompensated cirrhosis. Non-gastroenterologists and non-primary care physicians were the least likely to recommend against NSAID use, while gastroenterologists were the least likely to recommend against paracetamol in these patients. It was the recommendation of most respondents that *OTCAs should be avoided in patients with cirrhosis, and that paracetamol should be avoided or its dose reduced in the setting of daily alcohol use.*



## Renal events

Renal effects of NSAIDs are based on

***The signs of acute renal failure include weight gain and elevations in serum creatinine, blood urea nitrogen, and serum potassium. Onset of this complication is usually within days of the start of therapy and seems to be more rapid with agents that have a short half-life.***

their pharmacologic mechanism of action. Even with the advent of selective COX-2 inhibitors, nephrotoxicity still remains a concern. The adverse effects of NSAIDs are mediated via inhibition of prostaglandin synthesis

from arachidonic acid by non-specific blocking of the enzyme cyclooxygenase leading to vasoconstriction and reversible mild renal impairment in volume contracted states. When unopposed, this may lead to acute tubular necrosis and acute renal failure. NSAIDs also produce interstitial nephritis with or without nephrotic syndrome secondary to minimal change disease. Although this presents as acute renal failure, it can progress in some cases to chronic renal failure. Papillary necrosis has been incriminated in the development of chronic renal failure secondary to NSAIDs. In patients on long term NSAIDs without acute or chronic renal failure, subclinical renal dysfunction such as reduced creatinine clearance and impaired urine concentrating ability has been shown to be present. *Although this sub-clinical dysfunction is reversible on withdrawal of NSAIDs, some reports have suggested a persistent residual dysfunction. Even with a wide range of NSAIDs at our disposal, a renal safe NSAID is yet to be discovered.*

Inhibition of PGE<sub>2</sub> synthesis can lead

to increased sodium reabsorption, causing peripheral edema, which is the most common renal effect of NSAIDs. Edema and sodium retention are usually mild, resulting in weight gain of 1 to 2 kg, and typically occur within the first week of therapy. In rare serious cases, increased sodium reabsorption can result in marked edema, weight gain, and exacerbations of heart failure. The response to diuretic therapy can also be decreased, and usually moderate increases in blood pressure (BP) are sometimes observed. In addition to previously mentioned risk factors, diabetes mellitus, renal disease, circulatory compromise, and advanced age may predispose patients to NSAID-related sodium retention and edema. Hyperkalemia is another electrolyte disturbance that can occur as a result of inhibition of PG synthesis in the kidney. *The risk of hyperkalemia may be particularly high in patients receiving potassium supplementation, potassium-sparing diuretics, or ACE inhibitors. The effects of NSAIDs on electrolyte and water homeostasis seem to be dose-dependent.*



Acute renal failure is a rare but potentially serious complication of NSAID use. The signs of acute renal failure include weight gain and elevations in serum creatinine, blood urea nitrogen, and serum potassium. Onset of this complication is usually within days of the start of therapy and seems to be more rapid with agents that have a short half-life. Acute renal failure with NSAID therapy is mediated hemodynamically as a result of decreased renal perfusion after inhibition of prostacyclin synthesis. The risk factors are similar to those for electrolyte imbalance and also include sepsis, shock, systemic lupus erythematosus, hyperreninemia, and hyperaldosteronemia. Although renal blood flow is not thought to be dependent on PGs under normal physiologic conditions, some reported cases of renal failure after initiation of NSAID therapy include apparently healthy subjects. These effects are relatively mild and rare in healthy individuals but can be serious in patients whose renal function is prostaglandin-dependent. *Patients with contracted effective intravascular fluid volume as a result of congestive heart failure, cirrhosis, diuretic use, or restricted sodium intake are more likely to experience NSAID-related changes in renal function.*

Very rare adverse renal effects of NSAID therapy include nephritic syndrome and papillary necrosis. Acute interstitial nephritis can develop at any time during therapy and is usually combined with minimal-change glomerulonephritis. The exact risk factors for NSAID-related nephrotic syndrome have not been identified, but it seems that it occurs more frequently in women and the elderly. This adverse event may also be related to pharmacologic properties of the agent, as the majority of cases have been reported with fenoprofen. Leukotrienes increase vascular permeability in the glomerular and peritubular capillaries, leading to proteinuria and interstitial nephritis. Renal papillary necrosis is the least common but



***Aspirin and NSAIDs can induce dose-dependent asthma exacerbations and other adverse reactions. The potential for causing bronchospasm seems to correlate with the degree of prostaglandin inhibition.***

potentially most severe NSAID-related renal adverse effect, as it represents permanent renal parenchymal damage. *This can be caused acutely by a massive overdose of an NSAID in a dehydrated individual. Chronic renal papillary necrosis is associated with long-term use of multiple high doses of a single analgesic or combinations of analgesics.*

Again, the good news is; according to a new study which appears in the July 18 issue of *The Journal of the American Medical Association* occasional use of aspirin, acetaminophen, or other pain reliever for everyday aches and pains is not associated with kidney dysfunction among healthy men. This study, however, provides reassuring evidence that there does not appear to be a strong association between chronic analgesic use and chronic renal dysfunction. Researchers at Brigham and Women's Hospital in Boston analyzed self-reported use of these pain relievers among 11,032 men with no history of kidney problems who took part in the 14-year Physicians' Health Study, from 1982 to 1995. They compared analgesic use to measured creatinine levels and creatinine clearance from blood samples provided by the men. The authors defined elevated creatinine level as 1.5 mg/dL or higher, and a reduced creatinine clearance as 55 mL/min or less. Self-reported use of analgesics was classified as never (less than 12 pills), 12-1499 pills, 1500-2499 pills, and more than 2500 pills. Some earlier studies have suggested that regular use of popular pain relievers such as aspirin, acetaminophen, and other nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk of chronic kidney problems in generally healthy patients, but others have shown no association.

### **Bronchial events**

Aspirin and NSAIDs can induce dose-dependent asthma exacerbations and other adverse reactions (eg, angioedema). The potential for causing bronchospasm seems to correlate with the degree of prostaglandin inhibition. Patients at increased risk of bronchospasm include those with nonallergic rhinitis, nasal polyps, pansinusitis, and asthma. Up to 15% of adults with asthma may have aspirin-induced bronchospasm. The risk increases to 20% to 40% in patients with both asthma and nasal polyps<sup>5</sup>. An aspirin challenge may also cause diffuse flushing,



aspirin-induced bronchospasm. The risk increases to 20% to 40% in patients with both asthma and nasal polyps<sup>5</sup>. An aspirin challenge may also cause diffuse flushing, rhinorrhea, and ocular irritation. NSAID sensitivity is not IgE-mediated, so skin testing is not an effective means of ruling out the diagnosis. Instead, history taking or, if needed, a cautiously performed challenge is used to detect aspirin sensitivity.

Aspirin-induced asthma has been found to be associated with decreased prostaglandin levels and increased leukotriene levels. On challenge, elevations have been found in urine histamine and leukotriene levels as well as in serum tryptase levels, the latter presumably from mast cells. Although antihistamines are not effective for preventing aspirin-induced asthma, leukotriene antagonists have been shown to be inhibitory. These data suggest that leukotriene C4 may mediate bronchospasm associated with aspirin sensitivity. While it is not completely clear whether these two effects are additive, *a high index of suspicion should be maintained in any patient who develops pulmonary symptoms and is taking either an ACE-inhibitor or an NSAID.*

### **Rheumatologic concern**

Chronic pain affects 75 million US citizens. A number of pharmacologic treatments are available for chronic pain that does not respond adequately to nonpharmacologic methods. Long the mainstay of chronic pain management, nonsteroidal anti-inflammatory drugs (NSAIDs) are known to be associated with gastrointestinal (GI) and renal toxicities, a particular problem for the elderly population, which commonly experiences chronic pain, such as that associated with osteoarthritis (OA). Several non-NSAID, non-narcotic therapies are available for noninflammatory pain. Acetaminophen is as effective as NSAIDs for the management of mild-to-moderate OA

pain and is the recommended first-line therapy by the American College of Rheumatology (ACR). Propoxyphene, widely believed to be safe and effective, may, in fact, be no more effective and perhaps less effective than acetaminophen or ibuprofen. A relatively new analgesic, tramadol, appears to be a useful therapy for patients who do not receive adequate pain relief with acetaminophen and are at risk for NSAID-related side effects. For localized chronic pain associated

***Opioids may be safer than long-term NSAID therapy and should be considered for all patients with moderate-severe or quality-of-life-impacting pain. Breakthrough pain with opioids should be anticipated and treated with short-acting, immediate-release opioids.***

with OA, topical capsaicin is also an effective analgesic. The American Journal of Medicine, Volume 105.

### **Geriatric events**

If ignored or incorrectly treated, pain may cause falls, functional impairment, disruptions in sleep, depression and anxiety, and increased healthcare costs. However, the cardiovascular risk and gastrointestinal toxicity of NSAIDs usually outweigh the benefits

of using them. For most physicians, acetaminophen should be considered as "initial and ongoing pharmacotherapy in the treatment of persistent pain, particularly musculoskeletal pain". The presence of hepatic insufficiency and/or chronic alcohol use are relative contraindications.

Opioids may be safer than long-term NSAID therapy and should be considered for all patients with moderate-severe or quality-of-life-impacting pain. Breakthrough pain with opioids should be anticipated and treated with short-acting, immediate-release opioids. There is some consensus on geriatric use of NSAIDs (*Journal of the American Geriatrics Society*)

- Use of a proton pump inhibitor or misoprostol for gastrointestinal protection.

- Routine assessment of gastrointestinal and renal toxicity, hypertension, heart failure, and other drug-drug and drug-disease interactions.

- Use of no more than one NSAID or COX-2 inhibitor for pain control. Patients taking aspirin for cardioprophylaxis should not use ibuprofen.

The update also made recommendations for the use of adjuvant painkillers and other drugs for older persons with recalcitrant pain. These included:

- All patients with fibromyalgia are candidates for adjuvant analgesics, while those with neuropathic pain are candidates for a trial of these adjuvant agents.

- Avoid tertiary tricyclic antidepressants because of elevated risk of adverse effects, such as anticholinergic effects and cognitive impairment.

- Reserve long-term systemic corticosteroids for patients with pain-associated inflammatory disorders—not osteoarthritis- or metastatic bone pain.

- Patients with regional or localized pain may be candidates for topical lidocaine, menthol, or capsaicin treatment. ■



# NUTRITIONAL MANAGEMENT OF *Diabetes Mellitus*



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The link between diabetes and diet has been well documented, as has the importance of diet in conjunction with medical interventions for diabetes. Patients often look to their primary care physicians for advice about general diabetes care, including diet, but survey studies have revealed that doctors feel uncomfortable advising patients on the sensitive issues of weight loss and diet. Research is increasingly demonstrating that medical nutrition therapy (MNT), administered by a registered dietitian (RD) or nutrition professional, is a key component of diabetes management and a complement to treatment of diabetes by physicians.

## Recommendations

- All people with diabetes should receive nutritional counselling from a registered dietitian.
- People with diabetes should be encouraged to obtain optimal metabolic control through a balance of food intake, physical activity and medication (if required) to avoid complications.
- Specific dietary recommendations and medications should be individualized to accommodate the person's preferences and lifestyle.

## Carbohydrates

Dietary carbohydrates from cereals, breads, other grain products, legumes, vegetables, fruits, dairy products and added sugars should provide 50–60%

of the individual's energy requirements. Both the source and the amount of carbohydrate consumed influence blood glucose and insulin responses. Factors that influence blood glucose are not predicted by chemical composition alone; food form, ingested particle size, starch structure and cooking methods may all influence the carbohydrate absorption rate from the small intestine and the resultant blood glucose response.

## Recommendations

- Carbohydrates should provide 50–60% of daily energy requirements.
- The amount and source of carbohydrate in meal planning should be considered.
- Including low GI foods may be helpful in optimizing blood glucose control. A dietary pattern that includes carbohydrate from fruits, vegetables, whole grains, legumes, and low-fat milk is encouraged for good health.
- Monitoring carbohydrate, whether by carbohydrate counting, exchanges, or experienced-based estimation remains a key strategy in achieving glycemic control.
- The use of glycemic index and load may provide a modest additional benefit over that observed when total carbohydrate is considered alone.

## Protein

The Dietary Reference Intakes' acceptable macronutrient distribution range for protein is 10–35% of







Uncontrolled diabetes is often associated with micronutrient deficiencies. Individuals with diabetes should be aware of the importance of acquiring daily vitamin and mineral requirements from natural food sources and a balanced diet.

energy intake. The RDA is 0.8 g good-quality protein / kg body wt /day (on average, approx. 10% of calories). Good-quality protein sources are defined as having high PDCAAS (protein digestibility–corrected acid scoring pattern) scores and provide all nine indispensable amino acids. Examples are meat, poultry, fish, eggs, milk, cheese, and soy. Sources not in the “good” category include cereals, grains, nuts, and vegetables.

#### Recommendations

■ For individuals with diabetes and normal renal function, there is insufficient evidence to suggest that usual protein intake (15–20% of energy) should be modified.

■ In individuals with type 2 diabetes, ingested protein can increase insulin response without increasing plasma glucose concentrations. Therefore, protein should not be used to treat acute or prevent nighttime hypoglycemia.

■ High-protein diets are not recommended as a method for weight loss at this time. The long-term effects of protein intake >20% of calories on diabetes management and its complications are unknown. Although such diets may produce short-term weight loss and improved glycemia, it has not been established that these benefits are maintained long term, and long-term effects on kidney function for persons

with diabetes are unknown.

#### Fat and cholesterol

The primary goal with respect to dietary fat in individuals with diabetes is to limit saturated fatty acids, *trans* fatty acids, and cholesterol intakes so as to reduce risk for CVD. Saturated and *trans* fatty acids are the principal dietary determinants of plasma LDL cholesterol. In metabolic studies in which energy intake and weight are held constant, diets low in saturated fatty acids and high in either carbohydrate or *cis*-monounsaturated fatty acids lowered plasma LDL cholesterol equivalently.

#### Recommendations

■ Limit saturated fat to <7% of total calories.

■ Intake of *trans* fat should be minimized.

■ In individuals with diabetes, limit dietary cholesterol to <200 mg/day.

■ Two or more servings of fish per week (with the exception of commercially fried fish filets) provide n-3 polyunsaturated fatty acids and are recommended.

#### Micronutrients

Uncontrolled diabetes is often associated with micronutrient deficiencies. Individuals with diabetes should be aware of the importance of acquiring daily vitamin and mineral requirements from natural food sources and a balanced diet. Health care providers should focus on nutrition counseling rather than micronutrient supplementation in order to reach metabolic control of their patients. Research including long-term trials is needed to assess the safety and potentially beneficial role of chromium, magnesium, and antioxidant supplements and other complementary therapies in the management of type 2 diabetes. In select groups such as the elderly, pregnant or lactating women, strict vegetarians, or those on calorie-restricted diets, a multivitamin supplement may be needed.





Human insulin is grown in the lab inside common bacteria *Escherichia coli* is by far the most widely used type of bacterium, but yeast is also used.

# Insulin manufacturing a new era for Bangladesh

**Md. Shariful Islam**

There are four main types of insulin manufactured based upon how soon the insulin starts working, when it peaks, and how long it lasts in the body. According to the American Diabetes Association.

Rapid-acting insulin reaches the blood within 15 minutes, peaks at 30-90 minutes, and may last five hours.

Short-acting insulin reaches the blood within 30 minutes; it peaks about two to four hours later and stays in the blood for four to eight hours.

Intermediate-acting insulin reaches the blood two to six hours after injection, peaks four to 14 hours later, and can last in the blood for 14-20 hours. And Long-acting insulin takes six to 14 hours to start working, it has a small peak soon after, and stays in the blood for 20-24 hours. Diabetics each have different responses to and needs for insulin so there is no one type that works best for everyone. Some insulin is sold with two of the types mixed together in one bottle.

## Production in five steps

The plant for producing biosynthetic insulin is organized into these five processing sections:

- Fermentation
- Processing 1
- Processing 2
- Purification, and
- End product treatment.

## Conceptual design the key to success

In this planning phase, it was important to bring the process technology into harmony with these requirements:

- Building architecture
- clean room classification and HVAC (heating, ventilation, air conditioning)
- logistics and storage
- Information technology and

process control.

● functional descriptions as the basis for the formulating operation

● Product quality and GMP (Good Manufacturing Practice) concepts.

Plant-oriented design planning was established, starting from the basic data determined and specifications of process-oriented design principles.

- Building concept
  - Master plans for beginning-to-end quality.
  - Assurance, from design to start-up.
  - Plant design, connected to the existing infrastructure.
- This process was essential so that the documents needed for



the construction contract and for the Federal Environmental Protection Act contract could be produced as quickly as possible on an assured design basis and submitted to the authorities responsible.

The conceptual design produced in that manner was based on:

- Layout studies of critical plant areas (e.g., recrystallization) with respect to structure, GMP requirements, material handling, cleaning, and serviceability
  - Layout designs for medium supply and disposal, electrical engineering, measurement, and control technology, as well as HVAC.
  - Logistical concepts with respect to material, personnel and product flow.
- Aventis received approval for construction promptly in December 2000, so that the groundwork started in January 2001. The mechanical preparation was done building-by-building, oriented to the course of the process, until August 2002. After finishing the assembly, then begin the start-up in the same sequence.

The plant is distinguished by a high degree of complexity. It is a large-scale computer-controlled plant. Just one single person at the control room computer screen could manage it. It does require about 6,500 control points (connections to the process control system). The start-up of the entire process control system ran smoothly. By February 2002 the technology was available to start operations of the individual sections of the plant.



## Raw Materials

Human insulin is grown in the lab inside common bacteria. *Escherichia coli* is by far the most widely used type of bacterium, but yeast is also used. Researchers need the human protein that produces insulin. Manufacturers get this through an amino-acid sequencing machine that synthesizes the DNA. Manufacturers know the exact order of insulin's amino acids (the nitrogen-based molecules that line up to make up proteins). There are 20 common amino acids. Manufacturers input insulin's amino acids, and the sequencing machine connects the amino acids together. Also necessary to synthesize insulin are large tanks to grow the bacteria, and nutrients are needed for the bacteria to grow. Several instruments are necessary to separate and purify the DNA such as a centrifuge, along with various chromatography and x-ray crystallography instruments.

## The Manufacturing Process

Synthesizing human insulin is a multi-step biochemical process that depends on basic recombinant DNA techniques and an understanding of the insulin gene. DNA carries the instructions for how the body works and one small segment of the DNA, the insulin gene, codes for the protein insulin. Manufacturers manipulate the biological precursor to insulin so that it grows inside simple bacteria. While manufacturers each have their own variations,

there are two basic methods to manufacture human insulin.

### Working with human insulin

1. The insulin gene is a protein consisting of two separate chains of amino acids, an A above a B chain, that are held together with bonds. Amino acids are the basic units that build all proteins. The insulin A chain consists of 21 amino acids and the B chain has 30.

2. Before becoming an active insulin protein, insulin is first produced as preproinsulin. This is one single long protein chain with the A and B chains not yet separated, a section in the middle linking the chains together and a signal sequence at one end telling the protein when to start secreting outside the cell. After preproinsulin, the chain evolves into proinsulin, still a single chain but without the signaling sequence. Then comes the active protein insulin, the protein without the section linking the A and B chains. At each step, the protein needs specific enzymes (proteins that carry out chemical reactions) to produce the next form of insulin.

### STARTING WITH A AND B

3. One method of manufacturing insulin is to grow the two insulin chains separately. This will avoid manufacturing each of the specific enzymes needed. Manufacturers need the two mini-genes: one that produces the A chain and one for the B chain. Since the exact DNA sequence of each chain is known, they synthesize each mini-gene's DNA in an amino acid sequencing machine.

4. These two DNA molecules are then inserted into plasmids, small circular pieces of DNA that are more readily taken up by the host's DNA.

