July-September 2013

ISSN 2222-5188

# info MEDICUS

The essence of medical practice

Volume 10 Issue 3

# Silent Myocardial Ischemia

# Contents

# Editorial

Dear Doctor,

We would like to thank you for your continuous support and show our gratitude for being with us throughout our journey for the last 10 years.

In this issue, we would like to highlight the feature of "Silent Myocardial Ischemia" as Review Article. Presently, silent myocardial ischemia is becoming the burning issue worldwide for both developed and developing countries as about 40% of patients with ischemic heart diseases have acute episode of myocardial ischemia during their lifetimes while 75% of these episodes cause no symptoms and are considered as "silent".

Keeping continuation with the previous issue, we have also included section-3 - "Essentials of Evidence Based Clinical Practice" in Clinician's Corner which is the modern approach of updating knowledge in diagnosis, treatment and prognosis of the patient.

We have tried to incorporate some pictures in Visual Diagnosis section to refresh your memory, which, we hope will be an enjoyable exercise for you.

Addition to these in Case Review, we have presented a rare but interesting case on "Gynaecomastia, Galactorrhoea and Lung Cancer in a man". There are only two previously reported cases of lung cancer associated with galactorrhoea, including this case report and this case is the first case of lung cancer associated with galactorrhoea which was resolved with systemic chemotherapy.

Positive Pressure Ventilation is a lifesaving maneuver. Therefore, in Clinical Method some information about "Positive Pressure Ventilation with a face mask and bag valve device" along with the procedure is also given.

In addition, regular sections are presented as usual. We hope this issue will be more useful and informative for you.

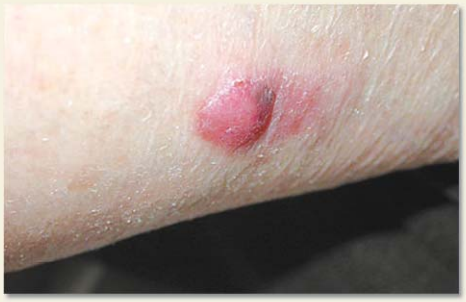
We always welcome and count your valuable comment regarding "Info Medicus" that helps us to make continuous improvement as we propel forward with new issues.

Last but not the least, on behalf of the editorial board, we wish you and your patients a happy and safe "Monsoon" season.

Thanks and best regards,

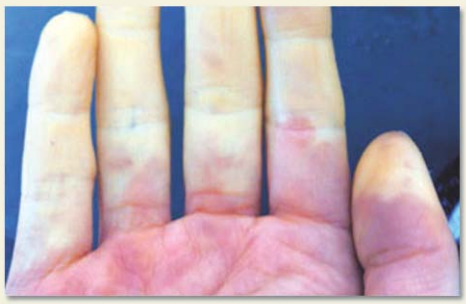
**(Dr. S. M. Saidur Rahman)**
Medical Services Manager

**(Dr. Rumana Dowla)**
Manager, Medical Information & Research



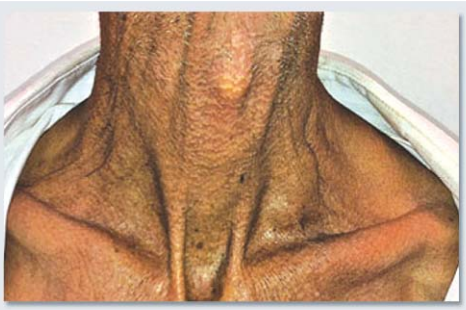
**1. What is the diagnosis?**

a. Amelanotic melanoma
b. Angioma
c. Dermal nevus
d. Pyogenic granuloma



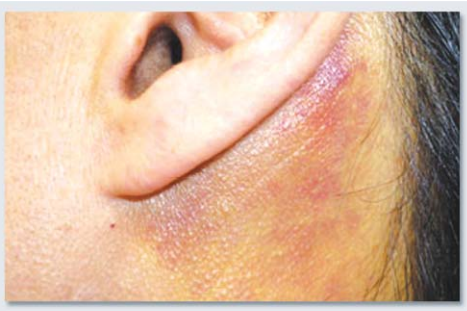
**2. What is the diagnosis?**

a. Carcinoid syndrome
b. Mastocytosis
c. Radial-artery occlusion
d. Raynaud's phenomenon



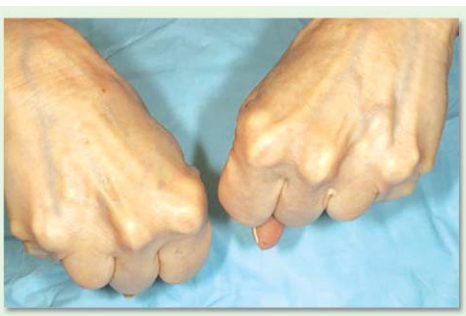
**3. This patient had presented with weight loss. What is the most likely diagnosis?**

a. Lung cancer
b. Gastric cancer
c. Melanoma
d. Nasopharyngeal cancer



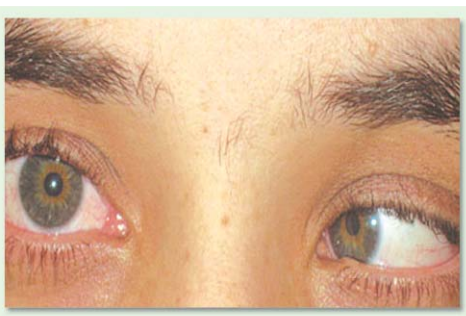
**4. This patient presented with hearing loss and left ear fullness. What is the diagnosis?**

a. Cholesteatoma
b. Fracture of the temporal bone
c. Ochronosis
d. Relapsing polychondritis



**5. What is the diagnosis?**

a. Albright's hereditary osteodystrophy
b. Hypertrophic osteoarthropathy
c. Osteoarthritis
d. Rheumatoid arthritis



**6. This patient was trying to look right when the image was taken. What is the diagnosis?**

a. Internuclear ophthalmoplegia
b. Left sixth cranial nerve palsy
c. Right sixth cranial nerve palsy
d. Right fourth cranial nerve palsy

Please see the answers → 1. a 2. d 3. b 4. b 5. a 6. c

# Silent Myocardial Ischemia

Silent Myocardial Ischemia (SMI)- objective documented ischemia in the absence of chest discomfort or other anginal equivalents is a major component of the total ischemic burden for patients with ischemic heart disease. In the United States, an estimated 2 to 3 million persons with stable coronary artery disease (CAD) have evidence of silent ischemia. About 40% of patients with ischemic heart disease have acute episodes of myocardial ischemia during their lifetime; 75% of these episodes cause no symptoms and are considered "silent."

Greater awareness of the incidence of silent ischemia in high-risk populations such as persons with diabetes can help reduce cardiovascular events and death rates. In this review, we outline the evidence that supports the relationship between SMI and the risk of future cardiovascular events.

## Cohn classification of silent ischemia

Patients at increased risk for cardiovascular events include those with stable angina, unstable angina, post-infarction angina, or variant angina; those who have survived cardiac arrest or have had a heart transplant or percutaneous coronary intervention or bypass surgery; and those who have diabetes or multiple coronary risk factors.

According to the Cohn classification, 4 types patients with silent ischemia are stratified into types I, II, or III:

- Type I silent ischemia is the least common form. It occurs in asymptomatic patients with obstructive CAD who do not experience anginal symptoms at any time.
- Type II silent ischemia most commonly occurs in patients with a documented previous Myocardial Infarction (MI).
- Type III is the most common form; it occurs in patients with chronic stable angina, unstable angina, or variant angina.

## Pathophysiology

### Pain studies

No discussion of silent ischemia is complete without consideration of the cardiac pain mechanism. Although much has been learned about this subject, much is still uncertain. The afferent fibers that run in the cardiac sympathetic nerves are usually thought of as the essential pathway for the transmission of cardiac pain. The atria and ventricles are abundantly supplied with sympathetic sensory innervations from the heart, the sensory nerve endings connect to afferent fibers in cardiac nerve bundles, which in turn connect to the upper 5 thoracic sympathetic ganglia and the upper 5 thoracic dorsal roots of the spinal cord. Within the spinal cord, impulses mediated by this sympathetic afferent route probably converge with impulses from somatic thoracic structures into the same ascending spinal neurons. This would be the basis for cardiac pain referred to the chest, wall, arm, back etc. In addition to this "convergence-projection theory," the contribution of vagal afferent fibers must be acknowledged for an explanation of cardiac pain referred to the jaw and neck. How these vagal fibers are activated remains unclear. Furthermore, somatic localization of ischemic pain cannot predict the site of myocardial ischemia (anterior, inferior, or lateral) from one patient to the next.

The actual "trigger" that stimulates the sensory nerve endings remains elusive. If a chemical pain stimulus is involved, the substance that has been most recently linked to the production of angina-like chest pain is adenosine. From a study it was observed that an adenosine infusion resulted in chest pain even in patients without obstructive coronary artery disease. Subsequently, it was also given in varying amounts to healthy volunteers and caused dose-dependent chest pain in all of the volunteers. Concomitant dipyridamole administration (which reduces cellular uptake of adenosine) increased the pain response, whereas theophylline (a nonspecific adenosine antagonist) reduced the pain response. From these studies and others, it appears that adenosine is a mediator of cardiac and muscular ischemic pain. At one time, a mechanical stimulus (stretching of the coronary arteries) was also proposed as a cause of pain even when ischemia itself was not induced. This was suggested after watching the behavior of laboratory animals whose coronary arteries were stretched. This theory has received increased support because of the observation that during percutaneous transluminal coronary angioplasty (PTCA) in humans, the greater the balloon inflation pressure, the more intense pain in the same individual.

The pioneering somatic pain threshold studies suggested differences between coronary patients either with or without angina during a positive exercise test. Their 3 different modalities of somatic pain perception were studied. When pain perception was determined by an electrical current applied to the thigh, asymptomatic patients had a significantly higher threshold. Subsequent studies from other laboratories confirmed their findings. A central mechanism was suggested in 1996, by using PET scanning to measure cerebral blood flow in patients with and without silent ischemia. On the basis of their data, it was postulated that abnormal central processing of afferent cardiac pain signals could be involved in the pathophysiology of this syndrome.

