

National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Disease and Stroke (NPCDCS)

A Manual for Medical Officer



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Collaborative Programme 2008-2009**

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Section 1:

INTRODUCTION

Non-communicable diseases (NCD), also known as chronic diseases include cardiovascular diseases, diabetes, stroke, most forms of cancers and injuries. Such diseases mainly result from lifestyle related factors such as unhealthy diet, lack of physical activity and tobacco use. Changes in lifestyles, behavioural patterns, demographic profile (aging population), socio-cultural and technological advancements are leading to sharp increases in the prevalence of NCD. These diseases by and large can be prevented by making simple changes in the way people live their lives or simply by changing our lifestyle.

Magnitude of NCD burden in India

During the year 2005, NCD accounted for 53% of all the deaths in the age group 30-59 years in India. Of these, 29% were due to cardiovascular diseases; It is estimated that, by 2020, cardiovascular disease will be the largest cause of disability and death, as a proportion of all deaths in India. In 2003 alone, in India, there were approximately 30 million people suffering from coronary heart disease. It is estimated that the overall prevalence of diabetes, hypertension, Ischemic Heart Diseases (IHD) and Stroke is 62.47, 159.46, 37.00 and 1.54 respectively per 1000 population of India. There are an estimated 25 Lakh cancer cases in India.

Diabetes which is a major risk factor for chronic disease on its own causes increased death and disability. According to the Diabetes Atlas 2006 published by the International Diabetes Federation, the number of people with diabetes in India is currently around 40.9 million and is expected to rise to 69.9 million by 2025, unless urgent preventive steps are taken. Similarly, 118 million people were estimated to have high blood pressure in the year 2000 which is expected to go up to 213 million in 2025. Not only this, **Indians succumb to diabetes, high blood pressure and heart attacks 5-10 years earlier than their western counterparts, during their most productive years. This leads to considerable loss of productive years, to the country.** It has been estimated that, by the year 2030, India will lose approximately 17.9 million potentially productive years which is higher than the expected combined loss in China, Russia, USA, Portugal and Brazil. This translates into a huge economic loss as high as 237 billion dollars by the year 2015. Development of diabetes and heart attacks at an early age is not largely because of

environmental causes such as low consumption of fresh fruits and vegetables along with other unhealthy diet, increasing use of tobacco, and higher prevalence of sedentary life-style.

To contain the increasing burden of Non-Communicable Diseases, Ministry of Health and Family welfare, Government of India, has revised the National Cancer Control Programme (NCCP) and formulated an integrated National Programme for Prevention and Control of Cancers, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS). The NPCDCS will focus on health promotion and prevention, strengthening of infrastructure including human resources, early diagnosis and management and integration with the primary health care system through NCD cells at different levels for optimal operational synergies.

Objectives of NPCDCS:

- a. Prevent and control common NCDs through behaviour and life style changes,
- b. Provide early diagnosis and management of common NCDs,
- c. Build capacity at various levels of health care for prevention, diagnosis and treatment of common NCDs,
- d. Train human resource within the public health setup viz doctors, paramedics and nursing staff to cope with the increasing burden of NCDs, and
- e. Establish and develop capacity for palliative & rehabilitative care

Strategies

The Strategies to achieve above objectives are as follows:

- 1) Prevention through behaviour change
- 2) Early Diagnosis
- 3) Treatment
- 4) Capacity building of human resource
- 5) Surveillance, Monitoring & Evaluation

The strategies will be implemented in 20,000 Sub-Centres and 700 Community Health Centres (CHCs) in 100 Districts across 21 States/UTs

Section 2:

RISK FACTORS OF NCDS

What gives rise to major NCDs (Diabetes, cardiovascular diseases, Stroke, Cancer)?

Major NCDs are caused by a set of risk factors like unhealthy diet (low fruit and vegetable intake), physical inactivity, tobacco use, harmful use of alcohol and stress. High blood pressure, dyslipidemia (high levels of total cholesterol, LDL-cholesterol, and triglycerides and low level of HDL-Cholesterol) overweight/obesity (both generalized and central) is other physiological risk factors. Other putative but not well proven factors include air pollution, food preservatives, adulterants, artificial color and indoor smoke from solid fuels. Alcohol consumption, specifically binge drinking, leads to acute hypertension, stroke and in some individuals atrial fibrillation and cardiomyopathy.

Risk factors and level of NCD prevention and management

Behavioral RF	Physiological RF	Disease Outcome
<input type="checkbox"/> Unhealthy Diet <input type="checkbox"/> Physical inactivity <input type="checkbox"/> Tobacco <input type="checkbox"/> Alcohol <input type="checkbox"/> Stress	<input type="checkbox"/> BMI (Obesity) <input type="checkbox"/> Hypertension <input type="checkbox"/> Hyper-cholesterolemia <input type="checkbox"/> High Blood sugar level	<input type="checkbox"/> Diabetes <input type="checkbox"/> Heart disease <input type="checkbox"/> Stroke <input type="checkbox"/> Cancer <input type="checkbox"/> Chronic respiratory disease
Primary Prevention Health promotion	Secondary Prevention Case management & HP	Tertiary Prevention Case management

Some attributes of risk factors

- Risky lifestyle behaviors are responsible for the risk factors. Risk factors are cumulative and operate on a life course perspective. (i.e. they influence the risk throughout the life course. For example childhood obesity is a major risk factor for adult obesity and consequently diabetes and CVD).
- Normally, for all practical purposes it is seen that these risk factors occur together. A person who has high blood sugar levels may also have high blood pressure, dyslipidemia and central obesity.

- Risk factors operate in a continuum. This means that even within the normal ranges, people with higher level have higher risks. For example individuals with systolic blood pressure of 140 mmHg have a higher risk of CVD, stroke and future death than those with 120 mmHg even though both are within "normal" range. This applies to all the risk factors of CVD and Stroke
- The risk factors are additive. This means cumulative small elevations of risk factors are much more harmful than isolated elevation of single risk factors.

It is important to note that all these risk factors are amenable to modification through lifestyle changes. **In nutshell, today's risky behaviors are tomorrow's risk factors. Today's risk factors are tomorrow's disease. Thus, primary and secondary prevention of chronic diseases and their common risk factors provide the most sustainable and cost-effective approach to chronic disease prevention and control**

Section 3:

ROLE OF MEDICAL OFFICER IN NPCDCS

1. Health promotion activities - Educate regarding common risk factors, increased intake of healthy foods (ii) increased physical activity through sports, exercise, etc. (iii) avoidance of tobacco and alcohol and (iv) stress management.
2. Risk assessment and management through opportunistic screening
3. Motivate and create role models in the community
4. Work closely with other sectors/ departments for NCD prevention
5. Management of patients suffering from Cancer, Diabetes, CVDs and Stroke referred from different centers
6. Establish an effective referral mechanism (two way) with the nearest medical colleges
7. Supervision of the activities undertaken by paramedical workers
8. Assist resource centers/ institution in organizing the training for different cadre of health workers

Section 4:

RISK ASSESSMENT AND MANAGEMENT

This section provides evidence-based guidelines on how to reduce the occurrence of first clinical events of coronary heart disease (CHD), cerebrovascular disease (CeVD) and peripheral vascular disease (PVD) in the population.

The evidence-based recommendations given in these guidelines provide guidance on which specific preventive actions to initiate, and with what degree of intensity. The accompanying World Health Organization/ International Society of Hypertension (WHO/ISH) risk prediction charts enable the estimation of total cardiovascular risk of people in the first category.

4.1. What are the goals of implementing these guidelines?

The goals are to prevent CHD, CeVD and PVD events and Cancer by lowering risk.

The recommendations assist people to:

- Quit tobacco use, or reduce the amount smoked, or not just start the habit
- Make healthy food choices
- Be physically active
- Reduce body mass index, waist hip ratio/waist circumference
- Lower blood pressure
- Lower blood cholesterol and low density lipoprotein cholesterol (LDL-cholesterol)
- Control hyperglycemia
- Take anti platelet therapy when necessary.

4.3. Who needs referral to a specialist facility?

Referral is required if there are clinical features suggestive of:

- Acute cardiovascular events such as: heart attack, angina, heart failure, arrhythmias, stroke, and transient ischemic attack.
- Secondary hypertension, malignant hypertension.
- Diabetes mellitus (newly diagnosed or uncontrolled).
- Established cardiovascular disease (newly diagnosed or if not assessed in a specialist facility).
- Suspected lesions for Cancer
- People needing medical therapy to quit smoking.

Once the condition of the above categories of people (except with suspected lesion) is assessed and stabilized, they can be followed up in a primary care facility based on the recommendations provided in these pocket guidelines. They will need periodic reassessment in specialty

4.3. When is grading cardiovascular risk using charts unnecessary for making treatment decisions?

Some individuals are at high cardiovascular risk because they have established cardiovascular disease or very high levels of individual risk factors. Risk stratification is not necessary for making treatment decisions for these individuals as they belong to the high risk category; all of them need intensive lifestyle interventions and appropriate drug therapy .

They include people:

- With established cardiovascular disease
- Without established CVD who have a total cholesterol \geq 320 mg/dl or low density lipoprotein (LDL) cholesterol \geq 240 mg/dl or TC/HDL-C (total cholesterol/high density lipoprotein cholesterol) ratio >8
- Without established CVD who have persistent raised blood pressure of \geq 160/ \geq 100 mmHg
- With renal failure or renal impairment.

4.4. Instructions for using WHO/ISH risk prediction charts

These WHO/ISH risk prediction charts indicate 10-year risk of a fatal or nonfatal major cardiovascular events (myocardial infarction or stroke), according to age, gender, blood pressure, smoking status, total blood cholesterol and presence or absence of diabetes mellitus. There are two sets of charts. One set can be used in settings where blood cholesterol can be measured. The other set is for settings in which blood cholesterol cannot be measured.

The charts provide approximate estimates of CVD risk in people who do not have established coronary heart disease, stroke or other atherosclerotic disease. They are useful as tools to help identify those at high cardiovascular risk, and to motivate persons, particularly to change behaviour and, when appropriate, to take antihypertensive, lipid-lowering drugs, and aspirin.

4.5. How do you use the charts to assess cardiovascular risk?

- If blood cholesterol can be measured, refer to chart 1.
- If blood cholesterol cannot be measured due to resource limitations, refer to chart 2.
- Before applying the chart to estimate the 10 year cardiovascular risk of an individual, the following information is necessary

Presence or absence of diabetes^{*}

Gender

Smoker (*All current smokers and those who quit smoking less than 1 year before the assessment*) or non-smoker^{**}

Age

Systolic blood pressure (SBP)^{***}

Total blood cholesterol.

^{*} *A person who has diabetes is defined as someone taking insulin or oral hypoglycemic drug(s), or with a fasting venous plasma glucose concentration ≥ 126 mg/dl or a postprandial (approximately 2 hours after a main meal) venous plasma glucose concentration ≥ 200 mg/dl on two separate occasions. For very low resource settings urine sugar test may be used to screen for diabetes if blood glucose assay is not feasible. If urine sugar test is positive a confirmatory blood glucose test needs to be arranged to diagnose diabetes mellitus.*

^{**} *All current smokers and those who quit smoking less than 1 year before the assessment are considered smokers for assessing cardiovascular risk.*

^{***} *Systolic blood pressure, taken as the mean of two readings on each of two occasions, is sufficient for assessing risk but not for establishing a pre-treatment baseline.*

Once the above information is available proceed to estimate the 10-year cardiovascular risk as follows:

Step 1	Select the appropriate chart depending on the presence or absence of diabetes
Step 2	Select male or female tables
Step 3	Select smoker or non smoker boxes
Step 4	Select age group box (if age is 50-59 years select 50, if 60-69 years select 60 etc)
Step 5	Within this box find the nearest cell where the individual's systolic blood pressure (mm Hg) and total blood cholesterol level (mg/dl) cross. The colour of this cell determines the 10 year cardiovascular risk.

4.6. WHO / ISH Risk prediction CHARTS

Chart 1: 10 year risk of a fatal or non fatal cardiovascular event by gender, age, and systolic blood pressure, total blood cholesterol, smoking status and presence or absence of diabetes mellitus

WHO/ISH risk prediction chart applicable for Indian population

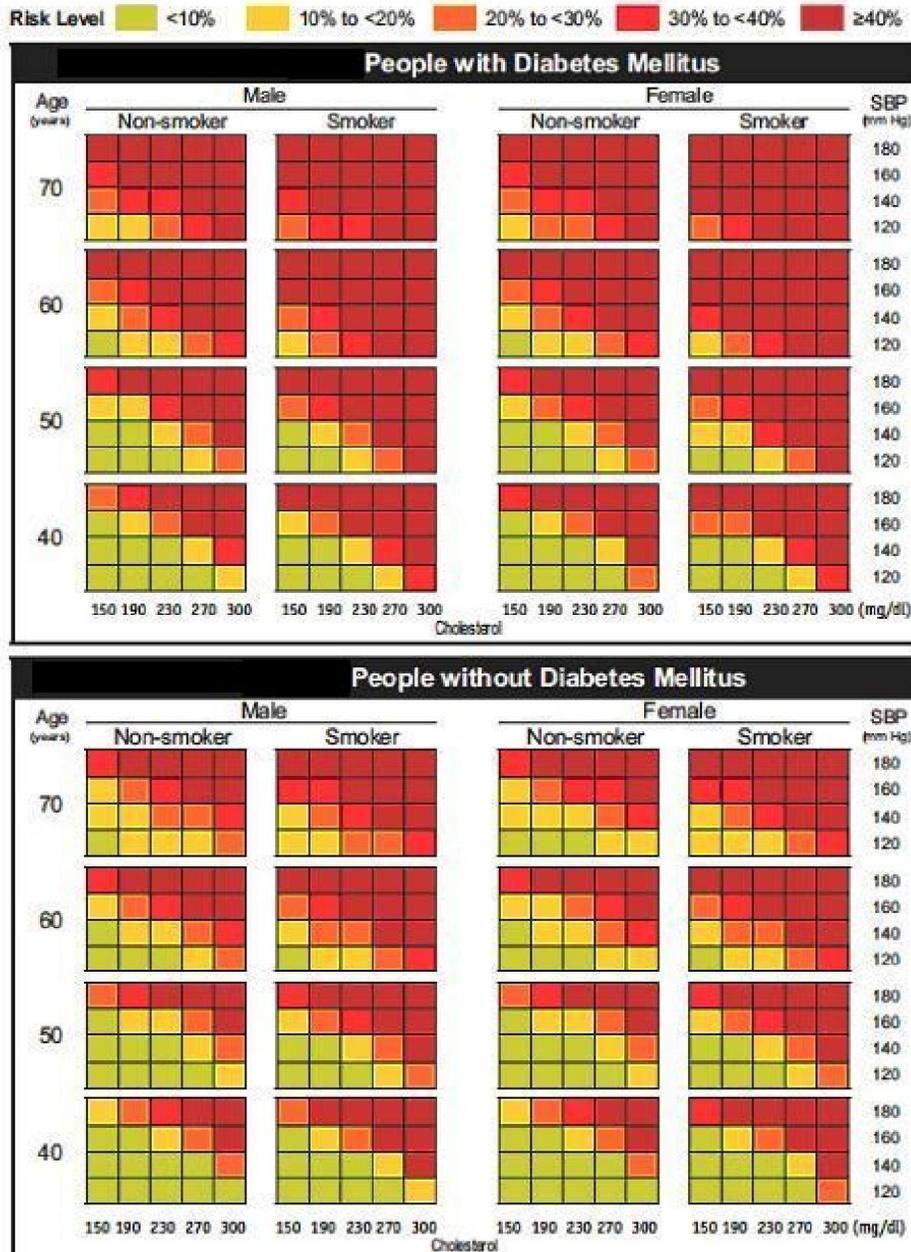
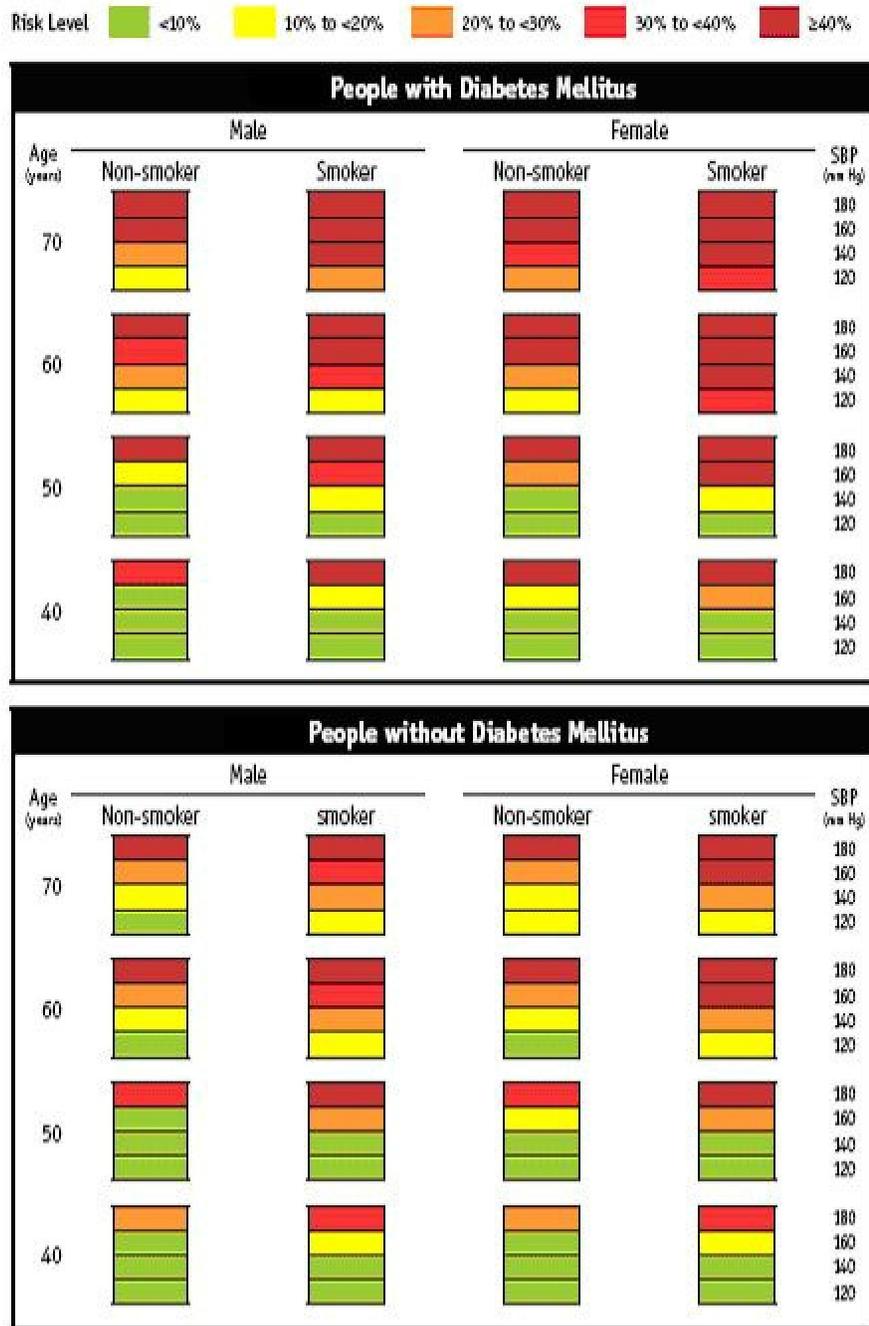


Chart 2: 10 year risk of a fatal or non fatal cardiovascular event by gender, age, systolic blood pressure, smoking status and presence or absence of diabetes mellitus



4.7. Practice Points

Please note that CVD risk may be higher than indicated by the charts in the presence of the following:

- Already on antihypertensive therapy
- Premature menopause
- Approaching the next age category or systolic blood pressure category
- Obesity (including central obesity)
- Sedentary lifestyle
- Family history of premature CHD or stroke in first degree relative (male <55 years, female < 65 years)
- Raised triglyceride level (≥ 150 mg/dl)
- Low HDL cholesterol level (≤ 40 mg/dl in males, ≤ 50 mg/dl in females)
- Fasting glycaemia, or impaired glucose tolerance
- Microalbuminuria
- Socioeconomic deprivation.