5. Manufacturers first insert the plasmids into a non-harmful type of the bacterium *E. coli*. They insert it next to the *lacZ* gene. *LacZ* encodes for 8-galactosidase, a gene widely used in recombinant DNA procedures because it is easy to find and cut, allowing the insulin to be readily removed so that it does not get lost in the bacterium's



DNA. Next to this gene is the amino acid methionine, which starts the protein formation.

6. The recombinant, newly formed, plasmids are mixed up with the bacterial cells. Plasmids enter the bacteria in a process called transfection. Manufacturers can add to the cells DNA ligase, an enzyme that acts like glue to help the plasmid stick to the bacterium's DNA.

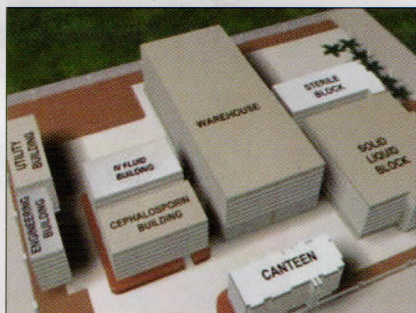
7. The bacteria synthesizing the insulin then undergo a fermentation process. They are grown at optimal temperatures in large tanks in manufacturing plants. The millions of bacteria replicate roughly every 20 minutes through cell mitosis, and each expresses the insulin gene.

8. After multiplying, the cells are taken out of the tanks and broken open to extract the DNA. One common way this is done is by first adding a mixture of lysozyme that digest the outer layer of the cell wall, then adding a detergent mixture that separates the fatty cell wall membrane. The bacterium's DNA is then treated with cyanogen bromide, a reagent that splits protein chains at the methionine residues. This separates the insulin chains from the rest of the DNA.

9. The two chains are then mixed together and joined by disulfide bonds through the reduction-reoxidation reaction. An oxidizing agent (a material that causes oxidation or the transfer of an electron) is added. The batch is then placed in a centrifuge, a mechanical device that spins quickly to separate cell components by size and density.

10. The DNA mixture is then purified so that only the insulin chains remain. Manufacturers can purify the mixture through several chromatography, or separation, techniques that exploit differences in the molecule's charge, size, and affinity to water. Procedures used include an ion-exchange column, reverse-phase high performance liquid chromatography, and a gel filtration chromatography column.

Manufacturers can test insulin batches to ensure none of the bacteria's *E. coli* proteins are mixed in with the insulin.



*The recombinant, newly formed, plasmids are mixed up with the bacterial cells. Plasmids enter the bacteria in a process called transfection. Manufacturers can add to the cells DNA ligase, an enzyme that acts like glue to help the plasmid stick to the bacterium's DNA.*

They use a marker protein that lets them detect *E. coli* DNA. They can then determine that the purification process removes the *E. coli* bacteria.

## PROINSULIN PROCESS

■ Starting in 1986, manufacturers began to use another method to synthesize human insulin. They started with the direct precursor to the insulin gene, proinsulin. Many of the steps are the same as when producing insulin with the A and B chains, except in this method the amino acid machine synthesizes the proinsulin gene.

■ The sequence that codes for proinsulin is inserted into the non-pathogenic *E. coli* bacteria. The bacteria go through the fermentation process where it reproduces and produces proinsulin. Then the connecting sequence between the A and B chains is spliced away with an enzyme and the resulting insulin is purified.

At the end of the manufacturing process ingredients are added to insulin to prevent bacteria and help maintain a neutral balance between acids and bases. Ingredients are also added to intermediate and long-acting insulin to produce the desired duration type of insulin. This is the traditional method of producing longer-acting insulin. Manufacturers add ingredients to the purified insulin that prolong their actions, such as zinc oxide. These additives delay absorption in the body. Additives vary among different brands of the same type of insulin.

## Analog insulin

In the mid 1990s, researchers began to improve the way human insulin works in the body by changing its amino acid sequence and creating an analog, a chemical substance that mimics another substance well enough that it fools the cell. Analog insulin clumps less and disperses more readily into the blood, allowing the insulin to start working in the body minutes after an injection. There are several different analog insulin. Humulin insulin does not have strong bonds with other insulin and thus, is absorbed quickly. Another insulin analog, called Glargine, changes the chemical structure of the protein to make it have a relatively constant release over 24 hours with no pronounced peaks.

Instead of synthesizing the exact DNA sequence for insulin, manufacturers synthesize an insulin gene where the sequence is slightly altered. The change causes the resulting.

Two Bangladeshi manufacturer marketing human insulin in different strength. ■



## Paradigm shift in the management of

# Back pain

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**B**ack pain is the fifth most common reason for physician visits. About nine out of ten adults experience back pain at some point in their life and five out of ten working adults have back pain every year. In up to 85% of people with low back pain, despite a thorough medical examination, no specific cause of the pain can be identified. For 90% of people, even those with nerve root irritation, their symptoms will improve within two months no matter what treatment is used, even if no treatment is given.

The trend of practice was prescribing bed rest for days together and this long period of inactivity further aggravated the situation. Earlier topics on back pain shows requesting of number of investigations; which may not be appropriate at the stage and state of the disease. Now the approach is changed and literatures are in favour of treating back pain keeping the patient active. This saves working hours and potentiates patient's functional abilities. Back pain in special situations like pregnancy, chronic kidney disease or in some other situations need special attention. This article highlights overview of the problem with graded approaches of evaluation and management.



### Overview of the problem:

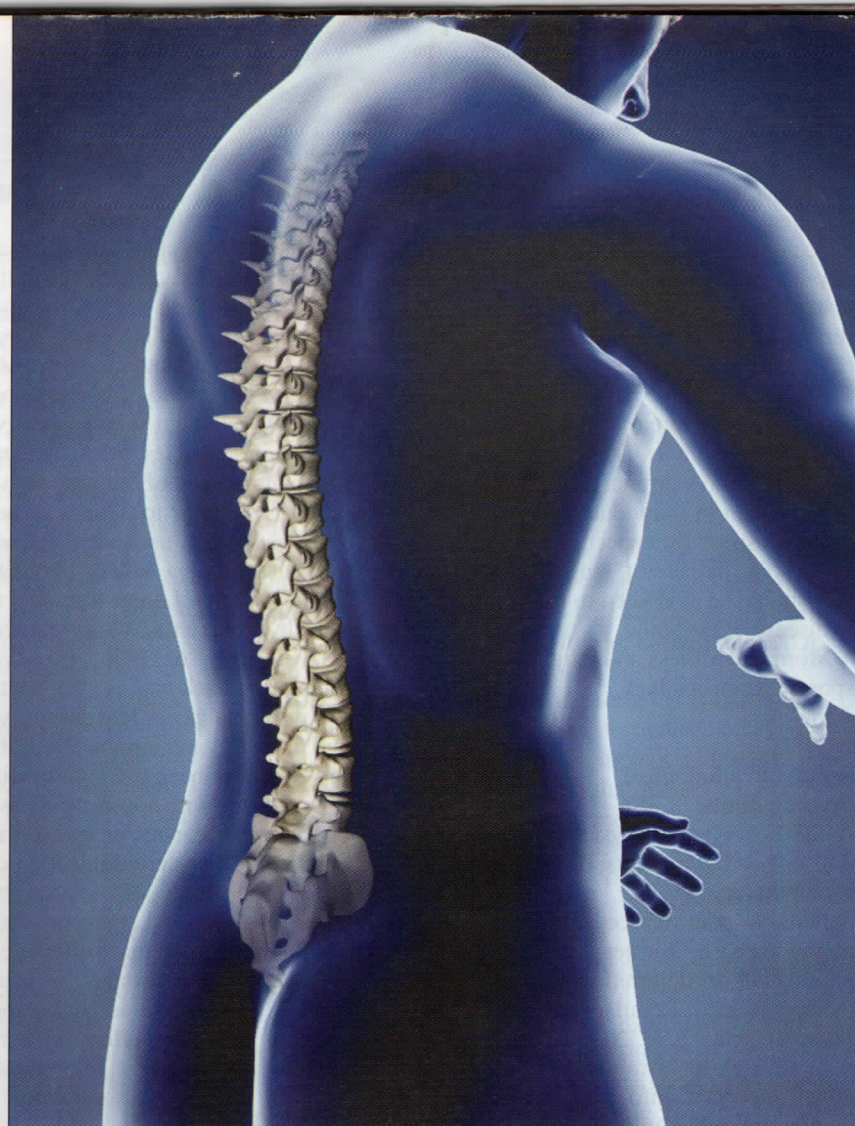
Back pain is a common symptom in clinical practice and classified as acute if it has been present for less than a month and chronic if it lasts for a longer period of time. Common causes of back pain involve disease or injury to the muscles, bones, and/or nerves of the spine. Pain arising from abnormalities of organs within the abdomen, pelvis, or chest may also be felt in the back.

A brief description of the commonest problems associated back pain with presenting features is discussed here

☐ Patient often presenting with buttock, back of thigh and leg pain (sciatica) is an example of nerve root impingement as a result of herniation (or bulging) of the spinal intervertebral disc. Discs begin to degenerate by the third decade of life. Herniated discs are found in one-third of adults older than 20 years of age. Only 3% of these, however, produce symptoms of nerve impingement. Spondylosis occurs as intervertebral discs lose moisture and volume with age, which decreases the disc height.

☐ Spinal disc degeneration coupled with disease in facet joints of the vertebrae can lead to spinal-canal narrowing (spinal stenosis). A person with spinal stenosis may have pain radiating down both lower extremities while standing for a long time or walking even short distances. Cauda equina syndrome is a medical emergency whereby the spinal cord is directly compressed. Disc material expands into the spinal canal, which compresses the nerves. This patient may present with pain, loss of sensation, and bowel or bladder dysfunction.

☐ Musculoskeletal pain syndromes that produce low back pain include myofascial pain syndromes and fibromyalgia. Both the condition can be differentiated as such : Myofascial pain is characterized by pain and tenderness over localized areas (trigger points), loss of range of motion in the involved muscle groups, and pain radiating in a characteristic distribution but restricted to a peripheral nerve. Relief of pain is often reported when the involved muscle group is stretched. Fibromyalgia results in widespread pain and tenderness throughout the body with history of non-restorative sleep. Diagnosis depends on finding of characteristic



**Back pain in special situations like pregnancy, chronic kidney disease or in some other situations need special attention. This article high lights overview of the problem with graded approaches of evaluation and management**

tender points on special areas of the body. Normal pregnancy can cause back pain in many ways, including stretching ligaments within the pelvis, irritating nerves, and straining the low back.

☐ A few studies suggest that psychosocial factors such as on-the-job stress and dysfunctional family relationships may correlate more closely with back pain than structural abnormalities revealed in x-rays and other medical imaging scans

☐ Patients with prior lumbar surgery and either recurrent or persistent low back pain, often termed failed back surgery syndrome, need mention. Knowing the type of surgery performed, the indications for and results of the surgery, and the time course and characteristics of any changes in the pattern and severity of postoperative pain is essential. Recurrent pain or progressive symptoms signal the need for further diagnostic evaluation.

☐ Back pain with following red flag/yellow flag signs are to be dealt



with special care and appropriate attention:

- Patient with bowel and/or bladder incontinence or progressive weakness in the legs.
- other signs of severe illness (e.g. fever, unexplained weight loss) may also indicate a serious underlying medical condition like TB or cancers
- Back pain that occurs after a trauma, indicate a bone fracture or other injury.
- Problems such as osteoporosis or multiple myeloma, also warrants prompt attention.
- Back pain in individuals with a history of cancer (especially cancers known to spread to the spine like breast, lung and prostate cancer) should be evaluated to rule out metastatic disease of the spine.
- Morning stiffness and fatigue may indicate spondyloarthropathies
- Pregnancy

### Scope of radiological investigations:

If the history and physical examination do not suggest the presence of infection, cancer, inflammatory disease, major neurological deficits, or pain referred from abdominal or pelvic disease, further evaluation can be eliminated or deferred while conservative therapy is tried. Regular radiograph of lumbosacral spine give 20 times the radiation dose of a chest -x-ray and provide limited, albeit important, information. Oblique films double the radiation dose and should not be routinely ordered.

MRI provides exquisite anatomic detail but is reserved for patients who are considering surgery or have evidence of a systemic disease or in emergency like epidural mass or cauda equina tumor. Radionuclide bone scan has limited usefulness. It is most useful in detection of vertebral body osteomyelitis or osteoblastic metastasis. The bone scan is normal in multiple myeloma because osteolytic lesions do not take up isotope.

### Management:

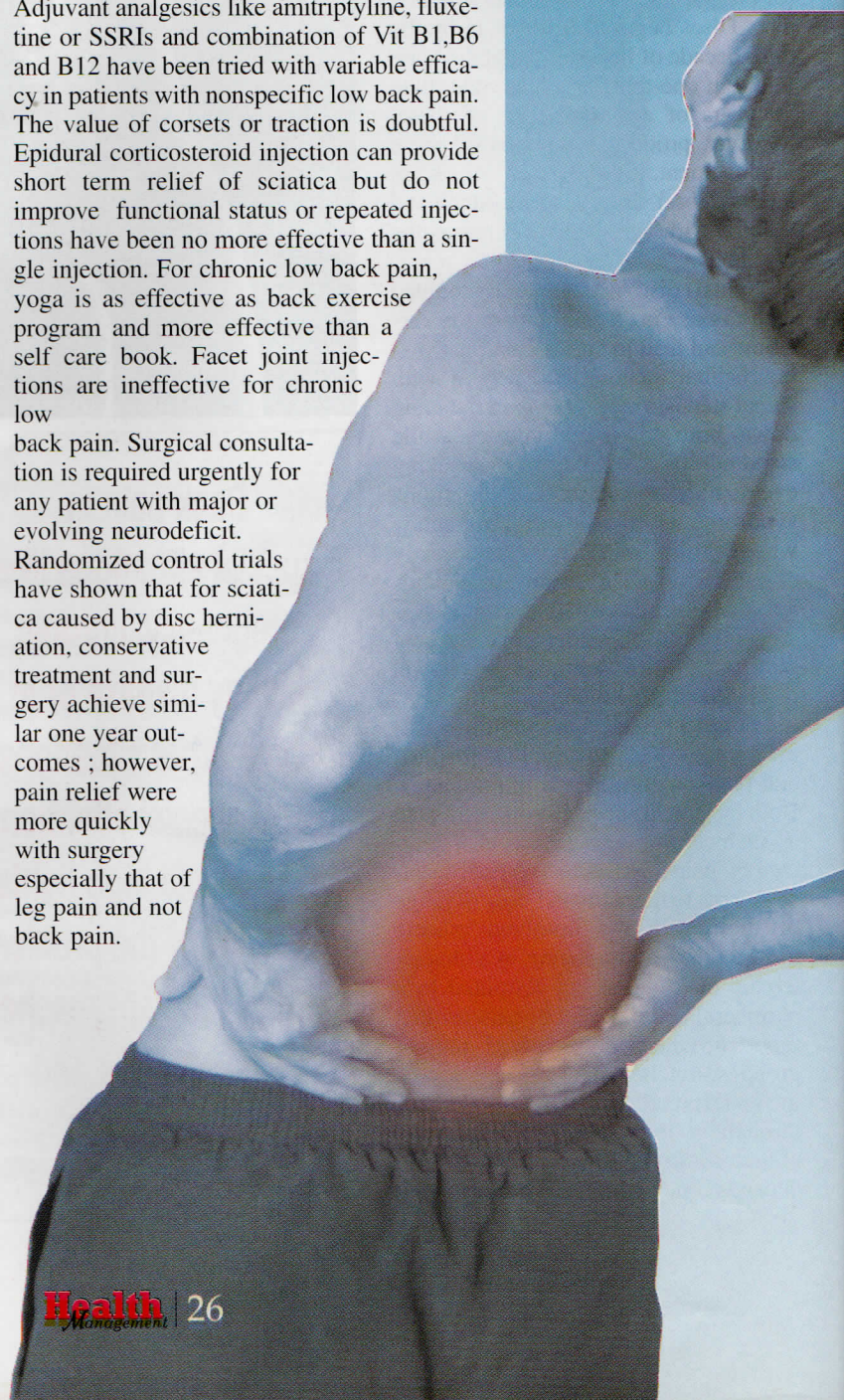
Goals: The management goals of treating back pain are to achieve maximal reduction in pain intensity as rapidly as possible; to restore the individual's ability to function in everyday activities; to help the patient cope with residual pain; to assess for side-effects of therapy; and to facilitate the patient's passage through the legal and socioeconomic impediments to recovery. For many, the goal is to keep the pain to a manageable level to progress with rehabilitation, which then can lead to long term pain relief. Also, for some people the goal is to use non-surgical therapies to manage the pain and avoid major sur-

gery, while for others surgery may be the quickest way to feel better.

Fortunately about 85-90% of the situations are nonspecific and improves with conservative care over 1-4 weeks. Management plan must be individualized with prescription of available appropriate modality. Absolute bed rest once thought to be cornerstones of therapy, are now known to be ineffective for acute back pain. Studies prove that no bed rest with continuation of ordinary activities as tolerated is superior to 07days of bed rest. For acute back pain, exercise therapy is ineffective. Use of pain killers like NSAIDs and Opioids should of short term and supervised. Muscle relaxants with paracetamol or NSAID may of help; however use of baclofen in back pain is very controversial. Adjuvant analgesics like amitriptyline, fluoxetine or SSRIs and combination of Vit B1,B6 and B12 have been tried with variable efficacy in patients with nonspecific low back pain. The value of corsets or traction is doubtful. Epidural corticosteroid injection can provide short term relief of sciatica but do not improve functional status or repeated injections have been no more effective than a single injection. For chronic low back pain, yoga is as effective as back exercise program and more effective than a self care book. Facet joint injections are ineffective for chronic low

back pain. Surgical consultation is required urgently for any patient with major or evolving neurodeficit. Randomized control trials have shown that for sciatica caused by disc herniation, conservative treatment and surgery achieve similar one year outcomes ; however, pain relief were more quickly with surgery especially that of leg pain and not back pain.

**Low back pain is not a specific disease. Rather, it is a symptom that may occur from a variety of different processes.**





## Graded recommendations for the management of Back pain:

**Grade A recommendations** (based on good-quality patient-oriented evidence): Patient is advised to stay active and continue ordinary activity within the limits permitted by pain, to avoid bed rest, and return to work early, which is associated with less disability. Consider McKenzie exercises may be considered, which are helpful for pain radiating below the knee as in some patients of herniated discs. Paracetamol or nonsteroidal anti-inflammatory drugs (NSAIDs) may be given if medication is necessary. COX-2 inhibitors, muscle relaxants, and opiate analgesics have not been shown to be more effective than NSAIDs for acute low back pain. Radiological investigations (X-Rays or MR scan) if patients have no improvement after 6 weeks, although diagnostic tests or imaging is not usually required.

**Grade B recommendations** (based on inconsistent or limited-quality patient-oriented evidence): Sympathetic reassurance of patients that 90% of episodes resolve within 6 weeks-regardless of treatment. Patient also told that minor flares-ups may occur in the subsequent year. Plain lumbosacral X-rays may be considered, if fracture is still suspected or the patient has multiple sites of pain. Possibility of cauda equina syndrome or severe or progressive neurological deficit if red flags are present. Complete blood count, urinalysis, and sedimentation rate is advised if cancer or infection are possibilities. If still suspicious, consider referral or perform other studies. Remember that a negative plain film x-ray does not rule out disease.

**Grade C recommendations** (based on consensus, usual practice, opinion, disease-oriented evidence, or case series): Recommend ice for painful areas and stretching exercises. Discuss the use of proper body mechanics and safe back exercises for injury prevention. Goal-directed manual physical therapy if there is no improvement in 1 to 2 weeks, modalities such as heat, traction, ultrasound, or transcutaneous electrical nerve stimulation. Do not refer for surgery in the absence of persistent neurological deficit.

**Newer techniques:** Vertebroplasty involves the percutaneous injection of surgical cement into vertebral bodies that have collapsed due to compression fractures has been tried in the treatment of compression fractures of the spine.

The use of specific biologic inhibitors of the inflammatory cytokine tumor necrosis factor-alpha may result in rapid relief of disc-related back pain.