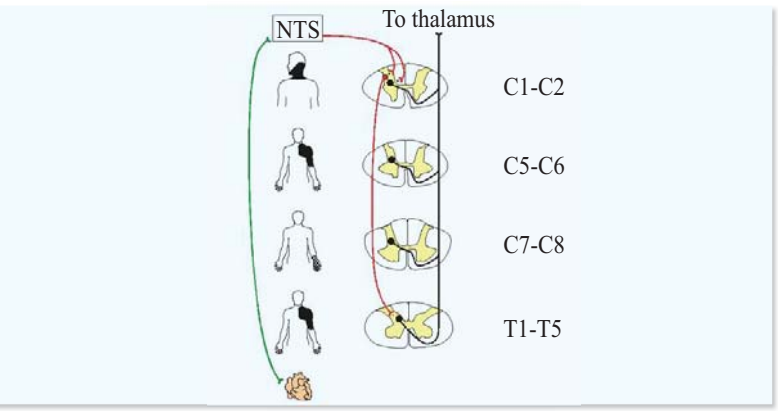



Fig: Vagal pathways to spinothalamic tract cells in upper spinal cord. Vagal pathways are shown (green) with a relay through the nucleus of the solitary tract (NTS. Vagal input probably reaches the T1-T5 segments through a propriospinal relay with cell bodies in the C1-C2 segments (red). Vagal excitation primarily excites spinothalamic tract neurons in C1-C2 and inhibits spinothalamic tract neurons in T1-T5

A possible role for endorphins in cardiac pain responses also has been studied. Varying concentrations of these opioid-like substances exist in plasma and cerebrospinal fluid and may be important in mediating pain sensitivity. The issue is not clear cut, as different laboratories that have measured plasma endorphin levels during and after exercise tests have produced conflicting results, and considerable overlap exists in values between patients with and those without silent ischemia. Data from PTCA studies by have suggested a link between endorphin levels and symptoms, but in another study, found endorphin release to be common during both spontaneous and provoked acute myocardial ischemia and to have no correlation with intensity of chest pain. Thus, the evidence linking endorphins to silent myocardial ischemia is suggestive but not conclusive. This is true in non diabetics as well as diabetics. Diabetics also have overt neuropathy as an additional contributing factor to their silent ischemia, although in many instances the neuropathy is subclinical and can only be detected by demonstration of autonomic impairment. According to a recent study, the combination of microalbuminuria and silent ischemia in asymptomatic diabetics identifies a particularly high-risk subgroup for future cardiac events.

Benzodiazepines have been shown to interact with opioid antinociception. Considering the importance of inflammation and leukocytes in myocardial ischemia, the expression of peripheral benzodiazepine receptors on leukocytes may be different in patients with and without angina during myocardial ischemia. Recently a study suggested that the expression of these receptors was indeed higher in patients with silent ischemia, also studied production of inflammatory cytokines in a similar patient population and reported that an "anti-inflammatory pattern" of cytokine production was observed in the patients with silent ischemia. So it concluded that the activation of the immune-inflammatory system may be crucial for production of anginal symptoms.

**Hemodynamic studies**

Hemodynamic abnormalities during silent ischemia unlike the endorphin controversy, this is an area where increasing data have proven useful in clarifying physiological mechanisms and it is apparent that hemodynamic abnormalities occur first and that pain follows electrocardiographic changes and is the final event in the sequence of events that characterizes an episode of myocardial ischemia. Holter monitoring has also proven useful in clarifying pathophysiologic mechanisms during silent ischemia. Early studies of ambulatory ischemia noted that almost 80% of total ischemic episodes were silent and that most of the asymptomatic episodes were short, whereas the symptomatic ones were just as likely to be long as short. As more and more studies using the Holter monitor have been published, it is apparent that there is a circadian variation in ischemic episodes, with most coming after arousal in the morning, or waking and rising at night. This circadian variation is the same in both men and women. What triggers myocardial ischemia during certain activities and not during others? This is a question to which ambulatory ECG monitoring has helped provide answers by correlating ECG data to diaries of daily events, concurrent drawing of blood catecholamines, etc. A relation to enhanced platelet aggregation or variations in vascular tone has been suggested. The importance of physical exertion, anger, smoking, and mental stress has all been well documented with the latter receiving special attention. It concluded that "autonomic change consistent with vagal withdrawal can act as a precipitating factor for daily life ischemia in episodes triggered by mental activity." One of the most intriguing physiological observations has been the steady increase in heart rate preceding the ischemic episode.

Even when not frankly tachycardia, this increased heart rate varies suggests more of a "demand" than "supply" imbalance as a basis for many of the episodes that were once thought to be vasospastic in origin. Documenting silent ischemia in patients with true variant angina represents a unique problem because in its purest form ST elevation is the predominant finding. Criteria for ST elevation on the ambulatory ECG are not as well developed as for ST depression, but it is generally accepted that the abnormality should be profound (>2 mm) to be considered significant.

## Risk factors

Factors that may increase risk of developing silent myocardial ischemia include:

- Tobacco: Smoking and long-term exposure to secondhand smoke damage the interior walls of arteries - including arteries of the heart - allowing deposits of cholesterol and other substances to collect and slow blood flow. Smoking also increases the risk of blood clots forming in the arteries that can cause myocardial ischemia.

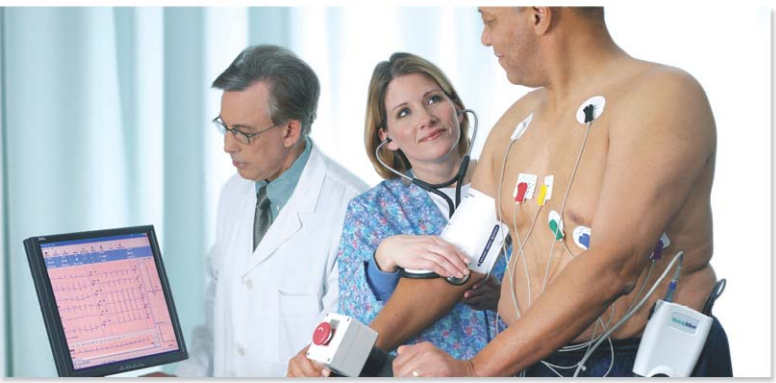


Fig: Exercise Treadmill Test (ETT)

- Diabetes: Diabetes is linked to an increased risk of myocardial ischemia, heart attack and other heart problems.
- Hypertension: Over time, high blood pressure can damage arteries that feed the heart by accelerating atherosclerosis.
- Dyslipidaemia: Cholesterol is a major part of the deposits that can narrow arteries throughout the body, including those that supply the heart. A high level of LDL cholesterol in blood is linked to an increased risk of atherosclerosis and myocardial ischemia. A high LDL level may be due to an inherited condition or a diet high in saturated fats and cholesterol. A high level of triglycerides, may also contribute to atherosclerosis.
- Lack of physical activity: An inactive lifestyle contributes to obesity and is associated with higher cholesterol and triglycerides and an increased risk of atherosclerosis.
- Obesity: Obese people have a high proportion of body fat, often with a body mass index of 30 or higher. Obesity raises the risk of myocardial ischemia because it's associated with high blood cholesterol levels, high blood pressure and diabetes.
- Family history: Positive family history of heart attack or coronary artery disease may be at increased risk of myocardial ischemia.

## Clinical assessment

On SMI, a large percentage of patients with ischemic heart disease have both symptomatic and silent episodes. Symptomatic ischemia may not present with classic anginal symptoms but with anginal equivalents such as

- Dyspnea
- Fatigue
- Palpitations
- Chest pain

Additional symptoms may include palpitations and fatigue Patients may describe fatigue as an inability to walk long distances or as feeling a sudden onset of weakness. Obtain a detailed history, including subjective changes as detailed above, and note any cardiovascular risk factors. Patients who exhibit these symptoms may need to be evaluated for CAD.

## Modalities in the diagnosis of SMI

The exercise treadmill test (ETT) and ambulatory (Holter) monitoring are the most readily available and frequently used tests to identify silent ischemia in clinical practice. Exercise testing Exercise testing appears to be the most suitable laboratory diagnostic test to document silent myocardial ischemia in asymptomatic individuals such as patients with no history of CHD and in those with a history of CHD or exertional angina. Exercise testing is frequently used to screen high risk, asymptomatic persons to identify those with asymptomatic CHD.

**Exercise ECG:** ECG during ETT was performed by using 12 standard leads on a treadmill according to Bruce protocol. The protocol had seven stages, each lasting 3 min resulting in 21 minute exercise for a complete test.

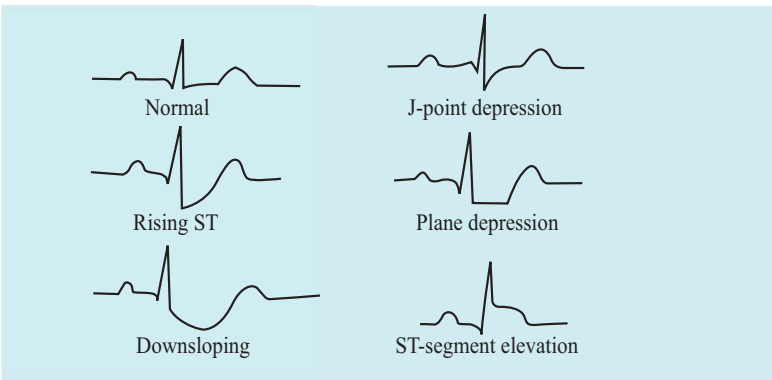



Fig: Variation of ECG in SMI

The exercise test was considered positive if there was a horizontal and down slopping ST segment depression of at least 1 mm occurring at least 0.08s after the J point. The test was considered negative when the heart reached the maximal predicted exercise heart rate (calculated without a change in ST segment with the ASTRAND formula, 220 - age) without a change in ST segment.

Conventional ST segment analysis during ETT is moderately sensitive in detecting CHD. However, it has low specificity because of an unacceptably high rate (10 to 35 percent) of false positive responses, particularly in asymptomatic persons and especially in women. As a result, the diagnosis of myocardial ischemia by ETT in asymptomatic individuals must be confirmed by radionuclide imaging techniques that is thallium perfusion scintigraphy or exercise ventriculography before the subject is labeled as having silent ischemia.