4.8. Recommendations for prevention of cardiovascular disease in people with cardiovascular risk factors (according to individual total risk)

10 year risk of cardiovascular event	Risk classification	Intervention
Risk <10%	LOW RISK	Low risk does not mean no risk. Conservative management focusing on lifestyle an intervention is suggested. Risk assessed after 5 years unless significant change in health status.
Risk 10% to <20%	MODERATE RISK	Monitor risk profile every 2 years.
Risk 20% to <30%	HIGH RISK	Monitor risk profile yearly.
Risk $\geq 30\%$	VERY HIGH RISK	Individuals in this category are at very high risk of fatal or non-fatal vascular events. Monitor risk profile every 36 months.

Note: Reassess a person after six months of lifestyle modification if there is isolated elevation of single risk factor.

4.9. LIFESTYLE MODIFICATION

a. DIET

- Increase intake of green leafy vegetables and fresh fruits.
- Consume less salt; avoid adding/sprinkling salt to cooked and uncooked food.
- Preparations which are high in salt and need to be moderated are: Pickles, chutneys, sauces and ketchups, papads, chips and salted biscuits, cheese and salted butter, bakery products and dried salted fish.
- Restrict all forms of sugar free and refined carbohydrates for example biscuits, breads, naan, kulchas, cakes, mathris etc.
- Steamed and boiled food should be preferred over fried food.
- Have fresh lime water instead of carbonated drinks.
- Avoid eating fast/junk foods and aerated drinks. Instead of fried snacks, eat a fruit.
- In practice, it is best to use mixture of oils. Either buy different oils every month or cook different food items in different oils.
- Oils which can be mixed and matched are mustard oil, soya bean oil, groundnut oil, olive oil, sesame oil, and sunflower oil.
- Ghee, vanaspati, margarine, butter and coconut oil are harmful and should be moderated.
- If you are a non vegetarian, try to take more of fish and chicken. They should not be fried. Red meat should be consumed in small quantities and less frequently

b. PHYSICAL ACTIVITY[#]

- Physical activity is a key determinant of energy expenditure.
- Regular exercise is important for promoting weight control or weight loss.
- Exercise regularly (moderate to vigorous) for 5-7 days per week; start slowly and work up gradually
 - At least 30 minutes (accumulated) of physical activities per day for cardiovascular disease protection.
 - 45 minutes/ day (accumulated) for fitness.
 - 60 minutes/ day (accumulated) for weight reduction.
- Discourage spending long hours in front of TV.
- Encourage outdoor activities like cycling, gardening etc.

- **Yoga:** A holistic life style which includes Asanas and all other components of healthy life style like low fat vegetarian diet (Satvik diet), stress management, tobacco avoidance and physical exercise. They have the potential for primary and secondary prevention of heart disease.

c. WEIGHT CONTROL

All individuals who are overweight or obese should be encouraged to lose weight through a combination of a low calorie diet and dynamic physical activity.

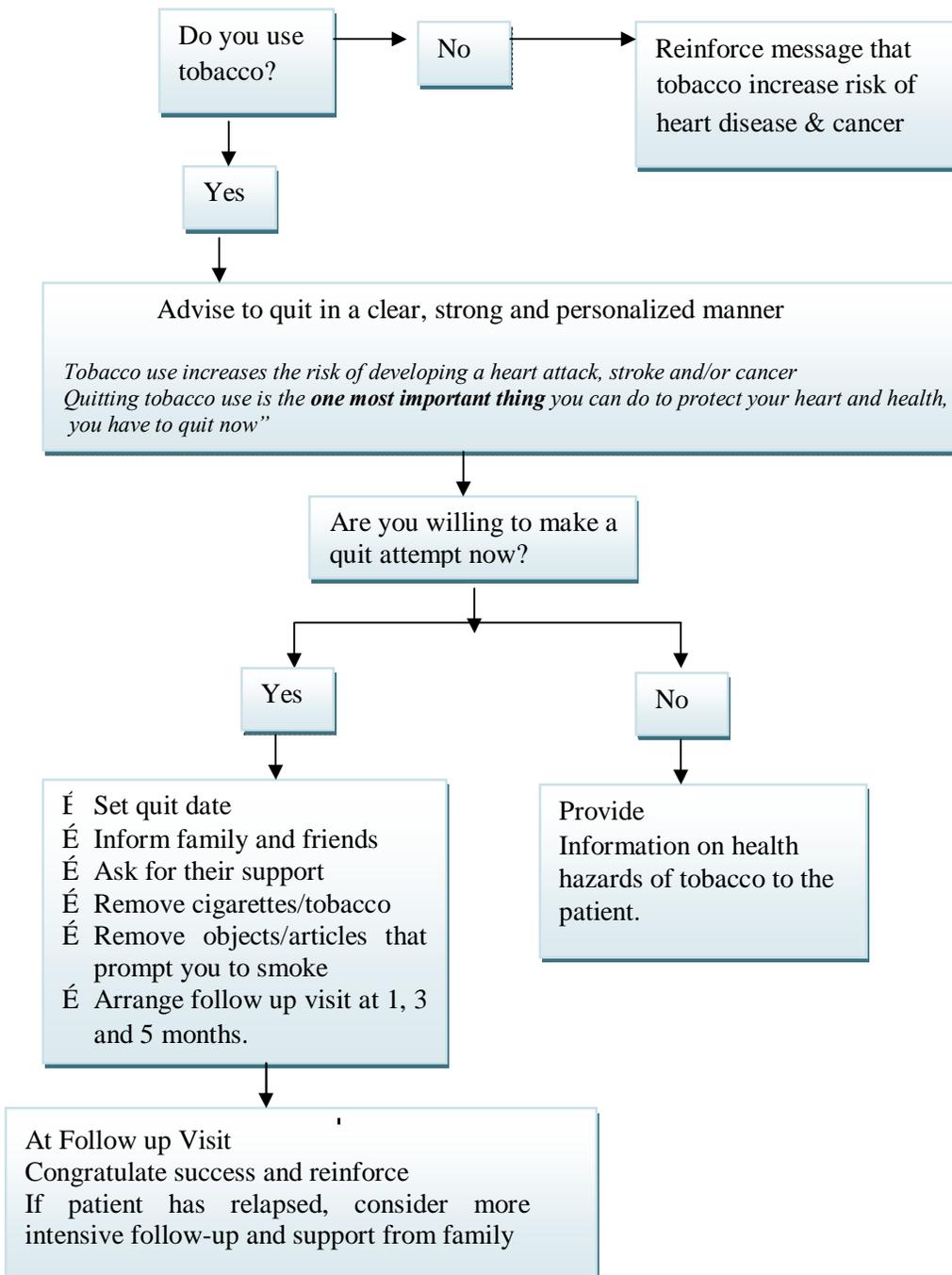
Overweight or obesity is assessed by measuring body mass index (BMI), which is calculated as weight in kg/height in meter². For Indian population 18.5 to 22.9 BMI is normal, 23 to 24.9 is considered as overweight and BMI of ≥ 25 is considered as obesity. Waist circumference is also an important measurement of central obesity and it should be <90 cm for men and <80 cm for women. Another measure of central obesity is Waist Hip Ratio (WHR). Normal WHR is <0.85 for women and <0.95 for men.

Patients with uncontrolled hypertension ($\geq 200/\geq 110$), uncontrolled diabetes (FBS ≥ 250 mg/dl), diminished vision due to diabetic/hypertensive retinopathy or for other reasons, recent myocardial infarction/unstable angina or stroke (within 6 weeks), and with uncontrolled angina (class III or more) are not advised to go for physical exercise.

d. TOBACCO CESSATION

- All non-smokers should be encouraged not to start smoking.
- All smokers should be strongly encouraged to quit smoking by a health professional through Lifestyle modification including YOGA and supported in their efforts to do so.
- It is suggested that those who use other forms of tobacco be advised to stop. The following flow chart depicts the protocol for counseling on tobacco cessation using the 5 steps -5 A approach

**PROTOCOL FOR COUNSELING ON CESSATION OF TOBACCO USE
(5 STEPS– 5As)**



Use 5 steps- 5 as- ask, advise, assess, assist, arrange

e. ALCOHOL INTAKE

All individuals should avoid alcohol as far as possible.

4.10. PHARMACOTHERAPY

10year risk of cardiovascular event	Risk classification	Anti-hypertensive drugs	Lipid lowering drugs	Antiplatelet drugs
Risk <10%	LOW RISK	<ul style="list-style-type: none"> <input type="checkbox"/> Persistent blood pressure ~ 140/90 mmHg should continue non pharmacologic therapy like lifestyle strategies <input type="checkbox"/> Total cardiovascular risk reassessed every five years 	<ul style="list-style-type: none"> <input type="checkbox"/> individuals with total cholesterol at or above 320 mg/dl <input type="checkbox"/> To follow a non pharmacologic therapy i.e., lifestyle modification 	<ul style="list-style-type: none"> <input type="checkbox"/> Aspirin should <i>not</i> be given to individuals in this low-risk category.
Risk 10% to <20%	MODERATE RISK	<ul style="list-style-type: none"> <input type="checkbox"/> Persistent blood pressure ~ 140/90 mmHg should continue non pharmacologic therapy like lifestyle strategies <input type="checkbox"/> Total cardiovascular risk reassessed every two years 	<ul style="list-style-type: none"> <input type="checkbox"/> individuals with total cholesterol at or above 320 mg/dl <input type="checkbox"/> To follow a non pharmacologic therapy i.e., lifestyle modification 	<ul style="list-style-type: none"> <input type="checkbox"/> Aspirin should <i>not</i> be given to individuals in this risk category.
Risk 20% to <30%	HIGH RISK	<ul style="list-style-type: none"> <input type="checkbox"/> Persistent blood pressure ~ 140/90 mmHg should continue non pharmacologic therapy like lifestyle strategies <input type="checkbox"/> Total cardiovascular risk reassessed every year <input type="checkbox"/> First line antihypertensive therapy may be considered. 	Adults >40 years with persistently high serum cholesterol (>200 mg/dl) and/or LDL cholesterol >120 mg/dl, despite a lipid-lowering diet and other lifestyle measures for a year, should be given a statin.	<ul style="list-style-type: none"> <input type="checkbox"/> Aspirin should <i>not</i> be given to individuals in this risk category.
Risk ≥30%	VERY HIGH RISK	<ul style="list-style-type: none"> <input type="checkbox"/> Persistent blood pressure ~ 130/80 mmHg should continue non pharmacologic therapy like lifestyle strategies <input type="checkbox"/> Total cardiovascular risk reassessed six months <input type="checkbox"/> First line antihypertensive therapy may be considered. 	Adults >40 years with persistently high serum cholesterol (>200 mg/dl) and/or LDL cholesterol >120 mg/dl, despite a lipid-lowering diet and other lifestyle measures for a year, should be given a statin.	<ul style="list-style-type: none"> <input type="checkbox"/> Aspirin should be given to individuals in this risk category.

Note: Reassess a person after six months of lifestyle modification if there is isolated elevation of single risk factor.

Section 5:

MANAGEMENT GUIDELINES

5. 1. PREVENTION AND MANAGEMENT OF DIABETES

What is diabetes?

Diabetes is a disease in which the body does not produce or properly use the hormone insulin. The body needs insulin to convert sugar, starches and other foods into energy. Impairment of insulin secretion and action in the body leads to abnormally elevated levels of glucose in blood, a condition classically termed as diabetes.

What are the different "types" of diabetes?

Diabetes is classified into three types namely Type 1 Diabetes, Type 2 Diabetes and gestational diabetes. A description of each of these types is given below while guidelines for management elaborated in the following sections are specific to type 2 diabetes.

Type 1 diabetes (T1DM):

Usually occurs in younger people, children and adolescents. The diagnosis of T1DM can be made throughout childhood but it is more likely below 15 yrs of age. The onset is usually acute and severe and insulin is required for survival. Type 1 diabetes results from autoimmune destruction of the beta cells in the pancreatic islets. Family history of diabetes is rare in T1DM. Presence of features of associated autoimmunity (autoimmune disorders, vitiligo) and absence of obesity and acanthosis nigricans are characteristics of T1DM. In addition, urine of T1DM patients with uncontrolled hyperglycemia is positive for ketone bodies.

Type 2 diabetes (T2DM):

Is the commonest type of diabetes. It usually occurs after the age of forty years but occurs frequently even at lower age among Indians. T2DM was previously known as non-insulin dependent diabetes mellitus. The onset is usually insidious and may be mild to severe. The family history is usually positive and strong. Obesity, metabolic syndrome and acanthosis nigricans are usually seen in these patients while there is no evidence of autoimmunity. Further, there is no insulin dependence till late in the course of illness.

When is a person at high risk for diabetes?

1. If he/she is of above the age of 30 years
2. If he/she is overweight (BMI is more than 23kg/m^2).
3. If he/she is physically inactive, that is, he or she exercises less than 3 times a week.
4. If he/she has high blood pressure
5. If he/she has impaired fasting glucose or impaired glucose tolerance.
6. If his/her triglyceride and/or cholesterol levels are higher than normal.
7. If his/her parents/siblings or grandparents have or had diabetes.
8. If she delivered a baby whose birth weight was 4 kgs or more.
9. If she has had diabetes or even mild elevation of blood sugars during pregnancy.

When to suspect diabetes?

- Symptoms of uncontrolled hyperglycemia: excess thirst, excess urination, excess hunger with loss of weight
- Frequent infections
- Non-healing wounds
- Unexplained lassitude
- Fatigue
- Impotence in men

Criteria for diagnosing T2DM

The criteria for diagnosing T2DM, as defined by the World Health Organization in 1999, are depicted in table-5.1.1.

Table-5.1.1: Criteria for diagnosis of T2DM using venous blood samples*		
	Fasting Glucose (mg/dl)	2-hour Post-Glucose Load (mg/dl)
Diabetes Mellitus	≥ 126	≥ 200
Impaired Glucose Tolerance	< 110	>140 to <200
Impaired Fasting Glucose	≥ 110 to <126	

**WHO Definition 1999*

Management of Diabetes

Management of T2DM should be initiated as soon as diagnosis is established even if the patient is asymptomatic. Initial assessment and management of the patients has to be carried out at Community Health Centre (CHC) level or at secondary care level. Management of T2DM comprises initial assessment, initial management and follow-up visits. Each of these components is elaborated here.

1. *Initial assessment* of individuals suspected of having T1DM need to be subjected to risk assessment which include:
 - History and physical examination;
 - Assessment of blood glucose level;
 - Presence of CVD risk factors (lipid profile); and
 - End-organ damage (urine for protein/ ECG/ fundus examination)

Assessment of history and physical examination of the patient is elaborated in table-5.1.2.