## Individual Patient Education for low-back pain

Low-back pain is a very common problem. It can cause a great deal of pain and lost activity. Health professionals use patient education to help people learn about low-back pain and what to do about it, including:

Staying active and returning to normal activities as soon as possible

Avoiding worry, cope with having a sore back, take little pain killing medications and do some aerobic and cardiorespiratory conditioning exercises with stretching regularly

Follow instructions on activities of daily living (ADLs) to avoid strain and avoid future back injuries.

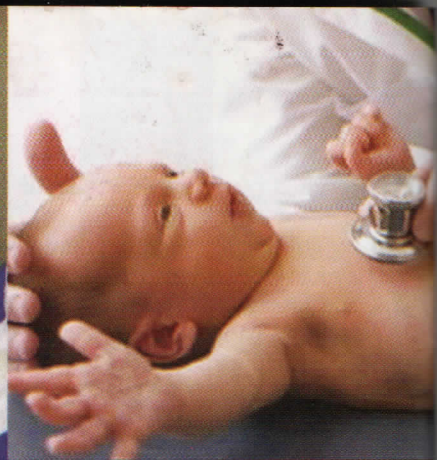
Patient education can mean a discussion with a health professional, a special class, written information such as a booklet to take home, or other formats such as a video are now available. One study found that patient education was more effective than exercises alone for some measures of function. Even some studies found that written information was just as effective as in-person education.

## Conclusion:

Low back pain is not a specific disease. Rather, it is a symptom that may occur from a variety of different processes. In up to 85% of people with low back pain, despite a thorough medical examination, no specific cause of the pain can be identified. Every patient with back pain should be examined carefully to find out any potential dangers that may warrant immediate intervention for specific measures. Physical therapy, generally consisting of stretching, strengthening, and aerobic exercise, is widely used and improves both pain and physical function in those with low back pain persisting beyond 6 weeks. Modalities such as heat, ultrasound, and transcutaneous electrical stimulation are often used; these may provide short-term symptomatic relief and should be used under professional supervision. Every effort should be applied for treating back pain keeping the patient active to save working hours and potentiates patient's functional abilities. ■







# Blood transfusion hazards of neonate



**Dr. Md Majharul Hoque**

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**Dr. Sumsul Arif Mohammad Musa**

**Dr. Md. Sazzad Hossain**

**A**lthough transfusion may be lifesaving, like all medical interventions, it is not without risk. An understanding of the potential risks of transfusion in neonates can help neonatologists make the most appropriate clinical care decisions and counsel the families of their patients. Suspected complications of transfusion, both acute and delayed, should be reported to the transfusion service to allow appropriate investigation. Here is a brief description on hazards of blood transfusion of neonate:

## Acute Immune-mediated Transfusion Reactions

Acute hemolytic transfusion reactions are the second most common cause of transfusion-related fatality in adult patients, but these are rare in neonates. Neonates do not produce red blood cell (RBC) antibodies; any antibodies present are of maternal origin. Prior to the first transfusion, neonates must be screened for passively transferred RBC antibodies, including ABO antibodies if non-O RBCs are to be given. If the initial screen result is negative, no further testing is needed for the first 4 postnatal months. Compared with adult patients, infants are at

increased risk of passive immune hemolysis from infusion of ABO-incompatible plasma. Although small quantities of ABO-incompatible plasma (eg, 5 mL/kg) typically are well tolerated, the quantity of plasma in the supernatant of platelet or RBC transfusions ordered for neonates may exceed this volume, particularly in the surgical settings should have procedures in place to limit the quantities of ABO-incompatible plasma transfused; platelets containing incompatible plasma can be volume reduced, and RBCs may be washed. In the neonate, an acute hemolytic event may be characterized by increased plasma free hemoglobin, hemoglo



binuria, increased potassium concentration, and decreased pH. Results of the direct antiglobulin (Coombs) test may confirm the presence of an antibody on the RBC surface. Treatment is supportive to maintain blood pressure and renal perfusion with intravenous normal saline at 10 to 20 mL/kg and diuresis with furosemide. Prevention is aimed at minimizing human errors and improving patient safety by strict regulations on patient identification before blood is drawn or administered.

Allergic reactions are rare in neonates. They occur when a patient has preformed immunoglobulin IgE antibody against an allergen in the donor plasma. Residual cytokines or chemokines (eg, RANTES) released by stored platelets also may contribute to allergic reactions. Most reactions respond to antihistamines. Severe anaphylactic reactions are rare; some are related to anti-IgA antibodies. These severe reactions are treated with epinephrine, steroids, or both as well as intubation and vasopressors if needed. Patients who have a history of anti-IgA antibodies or anaphylaxis to blood transfusion should receive washed cellular products.

Transfusion-related acute lung injury (TRALI) is the most common cause of transfusion-related fatality but often remains unrecognized. The recommended diagnostic criteria for TRALI are the acute onset of hypoxemia with bilateral infiltrates on chest radiograph within 6 hours of a blood transfusion and no evidence of circulatory overload. Patients who have circulatory overload respond to diuresis, but those who have TRALI do not. The treatment of TRALI is oxygen support and mechanical ventilation, resulting in recovery within 96 hours for most patients.

#### Acute Nonimmune-mediated Transfusion Reactions

Neonates are at increased risk of fluid overload from transfusion because the volume of the blood component issued by the TS may exceed the volume that may be transfused safely into neonates. Care should be taken to ensure that, in the absence of blood loss, volumes infused do not exceed 10 to 15 mL/kg. Metabolic complications are encountered primarily with massive transfu-

sions (>15 to 20 mL/kg) or exchange transfusions. Hypocalcemia can result from large infusions of citrate, which prevents clotting in blood components by binding calcium. The most feared symptom of hypocalcemia is myocardial depression. A prolonged QT interval may be observed on electrocardiography. Cardiac monitoring or regular checks of ionized calcium level are recommended in neonatal patients receiving massive transfusions.

Hyperkalemia can occur with rapid or massive infusion of stored RBCs. Washing to reduce supernatant potassi-



**Suspected complications of transfusion, both acute and delayed, should be reported to the transfusion service to allow appropriate investigation.**

um may be appropriate in massive transfusions in neonates. The quantity of free potassium is not clinically important for small-volume transfusions administered slowly (Hypoglycemia and hyperglycemia both have been reported in association with neonatal transfusions. An inadequate infusion rate of glucose may result if other sources of glucose are discontinued during transfusion.

Hypoglycemic episodes occur more commonly with transfusion of CPDA-1 RBCs rather than additive RBCs, which contain larger quantities of glucose. Large-volume transfusions of additive RBCs may cause transient hyperglycemia followed by rebound hypoglycemia from the insulin induced by the glucose load.

#### Delayed Transfusion Complications

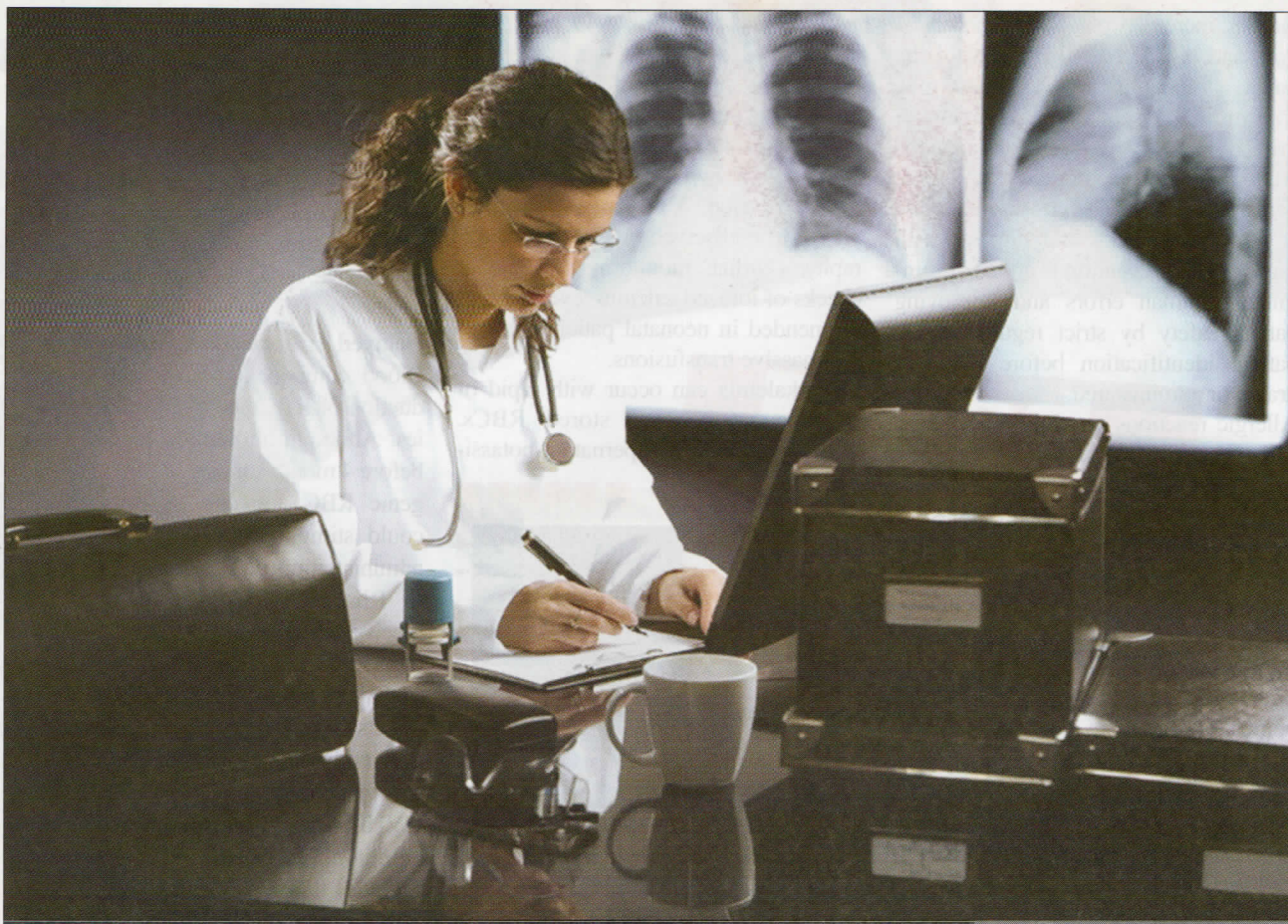
Blood components can stimulate production of RBC and WBC alloantibodies. Although alloimmunization is rare before 4 months of age, highly immunogenic RBC antigens, such as Rh D, could stimulate antibodies. Therefore, administration of Rh immune globulin to Rh-negative female infants who receive Rh D-positive platelets may be appropriate. Transfusion-associated graft versus host disease (TA-GVHD) results from the proliferation of donor-derived lymphocytes in response to histocompatibility antigens. Typically, TA-GVHD occurs in the severely immunocompromised patient. Neonates at risk include those who have congenital immunodeficiency syndromes, those who received intrauterine or exchange transfusions, and low-birthweight infants. No effective therapy is available for TA-GVHD, which is often fatal. TA-GVHD can be prevented by irradiating cellular products with at least 2,500 cGy. Because immunocompetent patients receiving products that are HLA-similar are also at increased risk of TA-GVHD, blood products donated by relatives of the recipient are irradiated.

#### Infectious risks of Transfusion

Some infectious agent which are transmitted by blood transfusion are Human immunodeficiency virus (HIV), Hepatitis B virus (HBV), Hepatitis C (HCV), Herpes virus, Human T-lymphotrophic virus (HTLV), Syphilis, Salmonella, Plasmodium species, Toxoplasma gondii, Leishmania donovani.

Knowledge on blood transfusion and carefulness can save neonates from complications of blood transfusion. So, it is our responsibility to become aware of this problem. ■





# TELEMEDICINE

## Scope in Bangladesh

Telemedicine may be as simple as two health professionals discussing a case over the telephone, or as complex as using satellite technology and video-conferencing equipment to conduct a real-time consultation between medical specialists in two different countries.

Telemedicine is a rapidly developing application of clinical medicine where medical information is transferred through the phone or the Internet and sometimes other networks for the purpose of consulting, and sometimes remote medical procedures or examinations. Telemedicine may be as simple as two health professionals discussing a case over the telephone, or as complex as using satellite technology and video-

conferencing equipment to conduct a real-time consultation between medical specialists in two different countries. Telemedicine generally refers to the use of communications and information technologies for the delivery of clinical care.

### Types of telemedicine

Telemedicine can be broken into three main categories: store-and-forward, remote monitoring and interactive services



## Store-and-forward telemedicine

involves acquiring medical data (like medical images, biosignals etc) and then transmitting this data to a doctor or medical specialist at a convenient time for assessment offline. It does not require the presence of both parties at the same time. Dermatology, radiology, and pathology are common specialties that are conducive to asynchronous telemedicine. A properly structured medical record preferably in electronic form should be a component of this transfer. A key difference between traditional in-person patient meetings and telemedicine encounters is the omission of an actual physical examination and history. The store-and-forward process requires the clinician to rely on a history report and audio/video information in lieu of a physical examination.

and home visits. Many activities such as history review, physical examination, psychiatric evaluations and ophthalmology assessments can be conducted comparably to those done in traditional face-to-face visits. In addition, "clinician-interactive" telemedicine services may be less costly than in-person clinical visits.

## Benefits and Uses of Telemedicine

Telemedicine is most beneficial for populations living in isolated communities and remote regions and is currently being applied in virtually all medical domains. Specialties that use telemedicine often use a "tele-" prefix; for example, telemedicine as applied by radiologists is called Teleradiology. Similarly telemedicine as applied by cardiologists is termed as telecardiology, etc.

Telemedicine is also useful as a commu-

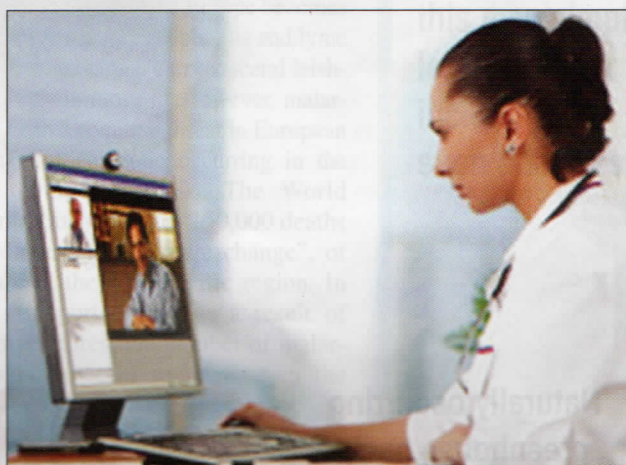
example, a rural community hospital) and a single source of consultants (such as an academic medical center) to complex "hub-and-spoke" networks involving many referring and consulting facilities.

Telemedicine has proven its feasibility in several challenging environments, including peacekeeping missions and the space shuttle.

## Improving health service in Bangladesh:

This emerging field can increase efficiency in health care; thereby decreasing costs, enhancing quality care; empowerment of consumers and patients; provide continuing medical education for health professionals and health education for consumers, bridging the urban- rural health facilities. Bangladesh, as a developing country, has a huge population (above 140 mil-

**Telemedicine is most beneficial for populations living in isolated communities and remote regions and is currently being applied in virtually all medical domains.**



## Remote monitoring

Also known as self-monitoring/testing, enables medical professionals to monitor a patient remotely using various technological devices. This method is primarily used for managing chronic diseases or specific conditions, such as heart disease, diabetes mellitus, or asthma. These services can provide comparable health outcomes to traditional in-person patient encounters, supply greater satisfaction to patients, and may be cost-effective.

## Interactive telemedicine

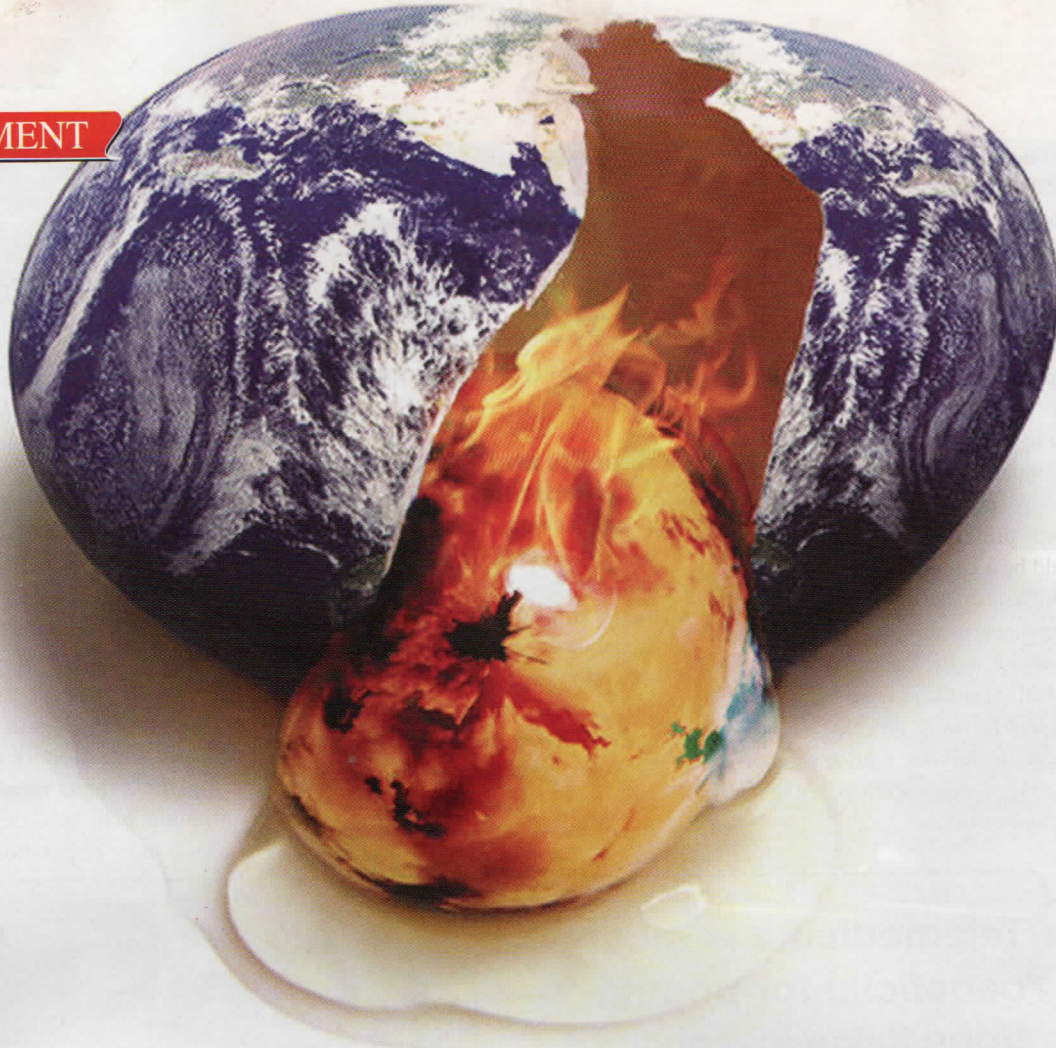
Provide real-time interactions between patient and provider, to include phone conversations, online communication

nication tool between a general practitioner and a specialist available at a remote location.

The clinical applications of telemedicine are even more varied than the technologies, although considerable attention has been focused on the use of interactive video for specialty and subspecialty consultation in rural areas. The generic interactive video telemedicine system typically uses fixed, studio-type video equipment to link a rural facility with an urban tertiary care center. Consultants communicate with patients and, often, with their primary care providers in an interactive situation. The precise configuration of these networks varies, ranging from a single source of referrals (for

lion) with inequitable distribution of resources. 70% of its population lives in rural areas whereas 75% of qualified consultants practice in urban centers. Due to non availability of health facilities in remote areas a large health service seeking people may need to travel for their appropriate health care in a few specialized health centers mostly situated in capital city or big cities. The use of information and communication technology (ICT) in the health sector is very limited in Bangladesh, though its use will make a significant contribution to the improvement of health sector and change the present scenario. ■





Naturally occurring greenhouse gases such as carbon dioxide, water vapor, methane, ozone and nitrous oxide hold heat in the atmosphere creating a greenhouse effect and keep the earth warm enough to sustain life.