**Holter monitoring**: Holter monitoring is the second most frequently used diagnostic test for silent ischemia. It has the advantage of providing long-term ECG recording of ischemic and arrhythmic events while patients are engaged in routine daily activities out of the hospital. An ACC/AHA task force has published guidelines for the use of ambulatory monitoring in the assessment of silent ischemia. Episodes of transient ischemia during Holter monitoring are diagnosed by a sequence of ECG changes that include a flat or downsloping ST depression of at least 1 mm, with a gradual onset and offset that lasts for at least one minute. Although ST segment depression during Holter monitoring has not always been accepted as unequivocal evidence of myocardial ischemia, recent studies have shown an excellent correlation between ST depression recorded during Holter monitoring, and other simultaneous objective evidence of ischemia by perfusion scintigraphy, radionuclide cardioangiography, and hemodynamic monitoring.

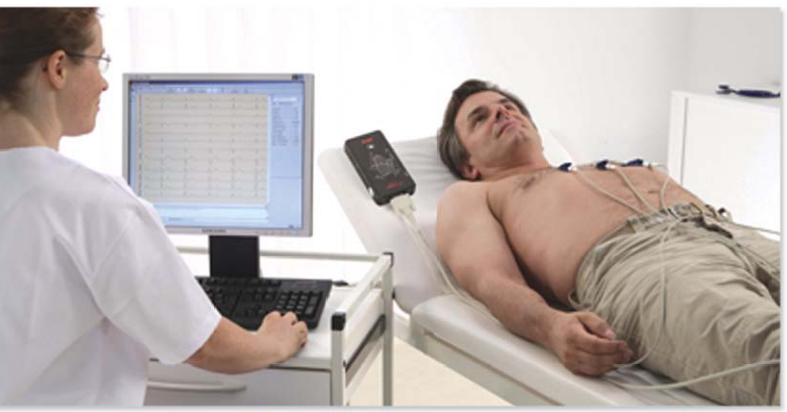


Fig: Holter Monitoring

One potential limitation to the use of outpatient Holter monitoring, especially for the evaluation of therapeutic interventions, is the marked day to day variability in the frequency and duration of ST depression and ischemic episodes. In one study, for example, 45 percent of patients had variability in frequency of ST depression while 42 percent showed variability in the duration of ischemia.

Although Holter monitoring is useful in further stratification of patients with a positive exercise test, it is important to emphasize that exercise testing remains the preferred diagnostic modality for initial identification of patients with silent ischemia. In this context it is also important to note that only a small fraction of patients with negative findings on exercise testing will demonstrate evidence of ischemia on Holter monitoring.

**Nuclear and echocardiographic imaging studies**: Tests other than routine ETT and ambulatory monitoring may be necessary in certain circumstances. As an example, nuclear imaging tests such as stress thallium scintigraphy or exercise radionuclide ventriculography are recommended for the evaluation of silent myocardial ischemia in patients who have an abnormal baseline ECG (e.g., left ventricular hypertrophy or strain, bundle branch block, preexcitation syndrome), and those receiving digitalis, phenothiazines, or other drugs that produce repolarization changes. Pharmacologic stress tests with dipyridamole or adenosine plus thallium scintigraphy, or dobutamine stress echocardiography, can be utilized in those patients who are unable to ambulate or exercise (e.g., due to advanced peripheral vascular disease).

However, all of these tests are costly and have limitations. It is therefore essential at the outset to critically evaluate the need for these tests and predetermine the steps to be taken based upon the results of the given test.

**Electron beam computed tomography**: The severity of coronary artery calcification on electron beam computed tomography (EBCT), as determined by a calcium score, can identify asymptomatic patients at high risk for coronary heart disease.

## Treatment

Because SMI increases the risk of cardiovascular events, it is reasonable to use pharmacological therapy in an attempt to decrease the patient's total ischemic burden.

**β-Blockers:** These seem to be the most effective agents; they reduce the incidence, frequency, duration, and severity of silent ischemia. The Atenolol Silent Ischemia Study (ASIST) evaluated the effects of atenolol in asymptomatic or mildly symptomatic patients who had abnormal results on exercise thallium testing and silent ischemia documented by ambulatory ECG monitoring treatment with atenolol, 100 mg/day, reduced daily ischemia, as well as the risk of future adverse cardiac events at 1 year. Another effective treatment is to combine a long-acting β-blocker with a long-acting nitrate.

Anti-ischemic efficacy can be evaluated by repeated Holter monitoring and titrating drug doses until the ischemic burden is suppressed by at least 50% or the maximum tolerated dose of a β-blocker is attained.

**Calcium channel blockers**: These agents, specifically amlodipine, long-acting nifedipine, and short- or long-acting diltiazem, have been shown to reduce ischemic episodes by 13% to 69%, and to decrease the duration of episodes by 6% to 68%. Combining a long-acting dihydropyridine calcium channel blocker (CCB) with a β-blocker has proved superior to either agent alone in reducing ischemia. If β-blocker therapy is not an option because of adverse effects or contraindications, consider combining a long-acting dihydropyridine CCB and a long-acting nitrate.

**Revascularization**: This is achieved with either percutaneous coronary interventions or coronary artery bypass grafting (CABG). Revascularization, regardless of the method, has not conclusively reduced the risk of MI or cardiovascular death in patients with chronic stable angina and preserved LV systolic function.

Consider revascularization for patients with unacceptably frequent or severe angina that has not responded to optimized medical therapy, and for patients with such high-risk features as symptomatic multivessel disease, proximal left anterior descending or left main artery disease, LV systolic dysfunction, diabetes, a large area of myocardium at jeopardy on nuclear or echocardiographic stress testing, early onset of ischemia on stress testing, or ST segment depression of 2 mm or more.

Revascularization currently is not recommended for patients without anginal symptoms unless they meet the above criteria. Focus instead on steps to modify risk factors, such as blood pressure control, lipid lowering, smoking cessation, and lifestyle modifications including diet and exercise.

## Prevention

In addition to other treatments, it is recommended that to adopt a heart-healthy lifestyle.

- Cessation of smoking.
- Avoid secondhand smoke. Secondhand smoke can damage the lining of arteries and increase the risk of developing myocardial ischemia.
- Control underlying health diseases. Treat diseases that can increase risk of myocardial ischemia, such as diabetes, hypertension and high blood cholesterol.
- Eat a healthy diet with limited amounts of saturated fat, lots of whole grains, and many fruits and vegetables.
- Exercise can improve blood flow to the heart. Before that one should consult with the physician about starting a safe exercise plan.
- Maintain a healthy weight.
- Decrease stress. Reduce stress as much as possible. Practice healthy techniques for managing stress, such as muscle relaxation and deep breathing.

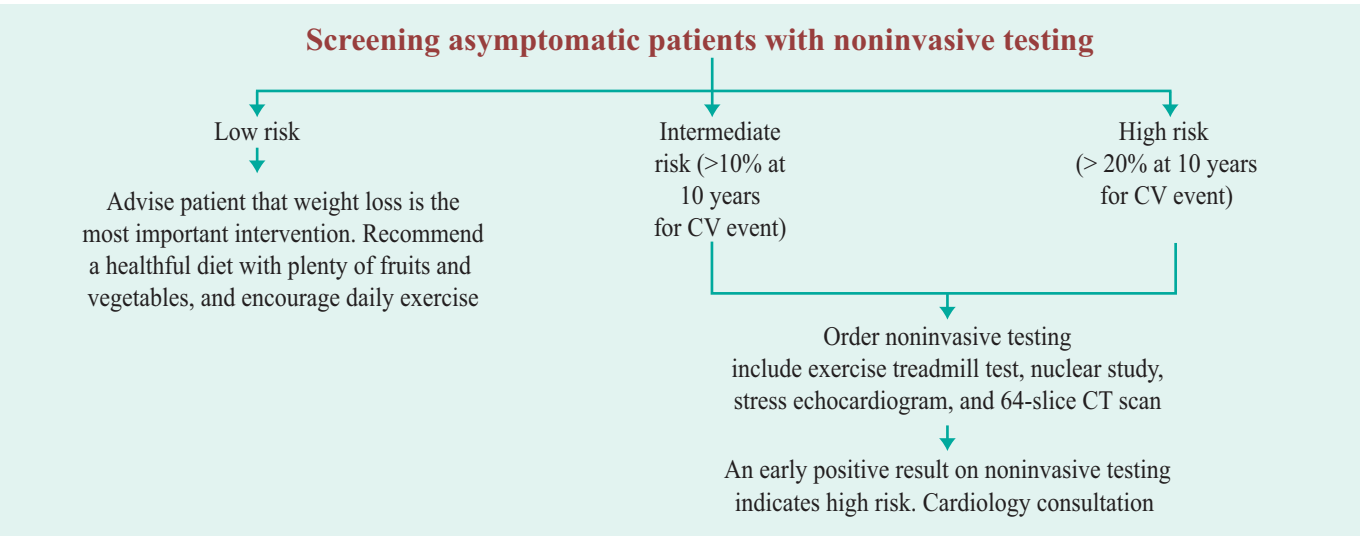
## Prognostic significance of SMI

**SMI and cardiovascular risk:** Patients presenting with SMI, 62% had 3-vessel CAD with abnormal LV function and experienced subsequent MI or sudden death, compared with only 10% of patients with 1-vessel CAD and preserved LV function.

**SMI and chronic stable angina:** Forty-six patients (43%) had evidence of SMI during monitoring by 24 hour ambulatory ECG monitoring while receiving antianginal medications

**SMI and unstable angina:** Unstable angina whose symptomatic ischemia had been nearly eliminated with therapy. In this population, persistent SMI evident on Holter monitoring was associated with more severe CAD. Compared with patients in whom SMI was absent, those with SMI were more likely to experience early (within 30 day s) adverse outcomes of MI or recurrent symptoms requiring revascularization, as well as late (after 2 years) adverse outcomes including death or recurrent MI. Similar observations were evident in patients after recent angioplasty.

**SMI following MI:** Unstable angina or MI found that 75% of the patients had evidence of SMI.




**SMI without documented CAD or angina:** 8.2% had a positive ETT and over the next 7.4 years (mean) the mortality rate from CHD was 6.7% (21/315) in the positive ETT group and 1.3% (46/3460) in the negative ETT group.