2. *Initial management* include:
 - Pharmacotherapy for the management of hyperglycemia and any other co-morbid conditions e.g. high blood pressure, dyslipidemia etc.;
 - Therapeutic lifestyle management (please refer the earlier section); and
 - Diabetes patient Education and counseling by dietician

Table-5.1.2 Initial Assessment of Diabetic Patients	
History (Ask for)	Physical Examination (Look for)
Symptoms of hyperglycemia	Weight
Duration since onset of symptoms	Body Mass Index
Precipitating factors such as recent infections, stress, change in dietary habits or physical activity levels	Waist circumference, Waist-hip ratio
Symptoms of Micro- and Macro-vascular Complications: visual disturbances, edema, breathlessness, angina, intermittent claudication, numbness, paraesthesiae	Acanthosis nigricans *
Hypertension, pre-existing cardiovascular diseases	Blood pressure
Drug history	Peripheral pulses
Diet	Feet: calluses, ulcers, prominent veins, edema, injuries
Physical Activity: type, frequency	Fundus examination [#]
Family History	Cardiovascular system
-Diabetes and complications -Age at onset -Cardiovascular disease	Peripheral nervous system
	Thyroid
<i>*Acanthosis nigricans is a brown to black, poorly defined, velvety hyperpigmentation of the skin, usually present in the posterior and lateral folds of the neck, the axilla, groin, umbilicus, and other areas. This occurs due to insulin spillover (from excessive production due to obesity or insulin resistance) into the skin which results in its abnormal growth, and the stimulation of color producing cells. The most common cause would be insulin resistance, usually from type-2 diabetes mellitus.</i>	
[#] Details of Fundus examination are provided in a later section	

T2DM: Principles of Management

Lifestyle management (diet and physical activity) accompanied by drug therapy or insulin are the corner stone of diabetes management. Apart from this other concurrent complications should be addressed. The basic principles in the management of type-2 diabetes are:

- Modify Lifestyle: diet and physical activity
- Reduce Insulin Resistance through reduction in weight, specifically reduction of fat mass
- Pharmacological treatment (if inadequate control):
 - ✓ *Sulfonylureas/ Metformin*
- Treatment for high blood pressure:
 - ✓ *ACE-Inhibitors, Calcium channel blockers such as amlodipine and diuretics such as hydrochlorothiazide*
 - ✓ *For details refer the section on hypertension*
- Lipid control with statins

The targets of control in Diabetes management in depicted in the Box 5.1.1

Box 5.1.1: Ideal Targets of control in the management of Diabetes	
Fasting blood glucose	: 80-110 mg/dl
Post meal blood glucose	: 120-140 mg/dl
HbA _{1C}	: < 7%
Total cholesterol	: < 180 mg/dl
LDL-chol	: < 100 mg/dl
HDL chol	: > 45 mg/dl
Blood pressure	: < 130/80 mmHg
Serum TG	: <150 mg/dl
<i>Source: ICMR</i>	

Note: The targets for diabetic population are lower than the non-diabetes

Box 5.1.2: Glycosylated haemoglobin (HbA_{1c})

A fraction of hemoglobin in the RBCs is found to be in a glycosylated form i.e. has glucose attached to it. The HbA_{1c} level is proportional to average blood glucose concentration over the previous two to three months and therefore is an excellent indicator of how well the patient has managed his/her diabetes over the last four weeks to three months. Glycated hemoglobin is recommended for monitoring blood sugar control in diabetic patients.

American Diabetes Association (ADA) recommends an HbA_{1c} goal of less than 7% for people with diabetes in general.

Pharmacotherapy

✓ **BIGUANIDES** (Metformin)

Mechanism of Action: Insulin sensitizer

Dose: The dose of metformin varies from 250mg to 2000mg/day. Since patients may complain of nausea and gastric irritation, the dose can be administered after a major meal. Dose of metformin can be titrated based on blood glucose monitoring at intervals of 2-4 weeks. Currently the preferred approach is to start the patient on metformin and increase the dose to at least 1g/day. If despite this dose, optimum glucose control is not achieved, a sulphonylurea should be added (see box-7 for targets of control).

Advantages

- No weight gain; some patients may experience weight loss. Hence metformin is useful in large majority of patients who are overweight
- No hypoglycaemia
- For monotherapy in obese patients
- Can be combined with other anti-hyperglycemic agents including insulin

Contraindications

- renal (Creatinine \geq 1.5mg% in men; Creatinine \geq 1.4mg% in women) / hepatic disease
- cardiac / respiratory insufficiency; other hypoxic condition ○ severe infections
- alcohol abuse
- history of lactic acidosis
- Use of I/V radiographic contrast media
- Pregnancy
- Temporarily withhold: surgery, acute illness

Caution: Phenformin is a banned drug and is not recommended

✓ **SULPHONYLUREAS (Glibenclamide)**

- The dose of glibenclamide varies from 2.5-20mg/day given in one or two doses. The dose can be titrated based on blood glucose monitoring at intervals of 1-2 weeks
- General rule: glucose lowering effect plateaus after half-maximal recommended dose
- APPROVED INDICATIONS: monotherapy; in combination with metformin and insulin
- Caution: Hypoglycemia can occur most likely to effect among elderly, those with worsening renal function and among those with irregular meal schedules

General Guidelines for using oral anti-diabetic agents:

The treatment should be individualized and the points mentioned below are only broad based Guidelines. The necessity of diet, exercise and life style modifications needs to be emphasized; in some cases these measures alone would suffice. When pharmacological treatment becomes necessary, the following points may be considered:

(i) Non-obese people with type 2 diabetes:

- In non-obese people with diabetes, start with a sulphonylurea / meglitinide or glitazone. If even after two to four weeks of initiation of treatment, symptoms still persist or blood sugar is not sufficiently controlled then a drug from another group like metformin can be added. If the initial blood sugar levels are very high, the symptoms are very severe or acute complications like ketosis are present, insulin has to be considered for treatment even at the onset, for a brief period.
- If the initial assessment shows presence of complications like diabetic retinopathy or nephropathy, this indicates a long period of undiagnosed diabetes and insulin therapy on a continuous basis should be considered.

(ii) Obese people with type 2 diabetes:

- In obese people with diabetes, the starting drug is ideally metformin.
- Similar Guidelines as mentioned above can be used to achieve good metabolic control with addition of other drugs like sulphonylureas/ meglitinides or glitazones and/ or insulin.

(iii) Lean people with type 2 diabetes:

- In India, many subjects with type 2 diabetes are lean or low body weight (BMI <18.5kg/m²). In these people with diabetes, metformin is better avoided and the use

of glitazones and sulphonylureas may be considered as first line of management. Quite often, such people with diabetes may require insulin for better control.

- With increasing duration of diabetes, most oral anti-diabetic agents tend to be less effective and hence poly-pharmacy becomes inevitable, with use of drugs from multiple classes. However, insulin use should not be delayed and, if and when necessary, insulin should be introduced for tight glycemic control.

Combination of oral drugs with insulin

When the glycemic control is not achieved with the maximum dose of an oral agent/combination therapy, this is called "secondary failure to oral hypoglycemic agents (OHA).

It has been the experience of most physicians in India that combination of oral drugs and insulin helps to achieve good control of diabetes. While using combination therapy, the oral drugs may be continued in optimal doses, while intermediate acting/long acting/short acting insulin is added either at bed time or in the morning depending on the blood sugar profile of person with diabetes. However, if indicated, one should not hesitate to use insulin in multiple doses to achieve tight metabolic control.

When to recommend hospitalization

- Uncontrolled infections;
- Severe cellulitis,
- Unresponsive UTI or other deep seated infections including bad diabetic foot needing intravenous antibiotics,
- Recurrent UTI not responding to oral antibiotics,
- Presence of ketones in urine

Diabetes patient education and diet counseling

Patient education on diabetes management and life style modifications is the corner stone of effective diabetes control and management and prevention of complications. If a diabetes educator is available then the patients and their families must visit him/her. At PHC level, nurses/multipurpose health workers can be trained to undertake this activity. At sub-district and district level hospital, dietician/counselor and nurses can undertake diabetes patient education. Counseling on diet need to be provided by a trained dietician at district and sub-district level hospital. Patient education topics that can be covered in the initial visit and follow-up visits are depicted in the table-5.1.3.

Table-5.1.3: Patient education topics to be covered in the initial and follow-up visits	
Initial Visits	Follow-up Visits
<p>What is Diabetes?</p> <p>Why does it occur?</p> <p>Lifestyle measures: Diet, Exercise</p> <p>Detailed lifestyle advice</p> <p>Use of Oral Drugs</p> <p>Advice on identifying signs and symptoms of hypoglycaemia and hyperglycaemia and their management</p> <p>Patient should be informed about the importance of factors other than glucose control: cholesterol, blood pressure, stopping smoking,/tobacco, etc</p>	<p>Importance of Glycaemic Control</p> <p>Prevention of Complications</p> <p>Foot Care (see box-5.1.3)</p> <p>Newer modalities of treatment</p> <p>Marriage Counseling</p> <p>Pre-conceptional counseling regarding the importance of good glucose control prior to pregnancy</p>

Box 5.1.3: Foot Examination

Foot care advice to the patients

Inspect your feet daily for cracks, blisters, infections, and injuries. You may be able to see a problem before you feel it. If you can't see the bottoms of your feet easily, use a mirror. A magnifying glass also may help you see better. If you can't check your own feet, have someone else do it for you.

Cleanse your feet daily as you bathe or shower, using warm water and mild soap. Dry your feet with a soft towel making sure to dry between the toes. Don't use hot water. You may burn your skin as you may not be able to feel the hotness of the water.

Moisturize dry skin by using oil. If it causes redness or irritation, discontinue its use and inform your doctor. If you are currently using a cream or lotion that keeps your skin soft and free of cracks, continue using it.

Clip toenails straight across. Use a nail cutter; don't use a scissor and also smooth down the edges.

If you can't easily reach your feet for have thick nails, have someone experienced trim your nails.

Always wear something on your feet (socks, slippers, shoes) to protect from injury - even in your house.

Choose soft good shoes. Let them be a size bigger than what you feel is appropriate. Wear socks made of cotton or wool (in winter).

Treat minor breaks in the skin promptly. Cleanse the area with soap and water, dry, and cover with clean gauze. Observe for signs of infection such as redness, swelling, warmth, pain or drainage. Don't put weight on the foot that has an injury.

See your doctor to check your feet during your regular visits for diabetes care. Take off your shoes and socks at every visit.

For more information and visual guidance visit

<http://www.healthy-india.org/preventdiabetes5.asp>

3. Follow-up visits

Annual assessment of the patients has to be carried out at CHC/secondary care level for follow-up of blood glucose, urinary microalbuminuria, fundus examination, blood lipids, creatinine, feet examination and patient education. Primary care physicians need to follow up the diabetic patients regularly for compliance with medicines, lifestyle management, blood glucose control, blood pressure control and control of other risk factors.

Eye Care in diabetes

The Retina/fundus of all diabetes patients need to be checked at least once a year by a trained ophthalmologist even if there are no eye symptoms and the vision is 6/6. The patient needs to be accordingly referred for the same to the CHC, where ophthalmologist is available. Early retinal problems don't show up as visual symptoms and a good vision should not mean that a fundus examination is not required.

Diabetes can damage blood vessels throughout our bodies. The vessels in the eyes seem especially vulnerable to damage. In the early stages of retinopathy, fluid can leak from small blood vessels in the retina. If this leaking occurs in the macula, then objects may appear blurry. However early damage can be diagnose through a retina/fundus examination and the blood vessels can be sealed with laser and vision can be saved and preserved.

Proliferative retinopathy is an advanced form of retinopathy. Proliferative retinopathy occurs when abnormal blood vessels grow on the retina and sometimes into other parts of the eye. If these vessels bleed into the vitreous - the clear fluid in the centre of the eye, light can't reach the retina and vision can become cloudy. The blood may be slowly reabsorbed and vision can return to normal but if the bleeding continues, vision may be cloudy until the problem is treated.

Tissue can also grow along with the abnormal blood vessels, distorting vision or making objects appear blurry. Over time, the tissue can shrink, pulling the retina away from its base.

If the blood doesn't reabsorb or if the tissue affects vision, the vitreous may need to be surgically removed to avoid loss of vision. All these problems of the eyes can be prevented if prevention is started early.

Checklist for preventing of diabetes complications

Every 3-6 months the patient should have a physical review by the physician. Checklist for the follow-up is as follows:

1. Test blood sugar levels
2. Test glycosylated haemoglobin levels(HbA_{1C}) (if facilities are readily available)
3. Examine feet for sensations and circulation; Also for calluses, dryness, sores, infections, injuries
4. Check blood pressure.
5. Help the patient to give up tobacco, if he/she continues to use tobacco
6. Reinforce of life style measures- increase physical activity levels and improve diet (please refer the earlier section on therapeutic lifestyle management).

Preconception counselling

Counselling on pregnancy must start before conception. All women with diabetes must know that they should not conceive till their blood glucose is well controlled for at least 2-3 months before conception as ascertained by HbA_{1C}. Hyperglycemia at conception increases the risk of complications during pregnancy as well as congenital defects in the foetus. A summary of services for diabetes management, appropriate at each levels of care, is depicted in the table 5.1.4:

Services	Levels of Care		
	Secondary care level	CHCs	PHCs
Screening for Diabetes	½	½	½
History and Physical Examination	½	½	½
Initial Assessment	½	½	X
Diabetic Patient Education	½	½	½
Pharmacotherapy			
Initiation	½	½	X
Follow-up	½	½	½
Foot care	½	½	½
Eye care	½	½	X
Annual Assessment	½	½	X
Pre-conception Counseling	½	½	½
Marriage Counseling	½	½	½

5.2. PREVENTION AND MANAGEMENT OF HYPERTENSION

Introduction

Abnormally elevated blood pressure is a pathological condition which increases the work load on the heart. This condition is termed as high blood pressure or hypertension. Based on the etiology, high blood pressure is of two types:

Primary/essential: Primary or "essential" hypertension has no known cause, however many of the above said lifestyle factors are associated with this condition. This constitutes majority of the high blood pressure in the world today.

Secondary: Secondary hypertension is caused by some other medical conditions/problem or the use of certain medications. Secondary hypertension is seen only in very few individuals in the community. The causes of secondary hypertension include: kidney diseases: reno-vascular disease and chronic renal disease, endocrine disorders: hyperthyroidism, cushing's syndrome and pheochromocytoma, sleep disorders, coarctation of the aorta and non specific aorto-arteritis. Some of these causes are often curable, and many others treatable.

Criteria for diagnosing high blood pressure

The table-5.2.1 provides a classification of blood pressure for adults ages 18 and older. The classification is based on consistent elevation during two or more properly measured BP readings in sitting position.

Table-5.2.1: Criteria for diagnosing high blood pressure		
Category	Systolic	Diastolic
Normal	Less than 120	Less than 80
Pre-hypertension	120-139	80-89
High Blood Pressure		
Stage 1	140-159	90-99
Stage 2	160 or higher	100 or higher

Source: JNC VII classification

MANAGEMENT OF HYPERTENSION:

The Risk assessment should cover:

- *Assessment of medical history*
- *Physical Examination*
- *Laboratory Investigation*

➤ ***Assessment of medical history:***

Ask for:

- a. Risk factors
 - Lack of physical activity (or sedentary lifestyle).
 - Obesity or being overweight
 - Abdominal obesity
 - High sodium intake/high salt intake
 - Excess alcohol consumption
- b. Family history
- c. Symptoms of consequences of hypertension
- d. Frequent intake of pain relieving drugs (NSAIDS)
- e. Steroid intake for asthma
- f. Breathing difficulty particularly on exertion
- g. Swelling of feet

- h. Urinary difficulties, history of passing stones in the past

➤ ***Physical examination:***

Physical examination should include

- a. BP measurement at least in one upper and one lower limb (Refer Appendix- for the procedure)
- b. Measurement of Body weight and height to obtain BMI
- c. Measurement of Waist circumference
- d. Palpating all peripheral pulses
- e. Auscultation for bruit (renal, carotid, abdominal and others)
- f. Eye evaluation if ophthalmology facility is available

➤ **Laboratory Tests:**
Essential:

- Blood Sugar
- Urine analysis for proteinuria

Desirable: (at CHC/sub-district/district level hospitals depending upon the available facilities for laboratory investigations)

- Haemogram,
- Serum creatinine
- Serum sodium and potassium levels
- Lipid profile
- Complete Urine analysis
- Electrocardiogram(ECG)
- X-Ray chest

Based on risk assessment, the management of high blood pressure cases can be initiated. The management should include the following:

- *Therapeutic life-style management (refer to section on lifestyle modification)*
- *Drug Therapy*

Drug Therapy

Whether a person requires medicines for his high blood pressure and **which** medicine is best for the patient would depend on:

- The blood pressure reading
- Whether the high blood pressure has already affected target organs in the body such as heart, kidneys, eyes and arteries
- Concurrent medical conditions such as diabetes, heart disease, kidney disease and other risk factors like use of tobacco, obesity and high blood fat levels(lipid profile) etc.
- Other considerations will be age, gender (male/female) and body weight.

Treatment Goals

Refer to the risk assessment section to manage hypertension.

1. Initial aim should be to obtain blood pressure level less than 130/85 mms of Hg
2. Ideally the aim should be to get to blood pressure levels of less than **120/80** without bothersome side-effects.
3. Don't accept blood pressure levels of **140/90** mms of Hg or more
4. Maintain healthy blood pressure throughout the person's lives

5. Prevent and control risk factors which could give rise to high blood pressure.
6. Always make sure that risk factors **are controlled**.
7. Prevent and control risk factors which could increase risk of complications due to high blood pressure.

In the Indian context, **diuretics (hydrochchlorthiozide), calcium channel blockers (amlodipine) and ACE inhibitors (Enalapril)** are relatively cheap. Drug therapy should be started in individuals at the time of diagnosis if they have blood pressure more than 160/100mmHg (despite non-pharmacological interventions) or if the blood pressure is more than 140/90 in diabetic subjects or end organ damage such as protinuria, high blood urea, ECG evidence of left ventricular hypertrophy, presence of heart diseases and evidence of retinopathy. In all other individuals life style modification should be tried for atleast six months before initiating drug therapy.

Medicines are tailored depending on the following factors

- Blood pressure level
- Patient characteristics (like age, body weight, occupation)
- Co-existing risk factors
- Type and extent of target organ damage
- Other associated diseases
- Affordability

It is better to start with calcium channel blockers (specifically if the person is older than 55 years) and ACE inhibitors if less than 55 years. Recheck the BP in 2 weeks. If BP is not under control adding diuretics (Hydrochlorothiazide 12.5 mg a day) may be helpful. Normally this should bring the BP under control. If the BP is not controlled by the combination of Amlodipine 10mg + Hydrochlorothiazide 25mg a day or Enalapril 10mg and Hydrochlorothiazide 25mg a day, a referral to a higher center may be necessary.