# GLOBAL WARMING

Dr. Samiur Rahman

Global warming is all about adverse climate change caused by the trapping of green house gases (like carbon dioxide) in the earth's atmosphere that affects biodiversity and poses a serious health hazard. Counter measures to facilitate living in hotter temperatures like air-conditioning and refrigeration will unfortunately consume more electricity from power plants that burn coal, releasing carbon dioxide. This will further spike global warming and have a seriously damaging influence on human health.

## Causes of Global Warming

Naturally occurring greenhouse gases such as carbon dioxide, water vapor, methane, ozone and nitrous oxide hold heat in the atmosphere creating a greenhouse effect and keep the earth warm enough to sustain life. Enhanced greenhouse effect or the abnormal increase of 'greenhouse gases' due to human activities like burning of solid waste, wood, fossil fuels like oil, natural gas and coal, deforestation and the release of hydrofluorocarbons (HFCs), perfluorocarbons (PFCs)



, and sulfur hexafluoride (SF<sub>6</sub>) from industrial processes cause more than normal heat to be trapped in the atmosphere and cause global warming.

### Consequences of Global Warming

The most direct effect of climate change on humans might be the impacts of hotter temperatures themselves. Rising temperatures have two opposing direct effects on mortality: higher temperatures in winter reduce deaths from cold; higher temperatures in summer increase heat-related deaths. The net local impact of these two direct effects depends on the current climate in a particular area.

Climatic changes triggered by global warming can bring in their wake extreme conditions like abnormal storms, drought and floods and can be of immediate threat to life.

Recent outbreaks of malaria, dengue fever ("breakbone" fever), Hanta virus and similar diseases in the West due to climate change are the consequences of global warming, according to some Harvard Medical School doctors. The incidence of kidney stones is likely to go up and so are many other conditions. The long term serious consequence to human health is likely to threaten our very existence on this planet.

In brief - global warming can soon become a risk factor for heat strokes, cardiovascular and respiratory problems. People with an ailing heart are especially vulnerable because the cardiovascular system has to work harder to cool the body in very hot weather.

High air temperatures increase the ozone concentration at ground level. Natural ozone

layer in the upper atmosphere protects the earth from the sun's harmful ultraviolet radiation; but at ground level ozone becomes a harmful pollutant that damages lung tissue and aggravates asthma and other breathing diseases. Even in healthy individuals exposure to modest levels of ozone can cause nausea, chest pain and pulmonary congestion.

### Increase risk of climate sensitive diseases:

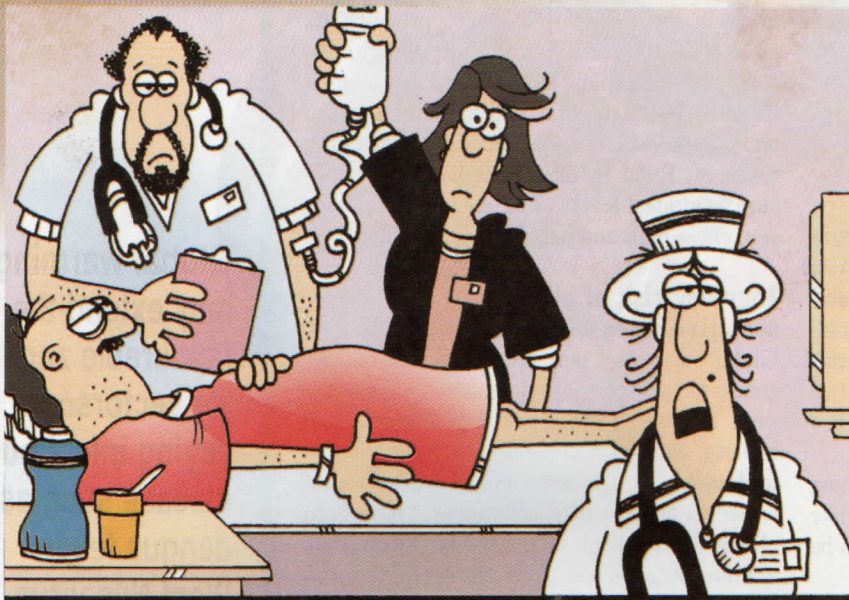
Global warming may extend the favourable zones for vectors conveying infectious disease such as dengue fever, West Nile virus, and malaria. In poorer countries, this may simply lead to higher incidence of such diseases. In richer countries, where such diseases have been eliminated or kept in check by vaccination, draining swamps and using pesticides, the consequences may be felt more in economic than health terms. The World Health Organization (WHO) says global warming could lead to a major increase in insect-borne diseases in Britain and Europe, as northern Europe becomes warmer, ticks-which carry encephalitis and lyme disease-and sandflies-which carry visceral leishmaniasis-are likely to move in. However, malaria has always been a common threat in European past, with the last epidemic occurring in the Netherlands during the 1950s. The World Health Organisation estimates 150,000 deaths annually "as a result of climate change", of which half are in the Asia-Pacific region. In April 2008, it reported that, as a result of increased temperatures, the number of malaria infections is expected to increase in the highland areas of Papua New Guinea. ■

Global warming may extend the favourable zones for vectors conveying infectious disease such as dengue fever, West Nile virus, and malaria. In poorer countries, this may simply lead to higher incidence of such diseases.





## MEDICAL JOKES



■ A doctor said to his car mechanic, "Your debit is several times more per hour than we get paid for medical care."

"Yeah, but you see, doc, you have always the same model, it hasn't changed since Adam; but we have to keep up to date with new models coming every year."

■ "Doctor, are you sure I'm suffering from pneumonia? I've heard once about a doctor treating someone with pneumonia and finally he died of typhus."

"Don't worry, it won't happen to me. If I treat someone with pneumonia he will die of pneumonia."

■ A man needing a heart transplant is told by his doctor that the only heart available is that of a sheep. The man finally agrees and the doctor transplants the sheep heart into the man. A few days after the operation, the man comes in for a checkup. The doctor asks him "How are you feeling?" The man replies "Not BAAAAD!"

■ Dentist: I have to pull the aching tooth, but don't worry it will take just five minutes.

Patient: And how much will it cost?

Dentist: It's \$90.00.

Patient: \$90.00 for just a few minutes work???

Dentist: I can extract it very slowly if you like.

■ Doctor: Did you take those pills I gave you to improve your memory?  
Patient: What pills?

■ A well known rich businessman's wife broke her hip. The businessman got the best bone surgeon in town to do the operation. The operation consisted of lining up the broken hip and putting in a screw to secure it. The operation went fine, and the doctor sent the businessman a fee for his services of \$5000. The businessman was outraged at the cost, and sent the doctor a letter demanding an itemized list of the costs. The doctor sent back a list with two things:

1 screw \$ 1

Knowing how to put it in \$4999

\$5000 total

The businessman never argued.







# AIDS

## BANGLADESH SCENARIO: THE BELL RINGS



**Dr. Md. Zahed Parvez Barbhuiyan**

Assistant Professor  
Skin and Venerology Department,  
Dhaka Medical College & Hospital.

**A**ids is defined as a disease indicative of defect in cell mediated immunity occurring in a person with no known cause for immunodeficiency other than the presence of HIV.

The Acquired Immunodeficiency Syndrome (AIDS) was first recognised in Los Angeles at New York in 1981 with an extraordinary outbreak of Pneumocystis Carinii Pneumonia and Kaposi's sarcoma in previously fit young men. Before the date in the USA both conditions had been very rare. In 1983 Barre-Sinoussi and colleagues in Paris isolated LAV (Lymphadenopathy Associated Virus). Later on, in the USA, Gallo and colleagues isolated HTLV111 (Human T Cell Lymphotropic Virus type 111) from several AIDS patients. These two isolates have subsequently been found to be identical and are now recognized to be the cause of AIDS.

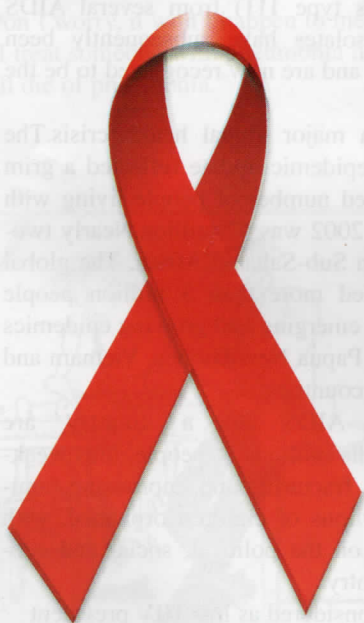
AIDS has created a major global health crisis. The UNAIDS and WHO epidemic update reflected a grim reality – the estimated number of people living with AIDS by the end of 2002 was 42 million. Nearly two-thirds of them live in Sub-Saharan Africa. The global AIDS epidemic killed more than 3 million people in 2003 and there are emerging and growing epidemics in China, Indonesia, Papua New Guinea, Vietnam and several central Asian countries.

The impacts of AIDS on a country are tremendous. AIDS kills millions of people, thus weakening the workforce, fracturing and impoverishing families and leaving millions of children orphaned, with concomitant effects on the political, social and economic fabric of a country.

Bangladesh is still considered as low HIV prevalent



However , the country's vulnerability is very high. National HIV surveillance indicates that the rate of HIV infection among street based sex workers in Bangladesh is high compared with sex workers in other parts of South Asia.



country. However, it is at a critical moment in the course of its AIDS epidemic. It is estimated that there are 13000 HIV -positive people in the country and that HIV prevalence in the adult population is less than 0.01%.

However , the country's vulnerability is very high. National HIV surveillance indicates that the rate of HIV infection among street based sex workers in Bangladesh is high compared with sex workers in other parts of South Asia. HIV among injecting drug users is already 4%. The presence of covert multi-partner sexual activity and denial, the low level of knowledge and low condom use, unsafe professional blood donations, lack of a desirable environment and violation of human rights, all contribute to the spread of HIV in Bangladesh.

So, NOW is the high time for Bangladesh to take appropriate measures to prevent the upcoming disaster. Although, current WHO supports like School Health Education (Teachers), School Health Education (Students), blood safety training programme, voluntary counseling and testing programme, HIV care and support centres are helping us a lot in preparing us to fight against AIDS. It is not enough at all. We need more Govt-Private partnership to fight against the situation. Everybody of us can join the fight against AIDS with

very simple daily personal practices like –

- Avoidance of illegal and riskful sexes
- Safe sex practices by condoms
- Treatment of sexually transmitted diseases
- Screening of blood and blood products for HIV
- Prevention of intravenous abuses
- Uses of disposable syringes
- Screening of HIV during pregnancy and child bearing age
- Ensure safe delivery
- Avoidance of breast feeding in case of HIV infected mothers and in those AIDS patients–HAART- highly active antiretroviral therapy with Government-NGO cooperation with processes of rehabilitations like good emotional, social ,occupational supports.

Every year, 1<sup>st</sup> December is celebrated as WORLD AIDS DAY throughout the world with the world with a view to fight against the disaster of AIDS. Now, we the people, the people of a least developed country should get up ,stand up and united to make appropriate policy with its implementation to combat against AIDS in Bangladesh, otherwise it would be more devastating than SIDOR. ■





# Geohelminth infestation *Among the children*

**Dr. Sunam Kumar Barua**

*Tropical Medicine Specialist*

**S**oil transmitted helminth infection or geohelminth infection is a cosmopolitan disease and more than 100 million people are supposed to be suffering from this infection. Soil transmitted helminthiasis are of several types; the hookworms which have a soil stage developing into larva that penetrate the host and a group of nematodes which survive as eggs that have to be ingested for the circle to continue. Man is the only reservoir. Infection rates are high in children causing malnutrition and ultimately lead to

growth retardation. It is mainly transmitted by oro-faecal route; i.e. by ingestion of infective eggs with food or drink. Foods that are eaten raw such as salads and vegetables readily convey the infection. Other methods of spread are the finger contamination with soil or by ingestion of contaminated soil (pica) as usually happen in case of children playing with soil. Simple diagnosis might be possible by the examination of eggs in stool in saline and iodine preparation to see under normal light microscope.



### Scenario in Bangladesh:

The infection rate was higher in female (29.6%) than in male (18.1%). In another study in Bangladesh, there was significant difference in the distribution of *Ascaris lumbricoides* in human hosts between males and females. In almost every studies the common helminths were *Ascaris lumbricoides* and *Trichuris trichura* in Bangladesh. In a recent study was done in Dhaka city revealed 40.7% positive cases for *Ascaris lumbricoides* or *Trichuris trichura* and only 7% had mixed infection. Soil transmitted infection was closely related with age and 30% students in that study were infected at the age of twelve. In other studies, the infection with nematodes was lower in neonates than in older children and children under ten years of age tended to be more heavily infected with *Ascaris lumbricoides* and *Trichuris trichura*. In that study didn't find any hookworm infection among the children. Among the Muslim students of Bangladesh the infection rate of hookworm was relatively high (53%).

More than two-thirds students (78%) used to take anti-helminthic drugs, while the outcome was not followed in that study. School is the best place to get health education but in the study only 9.3% students got information from their teachers and rest from their parents (72.1%) and from media (18.6%). Still most of the parents are illiterate, they fail to contribute much regarding health education. So we need a community based approach to helminthes control in combination with a school based programme.

Soil transmitted helminth infection is a preventable disease but it requires integrated approach. School going children needs proper health education on personal hygiene through more teachers involvement. Arrangement of parents counseling in schools for encourage community participation is also essential. Regular monitoring and evaluation of risk factors can minimize the soil transmitted infection among children.

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***Recommended drugs for use in public health programmes to control STH infection are the benzimidazole anthelmintics (BZAs), albendazole or mebendazole; older drugs including pyrantel pamoate and levamisole are also occasionally used in some developing countries.***

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### Global control strategies

Recommended drugs for use in public health programmes to control STH infection are the benzimidazole anthelmintics (BZAs), albendazole or mebendazole; older drugs including



pyrantel pamoate and levamisole are also occasionally used in some developing countries. In areas where STH infections co-occur with schistosomiasis, BZAs are co-administered with praziquantel (PQZ), the major drug used for the treatment of schistosomiasis.

Current efforts to control STH infection, as well as schistosomiasis, focus on the school age population. It is estimated that between 25 and 35 percent of school-aged children are infected with one or more of the major species worms. The most intense worm infections and related illnesses occur at school age.

Infection can result in significant consequences for health and development, affecting growth, promoting anaemia and causing some overt clinical disease, much of which is rapidly reversed by treatment. In addition to these impacts on health and physical development, infected school children perform poorly in tests of cognitive function; when treated, immediate educational and cognitive benefits are apparent only for children with heavy worm burdens or with concurrent nutritional deficits. Treatment alone cannot reverse the cumulative effects of lifelong infection nor compensate for years of missed learning, but studies suggest that children are more ready to learn after treatment for worm infections and may be able to catch up if this learning potential is exploited effectively in the classroom. In Kenya treatment reduced absenteeism by one quarter, with the largest gains for the youngest children who suffered the most ill health.



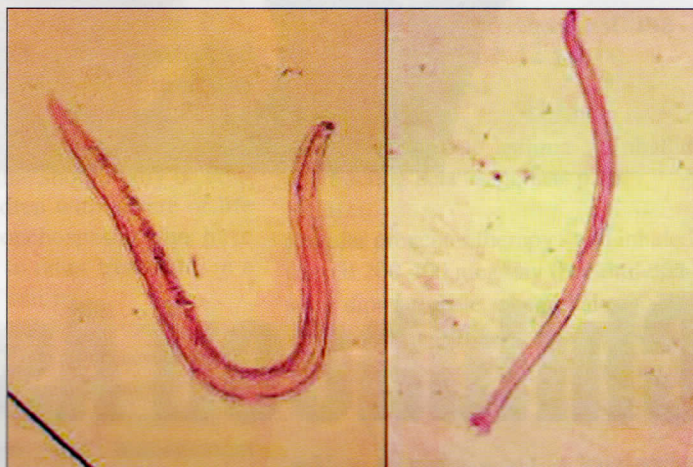
For these reasons, school age children are the natural targets for treatment, and school based treatment delivery programmes offer major cost advantages because of the use of the existing school infrastructure and the fact that school-children are accessible through schools. An important element of the approach is to minimize the need for clinical diagnosis, which is often more expensive than the treatment itself, and to focus on mass delivery of services. Evidence suggests that mass delivery of deworming is preferable on efficacy, economic and equity grounds to approaches that require diagnostic screening. School-based deworming also has major externalities for untreated children and the whole community by reducing disease transmission in the community as a whole.

Recognizing the centrality of school age children to the response to helminth infection, in 2001, the 54<sup>th</sup> World Health Assembly of the WHO passed a resolution to provide regular deworming treatment to 75 percent of school-age children at risk (an estimated target population of 398 million) by 2010. School health and nutrition programs provide the vehicle for delivering regular but infrequent (every 6 months or more) antihelminthic treatment to school children.

table and cost-effective if all of these components are made available, together, in all schools. The four components also provide the appropriate mix of interventions for responding to helminth infection globally: (1) *Policy*: health- and nutrition-related school policies that promote the nutrition and health of staff and children (and promote the role of teachers in delivering antihelminthic treatment); (2) *School environment*: access to safe water and provision of effective sanitation facilities (which helps break the helminth transmission cycle); (3) *Education*: skills-based education, including life skills that address health and hygiene issues and promotion of positive behaviors (including promoting handwashing and other hygienic behaviours that protect against helminth infection); and (4) *Services*: simple, safe, and familiar health and nutrition services that can be delivered cost-effectively in schools (such as deworming).

The common focus has encouraged concerted action by the participating agencies and has increased significantly the number of countries implementing school health reforms. The simplicity of the approach, combined with the enhanced resources available from donor coordina-

***The common focus has encouraged concerted action by the participating agencies and has increased significantly the number of countries implementing school health reforms.***



Operational research by Partnership for Child Development (PCD) has demonstrated how interventions can be implemented and evaluated at the country level, for example enabling mass deworming of school children.

A major step forward in international coordination and cohesion was achieved when a framework to Focus Resources on Effective School Health (FRESH) was launched at the World Education Forum in Dakar in April 2000. Among the early partners in this effort were UNESCO, UNICEF, the World Food Programme (WFP), the WHO, and the World Bank, with the Education Development Centre, Education International, and the Partnership for Child Development. The FRESH framework provides a consensus approach of agreed good practice for the effective implementation of health and nutrition services within school health programmes. The framework proposes four core components that should be considered in designing an effective school health and nutrition programme and suggests that the program will be most equi-

tion, has helped ensure that these programs can go to scale. For example, annual external support from the World Bank for these actions approaches US\$90 million, targeting some 100 million schoolchildren.

The FRESH framework does not prescribe the design of school based deworming programs, and in practice these are highly variable and country specific. In low income countries a public sector model is commonly used, involving the Ministry of Health in supervising the activity, and the Ministry of Education in implementing the intervention through teachers. In middle income countries, including Indonesia and, historically, Japan and South Korea, a private sector model involving nongovernmental organizations delivering treatment that is paid for by the community has proven sustainable and effective.

Whatever the design, identifying which schools and communities require treatment is an essential part of the process, and a key role for GIS. ■





# Childhood Asthma

**A**sthma is the commonest respiratory disorder of children. Chronic inflammation of the bronchial mucosa and hyper-reactive airways result in bronchoconstriction and reversible airway narrowing. It typically presents with wheeze, dry cough, difficulty breathing and/or chest tightness. Managing childhood asthma involves both an appreciation of current treatment practice but also a willingness to educate and support the child and their family in the longer term. Different phenotypes of childhood asthma are increasingly being recognised:

Transient early wheezers where wheezing is commonly associated with viral upper respiratory infections.

This is most likely to be grown out of by about 3 years, particularly in those children without a family or personal history of atopy.

Non-atopic wheezers who again are likely to outgrow symptoms by early school age.

Children who go on to develop a more persistent, atopic asthma associated with raised IgE levels.