*References*
*1. Consult live; Consultant. Vol. 49 No. 2*
*2. American Heart Association*
*3. www.bjmu.edu.cn*
*4. BSMMU J 2012; 5(1):42-45]*
*5. http://www.consultant360.com*

# Positive Pressure Ventilation with a face mask and a bag valve device

## Indications

Providing positive pressure ventilation with a face mask and a bag valve device can be a lifesaving maneuver. Although seemingly simple, the technique requires an understanding of the airway anatomy, the equipment, and the indications.

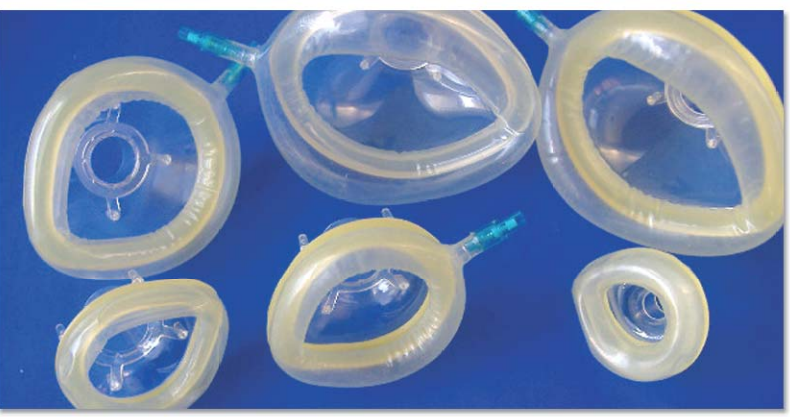


Fig: Different sizes of face mask

- Face-mask ventilation is used in patients who have respiratory failure but are still breathing spontaneously and in patients with complete apnea.
- Face-mask ventilation can be indicated in any situation in which spontaneous breathing is failing or has ceased, including cardiopulmonary arrest.

## Equipment

- There are many types of face masks, varying in design, size, and construction materials. Transparent masks are preferred because they allow for inspection of lip color, condensation, secretions, and vomitus. To maintain a good seal, the mask's size and shape must conform to the facial anatomy.

Fig: Positioning the mask

- Various bag-valve designs are available. All have a self-inflating bag and a non re-breathing, unidirectional valve. The valve is designed to function during both spontaneous and manually controlled ventilation. Because bag-valve devices can operate without an oxygen source, it is important to ascertain that supplemental oxygen is flowing through the bag-valve device when supplemental oxygen is indicated and available.
- Test the bag-valve device's capability for delivering positive-pressure ventilation before use. This can be achieved by sealing the bag-valve device connector with your thumb and squeezing the bag with reasonable force. If it is difficult to compress the bag or if air is forced between the connector and your thumb, positive pressure can be delivered.
- Whenever possible during face-mask ventilation, suction should be readily available. Disposable oral or nasal airways may be used for airway- management.
- Before beginning face-mask ventilation, examine the patient's oral cavity.

## One-hand technique

- The most common method used to hold the mask requires placing the thumb and index finger on the body of the mask while the other fingers pull the jaw forward and extend the head. Place the middle and ring fingers on the ridge of the mandible and the fifth finger behind the angle of the mandible.
- The tongue is the most common cause of airway obstruction. It is important to minimize the pressure applied to the submandibular soft tissues because pressure may further obstruct the airway by pushing the tongue against the palate.

## Two-hand technique

- It is difficult or impossible to maintain an adequate seal with only one hand in the case of obese or edentulous patients or those with abundant facial hair. In these situations, hold the mask with two hands, with each hand positioned as described in the one-hand technique. A second person should compress the bag-valve device.
- Regardless of the technique to ventilate the patient with a face mask, assess adequate ventilation by inspecting and auscultating the chest and abdomen. The rising and falling of the chest and breath sounds synchronous with the delivered tidal volume suggest adequate ventilation. Epigastric sounds and abdominal distension indicate gastric insufflation and poor ventilation.

## Using oropharyngeal and nasopharyngeal airways

- Occasionally, it may be difficult or impossible to provide ventilation unless a disposable oral or nasal airway is inserted. These devices are most helpful when the cough and gag reflexes are absent. Insertion in patients with intact reflexes

may precipitate coughing, vomiting, and laryngospasm. When the use of a disposable oral or nasal airway is necessary, must select the appropriate-sized device to avoid worsening the airway obstruction. Estimate the correct size of an oral airway by holding it next to the patient's mouth. The tip should reach the angle of the mandible.

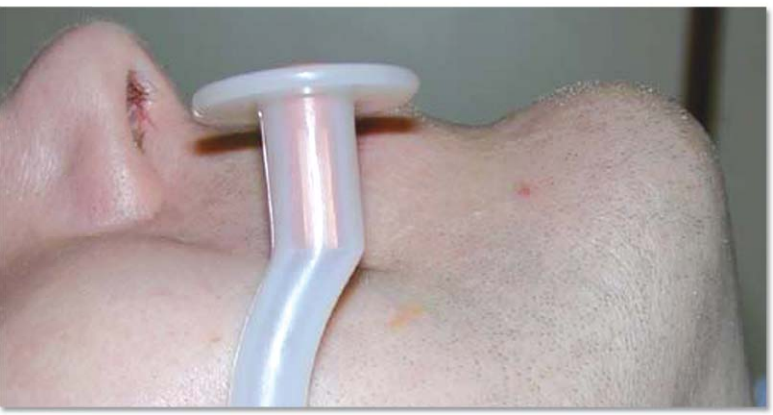


Fig: Measuring the oral airway

- Insert the oropharyngeal airway by depressing the tongue with a tongue blade and advancing the airway toward the base of the tongue. Alternatively, insert the airway upside down and then rotate it 180 degrees as it is being advanced posteriorly.
- Nasopharyngeal airways are better tolerated than oral airways when airway reflexes are present. They are useful when the patient's mouth cannot be opened. The simplest method of estimating their appropriate length is by correlating it with the external anatomy of the face and neck. Nasopharyngeal airways should be lubricated and advanced perpendicular to the face. Use them only with extreme caution in patients with facial injuries, basilar skull fractures, and coagulopathy, weighing the risk of further injury and bleeding against the need for oxygenation.
- When the patient is breathing spontaneously, must synchronize the delivered tidal volume with the patient's inspiration.

## Complications

- Corneal abrasions and blindness in the presence of eye injury
- Soft-tissue injuries, including injuries to the nose and lips, may result when excessive pressure is applied.

## Contraindications

Face-mask ventilation is rarely contraindicated. However, caution is advised in patients with

- Severe facial trauma
- Eye injuries
- Foreign material (e.g., gastric contents) in the airway may lead to aspiration pneumonitis.

## Summary

Discontinuation of face-mask ventilation depends on clinical circumstances. Patients may require a more permanent or effective method of airway management, such as endotracheal intubation or tracheostomy. On other occasions, all that is needed for patients to recover completely is effective face-mask ventilation with oxygen.

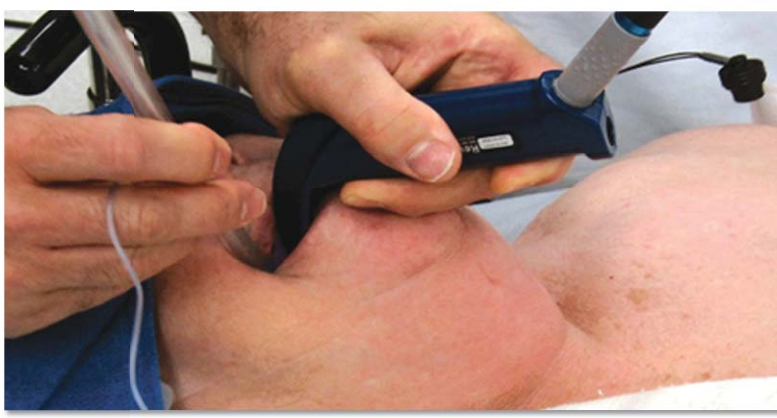


Fig: Procedure

*Reference: The New England Journal of Medicine, July 26, 2007*

## Info Quiz Participants

- Have you selected the correct answer (s) You still have time to put your entry submission together for Info Quiz Prize
- The closing date for entries is 16 August 2013
- We look forward to receiving your winning entry

**Info Quiz Answers**
**April-June 2013**

| | | | | |
|---|---|---|---|---|
| 1. d | 2. a | 3. b | 4. b | 5. d |
| 6. a | 7. c | 8. c | 9. b | 10. c |

# Essentials of Evidence Based Clinical Practice

## Section-3

### Three ways to use the medical literature

Consider a medical student, early in her training, seeing a patient with newly diagnosed diabetes mellitus. She will ask questions such as the following: What is type 2 diabetes mellitus? Why does this patient have polyuria? Why does this patient have numbness and pain in his legs? What treatment options are available? These questions address normal human physiology and the pathophysiology associated with a medical condition.

Traditional medical textbooks that describe underlying physiology, pathology, epidemiology, and general treatment approaches provide an excellent resource for addressing these background questions. The sorts of questions that seasoned clinicians usually ask require different resources.

### Browsing

A general internist scanning the September/October 2005 ACP Journal Club (http://www.acponline.org/journals/acpjc/ jcmenu.htm) comes across the following articles: "Intensive Insulin-Glucose Infusion Regimens With Long-Term or Standard Glucose Control Did Not Differ for Reducing Mortality in Type 2 Diabetes Mellitus and MI," and "Review: Mixed Signals From Trials Concerning Pharmacologic Prevention of Type 2 Diabetes Mellitus."

This internist is in the process of asking a general question-what important new information should I know to optimally treat my patients? Traditionally, clinicians address this question by subscribing to a number of target medical journals in which articles relevant to their practice appear. They keep up to date by skimming the table of contents and reading relevant articles. This traditional approach to what we might call the browsing mode of using the medical literature has major limitations of inefficiency and resulting frustration. Evidence-based medicine offers solutions to this problem.

The most efficient strategy is to restrict your browsing to secondary journals. For internal and general medicine, ACP Journal Club publishes synopses of articles that meet criteria of both clinical relevance and methodologic quality. We describe such secondary journals in more detail in Section 4, Finding the Evidence.