Life style advice is advocated for the first six month after the diagnosis of high BP in the following situations:

- If the BP is less than 160/100 mm of Hg
- There is no diabetes, co-existing heart disease stroke or peripheral vascular disease
- No evidence of LVH on ECG
- Absence of urinary proteinuria and
- Serum creatinine <1.6mg/dl

Table-5.2.2: Dosage and contraindications of Common anti-hypertensive medications			
Drug	Dose	Contra- indications	Cautions
ACE-Inhibitors	Enalapril: 5-40mg/day Captopril: 25-150mg/ day Ramipril: 2.5-20mg/day	Pregnancy Renovascular diseases	Renal impairment Peripheral vascular disease
Calcium- Channel blockers	Amlodipine: 2.5-10mg/day Nifedipine (Sustained Release): 30-60mg/day	-	Painless swelling of the feet and ankles may occur leading to its withdrawal in a few patients
Thiazides	Hydrochlorothiazide: 12.5-50 mg/day	Gout	
Beta-Blockers	Metoprolol (Sustained Release): 50-200mg/day Atenolol: 25-100mg/day	Asthma or chronic obstructive pulmonary disease, advanced Heart block	Heart failure (symptomatic) Peripheral vascular disease, Diabetes (except with coronary heart disease)

The summary of services for hypertension management, appropriate at each levels of care is depicted in table -5.2.3.

Table-5.2.3: Management of Hypertension at different levels of care			
Services	Levels of Care		
	Secondary care	CHCs	PHCs
Screening for Hypertension	½	½	½
<i>Initial Risk Assessment</i>			
Assessment of Medical History	½	½	½
Physical Examination	½	½	½
<i>Laboratory Investigation</i>			
Essential	½	½	½
Desirable	½	½	
Therapeutic Lifestyle Management	½	½	½
<i>Pharmacotherapy</i>			
Initiation (Uncomplicated cases)	½	½	½
Initiation (Complicated cases)	½	½	½
Follow-up	½	½	½
Annual Assessment	½	½	½

5. 3. PREVENTION AND MANAGEMENT OF DYSLIPIDEMIA

What is Dyslipidemia?

Dyslipidemia is characterized by elevation of plasma cholesterol, triglycerides (TGs), or both, or a low high density lipoprotein (HDL) level that contributes to the development of atherosclerosis.

Cholesterol is a fatty substance (lipid) that is present in cell membranes and is a precursor of bile acids and steroid hormones. Cholesterol exists largely as LDL-cholesterol, VLDL cholesterol, and HDL cholesterol. Along with triglycerides they are tightly packed in a central core and surrounded by surface lipoprotein particles. Several large epidemiological investigations of human populations incriminate high levels of cholesterol as being atherogenic.

The positive relationship between serum cholesterol levels and the development of first or subsequent attacks of CHD is observed over a broad range of LDL-cholesterol levels; the higher the level, the greater the risk. Prospective study data suggest that the risk of CHD plateaus at lower cholesterol levels, but this apparent plateau has disappeared in larger studies. In other words the risk of CHD is continuous at all levels of blood cholesterol therefore any definition is weighted based on risk-benefit and cost-effectiveness ratio and management is based on individualized risk of CHD.

Definition of High Blood Cholesterol

The definition of abnormal blood cholesterol is as indicated in the table 5.3.1. These are based on the Adult Treatment Panel (ATP) III recommendations of the USA as there are no indigenous Indian prospective epidemiological data on risks of high blood cholesterol on CHD. Low HDL cholesterol is an important risk factor for CHD while high HDL cholesterol has a protective effect and is considered a negative risk factor.

Table-5.3.1. Classification of blood lipid levels for therapeutic interpretation

Blood Lipids	Serum Level (mg/dl)
Total Cholesterol	
Desirable	<200
Borderline High	200-239
High	>240

Among Indians, based in the normal mean levels of cholesterol, it is preferred to have total cholesterol less than 160mg/dl

LDL Cholesterol

Optimal	<100
Near Optimal	100-129
Borderline High	130-159
High	160-189
Very High	≥ 190

Serum Triglycerides

Normal	<150
Borderline High	150-199
High	200-499
Very High	≥ 500

Serum HDL Cholesterol

Low	<40
High	≥ 60

MANAGEMENT OF HIGH BLOOD CHOLESTEROL

Management of high blood cholesterol would depend on the overall risk profile of an individual.

The broad guidelines to assess management would be based on:

1. Ascertaining whether patient has established Cardiovascular Disease like previous heart attack/ stroke/angina/peripheral vascular disease.
2. is a diabetic or not
3. what other CVD risk factors (hypertension/smoking/age/obesity) are present
4. Blood sugar/ total cholesterol/ HDL/LDL cholesterol levels(where available)

Treatment Goals

PHC Level

1. All patients with established CVD or diabetes should be counseled about non pharmacology treatment and also initiated on statins (Atorvastatin /Simvastatin).
2. Other patients should be counseled about non pharmacology treatment

CHC Level

1. All patients with established CVD or diabetes should undergo lipid profile (where a detailed profile is not available total cholesterol should be done). They must be counseled about non pharmacology treatment and also initiated on statins (Atorvastatin /Simvastatin) to achieve a LDL cholesterol of less than 100 mg/dl or Total cholesterol of less than 200 g/dl. Patients not achieving these goals with statins alone or developing complications due to them should be referred to higher centre.
2. Other patients with 2 or more CVD risk factors should undergo lipid profile/ total cholesterol testing. Their risk level should be assessed by using **risk assessment chart** and **manage accordingly**.
3. Patients with one or no risk factors should be counseled about non pharmacology treatment only.

Drug Treatment

Several classes of hypolipidemic drugs are available. However, statins are by far the most widely used first line drugs as most of evidence of proven benefit of lowering cholesterol on CVD is based on trials using them.

Table-5.3.2: Summary of Statins	
Lipid effects	LDL cholesterol - 18655% HDL cholesterol - 5615% Triglycerides - 7630%
Contraindications	Active or chronic liver disease
Major side/adverse effects	Myopathy, increased liver transaminases
Usual starting dose	Simvastatin - 20 mg Atorvastatin - 10 mg

5.4 MANAGEMENT OF CAD

Definitions

Coronary artery disease is a condition in which there is an inadequate supply of blood and oxygen to a portion of the myocardium. It typically occurs when there is an imbalance between myocardial oxygen supply and demand. The most common cause of myocardial ischemia is atherosclerotic disease of an epicardial coronary artery or arteries (fig.5.4.1) sufficient to cause a regional reduction in myocardial blood flow and inadequate perfusion of the myocardium supplied by the involved coronary artery.

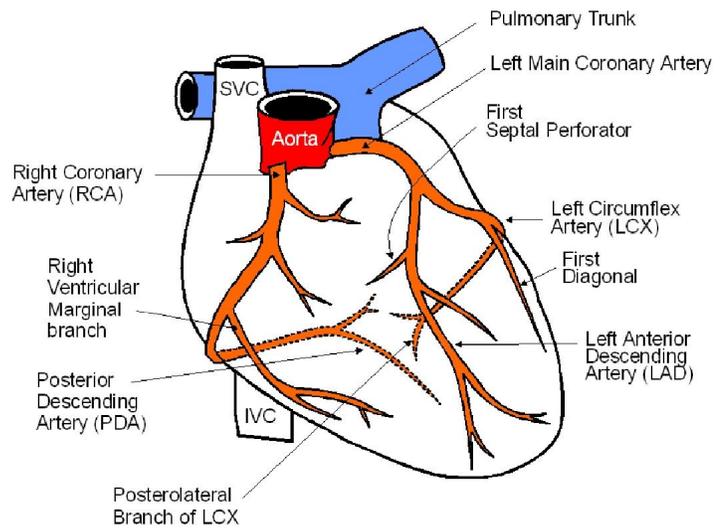


Fig 5.4.1: The coronary circulation representing specific arterial territory of the heart

“ **Coronary Artery disease (CAD):** Fifty percent or more stenosis of epicardial coronary arteries.

“ **Acute Coronary Syndrome (ACS):** A spectrum of clinical conditions from unstable angina to ST-elevation MI consequent to myocardial ischemia. Clinically, acute chest pain, typical in character, lasting more than 15 minutes. Typical defined as retrosternal discomfort (heaviness), brought about or increased with exertion and reduced with rest or nitrates.

“ **Unstable Angina (UA):** A clinical syndrome subset of ACS defined by ECG ST-segment depression or prominent T wave inversion and no elevation of cardiac biomarkers of necrosis (Troponins T/I or CPK_{MB}).

“ **NSTEMI:** A clinical syndrome subset of ACS defined by ECG ST-segment depression or prominent T wave inversion and/or positive biomarkers of necrosis in the absence of ST-segment elevation.

“ **STEMI:** A clinical syndrome subset of ACS characterized by ST-segment elevation or new onset LBBB due to myocardial necrosis.

“ **Chronic Stable Angina:** Chronic manifestation of CAD described as retrosternal discomfort (heaviness), brought about or increased with exertion and reduced with rest or nitrates lasting less than 10 minutes.

The clinical spectrums of CAD are shown in the diagram below (fig.5.4.2).

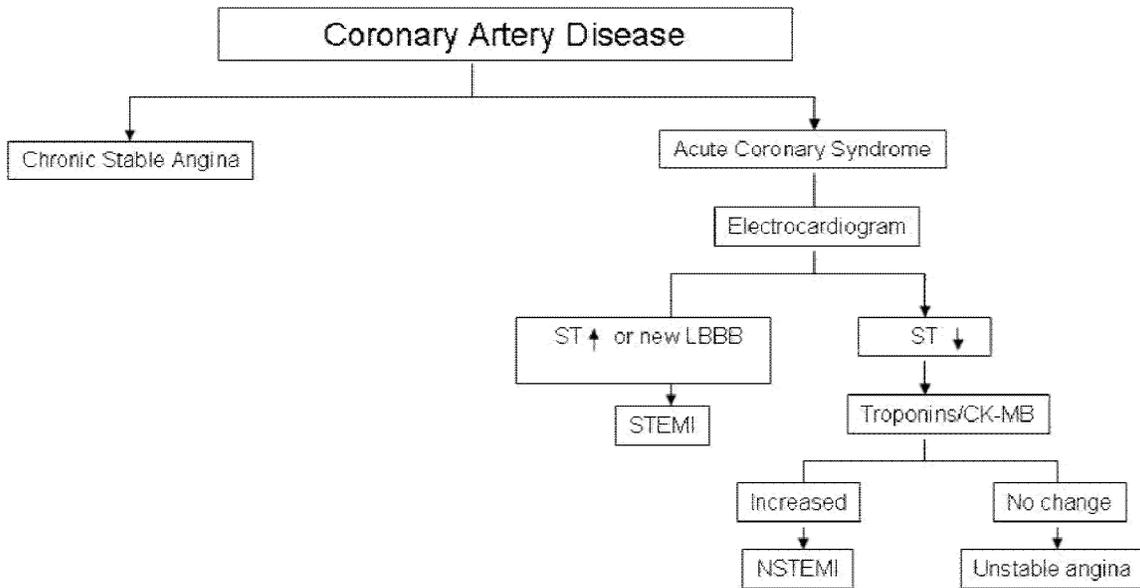


Fig.5.4.2: Flowchart showing the spectrum of CAD

Definition of myocardial infarction

MI was defined by a combination of two of three characteristics: typical symptoms (i.e., chest discomfort), enzyme rise and a typical ECG pattern. Pathologically, MI is defined as infarction of an area of the heart muscle, usually as a result of occlusion of an epicardial coronary artery.

Pathogenesis and patho physiology

Coronary artery occlusion is a dynamic process from deposition of atherosclerotic plaque and partial occlusion to complete artery occlusion (fig 5.4.3).

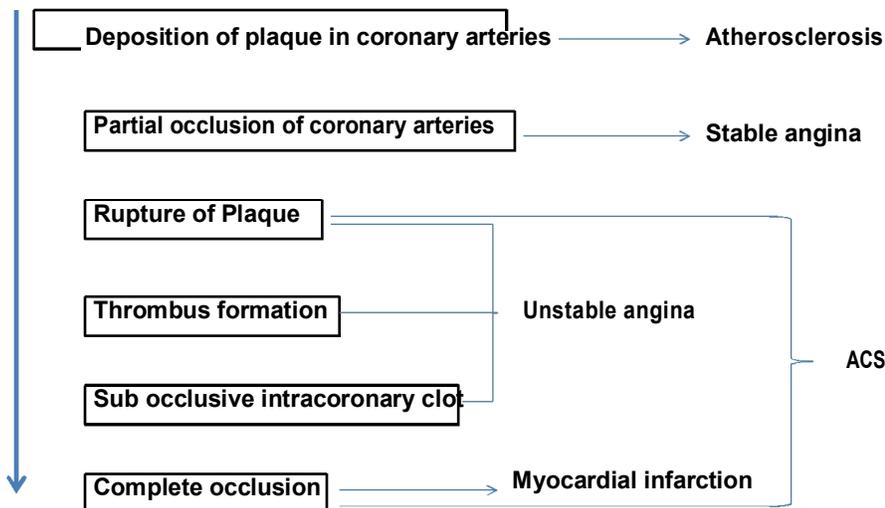
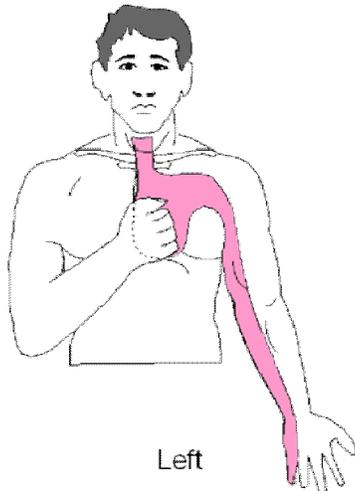


Figure 5.4.3 Spectrum of coronary artery disease

Usual distribution of pain with myocardial ischaemia



Less common sites of pain with myocardial ischaemia

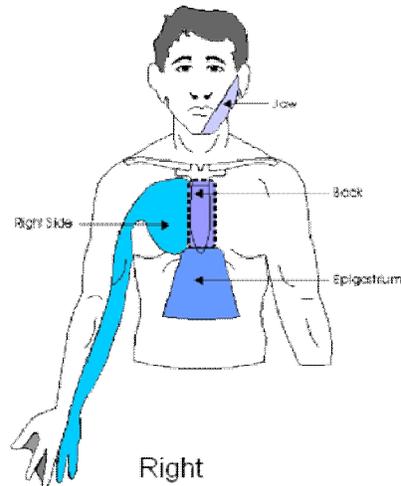


Fig.5.4.4: Figures showing the usual and unusual site of pain of angina

Clinical

Chest pain (angina) is the commonest symptom

- **Typical angina:** Substernal pressure radiating to neck, jaw, arm (Fig. 4) with duration <20-30 minutes which may be associated with dyspnea, diaphoresis, palpitations, nausea-vomiting, or lightheadedness; increases with exertion, decreases with rest or NTG. (**Note:** Rest angina is angina occurring at rest and prolonged, usually greater than 20 minutes)
- **MI:** Has increased angina intensity and duration >30 min. Twenty five percent of MIs are clinically silent. Proportion of painless STEMI is greater in patients with diabetes mellitus and increases with age.

Associated symptoms: Weakness, nausea/vomiting, sweating, apprehension, anxiety, sense of impending doom.

Other presentations, with or without pain

- “ Sudden-onset breathlessness, loss of consciousness confusional state or sensation of profound weakness
- “ Rhythm abnormalities or unexplained decrease in arterial pressure
- “ Evidence of peripheral embolism

Features not characteristics of myocardial ischemia:

- “ Sharp pain brought by respiratory movement or cough,

- “ Pain that may be localized by the tip of one finger, particularly over the left ventricular apex or a costochondral junction.
- “ Very brief episode of pain that lasts a few seconds
- “ Pain reproduced by movement or palpation over the chest
- “ Constant pain that lasts for many hours without other ischemic symptoms

Physical examination

- **Focused clinical examinations** for evidence of heart failure, peripheral hypo-perfusion (pallor, diaphoresis, cool extremities), heart murmur, elevated JVP, pulmonary edema should be noted quickly without delaying treatment.
- The presence of severe underlying coronary disease is suggested in patients with clinical **evidence of LV dysfunction, congestive heart failure**
- Pulse rate and blood pressure: Arterial pressure is variable. In most transmural infarctions, systolic pressure decreases by approximately 10-15 mmHg from the preinfarction state.
 - . Many patients have normal pulse rate and blood pressure within the first hour of STEMI.
 - . Patients with large infarctions have hypotension (systolic blood pressure <100 mmHg and/or sinus tachycardia >100/min)
 - . Anterior infarction: About one-fourth of patients have manifestations of sympathetic nervous system hyperactivity (tachycardia and/or hypertension).
 - . Inferior infarction: Up to half of patients show evidence of parasympathetic hyperactivity (bradycardia and/or hypotension).
- In right ventricular (RV) infarction, Jugular venous distention is common.
- Look for signs of ventricular dysfunction
 - . Third and fourth heart sounds
 - . Decreased intensity of the first heart sound
 - . Paradoxical splitting of the second heart sound
- Transient mid-systolic or late systolic apical systolic murmur due to dysfunction of the mitral valve apparatus may be present. New, loud (Gr 3/6) precordial systolic murmur may be present in ruptured ventricular septum and mitral regurgitation
- Pericardial friction rub in pericarditis (usually develops 24-96 hours after MI)

Electrocardiogram in ACS

- “ **A 12 lead resting ECG** (\pm RV3, RV4 for right ventricular MI) should be obtained immediately in patients with ongoing chest pain as rapidly as possible with in 10 minutes of presentation
- “ **A normal ECG does not exclude** the presence of severe CAD, and should be repeated if strong suspicion in every 4-6 hrs or earlier
- “ **ECG abnormality** includes:
 - . Resting **ST segment changes** (depression \geq 0.5 mm horizontal or down sloping in NSTEMI, convex elevation $>$ 1mm in \geq 2 consecutive leads in STEMI, pseudo normalization of ST segment or dynamic changes)
 - . New pathological **Q-waves** ($>$ 0.4 seconds) is considered diagnostic of MI, but may occur with prolonged ischemia
 - . **T wave-inversion**(\geq 2 mm symmetrical) or a peaked upright T waves may be the first ECG manifestations of Myocardial Ischemia
 - . Recent onset **LBBB**
 - . **RVTMI** is diagnosed with ST segment elevation in lead V4R, ST elevation in V1 in the presence of ST elevation in inferior leads
 - . **Non-specific ST and T changes:** ST depression $<$ 0.5 mm, T wave inversion $<$ 2mm, isoelectric T wave or asymmetric T inversion is less suggestive of myocardial ischemia.
- “ The **range of normal ST-segment** deviation differs between men and women. ST-elevation (concave upwards) in the V2 or V3 leads of 2.0 mV or less in men and 1.5 mV or less in women, or 1.0 mV or less in other leads, is normal
- “ **ECG changes that mimic MI** may result from pre-excitation, pericarditis, myocarditis, cardiomyopathy, COPD, pulmonary embolism, cholecystitis, and hyperkalemia; thus the treating physician should be aware.