Clinical assessment of the severity of an acute asthma attack in those aged over 2 years.

## Acute severe

Unable to complete sentences in one breath  
Unable to feed or talk  
Pulse >120 in those over 5 years or

>130 in 2-5 year olds  
Respiratory rate >30 in the over 5s and >50 in 2-5 year olds

Silent chest  
Cyanosis  
Poor respiratory effort  
Hypotension  
Exhaustion  
Confusion  
Coma

## Clinical assessment of the severity of an acute asthma attack in those aged under 2 years

Acute severe  
Oxygen saturations <92%  
Cyanosed  
Marked respiratory distress



Too breathless to feed  
Life threatening  
Apnoea  
Bradycardia  
Poor respiratory effort

### Management:

With children over 2 years old:  
Give calm reassurance at all times.  
Children with life-threatening asthma or  $SpO_2 < 92\%$  should receive high flow oxygen via face mask or nasal cannula.  
Inhaled beta2-agonists are the first line treatment for acute asthma:  
Delivery via a pMDI and spacer is preferred in mild to moderate asthma as there is less tachycardia and hypoxia compared to delivery via a nebuliser.  
Children under 3 years normally require a face mask attached to the spacer.  
2-4 puffs of beta2-agonists repeated every 20-30 minutes according to clinical response may be sufficient for a mild attack but severe attacks may require up to 10 puffs: drug dosing should be individualised according to severity of attack and response.  
Those children not improving after receiving up to 10 puffs of beta2-agonists in primary care should be referred to secondary care. Continue to give further doses of bronchodilator whilst awaiting transfer.  
Blue light those with poorly responding severe or life-threatening asthma, who should receive oxygen and nebulised beta2-agonists (2.5-5 mg salbutamol or 5-10 mg terbutaline) in transit.  
Nebulised beta2-agonists should be repeated every 20-30 minutes- frequent intermittent doses are as efficacious as equivalent continuous nebulised doses.  
Steroid therapy- early use reduces hospital admissions and can prevent symptom relapse.  
Oral steroids are of similar efficacy to intravenous preparations, which should be reserved for the acutely unwell child who cannot swallow.

### Oral prednisolone in an acute asthma attack:

#### Start early in the attack.

Use 20 mg prednisolone for children aged 2-5 years and 30-40 mg for those

over 5 years.

For children on maintenance steroid treatment, give 2 mg/kg prednisolone to a maximum of 60 mg.  
Repeat the dose in children who vomit. 3 days' treatment is usually sufficient, but tailor according to the length necessary for recovery.

### Additional emergency treatment:

IV salbutamol - early addition of a bolus dose (15 mcg/kg) can be a useful adjunct to nebulised treatment in some severe cases. Continuous infusion may be required where there is severe refractory asthma or concerns about reliability of inhalation. Doses exceeding 1-2 mcg/kg/min require PICU monitoring.

Nebulised ipratropium bromide- where symptoms are refractory to initial beta2-agonist treatment, the addition of ipratropium bromide (250 mcg/dose, mixed with the nebulised beta2-agonist solution) is of benefit in the first 2 hours of a severe asthma attack.

IV aminophylline should only be considered in children with severe or life threatening bronchospasm who have not responded to other treatment, in a HDU or PICU setting.

IV magnesium sulphate - inconclusive evidence of benefit in severe asthma. Intermittent wheezing attacks in the under 2s are usually in response to viral infection and management remains controversial:

Beta2-agonist bronchodilators may offer marginal benefits to those under two with wheeze and should be considered if the child is symptomatically distressed. If they are not effective, consider the use of other treatment options. For mild to moderate attacks, use a pMDI plus spacer and face mask. Do not use oral beta2-agonists, which have little evidence for efficacy in this context.

Oral steroid treatment- consider 10 mg soluble prednisolone for up to three days in the management of moderate to severe asthma in infancy in the hospital setting.

Ipratropium bromide can be combined with inhaled beta2-agonist where there are more severe symptoms.

### Management of chronic asthma in children under 5:

#### Step 1:

Mild intermittent asthma - inhaled short-acting beta 2-agonists p.r.n..

#### Step 2:

Regular preventer therapy - add inhaled steroid 200-400 mcg/day (beclomethasone dipropionate or equivalent) or leukotriene antagonist if inhaled steroid cannot be used. Start at the dose of inhaled steroid appropriate to the severity of the disease.

#### Step 3:

Add-on therapy - for the over 2s, consider the addition of a leukotriene antagonist or inhaled steroid 200-400 mcg/day (dependant on what drug they received already as step 2).

#### Step 4:

Persistent poor control- refer to respiratory paediatrician.

### Management of chronic asthma in children aged 5-12 years:

#### Step 1:

Mild intermittent asthma - inhaled short-acting beta 2-agonists p.r.n..

#### Step 2:

Regular preventer therapy - add inhaled steroid 200-400 mcg/day (beclomethasone dipropionate or equivalent). 200 mcg is an appropriate starting dose for most patients, but judge according to severity of disease.

#### Step 3:

Add-on therapies - add in long-acting inhaled beta2-agonist (LABA) but if response poor, stop. If asthma still not controlled, increase dose of inhaled corticosteroid to 400 mcg/day (beclomethasone dipropionate or equivalent) and then add either a leukotriene receptor antagonist or slow release theophylline.

#### Step 4:

Persistent poor control- increase inhaled steroid to 800mcg/day (beclomethasone dipropionate or equivalent).

#### Step 5:

Continuous or frequent use of oral steroids - use in the lowest dose to provide control whilst maintaining high-dose inhaled steroids and refer to respiratory



# New Hope with Biologics

**B**iologics include a wide range of medicinal products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins created by biological processes (as opposed to chemically).

Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources - human, animal, or microorganism - and may be produced by biotechnology methods and other technologies. Gene-based and cellular

biologics, for example, often are at the forefront of biomedical research, and may be used to treat a variety of medical conditions for which no other treatments are available.

■ In some jurisdictions, biologics are regulated in a different manner than are drugs and medical devices. As indicated above, the term "biologics" can be used to refer to a wide range of biological products in medicine. However, in most cases, the term "biologics" is used more restrictively for a class of medications (either approved or in development) that are produced by means of biological processes involving recombinant DNA technology. These medications are

## Examples

**A few examples of biologics made with recombinant DNA technology include:**

USAN/INN	Trade Name	Indication	Technology	Mechanism of Action
Abatacept	Orencia	Rheumatoid arthritis	Immunoglobulin CTLA-4 fusion protein	T-cell deactivation
Adalimumab	Humira	rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease	Monoclonal antibody	TNF antagonist
Alefacept	Amevive	Chronic plaque psoriasis	Immunoglobulin G1 fusion protein	Incompletely characterized
Erythropoietin	Epogen	Anemia arising from cancer chemotherapy, chronic renal failure, etc.	Recombinant protein	Stimulation of red blood cell production
Etanercept	Enbrel	Rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis	Recombinant human TNF-receptor fusion protein	TNF antagonist
Infliximab	Remicade	Rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease	monoclonal antibody	TNF antagonist
Trastuzumab	Herceptin	Breast cancer	humanized monoclonal antibody	HER2/neu (erbB2) antagonist



usually one of three types:

■ Substances that are (nearly) identical to the body's own key signalling proteins. Examples are the blood-production stimulating protein erythropoietin, or the growth-stimulating hormone named (simply) "growth hormone".

■ Monoclonal antibodies are similar to the antibodies that the human immune system uses to fight off bacteria and viruses, but they are "custom-designed" (using hybridoma technology or other methods) and can therefore be made specifically to counteract or block any given substance in the body, or to target any specific cell type; examples of such monoclonal antibodies for use in various diseases are given in the table below.

■ Receptor constructs (fusion proteins), usually based on a naturally-occurring receptor linked to the immunoglobulin frame. In this case, the receptor provides the construct with detailed specificity, whereas the immunoglobulin-structure imparts stability and other useful features in terms of pharmacology. Some examples are listed in the table below.

Biologics as a class of medications in this narrower sense have had a profound impact on many medical fields, primarily rheumatology and oncology, but also cardiology, dermatology, gastroenterology, neurology, and others. In most of these disciplines, biologics have added major therapeutic options for the treatment of many diseases, including some for which no effective therapies were available, and others where previously existing therapies were clearly inadequate. However, the advent of biologic therapeutics has also raised complex regulatory issues and significant pharmacoeconomic concerns, because the cost for biologic therapies has been dramatically higher than for conventional (pharmacological) medications. This factor has been particularly relevant since many biological medications are used for the treatment of chronic diseases, such as rheumatoid arthritis or inflammatory bowel disease, or for the treatment of otherwise untreatable cancer during the remainder of life. The cost of treatment with a typical monoclonal antibody therapy for relatively common indications is generally in the range of € 7,000-14,000 per patient per year.

Unlike the more common small-molecule drugs, biologics generally exhibit high molecular complexity, and may be quite sensitive to manufacturing process changes. The follow-on manufacturer does not have access to the originator's molecu-



lar clone and original cell bank, nor to the exact fermentation and purification process. Finally, nearly undetectable differences in impurities and/or breakdown products are known to have serious health implications. This has created a concern that generic versions of biologics might perform differently than the original branded version of the drug. So, unlike most drugs, generic versions of biologics are not authorized in the US or the European Union through the simplified procedures

allowed for small molecule generics. Notable exceptions include several of the earliest biopharmaceuticals made via recombinant DNA technology, including biosynthetic 'human' insulin and human growth hormone, which are grandfathered under the U.S. Federal Food, Drug & Cosmetic Act which addresses mainly small-molecule chemical drugs. By comparison, vaccines and most other biotech drugs are governed under the Public Health Service Act of 1944 (as amended), which would need to be further amended by U.S. Congress and signed into law by the President to allow for generics.

**Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues.**

In the EU a specially-adapted approval procedure has been authorized for certain protein drugs, termed "similar biological medicinal products". This procedure is based on a thorough demonstration of "comparability" of the "similar" product to an existing approved product. In the US the FDA has taken the position that new legislation will be required to address these concerns. Additional Congressional hearings have been held, but no legislation had been approved as of June 2008. Due to a lack of FDA manufacturing guidelines for generic versions of synthetic insulin and human growth hormone, generics manufacturers are caught in a bind.





# What is Sleep Apnea?

## Defining the Disorder

**Dr. Aminul Hoque**

During apnea events, there is a drop in blood oxygen levels, an increase in heart rate, a burst of stress hormones, and disrupted sleep when the body awakens slightly so that breathing will resume, sometimes with a gasp.

**S**leep apnea is a chronic disorder in which one repeatedly stops breathing during the night. Apnea literally means "no breath." These events last 10 seconds or longer, and may occur hundreds of times during a night. Someone with sleep apnea may be aware of snorting, gasping, or waking up short of breath, but may not realize it is happening at all.

### What Happens During Apnea?

During apnea events, there is a drop in blood oxygen levels, an increase in heart rate, a burst of stress hormones, and disrupted sleep when the body awakens slightly so that breathing will resume, sometimes with a gasp.

### What Are the Symptoms?

There are many common symptoms of sleep apnea, some of which are unexpected. These may include:

- Loud, chronic snoring
- Choking or gasping during sleep
- Excessive daytime sleepiness
- Morning headaches
- Memory or learning problems
- Feeling irritable
- Poor concentration
- Changes in mood, including depression

**The important Consequences:** This disorder can have major health con-

sequences and can be life threatening. Excessive daytime sleepiness may cause you to fall asleep while driving. Moreover, those affected may have increased risk of:

- Stroke or transient ischemic attacks
- Coronary heart disease
- Heart failure
- Irregular heartbeat
- Heart attack
- High blood pressure
- Heartburn and reflux
- Diabetes
- Erectile dysfunction
- Concentration and memory problems
- Depression
- Sudden death

Treatments for obstructive sleep apnea may include:

- Continuous positive airway pressure (CPAP): If someone has moderate to severe sleep apnea, he/she may benefit from a machine that delivers air pressure through a mask placed over your nose while in sleep. With CPAP the air pressure is somewhat greater than that of the surrounding air, and is just enough to keep your upper airway passages open, preventing apnea and snoring.

Although CPAP is a preferred method of treating sleep apnea, some people find it cumbersome or



uncomfortable. With some practice, most people learn to adjust the tension of the straps to obtain a comfortable and secure fit.

Don't just stop using the CPAP machine if problems arise. Consult with doctor to see what modifications can be made to make more comfortable. Additionally, contact doctor if still snoring despite treatment or begin snoring again. If weight changes, the pressure settings may need to be adjusted.

■ **Adjustable airway pressure devices:** If CPAP continues to be a problem one can use a different type of airway pressure device that automatically adjusts the pressure while sleeping. For example, units that supply bilevel positive airway pressure (BiPAP) are available. These provide more pressure when a person inhale and less when exhale.

■ **Oral appliances:** Another option is wearing an oral appliance designed to keep throat open. CPAP is more effective than oral appliances but oral appliances may be easier to use. Some are designed to open throat by bringing jaw forward, which can sometimes relieve snoring and mild obstructive sleep apnea.

■ **Surgery:** The goal of surgery for sleep apnea is to remove excess tissue from nose or throat that may be vibrating and causing to snore, or that may be blocking upper air passages and causing sleep apnea. Surgical options may include:

■ **Uvulopalatopharyngoplasty (UPPP):** During this procedure, doctor removes tissue from the rear of mouth and top of throat. Tonsils and adenoids usually are removed as well. This type of surgery may be successful in stopping throat structures from vibrating and causing snoring. However, it may be less successful in treating sleep apnea because tissue farther down throat may still block air passage. UPPP usually is performed in a hospital and requires a general anesthetic.

■ **Maxillomandibular advancement:**

In this procedure, the upper and lower part of jaw is moved forward from the



**If CPAP continues to be a problem one can use a different type of airway pressure device that automatically adjusts the pressure while sleeping. For example, units that supply bilevel positive airway pressure (BiPAP) are available.**

remainder of face bones. This enlarges the space behind the tongue and soft palate, making obstruction less likely. This procedure may require the cooperation of an oral surgeon and an orthodontist, and at times may be

combined with another procedure to improve the likelihood of success.

■ **Tracheostomy:** One may need this form of surgery if other treatments have failed and has severe, life-threatening sleep apnea. In this procedure, surgeon makes an opening in neck and inserts a metal or plastic tube through which breathing occur.

■ **Removing tissues in the back of throat with a laser (laser-assisted uvulopalatoplasty) or with radiofrequency energy (radiofrequency ablation) are procedures that doctors sometimes use to treat snoring. Although sometimes these procedures are combined with others, they aren't usually recommended as sole treatments for obstructive sleep apnea.**

Other types of surgery may help reduce snoring and contribute to the treatment of sleep apnea by clearing or enlarging air passages:

■ **Nasal surgery** to remove polyps or straighten a crooked partition between nostrils (deviated nasal septum)

■ **Surgery to remove enlarged tonsils or adenoids**

■ **Treatment for associated medical problems.** Possible causes of central sleep apnea include heart or neuromuscular disorders, and treating those conditions may help. For example, optimizing therapy for heart failure may eliminate central sleep apnea. ■





# Oriental Medicine

**Dr. Alak Barua**

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**O**riental Medicine Practitioner prescribes herbal medicine and provides acupuncture treatment. Herbal medicines are usually dispensed in tablet, capsule, liquid or in the decoction form and composed of one or more medicinal herbs. Most of the medicinal herbal formula contains five to fifteen medicinal herbs.

Though the side effects are significantly less than the pharmaceutical drugs, herbal medicine should be treated with the same care as any other type of medicine.

Acupuncture is effective for the pain and neuromuscular ailments. Several thousands years old acupuncture treatment still existing in this modern world, it has been significantly proven that acupuncture treatment increases endorphine, cortisol level, blood circulation, WBC counts and helps for cell, tissue healing.

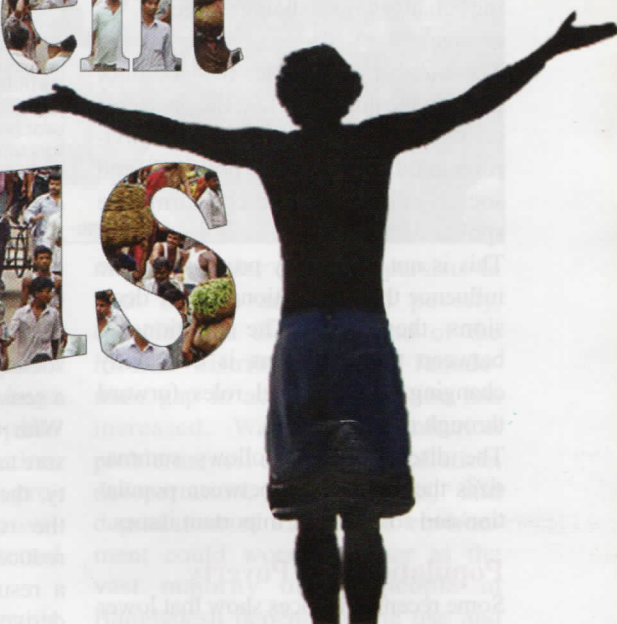
In the USA Oriental Medicine is one of the rapidly growing field. A candidate must require State license to practice Acupuncture & Oriental Medicine. There are twenty two accredited Oriental Medicine colleges in the USA. After successful completion of three years MS degree candidate requires to take National Certification Commission for Acupuncture & Oriental Medicine exam in order to qualify for the state licence.

The state license require certain continuing education hours each year for yearly renewal.

Acupuncture & oriental Medicine have used for countries as a major health care system in more than half of the world. Both the National Institute of Health, USA and the World Health Organization have recognized its effectiveness in treating a variety of clinical conditions. Acupuncture is one of the oldest, most commonly used systems of healing in the world. In 1993, the USA Food & Drug Administration estimated that Americans made up to 12 millions visits per year to Acupuncture & Oriental Medicine practitioners and spent Billions on Acupuncture treatments. ■



# Population Development Nexus



## Dr. Sheikh Md. Nazmul Hassan

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Any development effort should take into account the parameters of population for the sustained economic growth and welfare of the society. Because population and development are composite con-

cepts by nature and population issues do not exist in isolation. Since people in a society are both producers as well as consumers, any development process should consider the demographics of population,

*The number of people, the speed of growth, the quality of life, the pressures on them, etc. are influenced by environmental, economic, political and social conditions which form the spokes of the wheel.*





i.e., its structure, composition, distribution, behavior pattern, attitude, values, norms, beliefs, practices and the whole life-style pattern. As a way of demonstrating these links between population and development a population wheel (Nabi's wheel) has been adopted below.

### The Population Wheel

People lie at the hub of the wheel, causing changes and being affected by change.

The number of people, the speed of growth, the quality of life, the pressures on them, etc. are influenced by environmental, economic, political and social conditions which form the spokes of the wheel.

This is not a one way process. People influence these conditions by the decisions they take. The relationship between the conditions is constantly changing as the wheel rolls forward through time.

The discussion that follows summarizes the relationship between population and some of the important issues.

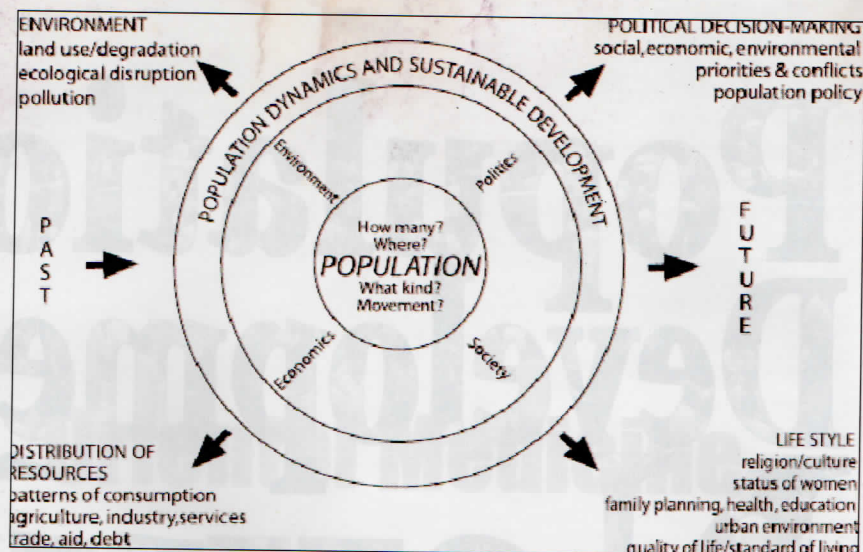
### Population and Poverty

Some recent evidences show that lower health status of the poor is an important determinant of poverty, and some argue that increasing population pressure is a major obstacle to improvement of health status of the people. In addition to accelerating poverty at present, the increasing population pressure contributes to further worsening of poverty in future in several ways.