Some specialties (primary care, mental health) and subspecialties (cardiology, gastroenterology) already have their own devoted secondary journals; others do not. The New York Academy of Medicine keeps a current list of available secondary journals in many health care disciplines (http://www.ebmny.org/journal.html). If you are not yet fortunate enough to have your own, you can apply your own relevance and methodologic screen to articles in your target specialty or subspecialty journals. When you have learned the skills, you will be surprised at the small proportion of studies to which you need attend and at the efficiency with which you can identify them.

### Problem solving

Experienced clinicians confronting a patient with diabetes mellitus will ask questions such as, In patients with new-onset type 2 diabetes mellitus, which clinical features or test results predict the development of diabetic complications? In patients with type 2 diabetes mellitus requiring drug therapy, does starting with metformin treatment yield improved diabetes control and reduce long-term complications better than other initial treatments? Here, clinicians are defining specific questions raised in caring for patients and then consulting the literature to resolve these questions.

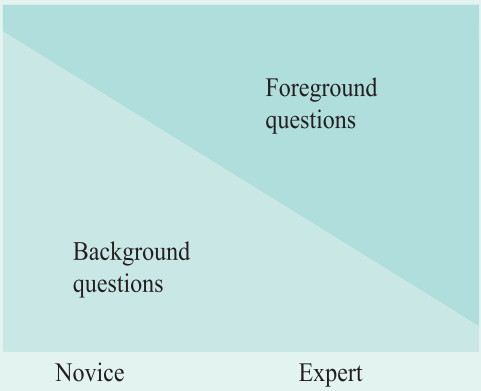
### Background and foreground questions

One can think of the first set of questions, those of the medical student, as background questions and of the browsing and problem-solving sets as foreground questions. In most situations, you need to understand the background thoroughly before it makes sense to address foreground issues.

A seasoned clinician may occasionally require background information, which is most likely when a new condition or medical syndrome appears ("What is SARS?") or when a new diagnostic test ("How does PCR work?") or treatment modality ("What are atypical antipsychotic agents?") appears in the clinical arena.

Figure 3-1

**Background and Foreground questions**




## Clarifying your question

### The structure: Patients, Exposure, Outcome

Clinical questions often spring to mind in a form that makes finding answers in the medical literature a challenge. Dissecting the question into its component parts to facilitate finding the best evidence is a fundamental skill. One can divide most questions into 3 parts: the patients, the intervention or exposure, and the outcome (Table 3-1).

### Five types of clinical questions

In addition to clarifying the population, intervention or exposures, and outcome, it is productive to label the nature of the question that you are asking. There are 5 fundamental types of clinical questions:

1. Therapy: determining the effect of interventions on patient-important outcomes (symptoms, function, morbidity, mortality, costs)
2. Harm: ascertaining the effects of potentially harmful agents (including therapies from the first type of question) on patient-important outcomes
3. Differential diagnosis: in patients with a particular clinical presentation, establishing the frequency of the underlying disorders
4. Diagnosis: establishing the power of a test to differentiate between those with and without a target condition or disease
5. Prognosis: estimating a patient's future course

### Finding a suitably designed study for your question type

You need to correctly identify the category of study because, to answer your question, you must find an appropriately designed study. If you look for a randomized trial to inform you of the properties of a diagnostic test, you are unlikely to find the answer you seek. We will now review the study designs associated with the 5 major types of questions.

To answer questions about a therapeutic issue, we identify studies in which a process analogous to flipping a coin determines participants' receipt of an experimental treatment or a control or standard treatment, a randomized controlled trial (RCT). Once investigators allocate participants to treatment or control groups, they follow them forward in time to determine whether they have, for instance, a stroke or heart attack-what we call the outcome of interest (Figure 3-2).

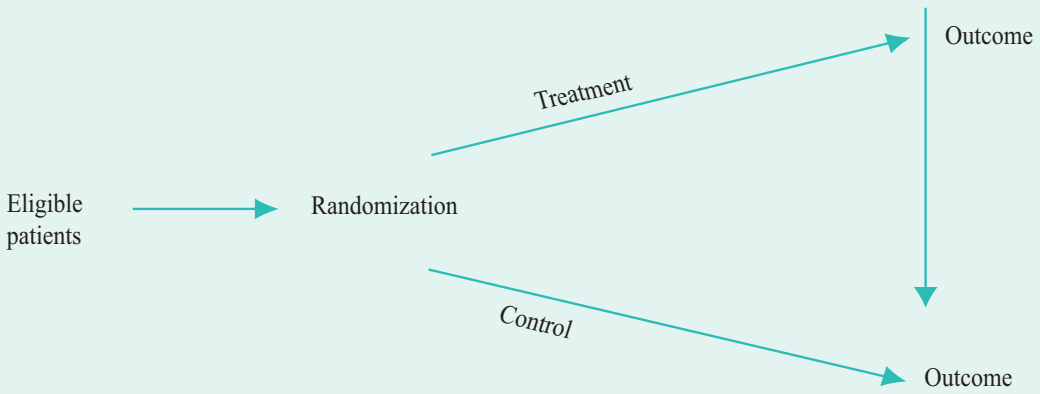
Table 3-1

**Framing clinical questions**

1. *The population.* Who are the relevant patients?
2. *The interventions or exposures* (diagnostic tests, foods, drugs, surgical procedures, time, risk factors, etc). What are the management strategies we are interested in comparing or the potentially harmful exposures about which we are concerned? For issues of therapy, prevention, or harm, there will always be both an experimental intervention or putative harmful exposure and a control, alternative, or comparison intervention or state to which it is compared.
3. *The outcome.* What are the patient-relevant consequences of the exposures in which we are interested? We may also be interested in the consequences to society, including cost or resource use. It may also be important to specify the period of interest.

**Figure 3-2**

## Structure of Randomized Trials




Ideally, we would also look to randomized trials to address issues of harm. For many potentially harmful exposures, however, randomly allocating patients is neither practical nor ethical. For instance, one cannot suggest to potential study participants that an investigator will decide by the flip of a coin whether or not they smoke during the next 20 years. For exposures like smoking, the best one can do is identify studies in which personal choice, or happenstance, determines whether people are exposed or not exposed. These observational studies (often subclassified as cohort or case-control studies) provide weaker evidence than randomized trials.

Figure 3-3 depicts a common observational study design in which patients with and without the exposures of interest are followed forward in time to determine whether they experience the outcome of interest. For smoking, one important outcome would likely be the development of cancer. For sorting out differential diagnosis, we need a different study design (Figure 3-4). Here, investigators collect a group of patients with a similar presentation (painless jaundice, syncope, headache), conduct an extensive battery of tests, and, if necessary, follow patients forward in time. Ultimately, for each patient they hope to establish the underlying cause of the symptoms and signs with which the patient presented.

**Figure 3-3**

## Structure of Observational Cohort studies

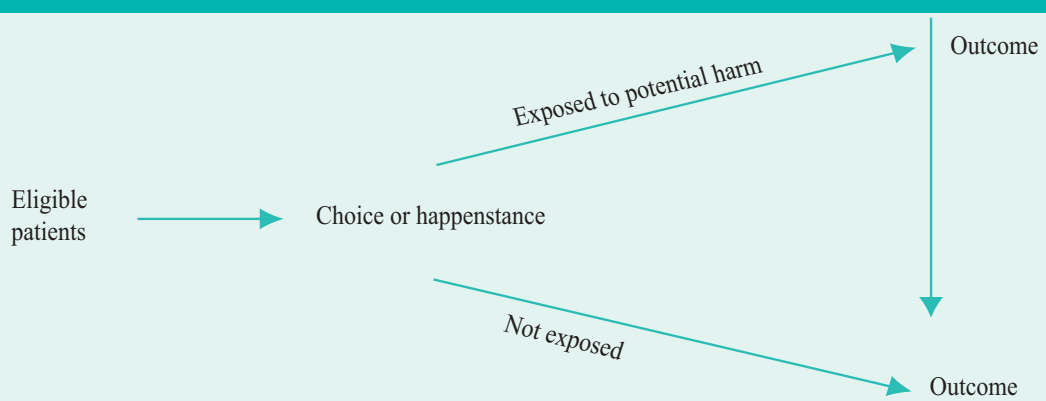



**Figure 3-4**

## Structure for studies of differential diagnosis

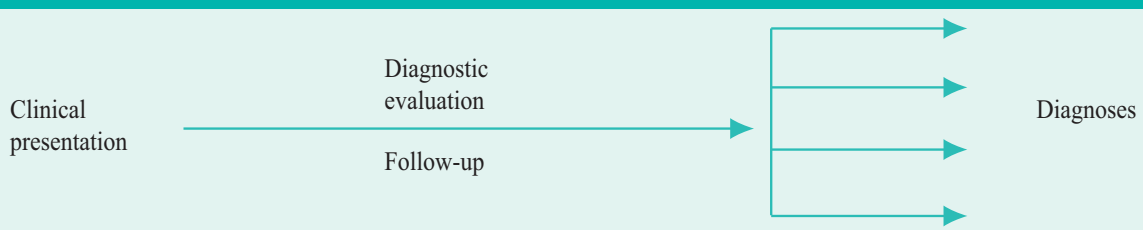
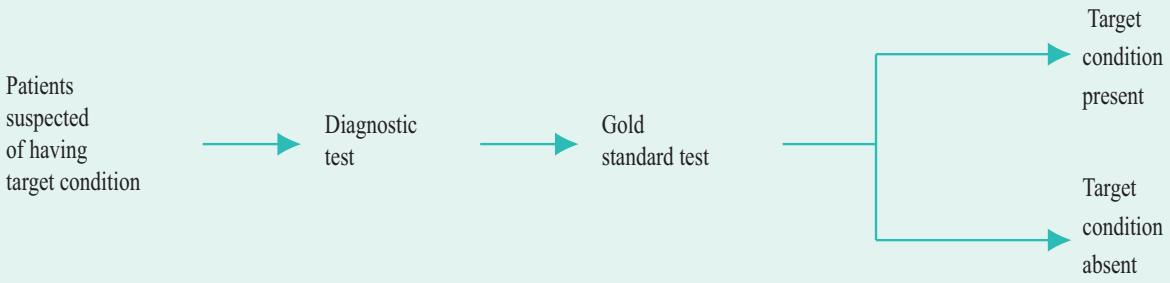


**Figure 3-5**

## Structure for studies of diagnostic test properties




Establishing the value of a particular diagnostic test (what we call its properties or operating characteristics) requires a slightly different design (Figure 3-5). In diagnostic test studies, investigators identify a group of patients in whom they suspect a disease or condition of interest exists (such as tuberculosis, lung cancer, or iron-deficiency anemia), which we call the target condition. These patients undergo the new diagnostic test and a reference standard, gold standard, or criterion standard. Investigators evaluate the diagnostic test by comparing its classification of patients with that of the reference standard (Figure 3-5).