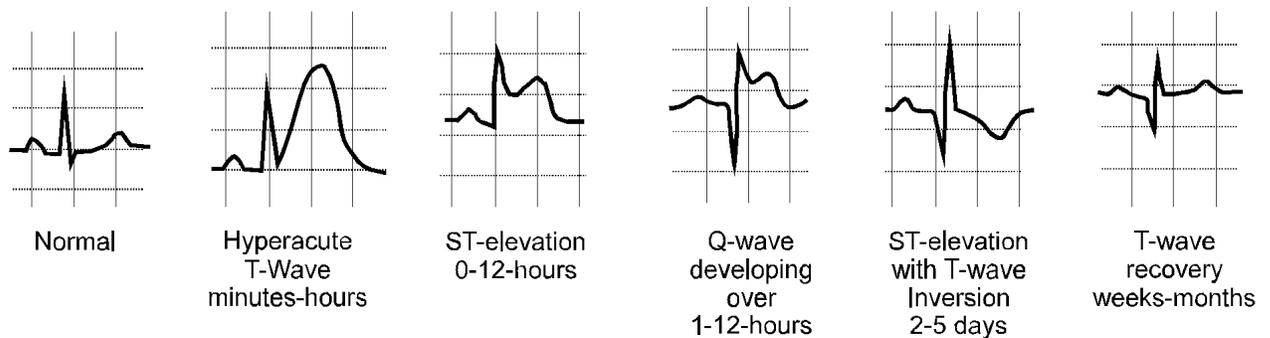


Figure 5.4.5. Evolution of ECG changes in Myocardial infarction

Laboratory studies (depending upon the facilities available):

- **Blood samples** should be sent for cardiac enzymes (biomarkers Troponin I or T and CK-MB)-for diagnosis of ACS; Hemogram, blood urea, creatinine, electrolytes, FBS -for monitoring and Fasting lipid profile- for secondary prevention. Cardiac specific troponin is the preferred biomarker (Table 5.4.1) for diagnosis of STEMI.

Table 5.4.1: Time course of serum markers in acute MI

Test	Onset	Peak	Duration
Creatine kinase - total and MB	3-12 hours	18-24 hours	36-48 hours
Troponins	3-12 hours	18-24 hours	Upto 10 days

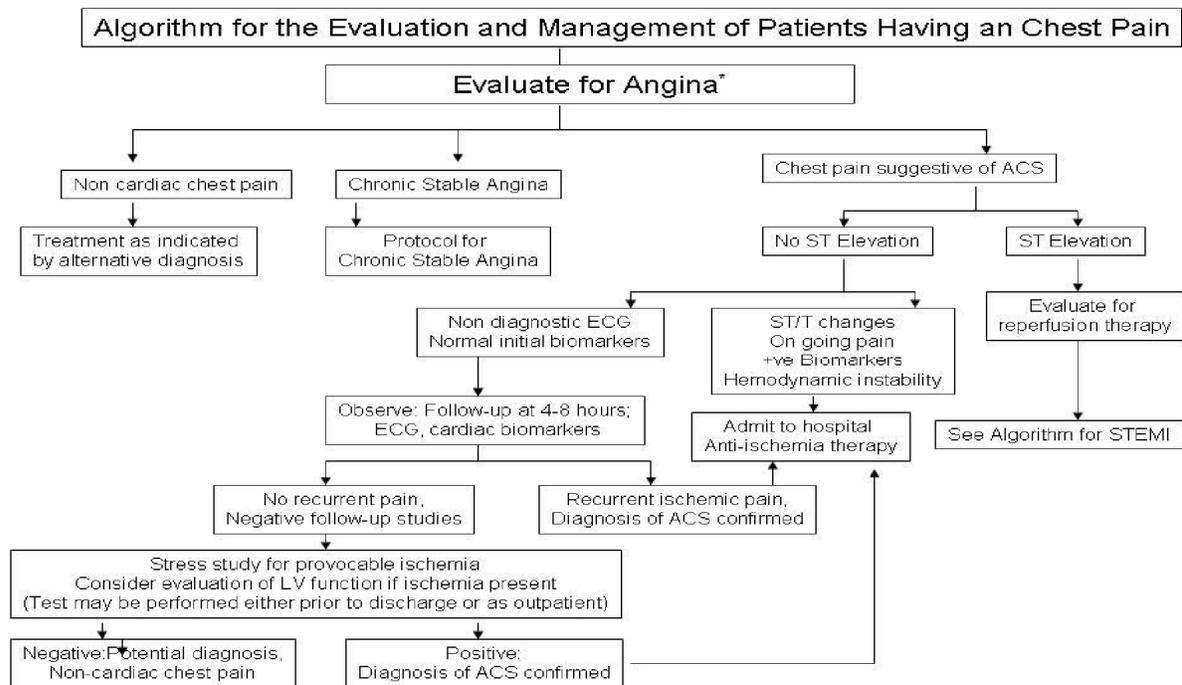
“ A portable **chest radiograph** is useful to exclude other causes of acute chest pain but it should not delay the initiation of therapy

“ Imaging: (if facilities are available)

2D echocardiography and Doppler echocardiography:

Algorithm for the Evaluation and Management of Patients with chest pain

Because symptoms are similar, the differentiation of CSA, UA/NSTEMI and STEMI from that of a non coronary chest pain requires medical evaluation and judgment (figure 5.4.6).



* History, ECG, stress tests

Figure 5.4.6. Algorithm for Evaluation and Management of Patients with Chest Discomfort.

1. Management of Chronic stable angina:

A. History: Clinical Classification of Chest Pain

“ Typical angina (**definite** if all 3 present)

2. Retrosternal chest discomfort with a characteristic quality and duration that is

3. Provoked by exertion or emotional stress and

4. Relieved by rest or nitroglycerin

“ Atypical angina (**probable**)

Meets 2 of the above characteristics

“ Non-cardiac chest pain

Meets **m1** of the typical angina characteristics

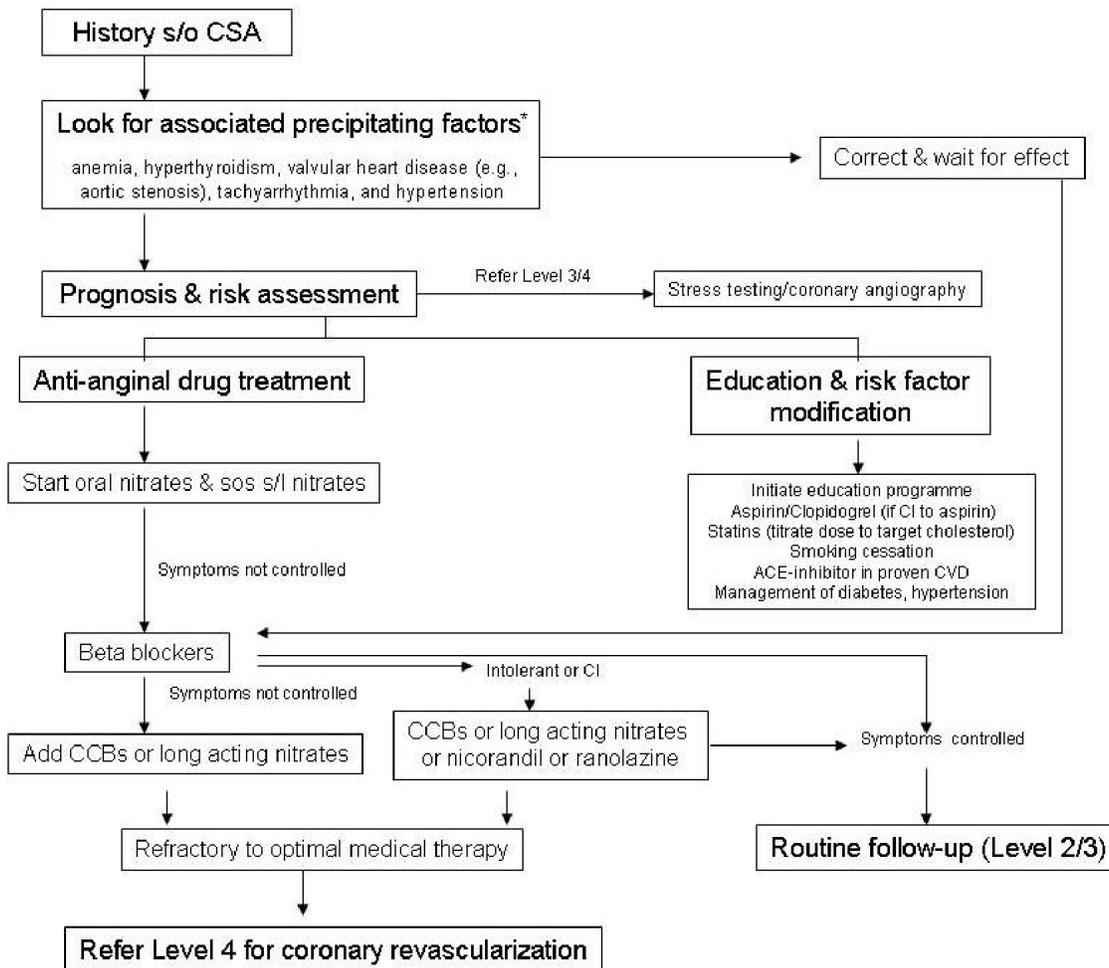


Figure 5.4.7. Management Algorithm of chronic stable angina

Table 5.4.2: Summary of Management of Chronic Stable Angina at Various Level of Health Care

Level 1 (PHC)	Level 2 (CHCs, Sub-divisional hospitals)	Level 3 (District Hospitals)	Level 4 (Medical colleges with facilities for PCI and Tertiary centers)
Diagnose and refer as soon as possible	<ul style="list-style-type: none"> <input type="checkbox"/> Detailed history <input type="checkbox"/> Investigation <ul style="list-style-type: none"> - ECG - Blood sugar, Serum creatinine, Cholesterol - Chest X ray <input type="checkbox"/> Treatment <ul style="list-style-type: none"> - Nitroglycerin (Sublingual)-sos - Oral nitrates - Beta blockers - Aspirin - Statins and ACE inhibitors - Reduce cholesterol < 200 mg/dl - Reduce LDL < 100 mg/ dl <input type="checkbox"/> Refer to level 3/ 4, if angina is not controlled despite medication 	<ul style="list-style-type: none"> <input type="checkbox"/> Management same as level 2 for new patient <input type="checkbox"/> Echocardiography for LV Function 	<ul style="list-style-type: none"> <input type="checkbox"/> Management same as level 2 for new patient <input type="checkbox"/> Angiography and revascularization if facilities are available for refractory cases

2. Initial management of ACS at emergency department

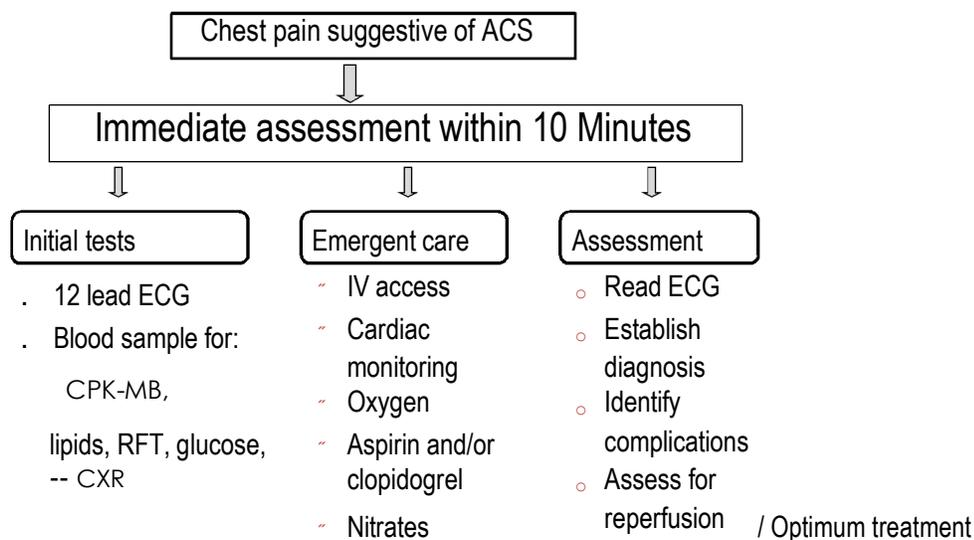


Figure 5.4.8: Flow chart for initial emergency measures in management of ACS

3. Management of Acute Coronary Syndrome (ACS)

Summary of recommendations for management of ACS at different levels				
Levels of care	Level 1 (PHC)	Level 2 (CHCs, sub-divisional hospitals)	Level 3 (District hospital)	Level 4 (Medical colleges with facilities for PCI & Tertiary centers)
History	Chest pain, associated symptoms angina equivalent, Orthopnea, presyncope/syncope	Reassess history	Reassess history	Reassess history
Examination	Pulse, BP, Cardiac auscultation, Chest auscultation	Directed physical examination	Directed physical examination	Directed physical examination
Investigations	ECG	ECG, Cardiac biomarkers (Trop T or I / CK-MB), Hemogram, FBS, Lipids, Serum electrolytes & Renal function tests	As for Level 2 and TMT & Echo (if available) - Risk stratification for CSA & low risk ACS	As for Level 3 and Cardiac catheterization lab & surgical facilities
Management	ECG Aspirin, clopidogrel, s/nitrate Prompt referral – Level 2 & higher (as per possibility)	Aspirin, clopidogrel, (if not given) s/nitrate Analgesia-morphine Anti-ischemic therapy (BB, nitrates) ACEI / ARBs if LV dysfunction Anticoagulant therapy (heparins) as per protocol Statins Thrombolysis for STEMI Refer – Level 3 for further evaluation of low risk ACS Level 4 for Primary PCI in case of CI to thrombolysis or Rescue PCI for failed lysis, Early intervention for high risk ACS Counselling & health education	Treatment protocol as for Level 2 and Thrombolysis for STEMI Refer – Level 4 for Primary PCI in case of CI to thrombolysis or Rescue PCI for failed lysis, Early intervention for high risk ACS Counselling & health education	State of the art management, including, Primary & rescue PCI.

* At sub-centre: give Tab. Aspirin 300mg stat with prompt referral to nearest Level 1 care

**Markers of successful lysis: decrease in chest pain, ST resolution of 50% or more and the development of a terminal negative T wave in the lead with the highest ST elevation

4. Medication Dosing and Administration:

Aspirin

É300 mg chewed and swallowed (150 mg × 2) upon presentation, then 150 mg daily indefinitely.

Clopidogrel

É300-mg oral loading dose, then 75 mg PO daily for 9 to 12 mo.

Heparin

ÉLMWH (Enoxaparin 1 mg/kg SC Q12 h or Dalteparin 120 IU/kg SC (max 10,000 IU) Q12h or, until PCI or till hospital admission)

β-Blockers (should be initiated in first 24 hours if no contraindications in small doses)

ÉOral Metoprolol 25-50 mg PO BD.

ÉCarvedilol 6.25-25mg BD. (if LV dysfunction)

ÉPatient with early contraindication should be reevaluated for b-blocker therapy for secondary prevention

Nitroglycerin

É0.4 mg sublingual Q 5 min × 3 for persistent ischemic pain or IV infusion starting at 5- 10 g/min with up titration for persistent ischemic pain. Oral long acting nitrates once/twice daily.

Morphine sulfate

É2-4 mg IV every 5-10 minutes until pain is relieved or side effects develop

ÉSide effects: Nausea, vomiting, respiratory depression and hypotension.

Oxygen

• 2-4 L/min by nasal cannula to maintain oxygen saturation > 90%

ACE inhibitors

• Captopril 6.25 mg TID, titrate up as tolerated

• Ramipril 2.5-5mg BD

• ARBs, (Valsartan 20-160 mg BD) in patients intolerant to ACE inhibitors with evidence of LV dysfunction.

• Aldosterone blockers (spironolactone 25mg OD, eplerenone 25-50 mg OD)

“ Post-STEMI patients who meets the following

“ No significant renal failure (Cr < 2.5 men or 2.0 for women)

“ No hyperkalemia > 5.0

“ LVEF < 40%

“ Symptomatic Congestive heart failure or Diabetes Mellitus

Insulin consider insulin infusion in first 48 hours to normalize blood glucose

5.5. PREVENTION AND MANAGEMENT OF STROKE

What is a Stroke?