*First*, due to current poverty the households are not able to invest for the productive activities which could increase income in future.

*Second*, due to current poverty, the households cannot spend for health and education of children. Thus, the potential of raising household productivity in future is also lost

*Third*, factors such as large number of births, early marriage, and early first birth adversely affect the reproductive health status of women and health status of children, the former contributing to current poverty and the latter to future poverty. Thus, poverty persists



over time and generations.

Population pressure contributes to persistence of poverty in another way too. Community resources comprising community land, water and forests in a society greatly benefit the poor and, in a sense, provide huge subsidy to them. With the increasing population pressure and the resultant increase in poverty, the households unscrupulously use the resources for survival and this reduces the amount of the resources. As a result, the poor households cannot derive any benefit from such resources in future. This will further worsen poverty in future. A vicious circle, thus, emerges.

### Population and Education

The increasing population pressure reduces the effects of education interventions in several ways:

*First*, as the size of population increases, the number of children eligible for obtaining education increases, and the amount of public resources required to cater to the rising demand for education increases enormously. It becomes increasingly difficult for the government to allocate the necessary fund.

*Second*, the increasing population pressure level reduces the capacity of the households to spend for education of their children.

*Third*, with the increasing number of household members, the possibility of the poor households to send their children to school becomes limited, despite

all assistance and support of the government.

### Population and Environment

Sustainable development connects the process by which human beings satisfy their present needs and improve their present quality of life, while at the same time safeguarding the ability of future generations to meet their own needs. Sustainable development is a function of: population size, per capita consumption, environmental damage caused by the technology used to produce what is consumed. The interaction between growth of population, production and unsustainable consumption patterns affects use of land, water, air, energy and other resources which are important elements of environment. A simple interaction between population and environment is that high growth of population may lead to over-consumption of natural resources and degradation of ecosystem and environmental potentials but this relationship could be further aggravated by a number of other social and environmental factors.

### Ageing in Bangladesh

Ageing in Bangladesh has emerged as a recent concern. Because of continuing rapid decline in fertility and improvement in life expectancy, the number and proportion of population aged 60 and over is increasing. Various projections show that both the population above 65 years and that above 60 years is going to reach staggering



proportions by the year 2051. This indicates that Bangladesh is entering a new phase of rapid growth of elderly population with its associated issues. The projections show that even after reaching replacement level fertility, the population will continue to get older compared to the younger generation. In other words, the declining fertility contributes lower share for the younger age groups due to fewer number of births, but the share of older age groups increases until the population stabilizes. This will continue for decades after reaching replacement level fertility. In terms of numbers the elderly population aged 65 and above is expected to double by year 2021 and reach nearly 30 million by the end of 2051. The demographic transformation is taking place in the context of other societal changes; the joint/extended large family, once seen as the source for providing the old age security and kinship network, is being replaced by smaller, nuclear family with no institutional safeguards to meet the needs of the elderly. There are no pension schemes/safety nets of any kind for these aged populations. Rural to urban migration further exacerbates the problem when the younger people move to the cities leaving their parents behind. Older women's conditions become extremely vulnerable in times of economic distress, structural reforms, environmental dangers and adjustment programs. Their lot worsens when they become widow or live without any support. In the face of weakening obligations of the children to parents and uncertain reliability of public health services on which the elders have to rely, new challenges emerge.

### Future Implications

The changes that have taken place in the population characteristics of Bangladesh have both bright sides as well as dark sides.

The bright sides are: reduction in growth rate, fertility levels, mortality levels, proportion of young population, rise in expectation of life at birth,



literacy rate, contraception prevalence rate, age at marriage and level of urbanization.

The dark sides are: a large population of more than 160 millions, a huge built-in momentum in the population, a growing old age population, very low man - land ratio, high proportion of rural exodus and relatively higher rates of infant and maternal mortality.

Before specifying the areas directly hit by the large population of the country, it is important to examine the projected future scenario of some selected population parameters. The projected population size will be about 170 million by the year 2020. The consequences of such a large population size, considering our limited resources and small land area, are very serious. The most affected area would be the social sectors. The rise in the expectation of life at birth implies a more elderly population and higher dependency ratio. The proportion of urban population is expected to be about 40 percent of the total population by the year 2020. This could place a tremendous pressure in urban lives which could become dangerously insecure, unhealthy, and environmentally unsustainable. Although the poverty situation has improved slightly in recent years, the head-count ratio is still very high. A sig-

nificant gender disparity persists in both income and human poverty, especially at the lower end of the income distribution. The female-male gap in acute malnutrition has increased. Water and sanitation problems, soil erosion, air pollution, deforestation, wetland loss, and degradation of the coastal environment could worsen further as the vast majority of the people in Bangladesh depend on the use and extraction of natural resources. The increasing number of women in the reproductive age group by the year 2020 implies a high impact of population momentum, i.e., more child births. This increase will pose the most formidable challenge to the targets and goals of the policy planners. Although limiting human fertility received high priority in national policy packages, reduction of malnutrition, action programs on meaningful education, and the empowerment of women has not received sufficient attention. According to FAO's estimate, only with high input of all kinds will Bangladesh be able to support about 178 million people. This figure will be attained around the year 2020, which implies the exhaustion of the carrying capacity of Bangladesh, if the population of Bangladesh is not planned and managed properly. ■



# Oral Prolonged Release Dosage Forms

**Md. Harun-or-Rashid**

*Pharmacist*

**B**efore formulating a drug substance into a dosage form, the desired product type must be determined into far as possible to establish the framework for product development.

Then various initial formulations of the product are development and examined for desired features (eg., drug release profile, bioavailability, clinical effectiveness) and for pilot plant studies and production scale-up. In recent years, with progress and innovation in the field of pharmaceutical technology, there has been an increasing effort to develop prolonged release dosage forms for many drugs. Prolonged release dosage forms have many advantages in safety and efficacy over immediate release drug products in that the frequency of dosing can be reduced, drug efficacy can be prolonged and the incidence and/or intensity of adverse effects can be decreased.

However, some prolonged release dosage forms have less clear rationale or are developed for active ingredients which are not appropriate for prolonged release dosage forms. In other cases, prolonged release dosage forms are designed without full consideration of the basic properties of the drugs. Moreover, standards for dissolution tests, which are important for evaluating prolonged release dosage forms, have not appropriately been established. As a result, it is often difficult to evaluate whether a prolonged release dosage form is acceptable or

not. Incomplete or undesirable prolonged release drugs may merely cause therapeutic confusion and, in addition may interfere with development and spread of good quality drugs. As part of the effort to ensure and promote drug reliability, it appears necessary to establish appropriate guidelines for the design and evaluation of prolonged release dosage forms.

and safety.

i) Elimination half life, ii) The first pass effect, iii) The absorption site, iv) Adverse reactions.

Therefore they should be sufficiently studied to fully characterize the drug.

It is desirable to clarify following factors: i) Correlation of clinical response with blood-drug concentrations or tissue concentrations at the



This article presents some general considerations regarding oral prolonged release dosage forms, mainly for drugs with new pharmaceutical forms. However, many of this general consideration are also applicable to other controlled release dosage forms.

## 1. Factors to be studied in dosage form design

The properties of the active ingredient The following characteristics of drugs are critical in ensuring their efficacy

site of action. ii) Induction or inhibition of drug metabolizing enzymes by the prolonged blood concentration, casual change of pharmacological response and the possibility of tolerance or addiction for the drug. iii) Interactions with other drugs due to protein binding.

## Pharmacodynamics

The major purpose for developing prolonged release formulations of the drug is generally to maintain the blood



concentration of the active ingredient at therapeutically effective levels. Therefore, it is desirable that average minimum effective concentration and optimal therapeutic concentrations be clarified for each drug by evaluating blood concentrations of the active ingredient or therapeutic moiety(s) including active metabolite(s) in relation to drug efficacy. It is also desirable to investigate toxic blood drug concentrations.

### **Biopharmaceutics**

Information on the biopharmaceutical properties of the active ingredient for a prolonged release dosage form is essential in rational formulation design. Particular attention should be given to the following six factors: 1) specificity in the site of absorption, 2) absorption rate, 3) the elimination half life of the drug, 4) first pass effects, 5) whether elimination is non-linear due to drug metabolism saturation or other factors, and 6) inactivation or metabolism of the drug in the body, including the gastrointestinal tract. In addition, it is useful to study effects of age, sex and smoking on the pharmacokinetics of the drug.

### **Chemistry and physicochemistry**

Chemical and physicochemical properties of drugs, especially, pH- solubility characteristics should be clarified.

### **Factors due to physiological condition**

The release of an active ingredient from a prolonged release dosage form, and its absorption are inevitably affected by physiological factors in the gastrointestinal tract. Prolonged release dosage forms are more susceptible to these factors than immediate release dosage forms. Therefore, the possible effects of the physiological factors should be fully considered for the dosage form design. If the drug is intended for use in a specific subpopulation, attentions should be paid to the specific physiology of the subpopulation.

### **2. Factors to be studied in the final dosage forms**

*Evaluation of the final dosage form*  
*Release characteristics*

**A. Evaluation of the release characteristics** The release of the active ingredient from the preparation in the gastrointestinal tract is affected by many physiological factors including the mechanical force exerted by the digestive tract in relation to its movement, and the volume, composition, pH, surface tension, and viscosity of the gastrointestinal fluid and gastrointestinal motility. Therefore, the in vitro release behaviors should be investigated under as many conditions as possible to understand possible effects of gastrointestinal variables on in vivo release. If it is anticipated that the release rate is influenced by the wettability, ionic strength and composition of the test medium, their effects should also be investigated.

**B. Specifications for dissolution testing** The specifications for drug releases should be established for quality control of prolonged release dosage forms. Basically, it is desirable to employ the release tests which can predict the blood level profile of the drug as precisely as possible.

### **C. Stability test**

Specimens for long term stability tests should be subject to dissolution testing and comply with the standards of the specifications.

### **Pharmacokinetics**

As far as possible, the pharmacokinetics of the prolonged release dosage form should be compared with the immediate release product in healthy volunteers. Pharmacokinetic evaluation should be made, based on blood concentration data, except for the case that the concentrations of the active ingredient can be determined at the site of action whose effective concentrations are known. Data on drug concentration in the urine, saliva, or other body fluids will be accepted only when the concentrations of the active ingredient in the blood or at the site of action are correlated with that in these fluids. Unless the drug shows linear pharmacokinetics within the clinical dose range, the investigation should be made at two dose levels, high and low.

### **Clinical efficacy**

The clinical usefulness of the prolonged release dosage form should be shown comparing it with its already approved immediate release product or its already approved prolonged release product (if a better prolonged release dosage form is claimed). If the relation between the pharmacological effectiveness and blood concentration is unclear, the usefulness should be proved by the well-controlled clinical studies where the effective and toxic concentrations should be investigated by monitoring blood concentrations of the drug.

### **Establishment of dosing regimen**

The appropriate dosing regimen should be established during Phase I and II clinical studies in which it is recommended that the blood concentrations are monitored during Phase II clinical trials to establish a better dosing regimen.

Overdose or dose, Disease state, Combination therapy are also importance in establishing dosing regimen

### **Dosing guidelines**

Recommendations for dosing conditions, frequency of dosing per day, and dose levels (initial dose, maintenance dose, dose adjustment for insufficient response, and the maximum tolerable dose) should be established, based on the available pharmacokinetic data during Phase II clinical studies. The action to be taken if toxic signs or adverse effects develop should also be specified.

The following factors should be consideration: A) drugs, blood concentrations of which may change strikingly by minimal changes in dose (drugs with non-linear absorption or elimination), B) drugs, the clearance and blood concentrations of which are susceptible to physiological conditions, age and so forth, C) drugs with a narrow therapeutic window, and D) drugs which might cause tolerance and/or severe adverse effects. ■





# Arsenic Poisoning

## SOURCE & SOLUTION

**A**rsenic contamination of groundwater is a natural occurring high concentration of arsenic in deeper levels of groundwater, which became a high-profile problem in recent years due to the use of deep tubewells for water supply in the Ganges Delta, causing serious arsenic poisoning to large numbers of people. Arsenic is a carcinogen which causes many cancers including skin, lung, and bladder as well as cardiovascular disease.

### Present situation in Bangladesh:

The story of the arsenic contamination of the groundwater in Bangladesh is a tragic one. Many people have died from this contamination. In the Ganges Delta, the affected wells are typically more than 20 m and less than

100 m deep. Groundwater closer to the surface typically has spent a shorter time in the ground, therefore likely absorbing a lower concentration of arsenic; water deeper than 100 m is exposed to much older sediments which have already been depleted of arsenic.



### Source

Arsenic is widely distributed throughout the earth's crust.

Arsenic is introduced into water through the dissolution of minerals and ores, and concentrations in groundwater in some areas are elevated as a result of erosion from local rocks.

Industrial effluents also contribute arsenic to water in some areas.

Arsenic is also used commercially e.g. in alloying agents and wood preservatives.

Combustion of fossil fuels is a source of arsenic in the environment through disperse atmospheric deposition.

Inorganic arsenic can occur in the environment in several forms but in natural waters, and thus in drinking-water, it is mostly found as trivalent



arsenite or pentavalent arsenate. Organic arsenic species, abundant in seafood, are very much less harmful to health, and are readily eliminated by the body.

Drinking- water poses the greatest threat to public health from arsenic. Exposure at work and mining and industrial emissions may also be significant locally.

### Water purification solutions Small-scale water treatment

A simpler and less expensive form of arsenic removal is known as the Sono arsenic filter, using 3 pitchers containing cast iron turnings and sand in the first pitcher and wood activated carbon and sand in the second. Plastic buckets can also be used as filter containers. It is claimed that thousands of these systems are in use can last for years while avoiding the toxic waste disposal problem inherent to conventional arsenic removal plants.



### Large-scale water treatment

In some places, such as the United States, all the water supplied to residences by water utilities must meet primary (health-based) drinking water standards. This may necessitate large-scale treatment systems to remove arsenic from the water supply. The effectiveness of any method depends on the chemical makeup of a particular water supply. The aqueous chemistry of arsenic is complex, and may affect the removal rate that can be achieved by a particular process.

### Coagulation/filtration

Removes arsenic by coprecipitation and adsorption using iron coagulants. Coagulation/filtration using alum is already used by some utilities to remove suspended solids and may be adjusted to remove arsenic.

Iron oxide adsorption filters the water through a granular medium containing ferric oxide. Ferric oxide has a high affinity for adsorbing dissolved metals such as arsenic. The iron oxide medium eventually becomes saturated, and must be replaced.

Activated alumina is another filter medium known to effectively remove dissolved arsenic. It has also been used to remove undesirably high concentrations of fluoride.

Ion Exchange has long been used as a

water-softening process, although usually on a single-home basis. It can also be effective in removing arsenic with a net ionic charge.

Both reverse osmosis and electrodialysis (also called electrodialysis reversal) can remove arsenic with a net ionic charge. Some utilities presently use one of these methods to reduce total dissolved solids and therefore improve taste. A problem with both methods is the production of high-salinity waste water, called brine, or concentrate, which then must be disposed of.

### SAR Technology:

A new solution to this problem has been proposed in the form of Subterranean Arsenic Removal (SAR) process where aerated groundwater is recharged back into the aquifer to create an oxidation zone which would coprecipitate iron & arsenic. The oxidation zone created by aerated water boosts the activity of the arsenic oxidizing microorganisms which can enzymatically oxidize arsenic from +3 to +5 state. In November 2009, the Blacksmith Institute- New York & the Green Cross- Switzerland selected the SAR Technology as one of the 12 Cases of Cleanup & Success in their World's Worst Polluted Places Report 2009. ■

**A new solution to this problem has been proposed in the form of Subterranean Arsenic Removal (SAR) process where aerated groundwater is recharged back into the aquifer to create an oxidation zone which would coprecipitate iron & arsenic.**



# EFFECTS OF ENVIRONMENT, SURGERY & DRUGS ON Thyroid Function

**Dramatic, although transient, increases in serum TSH levels have been observed in infants and young children during surgical hypothermia. Also, a prompt and important secretion of TSH occurs in the newborn, in the first few hours after birth, accompanied by an increase in thyroid hormone secretion and clearance.**

The sensitive and tightly regulated feedback control system, thyroid gland autoregulation, and the large intrathyroidal and extrathyroidal storage pools of thyroid hormone serve to provide a constant supply of thyroid hormone to peripheral tissues in the face of perturbations imposed by the external environment, chemicals and drugs, and a variety of diseases processes. The thyroid is subject to a

great number of exogenous and endogenous perturbations.

## RESPONSES TO ALTERATIONS IN THE EXTERNAL ENVIRONMENT

### Environmental Temperature

Changes in environmental temperature may cause alterations in TSH secretion and in the serum concentration of thyroid hormones and their metabolism.

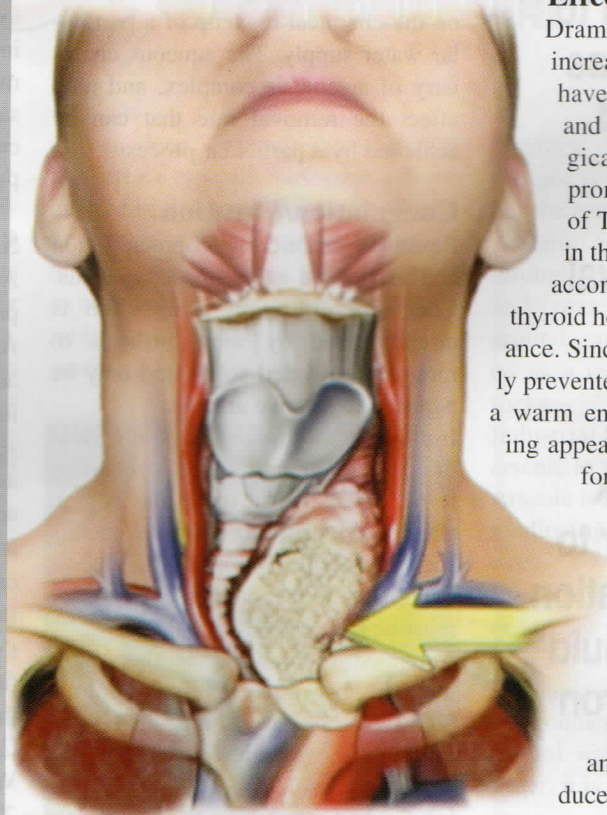
### Effects of Cold

Dramatic, although transient, increases in serum TSH levels have been observed in infants and young children during surgical hypothermia. Also, a prompt and important secretion of TSH occurs in the newborn, in the first few hours after birth, accompanied by an increase in thyroid hormone secretion and clearance. Since this TSH surge is partially prevented by maintaining infants in a warm environment, postnatal cooling appears to be responsible in part for the rise in TSH secretion.

In most studies, exposure of adults to cold or even intensive hypothermia has produced no changes.