A final type of study examines a patient's prognosis and may identify factors that modify that prognosis. Here, investigators identify patients who belong to a particular group (such as pregnant women, patients undergoing surgery, or patients with cancer) with or without factors that may modify their prognosis (such as age or comorbidity). The exposure here is time, and investigators follow patients to determine whether they experience the target outcome, such as a problem birth at the end of a pregnancy, a myocardial infarction after surgery, or survival in cancer (Figure 3-6).

### Three examples of question clarification

We will now provide examples of the transformation of unstructured clinical questions into the structured questions that facilitate the use of the medical literature.

**Example 1:** Diabetes and target blood pressure-
A 55-year-old white woman presents with type 2 diabetes mellitus and hypertension. Her glycemic control is excellent with metformin, and she has no history of complications. To manage her hypertension, she takes a small daily dose of a thiazide diuretic. During a 6-month period, her blood pressure is near 155/88 mm Hg.

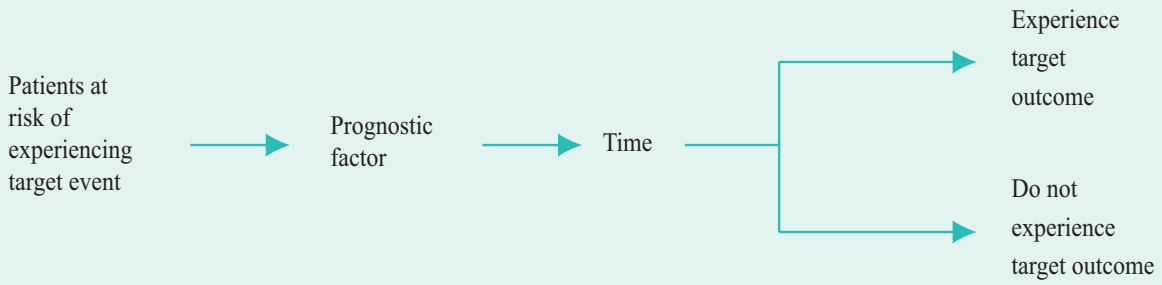
**Initial question:** When treating hypertension, at what target blood pressure should we aim?

Digging deeper: One limitation of this formulation of the question is that it fails to specify the population in adequate detail. The benefits of tight control of blood pressure may differ in diabetic patients vs nondiabetic patients, in type 1 vs type 2 diabetes, and in patients with and without diabetic complications.

The detail in which we specify the patient population is a double-edged sword. On the one hand, being very specific (middle-aged women with uncomplicated type 2 diabetes) will ensure that the answer we get is applicable to our patients. We may, however, fail to find any studies that restrict themselves to this population. The solution is to start with a specific patient population but be ready to drop specifications to find a relevant article.

**Figure 3-6**

## Structure of studies of prognosis



In this case, we may be ready to drop the "female," "middle-aged," "uncomplicated," and "type 2," in that order. If we suspect that optimal target blood pressure may be similar in diabetic and nondiabetic patients, and it proves absolutely necessary, we might drop the "diabetes."

We may wish to specify that we are interested in the addition of a specific antihypertensive agent. Alternatively, the intervention of interest may be any antihypertensive treatment. Furthermore, a key part of the intervention will be the target for blood pressure control. For instance, we might be interested in knowing whether it makes any difference if our target diastolic blood pressure is less than 80 mm Hg vs less than 90 mm Hg. Another limitation of the initial question formulation is that it fails to specify the criteria by which we will judge the appropriate target for our hypertensive treatment.

**Improved (searchable) questions:**

- **A question of Therapy**
  - Patients: Hypertensive type 2 diabetic patients without diabetic complications.
  - Intervention: Any antihypertensive agent aiming at a target diastolic blood pressure of 90 mm Hg vs a comparison target of 80 mm Hg.
  - Outcomes: Stroke, myocardial infarction, cardiovascular death, total mortality.

**Example 2:** Transient loss of consciousness-

A 55-year-old man, previously well, although a heavy drinker, presents to the emergency department with an episode of transient loss of consciousness. On the evening of presentation, he had his usual 5 beers and started to climb the stairs at bedtime. The next thing he remembers is being woken by his son, who found him lying near the bottom of the stairs. The patient took about a minute to regain consciousness and remained confused for another 2 minutes. His son did not witness any shaking, and there had not been any incontinence. Physical examination result was unremarkable; the electrocardiogram showed a sinus rhythm with a rate of 80/min and no abnormalities. Glucose, sodium, and other laboratory results were normal.

**Initial question:** How extensively should I investigate this patient?

Digging deeper: The initial question gives us little idea of where to look in the literature for an answer. As it turns out, there is a host of questions that could be helpful in choosing an optimal investigational strategy. We could, for instance, pose a question of differential diagnosis: If we knew the distribution of ultimate diagnoses in such patients, we could choose to investigate the more common and omit investigations targeted at remote possibilities.

Other information that would help us would be the properties of individual diagnostic tests. If an electroencephalogram were extremely accurate for diagnosing a seizure, or a 24-hour Holter monitor for diagnosing arrhythmia, we would be far more inclined to order the tests than if they missed patients with the underlying problems or falsely labeled patients without the problems.

Alternatively, we could ask a question of prognosis. If patients like ours had a benign prognosis, we might be much less eager to investigate extensively than if patients tended to do badly. Finally, the ultimate answer to how intensively we should investigate might come from a randomized trial in which patients similar to this man were allocated to more vs less intensive investigation.

**Improved (searchable) questions:**

- **A question of differential diagnosis**
  - Patients: Middle-aged patients presenting with transient loss of consciousness.
  - Intervention/Exposure: Thorough investigation and follow-up.
  - Outcomes: Frequency of underlying disorders such as vasovagal syncope, seizure, arrhythmia, and transient ischemic attack.
- **A question of diagnosis**
  - Patients: Middle-aged patients presenting with transient loss of consciousness.
  - Intervention/Exposure: Electroencephalogram.
  - Outcomes: Gold standard investigation (probably long-term follow-up).
- **A question of prognosis**
  - Patients: Middle-aged patients presenting with transient loss of consciousness.
  - Intervention/Exposure: Time.
  - Outcomes: Morbidity (complicated arrhythmias or seizures, strokes, serious accidents) and mortality in the year after presentation.
- **A question of therapy**
  - Patients: Middle-aged patients presenting with loss of consciousness.
  - Intervention/Exposure: Comprehensive investigation vs a comparator of minimal investigation.
  - Outcomes: Morbidity and mortality in the year after presentation.

**Example 3:** Squamous cell carcinoma-

A 60-year-old man with a 40-pack-year smoking history presents with hemoptysis. A chest radiograph shows a parenchymal mass with a normal mediastinum, and a fine-needle aspiration of the mass shows squamous cell carcinoma. Aside from hemoptysis, the patient is asymptomatic and physical examination result is entirely normal.

**Initial question:** What investigations should we undertake before deciding whether to offer this patient surgery?

Digging deeper: The key defining features of this patient are his non-small cell carcinoma and the fact that his medical history, physical examination, and chest radiograph show no evidence of intrathoracic or extrathoracic metastatic disease. Alternative investigational strategies address 2 separate issues: Does the patient have occult mediastinal disease, and does he have occult extrathoracic metastatic disease? For this discussion, we will focus on the former issue. Investigational strategies for addressing the possibility of occult mediastinal disease include undertaking a mediastinoscopy or performing a computed tomographic (CT) scan of the chest and proceeding according to the results of this investigation.

What outcomes are we trying to influence in our choice of investigational approach? We would like to prolong the patient's life, but the extent of his underlying tumor is likely to be the major determinant of survival, and our investigations cannot change that. We wish to detect occult mediastinal metastases if they are present because, if the cancer has spread to the mediastinum, resectional surgery is unlikely to benefit the patient. Thus, in the presence of mediastinal disease, patients will usually receive palliative approaches and avoid an unnecessary thoracotomy.

We could frame our structured clinical question in 2 ways. One would be asking about the usefulness of the CT scan for identifying mediastinal disease. More definitive would be to ask a question of therapy: what investigational strategy would yield superior clinical outcomes?

**Improved (searchable) questions:**

- **A question of diagnosis**
  - Patients: Newly diagnosed non-small cell lung cancer with no evidence of extrapulmonary metastases.
  - Intervention: CT scan of the chest.
  - Outcome: Mediastinal spread at mediastinoscopy.
- **A question of therapy**
  - Patients: Newly diagnosed non-small cell lung cancer with no evidence of extrapulmonary metastases.
  - Intervention: Mediastinoscopy for all or restricted to those with suspicious lesions on CT scan of the thorax.
  - Outcome: Unnecessary thoracotomy.

**Defining the question: Conclusion**

Constructing a searchable question that allows you to use the medical literature to solve problems is no simple matter. It requires a detailed understanding of the clinical issues involved in patient management. The 3 examples in this section illustrate that each patient encounter may trigger a number of clinical questions and that you must give careful thought to what you really want to know. Bearing the structure of the question in mind-patient, intervention or exposure and control, and outcome-is extremely helpful in arriving at an answerable question. Identifying the type of questions-therapy, harm, differential diagnosis, diagnosis, and prognosis-will further ensure that you are looking for a study with an appropriate design.