A stroke means that part of the brain is suddenly damaged. If an artery in the brain becomes blocked by a thrombus, it causes a stroke. If an artery in the brain leaks then too it damages the brain and causes a stroke.

Atheroma is also known as 'atherosclerosis' or 'hardening of the arteries'. Patches of atheroma are also called 'plaques' of atheroma. Patches of atheroma are like small fatty lumps that develop within the inside lining of arteries (blood vessels).The thrombus usually forms over some atheroma.

A temporary lack of blood supply to a part of the brain is known as TIA or transient ischemic attack.

Prevent Strokes

Stroke can be prevented by controlling high blood pressure, avoiding tobacco use and leading a healthy life style. Simple tips include the following:

- Keeping blood pressure well under control.
- In case of positive family history of stroke yearly evaluation of risk factors such as hypertension and diabetes.
- Eating healthy (plenty of whole grains, fruits and vegetables in the daily diet).
- Avoiding refined flours, sugars and foods rich in trans fat such as biscuits, deep fried foods etc.

Educate the patients that if there are stroke symptoms, including sudden weakness of the face or a limb, a blurring of vision, dizziness, or an intense headache, he/she should seek immediate medical attention

Box 5.5.1: Practical advice to patients on how strokes can be prevented

➤	Know the blood pressure . Have the blood pressure checked at least once a year, and, if it is elevated, treat it diligently, to keep it under control
➤	Stopping the use of both smoking and non-smoking forms of tobacco.
➤	It is preferable to avoid alcohol due to several other ill effects on health. However for individuals who consume alcohol the consumption should be moderate (daily consumption of not more than a glass of wine or 30-50ml of hard drinks such as whisky, brandy or similar products with high alcohol content). Avoid binge drinking. It is a major risk factor for stroke because it can acutely elevate blood pressure.
➤	Including exercise in the daily routine
➤	Consuming a low-salt, low-fat diet
➤	Preferring whole grains and whole pulses and eating 10-40 gms of unsalted non-fried nuts every day.
➤	Identifying circulatory problems that could increase the risk of stroke and Atrial fibrillation
➤	Screening for hypercholesterolemia. If more than 200mg/dl, lower it by lifestyle changes like regular exercise and change in diet along with statins.
➤	Controlling diabetes , if present concurrently.
➤	Avoiding deep vein thrombosis. If a patient is recovering from illness or a surgery and is in bed, then make sure he/she exercises the legs by raising it up and down 10-15 times every day

Management

Patients of stroke presenting within 6 hours of onset of symptoms should be referred to a secondary care for initial assessment and management. The follow-up of patients presenting with a completed stroke not requiring acute care (such as respiratory distress) can be managed at the PHC level.

Identification of an acute event

- Sudden onset of weakness of one half of body or one part of body
- Sudden onset of inability or difficulty in speech
- Sudden onset of imbalance
- Sudden onset of blindness
- Sudden onset of dizziness or spinning
- Sudden severe headache
- Seizures
- Sudden loss of consciousness

All patients with above symptoms should be examined by qualified medical practitioners

Guidelines for stroke treatment at a secondary health care level

1. If available a plain CT scan should be done in all cases; contrast if indicated.
2. Secure the airway by keeping the patients head to a side; if breathing is compromised assisted ventilation to be provided and circulation should be maintained by securing a good IV line and infusing 5% dextrose.
3. Elevated blood pressure should be managed by nitroprusside, labetalol (under monitoring) or captopril in titrated doses. *In most places only captopril will be available and this can be given sublingually too.* The BP should not be brought down rapidly. The systolic should be around 140 mmHg and diastolic between 80-90 mmHg.
4. Avoid cerebral decongestants (mannitol, glycerol) unless there is evidence of raised Intra-Cranial-Pressure with signs of decerebration.
5. Provide supportive care to prevent deep vein thrombosis by prophylaxis with 5000 units heparin BD (or equivalent units of low molecular weight heparin if available and affordable).
6. Acute rehabilitation includes proper positioning, dysphasia management, passive movements of limbs, bowel/bladder care with active involvement of family members

Guidelines for referral to a tertiary health care level

1. If CT shows significant mass effect, or middle cerebral artery (MCA) dense sign suggesting massive infarction, refer to tertiary centre
2. If CT shows intra-parenchymal hemorrhage with midline compression, or a cerebellar infarct or hemorrhage refer to higher centre.
3. If CT shows primary subarachnoid hemorrhage refer to higher centre

Guidelines for follow-up of stroke at all levels

1. First follow up at 2 weeks. Follow up to be kept at 3 or 6 monthly intervals depending on individual merits of the case.
2. Look for Functional recovery,
3. Check blood pressure and blood sugars,
4. Monitor compliance with rehabilitation measures.
5. Continue Aspirin. Use of clopidogrel or combination antiplatelet agents such as low dose aspirin plus extended release dipyridamole to be instituted on individual merits of the case after risk stratification at the secondary or tertiary care centers. Cardio-embolic strokes will need oral anticoagulants with monitoring of prothrombin time.
6. Dietary and lifestyle modification. Counseling regarding vocational guidance eventual return to work

Guidelines for stroke prevention:

1. Identification of those at high risk

- High blood pressure ,
- History of heart disease,
- History of TIA,
- Past history of stroke
- Diabetes,
- Tobacco users,
- Family h/o increased risk for vascular disease,
- Obesity- sedentary life style ,
- On oral contraceptives,
- Hyperlipidemia,
- Family history of stroke

Individuals belonging to the above category are at a higher risk for stroke. Such individuals have to undertake preventive measures for stroke. Refer the section on Therapeutic lifestyle management for lifestyle changes. Subjects with established vascular diseases have to take extra precautions as described below.

2. Primary prevention in high risk individuals

Advise to adopt a healthy life style and please refer to section on healthy life style.

5.6. PREVENTION AND MANAGEMENT OF CANCERS

Cancer is a group of diseases characterized by uncontrolled cell multiplication which can occur in any living tissue in any site in the human body. Cancer develops in several phases depending on the type of tissue affected. Figure 5.6 .1 shows the phases in cancer development.



(Source- National Cancer Control Programmes ó Policies and Managerial Guidelines. World Health Organization.2nd Edition, 2002)

Incidence of cancer is the most reliable indicator of occurrence of cancer and is generated from population based cancer registries (PBCRs). PBCRs also provide data on cancer survival and mortality. Prevalence (number of persons living with the disease at any given time) of cancer can be estimated using the information on cancer incidence and survival.

Global scenario

Cancer is emerging as a major problem globally; both in more developed and in less developed countries. Annually there are over 10 million new cases of cancer and more than 6 million deaths due to cancer (12% of all deaths) worldwide. The contribution of the developing world to this figure is more than half. By 2020, the number of new cancer cases is expected to reach at least 15 million a year and cancer deaths 10 million a year.

National scenario

As per the latest National Cancer Registry Programme (Two Year Population Based Cancer Registry 2004-2005) collected from eight PBCRs there were 70,600 cancer cases out of which 49.66% (35,061) were males and 50.34% (35,539) were females.

Prevention of Cancer

Table 5.6.1 illustrates approaches for some common groups of cancers.

Table 5.6.1 Approaches in cancer control		
Prevention	Tobacco-related cancers	Tobacco control/ cessation
Early detection	Oral/Breast/Cervix	Propagation of awareness and self-examination Opportunistic examination Diagnostic support
Diagnosis and treatment	Common cancers	Training Treatment guidelines Infrastructure Referral practices
Palliative care	All advanced cancers	Oral morphine availability, Human resource development Community participation

➤ Primary Prevention

Primary Prevention aims to reduce the incidence of disease by risk factor modification. A risk factor for a disease is an attribute or exposure that increases the probability of getting the disease. As exogenous risk factors including personal habits play a major role in the etiology of cancer, modifying risk factor exposure may prevent many cancers. Among the activities for prevention, emphasis should be placed on:

- Tobacco control
- Health education relating to sexual and reproductive factors associated with cancer
- Avoiding alcohol use
- Healthy diet
- Physical activity and avoidance of obesity

Tobacco

Tobacco is the single most important modifiable risk factor for cancer. Of all cancers in India, 34% are due to tobacco (48% of cancers in men and 20% of cancers in women). Tobacco smoke contains approximately 4000 chemicals of which at least 438 can cause cancer. Tobacco smoking causes cancer of the lung, larynx and oesophagus. Smoking is also associated with

cancers of the pancreas, bladder, pelvis of the kidneys, ureter and squamous cell carcinoma of the uterine cervix. Tobacco chewing is the most important risk factor for cancer of the oral cavity. Inhalation of secondary smoke, known as 'passive smoking' is a unique feature of smoking. It results in increased risk of cancers among non-smokers exposed to tobacco smoke.

➤ Alcohol

Increasing alcohol consumption is associated with cancers of the mouth, pharynx (excluding nasopharynx), larynx, oesophagus and liver. The risk relationship between cancer and alcohol is nearly a linear relationship with the risk increasing with increasing amount of alcohol consumed. Co-existence of tobacco habits can have a multiplicative effect on development of cancer.

Control of alcohol requires actions similar to those for tobacco control. The actions should be targeted towards individual and community and include *taxation, general public education, encouraging highly vulnerable groups like young people to avoid starting consumption etc.*

Sexual and Reproductive Factors

Sexual and reproductive factors are associated with cancer of the uterine cervix and breast. Sexual behaviour factors, like young age at first sexual activity, multiple sexual partners and poor sexual hygiene, are associated with cancer of the uterine cervix. Human Papilloma Virus (HPV) has now been identified as the etiological agent responsible for cervical cancer. HPV prevalence increases with high risk sexual behaviour and poor sexual hygiene.

Late age at marriage, nulliparity, and late menopause have been linked to breast cancer, but the underlying mechanism is probably uninterrupted exposure to oestrogen for prolonged periods in all these cases.

Education regarding sexual hygiene and safe sexual behaviour may be provided for prevention of cancer cervix. Safe sexual behaviour protects women from the risk of cervical cancer by preventing infection with HPV. Breast cancer is not preventable to any large extent. Early detection of breast cancer is the main strategy for improving survival in breast cancer.

Diet

Various studies in the past two decades suggest the role of diet in human cancers. It is generally agreed that diets rich in animal fats, especially red meats, increase the risk for cancer. It is also widely accepted that diets high in fresh vegetables and fruits, and fibre reduce risk for cancer.

Certain basic measures may help in reducing risk of cancer:

Avoid being underweight or overweight

Engage in regular physical activity

Consumption of alcohol is not recommended

Limit consumption of salted foods

Choose predominantly plant based diets rich in fruits and vegetables

Occupation

Occupational cancers constitute 5-10% of all cancers. Increased risk of lung cancer has been seen in workers engaged in manufacture of rubber tyres in developing countries, textile workers, ship and dockyard workers and wood workers. Higher risk of bladder cancer was seen in workers of chemical and pharmaceutical plants. Limiting exposure to potentially carcinogenic substances through protective gear, frequent rotation of workers, mechanized handling of such chemicals and similar mechanisms may help reduce cancers from occupational exposures.

Infection

Infections with various agents are implicated in the aetiology of certain cancers. Control of cancers caused by or associated with infections depends upon success in combating the infection concerned. Measures include eliminating reservoirs and source of infection, preventing transmission, increasing host immunity through vaccination, and effective treatment of those infected.

➤ **Early Detection**

Early detection of cancer is the detection of disease at a stage in its natural history where the chance of cure is high. Early detection is only part of a wider strategy that includes diagnosis, treatment and follow-up.

Many cancers that are potentially curable at early stages are detected only in advanced stages. Diagnosis of such cancers at a stage where treatment is effective could have a major impact on the disease outcome. Certain symptoms and signs may be early indicators of some cancers.

Warning signals for Cancer

C hange in bowel or bladder habits

A wound that does not heal

U nusual Bleeding or discharge

T hickening or Lump in the breast or elsewhere

I ndigestion or difficulty in swallowing

O bvious change in a wart or mole

N aging cough or hoarseness of voice

All people should be aware of these warning signs. The presence of any of these features does not mean a definitive diagnosis of cancer. Such changes may occur in other benign conditions also. However, any such sign not responding to appropriate treatment warrants immediate medical attention and prompt management.

It is also important to train people to detect cancers in the early stage with self-examination of the oral cavity and breast.

Screening

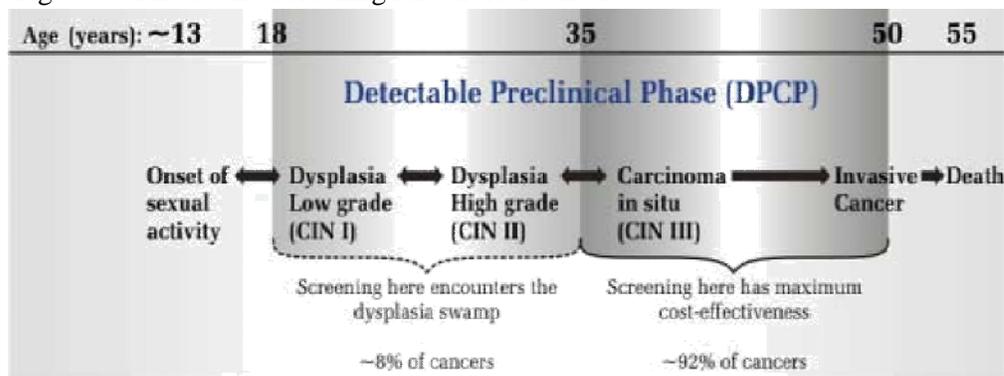
Screening is the presumptive identification of unrecognized disease or defects by means of tests, examination or other procedures that can be applied rapidly. Screening is based on the concept that there is a detectable pre-clinical phase of the disease being screened, and detection at this stage markedly alters disease prognosis. The success of screening depends on having

sufficient numbers of trained personnel to perform the screening tests with adequate coverage of target populations, and on the availability of facilities that can undertake subsequent diagnosis, treatment and follow-up. Screening is recommended for cancers of uterine cervix and breast, only if resources permit.

Screening for Cervical cancer

Cervical smear cytology is the standard screening test for cervical cancer. It is an easy and effective method revealing the presence of pre-cancerous lesions as well as in situ or very early invasive cancer. Screening should preferably begin at 35 years of age, as at younger ages dysplasia detected through screening rarely progresses to cancer, but adds to programme cost in treatment. The important requirement for cervical cytology is the availability of good laboratory services so that accurate diagnosis is possible. Fig 5.6.3 shows phases of cervical cancer and screening.

Fig 5.6.3: Phases and Screening for cervical cancer



➤ Diagnosis and Treatment

Diagnostic Methods

The diagnostic procedures in oncology are for diagnosis, determining the extent of the disease, deciding the treatment options available and evaluating the patient during follow-up. Clinical evaluation is the first and the most important step in the diagnosis of malignancy. It requires the health professional to be alert to the early warning signals. A thorough history and clinical examination of any suspicious symptom or sign is mandatory. Clinical suspicion of malignancy

can be confirmed by various diagnostic methods described below.

Radiological Evaluation

Various imaging methods are:

X ray

Fluoroscopy

Mammography

Ultrasound

C.T.Scan

Magnetic Resonance Imaging Medicine

Positron Emission Tomography Nuclear

Radio nuclide scan and Radioactivity uptake studies e.g. Thyroid, Bone

Biochemical Evaluation

This is generally done to know the organ functions, like liver function tests, and renal function tests.

Endoscopy

In oncology endoscopy is useful to:

Detect the site of primary cancer

Evaluate the extent of lesion

Perform biopsy

Perform certain therapies like endoprosthesis for oesophageal stenosis, laser therapy, etc.

Pathological Evaluation

Pathological evaluation is an important method for confirmation of clinical diagnosis and includes:

Haematological Examination: Examination of peripheral blood smear and bone marrow.

Cytological Examination:

- Exfoliative cytology: examination of exfoliated cells; e.g. female genital tract, oral cavity, urinary tract (urine examination), gastrointestinal lesions (gastric lavage) etc.
- Fine Needle Aspiration Cytology (FNAC): to obtain material from organs that do not shed cells spontaneously. Example: Breast, Thyroid, etc.
- Aspiration of body fluids: to rule out or confirm malignant effusions. Example: pleural fluid, peritoneal fluid.

Biopsy: A small chunk of tissue is removed from the suspicious site and subjected to histopathological examination. It may be:

- Excisional biopsy in small tumours
- Incisional / Punch biopsy in skin and mucosal lesions Cone biopsy in uterine cervix
- Needle biopsy in bone marrow, solid tumours of abdomen and pelvic organs.

Immunological Evaluation

Some cancers release biologic or biochemical substances, in the form of hormones, enzymes, and antigens, into the circulation. The measurement of these substances in blood can be useful in the detection and diagnosis of some types of cancers. Such chemicals are called tumour markers. Some common tumour markers and the conditions in which they may be raised are listed in Table 5.6.2

Tumour marker	Malignancies	Non-malignant conditions
Alpha feto protein (AFP)	Hepatoblastoma, Nonseminomatous germ cell tumour testis, Non-dysgerminomatous germ cell tumour ovary, Hepatocellular carcinoma,	Cirrhosis, Hepatitis
Beta human chorionic gonadotrophin (B-hCG)	Choriocarcinoma, Testicular germ cell tumours	Hypogonadism, Hydatidiform mole
Carcino embryonic antigen (CEA)	Colorectal cancers, Breast cancer, Cholangiocarcinoma, Stomach cancer	Smoking, Fatty liver, Hepatitis
CA-125	Epithelial ovarian cancer	Pregnancy, Menstruation, Endometriosis, Ascites, Pleural effusion
Prostate specific antigen	Prostate cancer	Prostatitis, Benign prostatic hyperplasia, Prostatic manipulation

Table 5.6.2 Some common tumour markers and the conditions in which they may be raised

Staging of cancer

Staging is used to assess the extent of the spread of the disease in the body. It is an indication of prognosis, and is used as a guide to determine the type and extent of treatment required.