### Effects of Heat

In general, an increase in ambient temperature has produced effects opposite to those





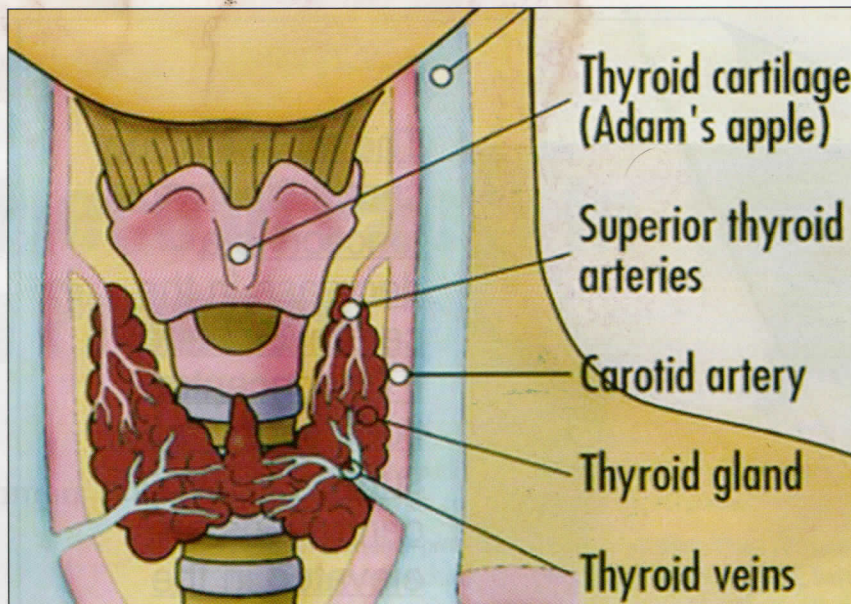
observed during cold exposure, although the effects of heat have not been extensively investigated. As indicated above, thyroid hormone levels in serum tend to be lower during the summer month.

### Nutrition

Since thyroid hormone plays a central role in the regulation of total body metabolism, it is not surprising that nutritional factors may profoundly alter the regulation, supply, and disposal of this thermogenic hormone. Although many dietary changes can affect the thyroid economy, the most striking and important effects are related to alterations in total caloric intake and the supply of iodine. The changes associated with caloric deprivation appear homeostatic in nature producing alterations in thyroid hormones which would conserve energy through a reduction in catabolic expenditure. The changes observed with a deficiency or excess of iodine supply generally serve to maintain an adequate synthesis and supply of thyroid hormone, principally through modifications in thyroidal iodide accumulation and binding.

### Overfeeding and Obesity

Overfeeding produces an increase in the serum T3 concentration as a result of an increased conversion of T4 to T3. It is particularly marked when the excess calories are given in the form of carbohydrates. Thus, it appears that



the effect of overnutrition on iodothyronine metabolism is the opposite of that of starvation. This finding gives further credence to the speculation that changes in thyroid hormone may serve to modulate the homeostasis of energy expenditure.

Although it has been reported that serum T3 concentrations correlate with body weight, it appears that this phenomenon reflects the effect of an increase in caloric intake on T3 production. Most studies find that obese subjects have normal thyroid function and hormone metabolism.

### Physical and Emotional Stress

Perhaps the most dramatic study of emotional stress is that reported by

Kracht, who found that stress provoked thyrotoxicosis in wild rabbits. Although some stress models may prompt secretion of thyroid hormone in animals, this effect is unlikely to occur in humans, at least for a sustained period of time. The stress-induced increase in adrenocortical activity tends not only to suppress TSH release but also to inhibit T3 production. A major problem in the analysis of available data is the difficulty in separating effects produced by non-specific stress from the effects caused by the agents used to induce the stress.

### Surgery

The most striking change in thyroid function is a decrease in the serum TT3 and FT3 concentrations shortly after surgery; rT3 concentrations are elevated in the postoperative period. The combined findings suggest a diversion in the normal deiodinative pathways of T4. FT4 levels may also be depressed in the postoperative period, but to a lesser degree. The TTR but not the TBG level is sharply reduced. This clear reduction in the concentration of the active forms of thyroid hormone during the postoperative period is preceded by a small, short-term increase in FT4 and FT3 concentrations during surgery. The magnitude of the subsequent reduc

**Overfeeding produces an increase in the serum T3 concentration as a result of an increased conversion of T4 to T3. It is particularly marked when the excess calories are given in the form of carbohydrates**





The most striking change in thyroid function is a decrease in the serum TT3 and FT3 concentrations shortly after surgery; rT3 concentrations are elevated in the postoperative period.

tion in T3 level appears to correlate with the severity of trauma and the morbidity during the postoperative course. The serum TSH concentration also tends to diminish, except during surgery performed in children under the conditions of hypothermia.

Because surgical trauma produces a prompt elevation in plasma cortisol levels and food intake is curtailed during the pre-, intra-, and postoperative periods, the possibility that glucocorticoids and starvation are the principal contributors to the observed changes in thyroid function has been given strong consideration

### Acute Mental Stress

Data on the effect of emotional stress on thyroid function in humans are principally derived from studies in patients with psychiatric disturbances. Thus, even if only patients with acute psychiatric decompensation are considered, the results are colored by the nature of the mental illness, its antecedent history, and the use of drugs. An early suggestion of enhanced hormonal secretion came from the observation of elevat-

ed protein-bound iodine (PBI) levels in the serum of psychiatric patients presumably under emotional stress and in medical students in the course of examinations.

### Goitrogens

Numerous dietary goitrogens, including cyanogenic glucosides, thiogluco-

sides, thiocyanate, and goitrin, are present in a wide variety of foods, and are believed to contribute to the occurrence of endemic goiter in some areas of the world. Monovalent anions such as thiocyanate and perchlorate inhibit iodide transport into the thyroid and cause goite

### DRUGS

A growing list of drugs and diagnostic agents have been found to affect thyroid economy by modulating the regulation of the hypothalamic-pituitary-thyroid axis, as well as by interfering with thyroid hormone transport, metabolism, excretion, and action. Some drugs, such as salicylates, diphenylhydantoin, and glucocorticoids, act at several levels. Several compounds, most notably estrogens, diphenylhydantoin, diazepam, heparin, halophenate, fenclofenac, and some biologically inactive thyroid hormone analogs compete with binding of thyroid hormone to its carrier proteins in serum. The only consequence of drugs affecting hormone transport is a decrease or increase in the concentration of total but not free hormone in serum. ■

## ATTENTION!

In case of hyperthyroidism, treatment usually continue with carbimazole. In our country Tab.Carbiroid is available which is a product of White Horse Pharmaceuticals and also Tab. Neo-mercazole from Roche Pharmaceuticals. It is sad but true that along with Roche's Neo-mercazole there is low quality product which has the same brand name and is imported illegally from India. In many cases, desirable result is not obtained because of the use of low quality drugs. So, it is a responsibility for all clinicians to make awareness on the use of appropriate drug.



## Prescription

# The Prime Piece of Paper in Purchasing Process



**Md. Mamunur Rahman**

M Pharm, MBA

***Trials are medicines which are gracious and wise physician prescribes because we need them; and he proportions the frequency and weight of them to what the case requires. Let us trust his skill and thank him his prescription.***

Sir Isaac Newton

Mathematician and Physicist  
Father of the Modern Science  
1642-1727

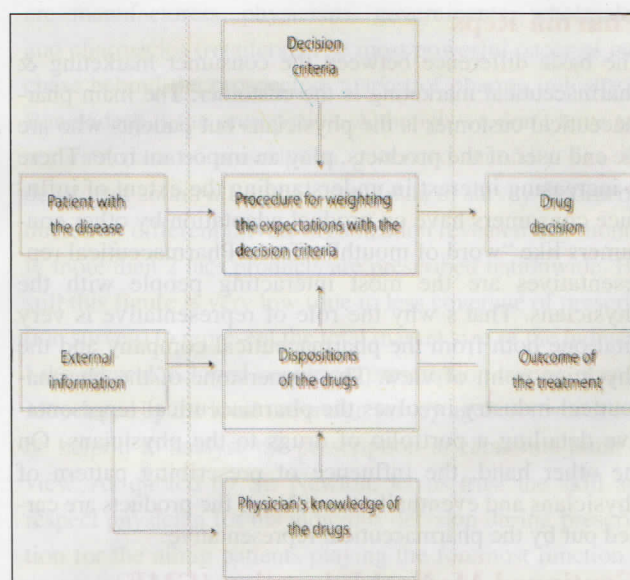
Physicians prescribe medicines for the patients to alleviate the symptoms of ailing humanity. This is the traditional process of how physicians treated patients. Several important factors are involved that incorporate the utilities of both the physician and patient in arriving at the prescription decision. There are two types of physicians: those who strongly value patient utility and those who value it less for both the two types of patients—new and continuing. Considering the patient, disease and time specific medication needed, prescription plays not only as a medical paper of medication for the patients, it is the main underlying factor of consumption pattern in healthcare system. Apart from the ethical and medical perspective of prescription, it plays the pivotal role for the pharmaceutical company in the business perspective.

When a physician prescribes a medication for the patient, it is also important to pay attention to certain economic factors like the various cost dimension related to drugs which eventually affect the consumption pattern. The compliance affects the performance of the patient positively or negatively. A patient cannot comply unless he or she takes the prescription filled i.e. consumed. But it is difficult to know the phenomenon of unfilled prescriptions due to identify the dimensions of the problem. There are several fac-

tors that affect the patient's compliance such as patient income, compliance behavior, cost factors & patient response.

Decision making is probably the vital factor concerning prescribing that leads to the consumption of drugs. Decision making have classified the behavior of decision makers into two types, rational (evaluates all alternatives completely, matches his needs with the respective abilities of the products available to fulfill these needs and, theoretically at least, makes his purchase with clear goals in mind) and emotional (swayed by product attributes (or the advertising) having nothing to do with the actual need-satisfying properties of the product). It should also be pointed out that rational and emotional motives may occasionally be combined.

A physician, for example, may use the most rational therapeutic approach when choosing the proper chemical entity for treating a given condition, and then may use completely emotional criteria for the choice of the brand of that drug to employ. The basic motivations behind a physician's choice of drug therapy must be considered to be rational. But both the emotional and rational choice of drugs are thought to be happened in the following way:



**Exhibit: Physician's Non-habitual Choice Process**



It is obvious that a physician's drug selection decision process, like any consumer purchasing decision, involves the input of many variables. Unlike a consumer, however, the physician's decision to prescribe involves the input of unique parameters and carries with it a high degree of responsibility. Factors that may influence the decision making process is mostly:

### **Patients**

Patients were found to have only a slight influence on physician prescribing. But due to the e-promotion of drugs and DTC (Direct to Consumer) advertising make more health awareness to the patients that eventually create some impact to the prescribing pattern. Drugs like the birth control medications, vaccines and the life style type medications are sometimes thought to be influenced by the patients to the physicians to prescribe.

### **Physician Samples**

Giving product sample to the physicians for trial is a common practice worldwide. Accepting samples by the physicians is also associated with awareness, preferences and rapid prescription of new drugs and existing drugs as well. Considering the use and utility of the samples it has a huge impact to the physicians to the prescription.

### **Gift & Gimmicks**

Although it is a question of doubt and a conflict of interest by the company as done the medical research whether receiving a gift and the number of gifts are correlated with the impact on prescribing behavior. But it is evident that the gifts from the pharmaceutical industry contribute to the rapidly increasing cost of medical care and more specifically to the increase in expenditures on prescription drugs.

### **Pharma Reps**

The basic difference between the consumer marketing & pharmaceutical marketing is the customer. The main pharmaceutical customer is the physicians but patients who are the end user of the products, play an important role. There is increasing interest in understanding the extent of influence consumers have on product adaptation by other consumers like "word of mouth" effects. Pharmaceutical representatives are the most interacting people with the physicians. That's why the role of representative is very vital one both from the pharmaceutical company and the physician point of view. The cornerstone of the pharmaceutical industry involves the pharmaceutical representative detailing a portfolio of drugs to the physicians. On the other hand, the influence of prescribing pattern of physicians and eventually the sales of the products are carried out by the pharmaceutical representative.

### **Continued Medical Education (CME)**

CME has now become a substantial subject of greater interest to a large number of pharmaceutical companies to

generate a positive impact in prescribing pattern of physicians. Most of the big companies did pay all the expenses & logistic support to the physicians for the research and clinical trials of the product. On occasion, pharmaceutical companies pay the cost of scientific exhibit like disease oriented symposia and conferences, disease oriented printed and audiovisual educational materials for the healthcare professionals, drug utilization reviews play a significant role in prescribing pattern.

### **Advertising**

The advertising of drugs is strictly restricted and regulated from country to country. Although the contribution of advertising to prescribe is debatable, it has both positive and negative impact on prescribing habit of physicians. After the drug disasters like the thalidomide, consumers have lobbied governments for the increased controls over pharmaceutical advertising and claims. But in some cases like the DTC advertising of different disease like HIV, birth control medications play a positive impact in prescribing pattern.

### **Peer Groups**

Physicians use more professional sources, particularly colleagues, when called upon to treat difficult conditions in which the effects of drug therapy are less clearly defined. Colleagues sharing an office with a physician will use a colleague as a source of information for drugs not presently used by the physician. Colleagues do have a positive effect on prescribing, but the influence, of a colleague is always secondary to other factors, such as advertising and education. Sometimes the junior physicians follow the prescription of senior professor who are called Key Opinion Leader (KOL).

### **Other Health Professionals**

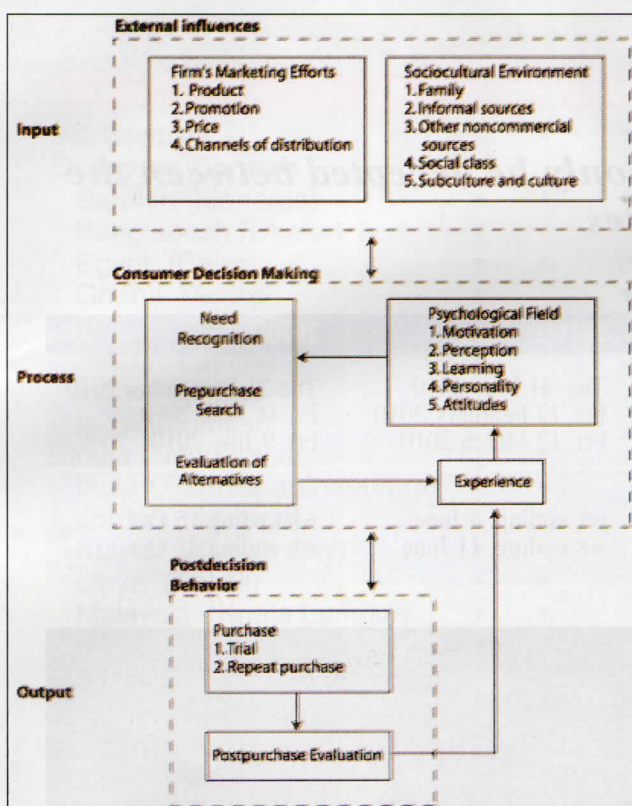
Physicians are not only the healthcare personnel who are influential in ultimate destination of prescription pharmaceuticals. Others healthcare professionals must be considered including the nurses, physicians assistants etc. Although it is difficult to quantify the influence of nurse on prescription and nonprescription (OTC) drug use but it is substantial in practice. Physicians Assistants (PAs) is another group of non-physicians who influence drug use. Both of the later two groups most frequently prescribe analgesics, antibiotics, antihistamines, antihypertensives, cough & cold remedies.

Research discovered that consumers are just as likely to purchase impulsively and to be influenced not only by family and friends but by advertising and also by mood, situation and emotion. All of these factors combine to form a comprehensive model of consumer behavior that reflects both cognitive and emotional aspects of consumer decision making. The basic difference between FMCG (Fast Moving Consumer Goods) & PMG (Pharmaceutical Medicinal Goods) is the customer or consumer point of



view. In PMG, physicians are thought to be the key customers and the patients are the end customers or consumers. Physician's drug selection decision process, like any consumer purchasing decision, involves the input of many variables. Describing the consumer decision of marketing model in pharmaceuticals perspective, physicians, patients are interlinked along with the key factor-the prescription.

According to the marketing model of consumer behavior, the decision-making process has three interlocking stages such as input stages, the process stages and the output stages as described below:



**Exhibit: Simplified Model of Consumer Decision Making**

### Input Stages

The input stage influences the consumer (both physicians and patients) recognition of product (medicine) need and consists of two major sources of information: the company's marketing efforts i.e. the marketing mix (product, price, place and promotion) offered by the pharmaceutical companies and the sociological influences on the consumer (family, friends, neighbors for the patients and peer group) influence to the physicians. There are also some other informal and noncommercial sources, social class, cultural and sub-cultural membership for the patients.

### Process Stages

The process stage of the model focuses on how con-

sumers (physicians) make decision about prescription. The psychological factors inherent in each physician (motivation, perception, learning, personality and attitudes) affect how the external input stage influence the physician's recognition of a need pre-purchase research for information and evaluation of alternatives. The experience gained through evaluation of alternatives, in turn, affects the consumer's (patient and physician) exiting psychological attributes.

### Output Stages

The output stage of the consumer decision-making (i.e. the prescribing habit of physicians) model consists of two closely related post-decision activities: purchase behavior and post-purchase behavior and these are related to the patients as a whole. But these factors influence the prescribing pattern of physicians.

Physicians are thought to be the key customers and the patients are the end customers or consumers. Physician's drug selection decision process, like any consumer purchasing decision, involves the input of many variables. Unlike a consumer, however, the physician's decision to prescribe involves the input of unique parameters and carries with it a high degree of accountability and responsibility as well. Describing the consumer decision of marketing model in pharmaceuticals perspective, physicians, patients are interlinked along with the key factor-the prescription.

The pharmaceutical industry of Bangladesh is a large and important industry both in terms of size (more than 400 manufacturers, 800 molecules & 7500 brands with yearly sales value more than Tk. 5,183 Crore) and growth (13.78%). The main participants in this industry, besides the end consumer are manufacturers, physicians, governments, wholesalers and pharmacies (retailers). The most powerful paper of purchase behind the prospective market of pharma industry of Bangladesh is the prescription. Although we don't have any accurate data of prescription generated annually like the developed country. But the sample data of survey report conducted by different private organization revealed that monthly more than 2 lacs products are prescribed nationwide. But still this figure is very low (due to less coverage of prescription survey) to represent the total market size of the industry. Like other developed countries, prescription census may be introduced by the local or foreign survey agencies which will be helpful to analyse the prescription in economic point of view. As quoted by Sir Newton, let us trust the skill and respect physician for his judicious decision during prescription for the ailing patients playing the foremost function in purchasing process of pharmaceuticals.