Careful definition of the question will provide another benefit: you will be less likely to be misled by a study that addresses a question related to the one in which you are interested, but with 1 or more important differences. For instance, making sure that the study compares experimental treatment to current optimal care may highlight the limitations of trials that use a placebo control. Specifying that you are interested in patient-important outcomes (such as long bone fractures) makes vivid the limitations of studies that focus on substitute or surrogate endpoints (such as bone density). Specifying that you are primarily interested in avoiding progression to dialysis will make you appropriately wary of a composite endpoint of progression to dialysis or doubling of serum creatinine level. You will not reject such studies out of hand, but the careful definition of the question will help you to critically apply the results to your patient care.

A final crucial benefit from careful consideration of the question is that it sets the stage for efficient and effective literature searching to identify and retrieve the best evidence.

*Reference: JAMA evidence, 2nd edition, pp: 17-31*

*In the next issue of Info Medicus we will publish the subsequent sections of Essentials of Evidence Based Clinical Practice.*

# Gynaecomastia, Galactorrhoea and Lung cancer in a man

A 60 year old man presented with right shoulder pain, productive cough, and dyspnoea of 3 months duration, with 5 kg weight loss and anorexia. He was a manual laborer and had no history of chest pain, fever, or haemoptysis. He had smoked 20 bidis (thin hand-rolled cigarette-like tobacco wrapped in dried tend leaf) per day for the past 40 years. He reported no other substance misuse or supplements intake.

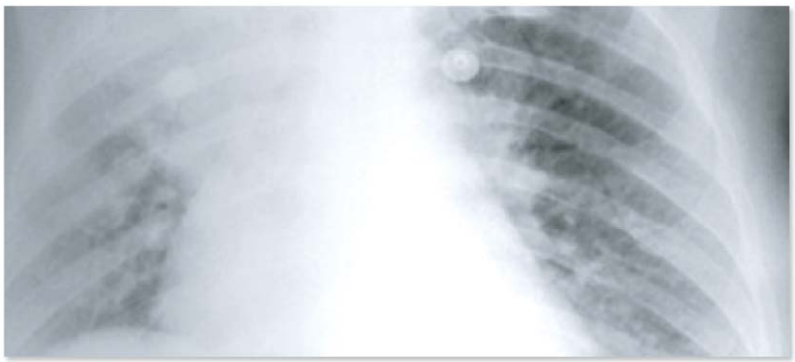


Fig: (A) Chest radiograph showing a large mass involving right upper and middle zones.

On examination, no clubbing or lymphadenopathy was found. Testicular examination was normal. Bilateral gynaecomastia with watery discharge from nipple on squeezing was seen.

Radiography (figure A) and CT of the chest showed a mass lesion 9·9 × 9·4 cm in the right upper lung lobe, with loss of fat planes in the aortic arch and chest wall, multiple nodules in both lower lobes, and enlarged lymph nodes. Fibreoptic bronchoscopy showed a growth in right upper lobe bronchus. Endobronchial biopsy showed squamous cell carcinoma.

Immunohistochemistry for β-HCG (figure B) was positive, and negative for oestrogen and testosterone. Serum β-HCG was 20 000 IU/L (normal <5 IU/L). Serum 17-β oestradiol was 1160 pmol/L (normal 45-609 pmol/L). A urine pregnancy card test was positive. Liver and renal function tests, and serum concentrations of prolactin, testosterone, luteinising hormone, follicle stimulating hormone, thyroid stimulating hormone, and cortisol, were normal. Visual acuity, visual fields, and fundus examination were normal. Non small cell lung carcinoma (squamous cell) stage T4N2M1a with choriocarcinomatous differentiation, and paraneoplastic galactorrhoea/gynaecomastia was diagnosed.

Chemotherapy (paclitaxel 175 mg/m² and cisplatin 65 mg/m² each on day 1 of 3 weekly cycle) were started as per our protocol. After the first cycle of chemotherapy, the patient's chest pain and cough subsided and the dyspnoea improved substantially. The gynaecomastia showed striking regression and the galactorrhoea disappeared.

At the time of subsequent sixth cycle of chemotherapy the patient was well. Gynaecomastia is an infrequent manifestation of lung cancer and is usually caused by an increased oestrogen/androgen ratio. Raised β-HCG concentrations stimulate Leydig cell-mediated oestrogen synthesis. Although β-HCG is produced from placenta, it has been used as a marker for gestational trophoblastic diseases and testicular germ cell tumours.

Raised β-HCG concentrations in serum are seen in 12-14% of lung cancer patients, and increased urinary β-HCG in up to half of lung cancer patients. Increased serum β-HCG and tumour β-HCG expression are more common in non-squamous nonsmall-cell lung carcinoma histological types. Clinical manifestations related to raise β-HCG are uncommon. Around 18% of all cases with galactorrhoea occur because of tumours, most commonly prolactinomas, and rarely non-pituitary malignancies. Irritative lesions of the chest wall can induce hyperprolactinaemia and galactorrhoea. This patient, although there was chest wall involvement, serum prolactin was normal and galactorrhoea was caused by ectopic β-HCG production from the malignant lung cancer (squamous) cells. Gynaecomastia that is associated with galactorrhoea is, however, a very rare paraneoplastic manifestation of lung cancer.

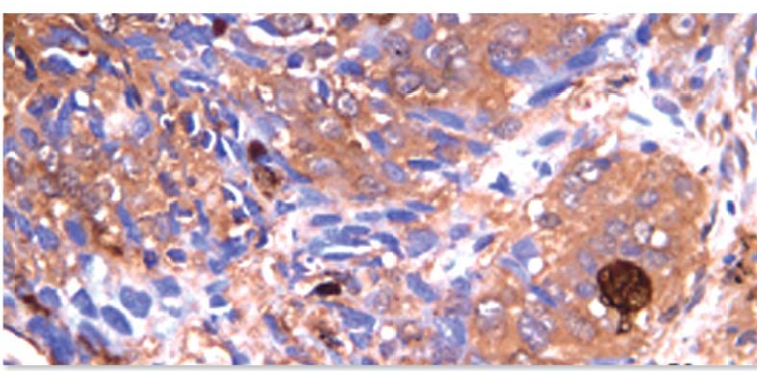


Fig: (B) Photomicrograph of endobronchial biopsy specimen showing β-HCG positive cytoplasm of tumour cells on immunohistochemistry (β-HCG immunostaining 400 X).

There are only two previously reported cases of lung cancer associated with galactorrhoea, including this patient. He is reported as first case of lung cancer associated with galactorrhoea which resolved with systemic chemotherapy. Regression of gynaecomastia took place without any specific anti-oestrogen therapy. Lung cancer should be considered in a male patient presenting with gynaecomastia and/or galactorrhoea.

*Reference: The Lancet 27 April, Vol. 381, page 1510*

## Amniotic fluid 'may heal premature baby gut'

Babies born too soon are not ready for the world outside the womb and their guts are ill-prepared to deal with food and they will develop necrotizing enterocolitis. The inflammation can cause tissue death and lead to a hole in the baby`s intestines which can result in a serious infection.

Amniotic fluid may hold the key to healing a fatal gut disease which affects premature babies. Scientists said Stem cells are well known to have anti-inflammatory effects, but this is the first time they have shown that amniotic fluid stem cells can repair damage in the intestines. Early animal tests, published in the journal Gut, showed that stem cells inside amniotic fluid could heal some of the damage and increase survival.

The scientists of Institute of Child Health at University College London have taken the stem cells from the amniotic fluid which surrounds a developing foetus in the womb and experiments on laboratory rats, which are programmed to develop fatal necrotizing enterocolitis, injections of stem cells appeared to increase survival times but they said further tests are still needed before it is tried in premature babies.

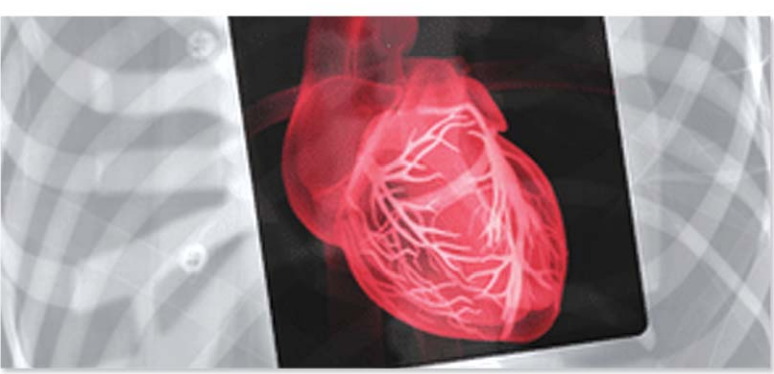
## Brain implant 'predicts' epilepsy seizures

A brain implant may be able to predict epilepsy seizures by picking up the early warning signs. The device uses the brain's electrical activity to tell patients if their risk of a seizure is high, moderate or low. The device collected signals from the surface of the brain and sent down wires to another implant in the chest. This beamed the data to a hand-held device which worked out the odds of a seizure. If a person is able to be alerted when they are about to have a seizure, this could help them to take steps to make sure they are safe during the seizure.

The trial was run at few hospitals in Europe. The results were mixed. For the first four months the brain was monitored so the system could learn a patient's brainwaves before a seizure. Only eight patients then progressed to the stage where the device was fully activated and they were constantly informed of their chance of a seizure. It was between 56% and 100% effective in those patients. Researches described the results as a major milestone showing for the first time that prospective seizure prediction is possible. Predicting seizures may help to understand more about the ways seizures can be managed and ultimately prevented.

## Gene therapy: 'Heart-healing virus' trial starts

Heart failure is increasingly common in the whole world. Patients have been enrolled into a trial to see if an engineered virus can be used to heal their damaged and struggling hearts.



The trial will use a virus to introduce genetic material into heart muscle to reverse the organ's decline. The concept of gene therapy is if there is a problem with a patient's genetic code, then correct that part of the code. It treats patients with lipoprotein lipase deficiency - which is otherwise unable to digest fat.

Researchers at Imperial College London found levels of the protein SERCA2a were lower in heart-failure patients. So they devised a genetically modified virus, with the instructions for producing more of the protein that can infect the heart. The virus will be released into the damaged heart muscle of the 200 patients involved in the trial via a tube inserted into the leg and pushed up through the blood vessels. Gene therapy aims to improve the function of weak heart muscle cells that offers a great potential for the future. The first gene therapy was finally approved for commercial use in Europe in November 2012.