TNM classification- The TNM classification for tumours has been adopted by the International Union against Cancer, and has been extended for many sites of cancer. This is a detailed clinical staging which is arrived at by the clinician by ascertaining the extent of the primary tumour (**T**), lymph node involvement (**N**), and presence of metastases (**M**). The information so obtained is scored. The details of scoring are specific to each type of cancer. Other systems of staging include the FIGO (International Federation of Gynaecology and Obstetrics) staging for cancers of the uterine cervix and body of the uterus, and the Duke's system of staging for cancer of the rectum.

Principles of Treatment

The primary goals of cancer treatment are cure ideally, prolongation of useful life if possible, and improvement in quality of life always. The principal methods of treatment are surgery, radiotherapy, and chemotherapy (including hormonal manipulation). Each of these modalities has a well-established role, and can be used for cure or for palliation. Appropriate combination and sequencing of these modalities can be adopted for specific cancers.

Surgery

Surgery plays an important role in the diagnosis, staging and treatment of localised cancers. Where other modalities form the mainstay of treatment, surgery can contribute through removal of tumour masses, palliation and treatment of some complications.

Surgery requires the support of other specialties including anaesthesiology, blood transfusion services, pathology (specially oncopathology) and critical care nursing. In early stage solid tumours, surgery that encompasses a sufficient margin of normal tissue is curative. These include early stage cancers of the breast, oral cavity, uterine cervix, colon, prostate and the skin. Surgery is also used post chemotherapy or radiotherapy to provide local cancer control and better chances for adjuvant therapy. In certain solid tumours, surgery is critical for reducing bulk (cytoreduction). Surgery is valuable in oncology emergencies, to relieve bowel obstruction, promote cessation of bleeding, close perforations, relieve compression, and drain ascites or pleural effusions. Apart from treatment, surgery for reconstruction and rehabilitation can improve function and cosmetic appearance and enhance quality of life for patients.

Radiotherapy

Radiotherapy is one of the most important methods of curing local cancer. Radiotherapy is the method of treating diseases with ionising radiation. The ionising radiation causes damage to certain vital structures within the cells. The cells are either damaged or are rendered incapable of further multiplication. These damaging effects on normal cells are less and reversible whereas the damage in the abnormal cell is irreversible. This differential is the principle of radiotherapeutic treatment.

Radiotherapy may be teletherapy (administered from a distance) or brachytherapy (treatment with radioactive substances within body cavities or tissues). Teletherapy may be administered by cobalt machines or by accelerators. Clinical outcomes are identical with both machines. Brachytherapy may be delivered by low dose rate (LDR) devices using caesium and high dose rate (HDR) devices using iridium or cobalt. HDR can be used for treatment of a wider variety of cancers than LDR and reduces the need for hospital bed occupancy, but demands more expertise and has higher costs.

Radiotherapy is one of the most important methods of curing local cancer. It is also often administered before or after surgery. Such treatment either facilitates surgery or consolidates surgical gains, and reduces local recurrence of disease. Palliative radiotherapy is of value in cases of pain secondary to bone metastasis and tumours causing bleeding or compressive syndromes.

Radiotherapy can cause various side effects. Patients may notice loss of appetite, nausea, and occasionally vomiting persisting for a week. The symptoms are mild in nature and seen in about 10% of patients, and are easily controlled by medicines. Other side effects depend on the site irradiated and can include mucositis and bone marrow depression. Long-term side effects are also observed.

Chemotherapy

Chemotherapy is the use of cytotoxic drugs against cancer. Cancer cells are damaged to the extent that they cannot survive. Normal cells are also damaged but to a lesser degree.

Chemotherapy is curative in certain cancers e.g. Hodgkin disease, high-grade non-Hodgkin lymphomas; palliative in many cancers, and used as adjuvant therapy for some cancers including breast cancer, ovarian cancer and colorectal cancer. The goal of adjuvant therapy (treatment given in addition to primary definitive therapy in the absence of macroscopic residual disease) is to avoid metastases, prolong life and improve quality of life. Chemotherapy is ineffective in hepatobiliary cancers, pancreatic cancer, thyroid cancer, and central nervous system cancers among others.

Acute side effects of chemotherapy are usually self-limited and reversible. Fall in blood count, hair loss, nausea, vomiting, constipation, diarrhea, anaemia, and depression of the immune system are some of the side-effects. There may be drug specific side effects like cardiotoxicity, nephrotoxicity, neurotoxicity.

Palliative care

Palliative care is an approach that improves the quality of life of patients and their families facing a life-threatening illness. This is done through prevention and relief of suffering by means of early identification, accurate assessment and treatment of pain and physical, psychosocial and spiritual problems. Palliative care involves a multidisciplinary team approach. Further details on palliative care are provided in the Manual on Palliative Care

In summary, primary prevention, early detection, prompt diagnosis and appropriate treatment, and palliative care are the main strategies for cancer control. Each cancer requires a distinctive mix of these strategies for its control. The matrix given in Table 5.6.3 suggests the options on a prevention-treatment-palliation continuum, for each cancer.

Tobacco-related cancers like cancers of the lungs, pharynx, and oral cavity are highly amenable to primary prevention. Early detection and treatment is possible for cancers of the oral cavity, uterine cervix, and breast. Palliative care is a key intervention for all types of

cancers.

Cancers of the oral cavity, uterine cervix, and breast are discussed in detail subsequently in view of the opportunity they offer for early detection and treatment with curative intent.

Table 5.6.3: Relative importance of various interventions in different cancers

Cancer	Early Detection	Surgery	Radiation	Chemotherapy/ Hormonal adjuvant the	Palliative Care
Mouth/Pharynx	+	++	+++	+	+++
Oesophagus	-	+	++	-	+++
Stomach	+	+	-	-	+++
Colon/Rectum	++	+++	++	+++	+++
Liver	-	+	-	-	+++
Lung	-	+	++	-	+++
Breast	+++	+++	++	+++	+++
Cervix	+++	++	+++	-	+++

Key: 0 = no role; + = small role; ++ = modest role; +++ = major role

(Source- National Cancer Control Programmes ó Policies and Managerial Guidelines. World Health Organization. 2nd Edition, 2002)

Issues that need to be kept in mind for all cancers

- Prompt referral of patients with any suspicion of cancer for appropriate management
- Compliance of the patient with medical advice
- Provision of psychosocial services for the patient, and the family
- Rehabilitation: Physical, psychological and social rehabilitation so that the affected individual is able to take care of self, be emotionally stable, and be able to work and socialize, to the extent possible.

Key messages

Primary prevention

- Avoid use of tobacco in any form
- Avoid alcohol
- Promote physical activity
- Eat plenty of fruits and vegetables
- Practise Safe sexual behaviour

Early detection of cancers

- Breast awareness
- Awareness in community regarding early warning signs of common cancers (Oral/Breast/Cervix)
- Opportunistic check up for oral, breast and cervical cancer
- Prompt referral and appropriate management
- Prompt referral of any suspicious case is the most important step towards cure.

Diagnostic methods:

- Clinical history & examination ó first and most important
- Radiological examination
- Pathological examination
- Diagnostic procedures help us to know:
 - The type of cancer
 - The extent (staging) of cancer
 - Treatment options and prognosis
 - Follow-up evaluation

Treatment Modalities: Surgery Radiotherapy Chemotherapy

- Treatment modalities can be used with intention of cure or palliation, and alone or in combination depending on type and extent of disease.
- Goal of treatment is ideally cure if possible and improvement in quality of life always

Role of Health Professionals in Cancer Prevention and Control

Health professionals have the following roles to play for prevention and control of Cancer

Prevention of cancers

- Create awareness about the ills of tobacco and advocate avoidance
- Encourage and assist habitual tobacco users to quit the habit
- Promote healthy dietary practices and physical activity

Early detection of cancers

- Create awareness about the early warning signs of cancer
- Encourage breast awareness
- Encourage oral self-examination
- Create awareness about symptoms of cervical cancer
- Examine, as a routine, the oral cavity of patients with history of tobacco use
- Offer clinical breast examination to any woman over 35 years presenting to the health centre
- If facilities exist, perform a pap smear test for every woman at least once in her lifetime, between 35 and 40 years of age
- Promptly refer any person with a suspicious lesion for accurate diagnosis and appropriate treatment

Treatment of cancers

- Ensure that every patient complies with therapy advised
- If follow up care is required at the health centre level, make sure that detailed instructions are provided by the treating institution

Palliative care

- Ensure that the patient is free from pain as far as possible. Learn and practice the WHO step-ladder approach of pain management; refer to the appropriate centre for oral morphine
- Achieve control of unwanted symptoms to the extent possible
- Provide psychological support to the patient to accept the diagnosis and treatment
- Involve the family in diagnosis, treatment and care as far as possible

Common Cancers

1. Cancer of the Oral Cavity

Oral cancer is one of the ten most common cancers in the world. In India, oral cancer, including cancers of the lip, tongue, gum and floor of mouth, is one the most common cancers, and may be the commonest in many regions. Oral cancer is both preventable and curable. There is usually a long natural history and most cases of oral cancer arise from pre-cancerous lesions. Therefore there is ample opportunity for intervention before actual malignancy develops. Also oral cancer responds well to surgery and radiation if detected early.

Risk factors

Tobacco chewing is the single most important risk factor for oral cancer. Other risk factors include alcohol use, betel nut chewing, and chronic trauma to oral mucosa by sharp tooth or ill-fitting dentures. Chronic exposure to these risk factors causes changes in the oral mucosa and these changes are visible as pre-cancerous lesions. Over time, malignancy may develop in these lesions.

Pre-cancerous lesions

Pre-cancerous lesions or conditions are local or generalized disturbances that predispose to malignancy in a particular site. Leucoplakia, erythroplakia, palatal changes associated with reverse smoking or beedi smoking and submucous fibrosis are local pre-cancerous lesions. Plummer Vinson syndrome, syphilis, and erosive lichen planus are generalized pre-cancerous conditions. All these conditions are amenable to early diagnosis, and treatment is possible in many cases.

Leucoplakia

This is defined as a white patch that cannot be characterized as any other disease clinically or pathologically (Figure 5.6.4).

They can be of 4 types:

- a. Homogeneous leucoplakia: Low risk of cancer
- b. Ulcerated or erosive leucoplakia: High risk of cancer
- c. Speckled or nodular leucoplakia: High risk of cancer
- d. Verrucous leucoplakia: Very high risk of cancer

Two or more types of leucoplakia may be present



Figure 5.6.4: Homogeneous leucoplakia involving dorsum and right lateral border of tongue

in the oral cavity at the same time. Confirmatory diagnosis is by biopsy

Erythroplakia:

This is a bright, velvety area sometimes surrounded by faint plaques which cannot be characterized as any other lesion clinically or pathologically (Figure 5.6.5). About 90% of these lesions show cellular dysplasia or malignancy. The risk of malignancy in erythroplakia is higher than in leucoplakia.



Figure 5.6.5: Erythroplakia

The most common cancer seen in the oral cavity is **squamous cell carcinoma**. It presents as a painless ulcer, mass or fissure. As the disease advances, patient may have excessive salivation, trismus, and difficulty in chewing, swallowing or cervical lymphadenopathy. Distant metastases are uncommon in oral cancers.

Early detection: This is important for detecting oral lesions at an early stage

I. Self Examination of oral cavity



Figure 5.6.6: Self Examination of oral cavity

II. Examination by a health professional

Utilize every opportunity to examine the oral cavities of tobacco users. All parts of the oral cavity should be examined; oral cavity includes lip, anterior 2/3 of tongue, floor of mouth, buccal mucosa, gingival mucosa, hard palate and retromolar trigone (Figure 5.6.7).

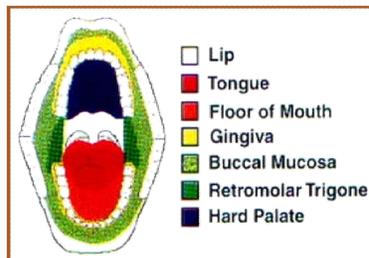


Figure 5.6.7 Oral Cavity

Management of Oral Cancer

Management may be through surgery, radiotherapy, chemotherapy, or a combination of modalities. Figure 5.6.8 presents a flow chart of management of any person with a suspicious oral lesion.

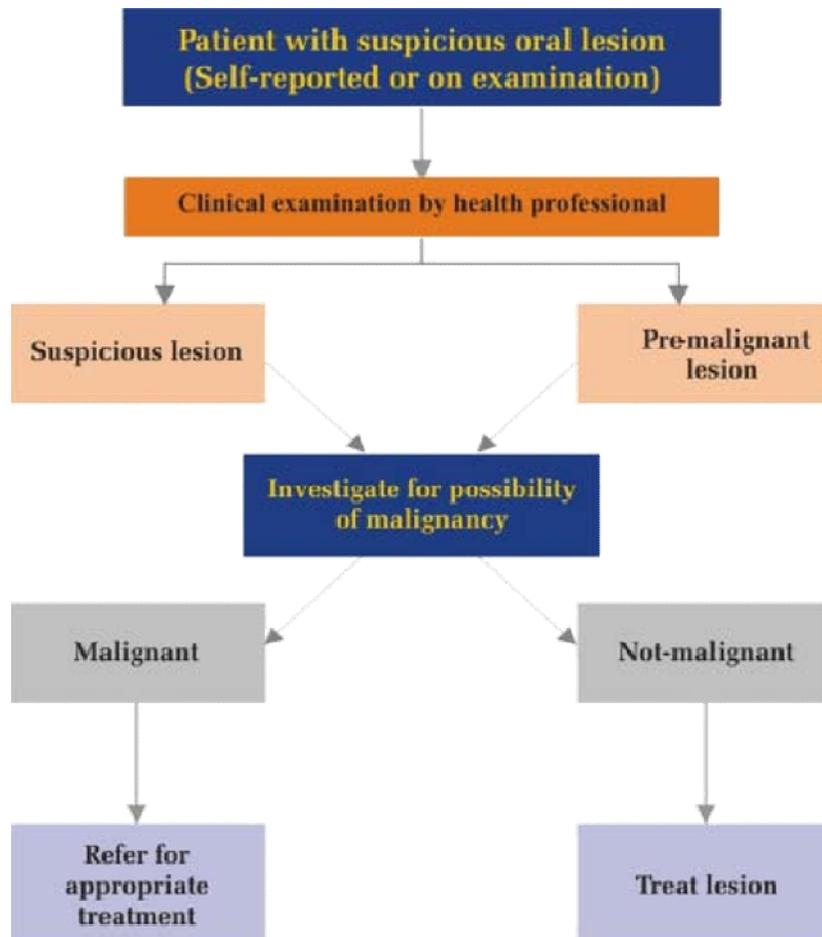


Figure 5.6.8: flowchart for management of patient with an oral lesion

2. Cancer of the Uterine Cervix

Cervical cancer is the third most common cancer among women in the world and the leading cause of death from cancer among women in developing countries. In India more than 100,000 new cases of cervical cancer occur each year and nearly 75,000 women die annually from this disease.

Human Papilloma virus infection, which is a sexually transmitted infection, is the primary cause of this cancer. HPV prevalence increases with multiple sexual partners for both spouse, and poor genital hygiene of both partners.

Symptoms of cancer of the uterine cervix:

In the early stages, there will be no symptoms. By the time symptoms appear, disease may have already spread. Common symptoms are:

- Post-menopausal bleeding
- Post-coital bleeding
- Intermenstrual bleeding
- Blood stained discharge per vaginum
- Excessive seropurulent discharge
- Backache
- Lower abdominal pain

Screening for Cervical Cancer

Screening for cervical cancer can be considered in women aged 30 to 59 years, as the chances of detecting pre-cancerous lesions are maximum in this age group. Regular population Based Screening using Pap Smear cytology is internationally accepted screening method for cervical cancer. In low resource setting, Visual Inspection with Acetic Acid is a useful alternative to categorise women as 'high risk' and 'low risk'.

Pap smear:

The ectocervix and the endocervix are scraped to collect cells that are spread on a glass slide, stained in the laboratory and examined under microscope. Depending on the features of the cells seen under microscope the cytopathologist (or a trained technologist) can report the smear as 'negative' (normal) or 'positive' (abnormalities suspicious of low grade or high grade CIN).

Requirement for Pap smear

- Examination gloves
- Speculum (Cusco's self-retaining type preferred)
- Ayre's spatula (Figure 5.6.9) and endocervical brush (if available)
- Glass slide
- Diamond tipped pencil to write on glass slide (if the glass slide has frosted edge an ordinary pencil can be used to label it)
- Focusing light
- Coplin's jar
- 95% ethyl alcohol
- Cytology form

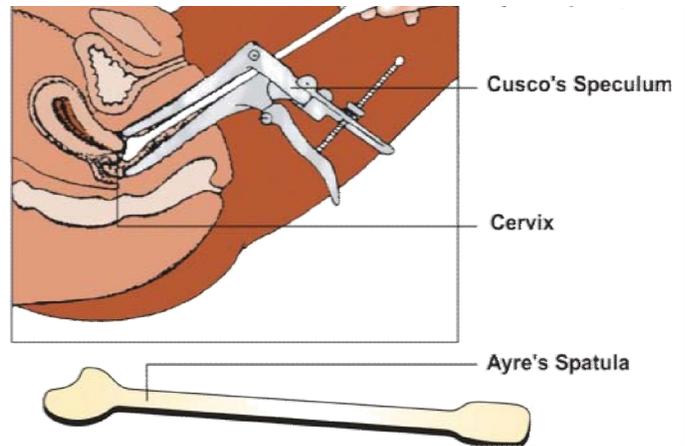


Figure 5.6.9: Cusco's Speculum and Ayer's Spatula

Procedure:

- Procedure should be explained to the woman.
- Clean a glass slide with dry cotton and label it.
- The woman should lie down on her back with legs folded (lithotomy position not required).
- Insert the speculum gently and expose the cervix.
- Note any abnormal discharge, bleeding or growth in the cervix.
- Insert the long tip of the Ayre's spatula into the os so that the curvature touches the ectocervix. Maintaining gentle pressure, rotate the spatula a full 360 degrees circle (Fig. 5.6.10).
- Spread the content of either side of the spatula on one side of the glass slide by one or two swipes.