*\*Writer is a Manager, Product Management Department (PMD), Orion Laboratories Ltd.*



# MRCP(UK) Part 1

## Examination Dates for 2010

*Online or paper applications will only be accepted between the published opening and closing dates.*

Date	2010/1	2010/2	2010/3
Examination date: Application opening date: Application closing date:	Tue 19 January 2010 Fri 2 October 2009 Fri 6 November 2009*	Tue 11 May 2010 Fri 12 February 2010 Fri 12 March 2010	Tue 21 September 2010 Fri 11 June 2010 Fri 9 July 2010
Results release dates: Results web Results posted	wk ending 12 Feb wk ending 19 Feb	wk ending 4 June wk ending 11 June	wk ending 15 Oct wk ending 22 Oct





## POST GRADUATE COURSE

### Bangkok School of Tropical Medicine, Mahidol University Thailand

Centres	2010/01	2010/2	2010/3	Application Type
<b>UK Centres</b>	•	•	•	Paper / Online
<b>Overseas Centres</b>				
Bahrain (Manama)	•	•	•	Paper
Bangladesh (Dhaka)	•	•	•	Paper / Online
Egypt (Cairo)	•	•	•	Paper / Online
Ghana (Accra)	•			Paper / Online
Hong Kong	•	•		Paper
India (Chennai)	•	•	•	Paper / Online
India (Kolkata)	•	•	•	Paper / Online
India (Mumbai)	•	•	•	Paper / Online
India (New Delhi)		•	•	Paper / Online
India (Thiruvananthapuram)	•	•	•	Paper / Online
Jordan (Amman)		•		Paper / Online
Kuwait (Kuwait City)	•	•		Paper / Online
Libya (Tripoli)	•	•	•	Paper / Online
Malaysia (Kuala Lumpur)	•	•		Paper / Online
Malta	•	•		Paper / Online
Myanmar (Yangon)*				Paper / Online
Nepal (Kathmandu)			•	Paper / Online
Oman (Muscat)	•	•	•	Paper / Online
Pakistan (Karachi)	•	•	•	Paper / Online
Pakistan (Lahore)	•	•	•	Paper / Online
Qatar (Doha)	•	•	•	Paper / Online
Saudi Arabia (Jeddah)	•			Paper / Online
Saudi Arabia (Riyadh)	•	•	•	Paper / Online
Singapore	•		•	Paper
Sri Lanka	•	•	•	Paper / Online
Sudan (Khartoum)	•	•	•	Paper / Online
Syria (Damascus)	•	•		Paper / Online
UAE (Abu Dhabi)	•	•	•	Paper / Online
UAE (Dubai)	•	•	•	Paper / Online
West Indies (Barbados)	•	•	•	Paper / Online
West Indies (Jamaica)	•	•	•	Paper / Online
West Indies (Trinidad)	•		•	Paper / Online
Zimbabwe (Harare)			•	Paper/ Online

Please note that the Part 1 examination will not be held in Myanmar in 2010. It will next be held in 2011

#### Academic Calendar

##### D.T.M. & H.

Course opens

First week of April

Pre-clinical Field Trip

June

Clinical Field Trip

July

Course closes

Last week of September

##### M.C.T.M. &

##### M.C.T.M.(Trop.Ped)

Course opens

First week of April

Pre-clinical Field Trip

June

Clinical Field Trip

July

Data Collection

November –December

Thematic paper Examination

March

Course closes

Last week of March

##### M.Sc. & Ph.D. (Trop.Med.),

##### Ph.D. (Trop.Med)

Start of First Semester

June

Start of Second Semester

November

#### CONTACT INFORMATION

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1327, 1318, 1345, 1315

Fax: 66 (0) 2354-9141

E-mail:

[tmirunit@diamond.mahidol.ac.th](mailto:tmirunit@diamond.mahidol.ac.th)



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House No – 14/E  
Dhanmondi R/A, Dhaka.  
Phone : 670397

#### A.M. Drug Store

Shabag Biponi Bitan  
Shabag, Dhaka

#### Al-Razi Hospital

Farmgate, Dhaka.  
Phone: 9117775

#### Antara Pharmacy

Shop No-5  
Sarwardi Complex  
College Gate, Dhaka.  
Phone : 8112503

#### Bismillah Pharmacy

P.G. Campus  
Shabag , Dhaka

#### BMCH Pharmacy

BMCH Campus  
Road No-14/A  
Dhanmondi R/A, Dhaka.  
Phone : 9118202, 9120792

#### Cash & Carry Pharma

Arambag, Dhaka.  
Phone: 7100407

#### Day Night Pharmacy

2/1, Secretareate Road  
Emergency Gate  
BMCH, Dhaka.

#### Emon Pharmacy

Johnson Road, Dhaka.\

#### Gazi – Medical Hall

BIRDEM  
Shabag , Dhaka  
Phone: 8615271



### Ambulance Services

#### Al-Markajul Islami

19/1, Babar Road, Mohammadpur, Dhaka.  
9129217, 8114980

#### Anjuman-e-Mofidul Islam

9336611, 7119808

#### Day Night Ambulance Services

8122041, 9123073, 0171544328

#### Fire Service

9556666-7, 9553333-7, 9555555

#### Green Ambulance Service

8612412, 0175088814

#### Holy Family Red Crescent Hospital

8311721-25

#### ICDDRDB (Mohakhali Diarrhoea Hospital)

8811751-60

#### Medinova Medical Services

8620353, 8113721

#### Red Crescent Ambulance

8311721-25

#### Shishu Hospital

8116061, 8116062, 8114571-2



### Blood Bank

#### Dhaka Medical College Hospital

8616744, 8626812-19, 9663429

#### DMC Sandhani

9668690, 018284878 (M)

#### Red Crescent Blood Bank

7/5, Aurangazab Road, Mohammadpur  
9116563, 326320

#### Sir Salimullah Medical College Hospital

7319123

#### SSMC Sandhani

7319123



## Hospitals

### Ad-din Hospital

2 Baro Maghbazar, Dhaka., 9353391-3

### Ahsania Mission Cancer Hospital

Plot No: M-1/C, Mirpur-14, Dhaka, 9008919

### Al-Barakah Kidney Hospital

129, New Eskaton Road, Dhaka 9350884, 9351164, 9337521

### Al-Manar Hospital Ltd.

H-5/4, Block-F, Lalmatia, Dhaka 9121387, 9121588

### Al-Rajhi Hospital Pvt. Ltd.

12, Farmgate, Dhaka 8119229, 8121172, 9140749, 9133563-4

### Apollo Hospital Dhaka

Rd-81, Block-E, Bashundhara R/A, Dhaka. 9891661-2, 9891680-1, 0173046684-5

### Bangladesh Eye Hospital

H-19/1, Rd-6, Dhanmondi, Dhaka 8651950-3

### Brighton Hospital & Diagnostic Centre

163-164, Sonargaon Road, Hatirpool 8626901-2, 8651128-35, 9677792-5

### Central Hospital

H-2, Road-5, Dhanmondi, Dhaka 9660015-19

### City General Hospital

H-120, Rd-9/A, Dhanmondi, Dhaka 9120862, 8130778

### Comfort Nursing Home

167/B, Green Road, DRA, Dhaka 8124990, 8124380, 8127394

### Crescent Gastro Liver & General Hospital Ltd.

25/I, Green Road, Dhanmondi 8621612, 8611936

### Delta Medical Centre

H-20, Rd-4, DRA 8617141-3

### Dhaka Community Hospital

190/1, Bara Moghbazar, Wireless Railgate 9351190-1, 8314887

### Dhaka Hospital

17, D.C Roy Road, Mitford 7320709, 7310750, 7320212, 7316643

### Fuad Al-Khatib Hospital

Almas Tower, 282/1 Majar Road, Mirpur, Dhaka 9007188, 8013638, 9004317

### Gonoshasthya Nagar Hospital

14/E, Rd-6, Dhanmondi 8613567

### Ibn Sina Hospital

H-68, Rd-15/A, DRA 8113709, 8119513-5

### Islami Bank Central Hospital

30 V.I.P Road, Kakrail, Dhaka 9338810, 8316166, 9355801-2, 9360331-2

### Japan Bangladesh Friendship (Pvt.) Hospital

H-27, Rd-114, Gulshan-2 8817575, 8828855, 8827575, 8828855

### Lab Aid Cardiac Hospital

H-1, Rd-4, Dhanmondi, Dhaka 8610793-8, 9670210-3 (C), 0176585828 (M)

### Lab Aid Specialized Hospital

H-6, Rd-4, Dhanmondi Dhaka 8610793-8, 9670210-3

### Metropolitan Medical Centre

Mohakhali (Opposite to Bus Terminal) 9899209, 8824155

### Millennium Heart & General Hospital Ltd.

4/9, Block-F, Lalmatia, Dhaka 9124046, 9122115, 8120097

### Monoara Hospital (Pvt.) Ltd.

54, Siddesari 8318135, 8318529, 8319802, 8318135

### Padma General Hospital Ltd.

290, Sonargaon Road, Dhaka 8620889-19, 9661528, 9662502

### Paedihope Hospital For Sick Children

H-32/A, Rd-6, Dhanmondi, Dhaka 9671345, 9631375

### Renaissance Hospital & Research Institute Ltd.

H-60/A, Rd-4/A, Dhanmondi 9664930, 8615792, 8611455

### Rushmono General Hospital

208-9, Outer Circular Road, Moghbazar 8317606, 8317819, 9357354, 9332358

### Samorita Hospital (Pvt.) Ltd.

89/1, Green Road (Panthapath) 8611307, 9131901

### SPRC & General Hospital

135, Ne Eskaton Road 9339089, 9342744, 8313185

### Sumona Clinic General Hospital

3-4 Patuatuly, Dhaka 7112583, 7115531, 9561786

### The Barakah General Hospital

937, Outer Circular Road Rajarbag, Dhaka 8317765, 9337534, 9346265

### Udayon Poly Clinic

16-17/1, Ne Eskaton, Dhaka 8016300-1, 9351100-1, 9357095



# Upcoming events in Medical Science

## February 2010

02 8th Asia Pacific Evidence-Based  
Medicine & Nursing Workshop and  
Conference George Town Malaysia

05 7th International Winter  
Arrhythmia School Blue Mountain  
Canada

09 International Conference on  
Climate Change and Bioresource  
(ICCCB-2010) Tiruchirappalli, India  
India

11 15th Annual Psychopharmacology  
Update Las Vegas Nevada  
The 15th Annual

Psychopharmacology Update pro-  
vides comprehensive information for  
treatment of psychiatric disorders. 24  
AMA PRA Category 1 credits.

12 East Asia Regional Biometric  
Conference and X Biennial  
Conference of International  
Biometric Society (Indian Region)  
Manipal India

13 5TH INTERNATIONAL CON-  
FERENCE ON SEXOLOGY CHEN-  
NAI India

This is the largest and biggest confer-  
ence of its kind in India. Sexologists,  
urologists, psychiatrists, venerologists,  
endocrinologists and general practition-  
ers, hiv specialists, psychologists, and  
therapists are contributing.

13 Pediatric Potpourri®: State of the  
Art 2010 Maui Hawaii

15 1st Global Conference - Making  
Sense Of: 'Care' in Health Care  
Sydney Australia

This inter- and multi-disciplinary  
project seeks to address the meanings,  
the role and the realities of the term  
'Care' as used in conjunction with

practices that relate to health and ill-  
ness matters.

17 1st Global Conference - Making  
Sense Of: Pain Sydney Australia  
This interdisciplinary conference pro-  
vides a forum for inquiry into the  
vicissitudes of pain: its nature and  
existential significance, and the  
many ways in which pain plays a part  
in our lives.

25 Pharmacon - Pharmacy  
Conference: Medicines

Counterfeiting Belgrade Serbia

26 2010 International Conference on  
Agricultural and Animal Science

Singapore Singapore

CAAS 2010 proceeding will be pub-  
lished by World Academic Press, and  
all papers in the proceeding will be  
indexed by the Thomson ISI  
Proceeding.

## March 2010

05 12th Annual Health and Human  
Rights 2010 - University of Toronto's  
International Health Programme  
Toronto Canada

06 3rd International Online Medical  
Conference (IOMC 2010) Online  
Conference Other





Building upon the success of previous conferences, IOMC 2010 will bring together medical researchers, experts, professors & students to discuss their research findings and share their knowledge ONLINE. Abstract/Paper submission is now Open.

08 1st Kuwait Conference on HPB and Transplantation Kuwait Kuwait

12 Fruehjahrstagung der Arbeitsgruppe Paediatric der Deutschen Gesellschaft fuer Schlafforschung und Schlafmedizin Cologne Germany

20 World Congress of Internal Medicine Melbourne Australia

24 15th Anniversary Congress of the European Association of Hospital Pharmacists Nice France

25 The 3rd International Conference on ICT for Africa 2010 YAOUNDE Cameroon

The International Conference on ICT for Africa 2010 (ICIA 2010) is themed 'ICT for Development - Contributions of the South'. This conference will bring together a fine mix of practitioners and academicians in the area of ICTs for susta

29 The Intimate Side of Sexual Health Pattaya Thailand

#### April 2010

03 5th International APOCP Conference Istanbul Turkey

07 BSA Annual Conference 2010: Inequalities and Social Justice Glasgow United Kingdom

The BSA 2010 Annual Conference includes presentations on topics that reflect the core research areas. The theme Inequalities and Social Justice will be addressed in both the main plenary sessions and the sub-plenary sessions.

09 Exploring Childhood Studies Camden NJ

12 Healthcare Tourism Congress 2010 Kuala Lumpur Malaysia

14 Fourth International Conference on Development Studies Abuja Nigeria

22 First Croatian Congress on Pharmacoeconomics and Outcomes Research with International Participation Rijeka Croatia (Hrvatska)

22 Internal Medicine 2010 Toronto Canada

23 Shoulder instructional course 2010 Zagreb Croatia (Hrvatska)

28 3rd Central European Congress of Surgery Dubrovnik Croatia (Hrvatska)

#### May 2010

04 QMEDIC 2010 - 2nd Qatar International Medical and Hospital Show Doha Qatar

10 Changing Cultures.... Veterinary Medicine & Literature Guelph Canada

15 Death Day Winchester United Kingdom

#### June 2010

03 OSSD Fourth Annual Meeting Ann Arbor Michigan

19 20th Meeting of the European Neurological Society

Berlin Germany

#### July 2010

01 6th Asian Interventional Cardiovascular Therapeutics (AICT) Congress Singapore

01 Health of the Nation Summit 2010 London United Kingdom

03 Pediatrics in the Islands ... Clinical Pearls 2010 Maui Hawaii

06 The Body on Display, from Renaissance to Enlightenment Durham United Kingdom

07 International Conference on Biomedical Data & Knowledge Mining: Towards Biomarker Discovery Chania Greece

11 International Obesity Conference Stockholm Sweden

12 Industrial Conference on Data Mining, ICDM 2010 Berlin Germany

This conference is the eleventh conference in a series of industrial conferences on Data Mining that will be held on yearly basis. Experts will present theoretical work and their applications and the results obtained by applying data mining

#### August 2010

04 Second World Congress on Research and Development Ibadan Nigeria

30 ITBAM: International Conference on Information Technology in Bio- and Medical Informatics Bilbao Spain

#### September 2010

01 Biofilms 4 International Conference, 2010 Winchester United Kingdom

15 ICBST 2010 : International Conference on Biomedical Science and Technology Amsterdam Netherlands

17 Pharmaceuticals in Developing and Emerging Economies: Production, Innovation, and Access to Medicines in the wake of TRIPS Hyderabad India

21 2nd conference of the European Paediatric Formulation Initiative EuPFI on Formulating Better Medicines For Children Berlin Germany

28 ICBST 2010 : International Conference on Biomedical Science and Technology Houston

#### October 2010

21 42nd Annual Congress of the International Society of Paediatric Oncology (SIOP) Boston MA

23 Aloha Update: Pediatrics® 2010 Kauai Hawaii

#### November 2010

06 International Seafood and Health Conference and Exhibition Melbourne Australia

Grand Patron, Professor Michael Crawford says This Conference will be to Human Health and Nutrition to what Kyoto was to Global Warming.

15 Academic Medical & Health Science Centers 2010 Scottsdale Arizona.



# CARDIOLOGIST

**Prof. (Dr.) Md. Abu Siddique**

Ph.D (Cardiology), FPGCS (Medicine), MBBS (DMC)  
Cardiologist and Physician  
Fellow Interventional Cardiology  
Professor of Cardiology, BSMMU.

**Chamber :**

Popular Diagnostic Centre Ltd.  
32, New Circular Road  
(Shantinagar Chowrasta) Dhaka.

**Prof. (Dr.) Md. Afzalur Rahman**

MBBS, MD(Cardiology), PhD(Cardiology),  
FRCP (Glasgow), FRCP(Edin), FACC (USA)  
Professor and Head, Department of Cardiology  
Sir Solimullah Medical College & Mitford Hospital.

**Chamber :**

Labaid Cardiac Hospital  
House-1, Road-4, Dhanmondi,  
Dhaka-1205

**Prof. (Dr.) H.I.Lutfor Rahman Khan**

MBBS, MD (Cardiology), D-Card ,  
Professor and Head, Department of Cardiology  
Dhaka Medical College & Hospital.

**Chamber :**

Comfort Tower  
167/B, Green Road, Dhaka-1205

**Prof. (Dr.) Abdur Zaher**

MBBS, FCPS (Medicine), FACC(USA), FRCP  
Professor Cardiology

**Chamber :**

LAB AID CARDIAC HOSPITAL  
House-1, Road-4, Dhanmondi, Dhaka-1205

**Prof. (Dr.) Md. Faruque**

MBBS, MD (Card), WHO Fellow (USA)  
Professor of Cardiology, NICVD.

**Chamber :**

Modern Diagnostic Centre Ltd.  
House-17, Road-8, Dhanmondi, Dhaka-1205

**Dr. A P M Sohrabuzzaman**

MD, FCPS  
Senior Consultant in Cardiology

**Chamber :**

LAB AID CARDIAC HOSPITAL  
House-1, Road-4, Dhanmondi, Dhaka-1205

**Professor Dr. M.A.Rashid**

MBBS, MPH, DTM. D-CARD, FACC, FRCP(Glasgow)  
Chief, Executive Officer & Senior Consultant, Cardiology

**Chamber :**

IBRAHIM CARDIAC HOSPITAL &  
RESEARCH INSTITUTE  
122, Kazi Nazrul Islam Avenue, Shahabag, Dhaka-1000.

**Prof. (Dr.) Baren Chakraborty**

MBBS(Dhaka), MCPS(Med),  
FCPS(Med), FACA(USA),  
FCCP(USA), FRCP (Ireland), FRCP  
(Edin), FRCP (Glasgow),  
FACC(USA)

Senior Consultant Cardiologist

**Chamber :**

Labid Aid Cardiac Hospital  
House-1, Road-4, Dhanmondi,  
Dhaka. ■

## ANNOUNCEMENT

It's our pleasure and appreciation to welcome articles on different specialities from concerned specialists and interesting case findings or exciting experiences in your daily practices for next edition. Obviously your active contribution enrich this journal indeed.



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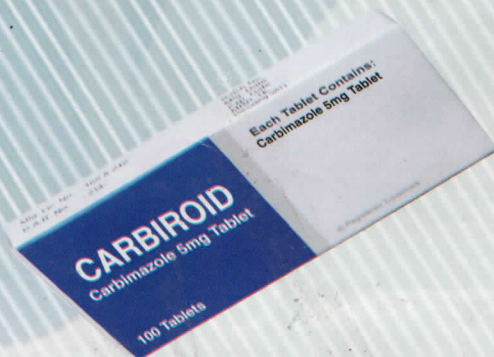
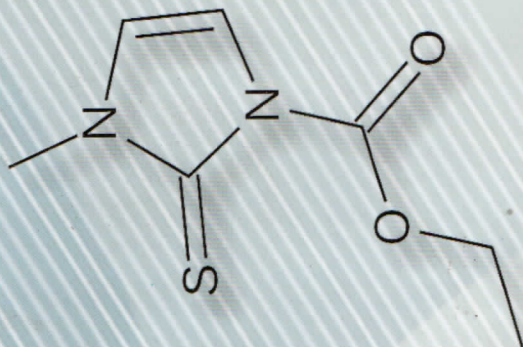
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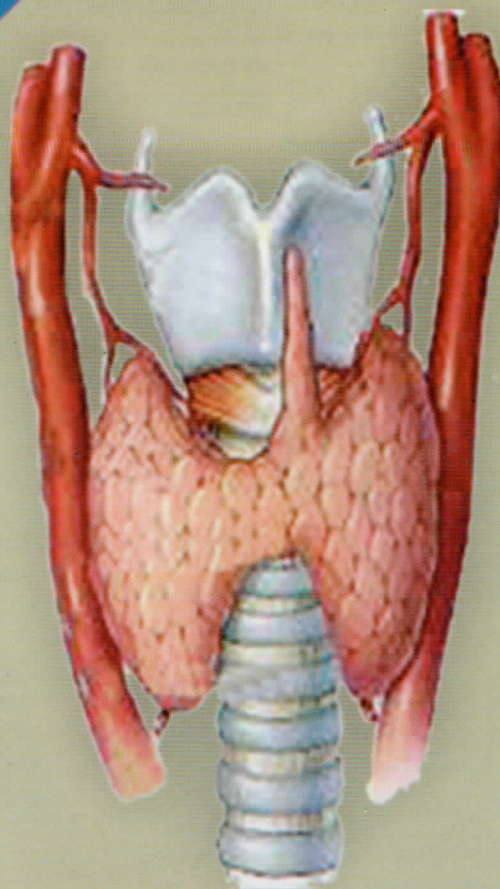


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- ☐ NODULAR GOITRE
- ☐ MULTINODULAR GOITRE
- ☐ SOLITARY TOXIC ADENOMA
- ☐ EXCESS **TSH**  
DUE TO PITUITARY TUMOUR
- ☐ THYROIDITIS