*Reference: BBC Health*

InfoQuiz

## Jog your memory

Please select the correct answer by (√) against a, b, c, d of each questions in the Business Reply Card and send it through our colleagues or mail within 16 August 2013; this will ensure eligibility for the Raffle Draw and the lucky winners will get attractive prizes!

1. **Oral Contraceptive Pills increases the risk of**
   a) Thromboembolisim
   b) Breast Carcinoma
   c) Endometrial Carcinoma
   d) Liver Cirrhosis

2. **In stage of starvation which type of sequence is correct?**
   a) Carbohydrate-fat-protein
   b) Carbohydrate-protein-fat
   c) Fat-carbohydrate-protein
   d) Protein-fat-carbohydrate

3. **BMR mainly increased by**
   a) Thyroxine
   b) Pregnancy
   c) Exercise
   d) Phenobarbital

4. **A middle aged old male taking betel nuts and pan. He is most likely to develop**
   a) Keratinization
   b) Erythroplakia
   c) Leukoplakia
   d) Sub mucous fibrosis

5. **A 5 years old child with generalized edema and protienuria of 3.6 gm in 24 hours.The most important underlying mechanism of edema**
   a) Increased hydrostatic pressure
   b) Decreased hydrostatic pressure
   c) Decreased colloidal osmotic pressure
   d) Increased colloidal osmotic pressure

6. **A 26 years old women presented with 36 weeks of gestation & bilirubin 30 mmol /l. The most life threatening hepatitis to mother in near future would be**
   a) Hepatitis C
   b) Hepatitis E
   c) Hepatitis B
   d) Hepatitis A

7. **Which is the most specific test for excessive growth hormone?**
   a) Arginine
   b) Exercise tolerance test
   c) Benedict's test
   d) Insulin tolerance test

8. **A child having loss of sensation on little finger due to the fracture of posterior aspect of elbow. Which ligament / tendon may rupture?**
   a) Ulnar collateral
   b) Radial collateral
   c) Flexor carpi ulnaris tendon
   d) Extensor carpi radialis longus

9. **Which of the following doesn't cause hypocalcaemia?**
   a) Prostate carcinoma
   b) Hepatocellular carcinoma
   c) Bronchogenic carcinoma
   d) Ovarian carcinoma

10. **Which Antacid delay gastric emptying?**
    a) Magnesium hydroxide
    b) Aluminium hydroxide
    c) Sodium bicarbonate
    d) Magnesium carbonate

CONGRATULATIONS

# Info Quiz Winners

January-March 2013

## Dhaka

***Dr. BR. GEN Md. Sayedur Rahman***
*MBBS, FCPS, FRCP*
*Advisor Specialist in Medicine*
*74, Rojonighonda super market*
*Dhaka Cantontment*

***Dr. Shamsoon Nahar***
*MBBS, FCPS, MS*
*Kaligonj UHC*
*Kaligonj, Gazipur*

***Dr. Rajib Kumar Saha***
*MBBS*
*Medical Officer*
*BSMMU, Dhaka*

***Dr. Md. Yeasir Arshad Rajan***
*MBBS, MPH, CCD, PGT (Medicine)*
*Rajan's Care, House-1, Road-2, Block-F*
*Banasree, Rampura, Dhaka*

***Dr. Sojol Ashfaq***
*MBBS, DLO, MS (ENT)*
*Insaf Barakah Kidney & General Hospital, Maghbazar, Dhaka*

***Dr. Jalal Uddin Ikbal***
*MBBS, M. Phil*
*Ajom Road, Mohammadpur, Dhaka*

***Dr. Mostaq Ahmed Chowdhury***
*MBBS, DTCD*
*Alam Pharmacy*
*Doyagonj, Dhaka*

***Dr. Aparna Das***
*MBBS, FCPS (Medicine)*
*Dhaka Hospital, Dhaka*

***Dr. Ariful Islam Joarder***
*MBBS, D-Card*
*Appolo Pharmacy*
*51, DIT Plot, Gandaria, Dhaka*

***Dr. Jinat Rehana***
*MBBS, CCD*
*House # 7, Road # 23, Sector # 4*
*Uttara, Dhaka*

***Prof. Dr. Sayed Wahidur Rahman***
*FCPS (Medicine)*
*Popular Diagnostic Centre*
*Dhanmondi, Dhaka*

***Dr. Durul Hoda***
*MBBS, FCPS, MD (Cardiology)*
*Radiam D/C, Joydabpur, Gazipur*

***Dr. Chandan Kumar Shaha***
*MBBS, MCPS*
*Al- Baraka General Hospital*
*Jatrabari, Dhaka*

***Dr. A K M Monwarul Islam***
*MBBS, FCPS (Medicine)*
*MD (Cardiology), MACP, FACC FESC*
*Consultant Popular Diagnostic Centre*
*Shyamoli, Dhaka*

***Dr. Sk. Md. Abu Zafar***
*MBBS, FCPS (Medicine)*
*Popular Diagnostic Centre*
*Narayangonj*

***Dr. Samsul Hoque Gazi***
*MBBS, FCPS*
*Nipun Diagnostic Centre, Tongibari*

***Dr. M. Atahar Ali***
*MBBS, FCPS, MD*
*Padma Diagnostic Centre*
*Malibagh, Dhaka*

***Dr. Sajal Asfaq***
*MBBS, DLO*
*Insaf Baraka Kidney & General Hospital*
*335 Mogbazar, Dhaka*

***Dr. Md. Mahid Khan***
*MBBS, MRCP*
*"Comfort doctor" Chamber*
*Green Road, Dhaka*

***Dr. Md. Mosharof Hossen***
*MBBS, DTCD*
*NIDCH, Dhaka*

***Dr. A S M Manzur Morshed***
*MBBS, MD (Nephrology)*
*Coloni bazaar, Tajgaon, Dhaka*

***Dr. Md. Abu Zayed***
*MBBS, DTCD (Chest)*
*The Doctor's Chamber,Tarua Narsingdi*

## Mymensingh

***Dr. Nurul Alam Bashar***
*MBBS, FCPS (Medicine), MD (Neuromedicine)*
*Swadesh Hospital Pvt. Ltd, Mymensingh*

***Dr. MD. Saiful Bari***
*MBBS, MD (Cardiology)*
*Nexus cardiac hospital, Mymensingh*

***Dr. Nargis Ara Bithi***
*MBBS, PGT, DLP*
*2 No. Horikrishno Roy Road*
*Mymensingh Diabetic Somitee*
*Mymensingh*

## Chittagong

***Dr. Hossain Khurshid***
*MBBS*
*Royal Hospital Ltd*
*O.R.Nizam Road, Chittagong*

***Dr. Komol Krishno Pramanik***
*MBBS, FCPS (ENT)*
*Medical Centre, Chittagong*

***Dr. Abdur Rahim***
*MBBS*
*Steel Mill Bazar*
*Chittagong*

***Dr. Md. Shaheen Abdur Rahman***
*MBBS, BCS (Health)*
*Medical Officer*
*Sadar Hospital*
*Cox's Bazar*

***Dr. J Q Nila***
*MBBS, DMU, M.Phil*
*Pahartali, Chittagong*

***Dr. Safiul Alam***
*MBBS, MD (Cardiology)*
*Sergiscope PVT. Ltd*
*Katalgong, Chittagong*

***Dr. Md Solim Ullah***
*MBBS, D-Card*
*Chittagong Diabetic General Hospital*

***Dr. Nurul Karim Rashed***
*MBBS, D-Card*
*Nuhash Medical Hall*
*Sitakunda Bazar*
*Sitakundo, Chittagong*

## Comilla

***Dr. Liakat Ali Khan***
*MBBS*
*Rajgonj, Comilla*

***Dr. Md. Monirul Islam Chowdhury***
*MBBS*
*Medical Officer, UHC*
*Chouddagram, Comilla*

## Rangpur

***Dr. Saki Md Jakiul Alam***
*MBBS, FCPS (Medicine)*
*Dinajpur Medical College*
*Dinajpur*

***Dr. Mostofa Moinuddin Ahmed***
*MBBS, BCS (Health)*
*UHC, Baragari, Domar*
*Nilphamari*

***Dr. Md. Shafiqul Haque***
*MBBS*
*Pulse clinic*
*Master para, Gaibandha*

## Faridpur

***Dr. Arun Kanti Biswas***
*MBBS*
*Gopalgonj Nursing Home, Gopalgonj*

***Dr. Md. Musa Khan***
*MBBS*
*RMO*
*Upazilla Health Complex*
*Damudya, Shariatpur*

## Tangail

***Dr. Noren Kumar Roy***
*MBBS*
*Niramoy clinic*
*Manikgonj*

***Dr. Pabon Kumar Saha***
*MBBS*
*Kumudini Medical College Hospital*
*Mirjapur, Tangail*

## Jessore

***Dr. Tapankor Biswas***
*MBBS*
*Jessore Medical College & Hospital*
*Jessore*

***Dr. Abu Md. Zahurul Islam***
*MBBS, DTCD*
*Alamdanga, Jessore*

## Maizdee

***Dr. Md. Shahidullah Dider***
*MBBS, FCPS (Medicine)*
*Upasham General Hospital*
*S.S.K.Road, Feni*

***Dr. Salma Chowdhury***
*MBBS, EOC (Gynae)*
*Upasham General Hospital*
*Laxmipur*

***Dr. Shamim Ara Nasrin***
*MBBS, DGO*
*Feni Clinic, S.S.K.Road*
*Feni*

***Dr. Md Safayet Hossain***
*MBBS, D-Card*
*Jahan Pharmacy*
*Main road, Maijdee court*
*Noakhali*

## Bogra

***Dr. Md. Mahabub Alam Siddiqui***
*MBBS, DTCD*
*Chest specialist*
*Nowgaon Chest Care*
*Kazir more, Nowgaon*

## Rajshahi

***Dr. Md. Jahirul Haque***
*MBBS, FCPS (Medicine)*
*Assistant Professor*
*Rajshahi Medical College*

**Published by**

Medical Services Department
ACI Pharmaceuticals
Novo Tower, 9th Floor, 270 Tejgaon Industrial Area, Dhaka-1208

**Designed by**

Creative Communication Ltd.
Road # 123, House # 18A , Gulshan 1, Dhaka 1212

ACI Limited