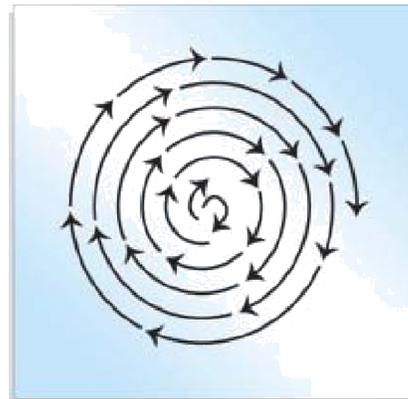


Figure 5.6.10: Preparation of smear

Visual Inspection using 4% Acetic acid (VIA):

Acetic acid causes dehydration of the cells and some surface coagulation of proteins thereby reducing the transparency of the epithelium. These changes are more prominent in abnormal epithelium and can be easily distinguished on naked eye inspection.

Requirements:

- Examination gloves
- Speculum (Cusco's self-retaining type preferred)
- Cotton tipped swabs
- Freshly prepared 5% acetic acid (to be produced at least once a week by diluting 5 ml of glacial acetic acid with 95 ml of distilled water)
- Focusing light (with halogen bulb preferred)

Procedure:

- Procedure should be explained to the woman.
- The woman should lie down on her back with legs folded (lithotomy position not required).
- Insert the speculum gently and expose the cervix.
- Note any abnormal discharge, bleeding or growth in the cervix.
- Apply adequate amount of acetic acid to the cervix using the cotton swabs.
- Wait for 1 minute to note the changes.
- Identify the squamo-columnar junction(SCJ) as the line joining the pink smooth squamous epithelium with the red velvet like columnar epithelium
- Look for white patches.
- If there are no white patches in the ectocervix the test is negative
- All the aceto-white patches are not considered positive.
- If there is a white patch, its density, margin and the relationship to the SCJ should be noted.



Figure 5.6.11: Normal Cervix



Figure 5.6.12: Visual inspection with acetic acid showing acetowhitening

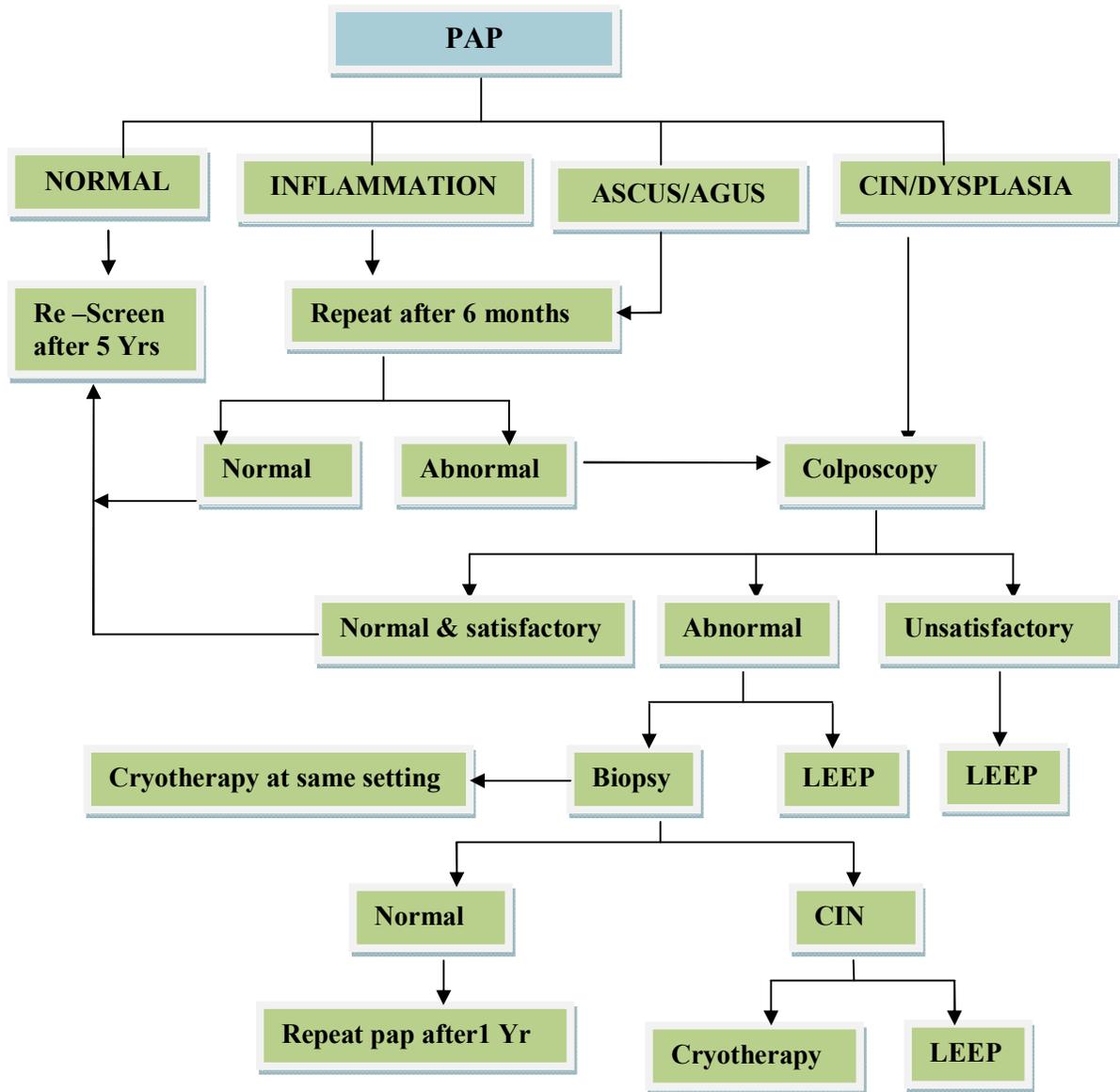
Table 5.6.4 gives the detailed criteria categorizing VIA test results as negative or positive or invasive cancer

Criteria for categorizing VIA test results as negative or positive or invasive cancer

VIA category	Description
Negative	<ul style="list-style-type: none"> • No aceto-white lesions • Transparent lesions or faint patchy lesions without definite margins • Nabothian cysts becoming aceto-white • Faint line like aceto-whitening at the junction of columnar and squamous epithelium • Aceto-white lesions far away from the transformation zone
Positive	<ul style="list-style-type: none"> • Distinct, opaque aceto-white area <p>Margin should be well defined, may or may not be raised</p> <p>Abnormality close to the squamocolumnar junction in the transformation zone and not far away from the os.</p>
Invasive cancer	<p>Obvious growth or ulcer in the cervix. Acetowhite area may not be visible because of bleeding</p>

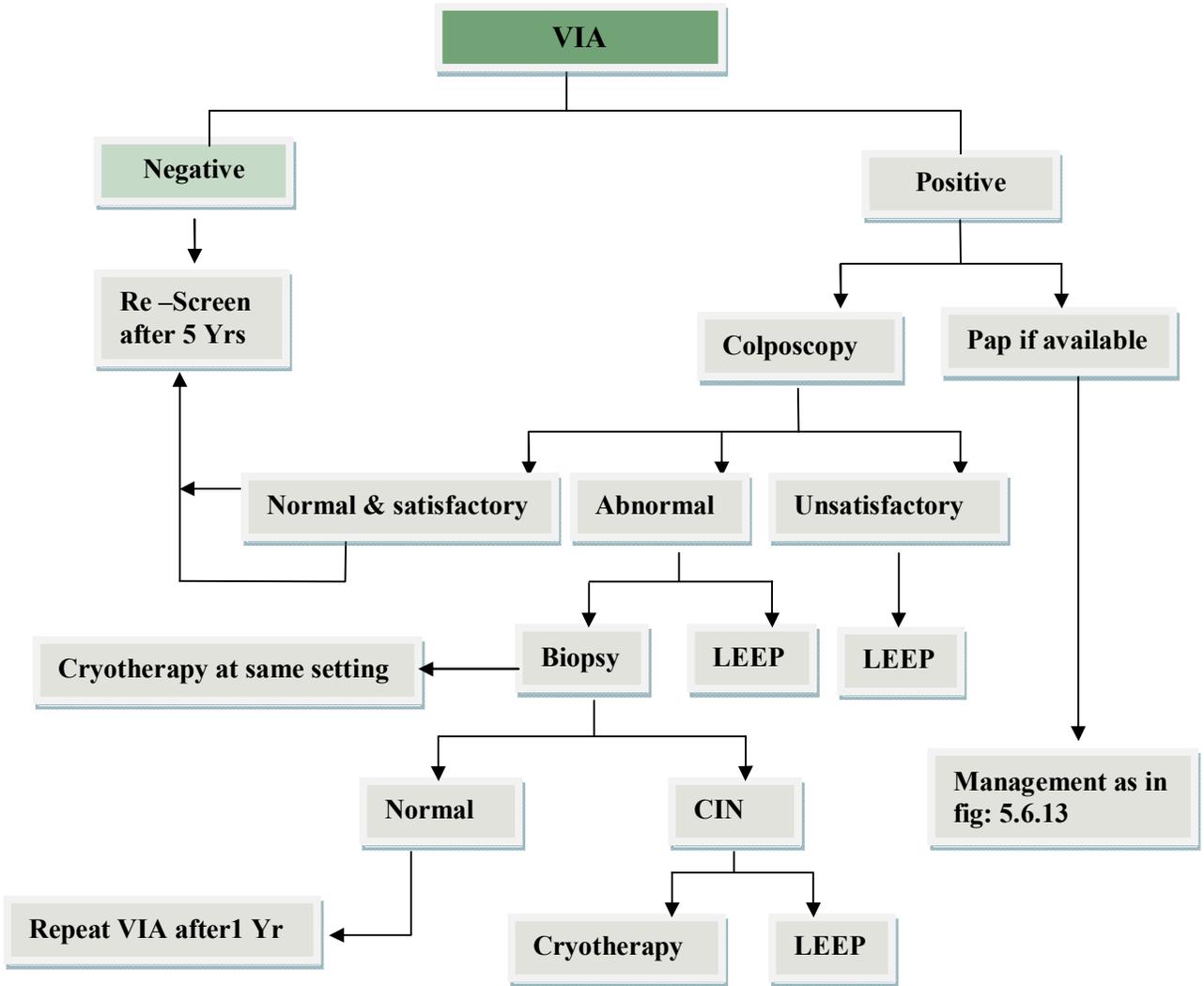
Management of women with abnormal tests

All cases of suspicious smears or visual inspections should be subjected to colposcopy for better visualization. Biopsy, either by endocervical curettage or cervical cone biopsy should be done in all suspicious cases on colposcopy. For such investigations, women should be promptly referred to the nearest centre performing these investigations. Figures 5.6.13 and 5.6.14 depict the sequential management of women with abnormal test results on Pap and VIA.



CIN: Cervical Intraepithelial neoplasia
 LEEP: Loop Electricosurgical Excisional Procedure
 ASCUS: Atypical Squamous cells of unspecified significance
 AGUS: Atypical glandular cells of unspecified significance

Figures 5.6.13: Sequential management with abnormal test results on Pap



Figures 5.6.14: Sequential management with abnormal test results on VIA

3. Cancer of the Breast

Breast cancer is the commonest cancer among women all over the world. In India, it is the second most common cancer among women after cancer of the uterine cervix and is emerging as the commonest cancer in urban centres. Data from Hospital Based Cancer Registry (HBCR) show that only about 15% of patients present in localized stage. Regional Lymph nodes are involved in around 75% at the time of presentation and about 10% have distant metastases at the time of presentation

Risk factors

Some of the risk factors for breast cancer are

- Reproductive and hormonal factors ó the older a woman is when she has her first child, the greater her chance of having breast cancer. Women who begin menstruation early (before age 12), have menopause late (after age 55) or never had children are also at greater risk. Women who take menopausal hormone therapy (oestrogen and progesterone) for five years or more after menopause also appear to have an increased risk.

- Family History: Risk of cancer increases in women with a first-degree relative with bilateral breast disease

- Other factors:

Being obese after menopause: women who are obese after menopause are at higher risk of breast cancer.

Physical inactivity: women who are physically inactive throughout life have a greater risk of having breast cancer.

Alcohol intake: some studies suggest that the risk of breast cancer increases with increased intake of alcoholic beverages.

Prompt diagnosis of breast cancer in the early stage is very important. This is possible by increasing the level of awareness among women and health care professionals. The following methods may be used for early detection

Breast awareness and breast self examination (BSE): The first person to detect any lump in the breast is the woman herself. For this, it is essential that every woman be aware of the size, shape and consistency of her breasts, and know when there is an abnormal change in any of these

Every woman should be aware of the following signs ó

- A change in size
- A nipple that is pulled in or changed in position or shape
- A rash on or around the nipple
- Discharge from one or both nipples
- Puckering or dimpling of skin
- Lump or thickening in the breast
- Constant pain in the breast or armpit

In case a woman notices any such change, she should promptly visit the health centre or a health professional.

Clinical Breast Examination (CBE): This is to be performed by a physician, trained nurse or a health worker. It is recommended that women may be examined for any lump in the breast when they have come for other reasons.

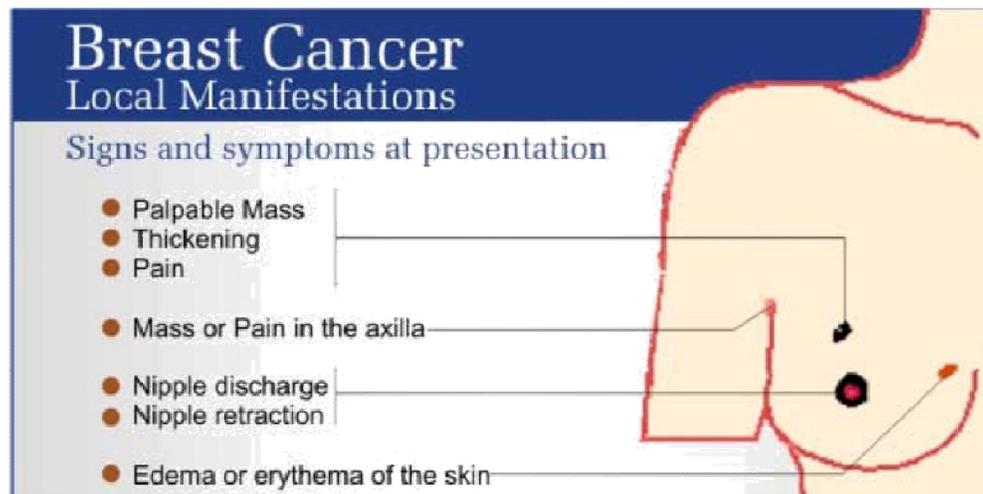


Fig.5.6.15 Sign and Symptoms of Breast Cancer

Management of breast cancer

Breast cancer is managed by surgery, radiotherapy, chemotherapy (including hormone therapy), or a combination of the three. Figure 5.6.10 shows the management of a person with a suspicious breast lump in a flowchart.

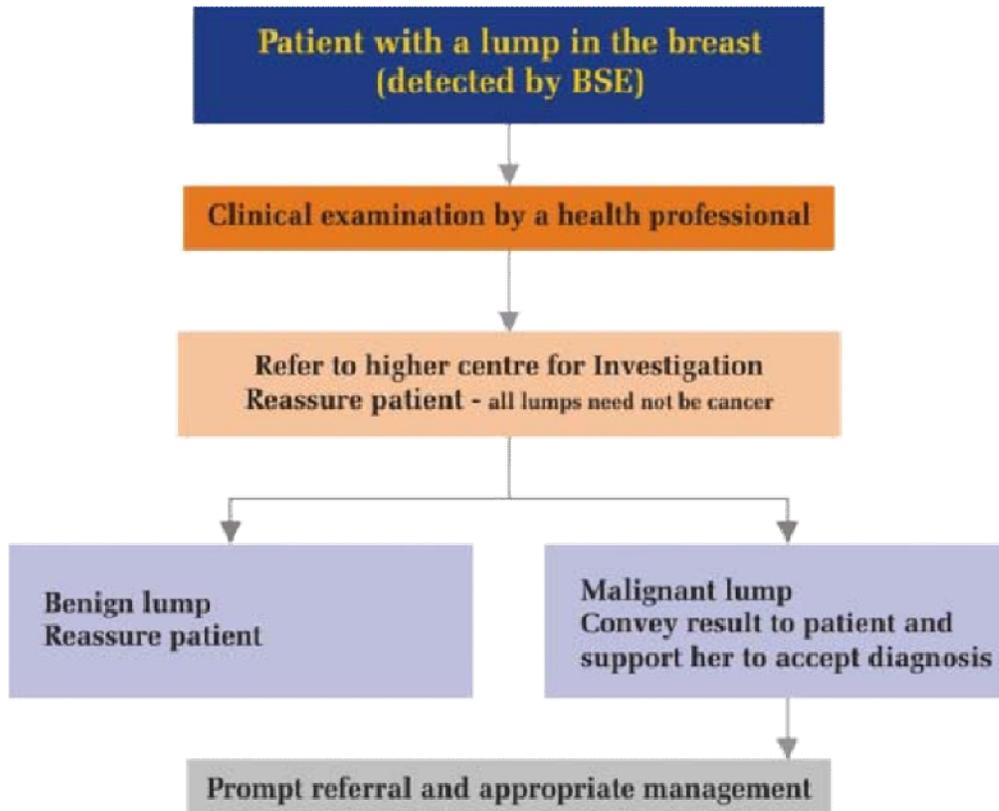


Figure 5.6.16: Flowchart of management of a suspicious breast lump

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