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ФЕДЕРАЛЬНОГО АГЕНСТВА ПО ЗДРАВООХРАНЕНИЮ
И СОЦИАЛЬНОМУ РАЗВИТИЮ»
КАФЕДРА ПРОПЕДЕВТИКИ ВНУТРЕННИХ БОЛЕЗНЕЙ

Пропедевтика внутренних болезней

Учебно-методическое пособие
Часть VII

Introduction to Internal Diseases

Manual
Part VII

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Учебно-методическое пособие составлено в соответствии с Государственным образовательным стандартом высшего профессионального образования (2000), Государственными требованиями к минимуму содержания и уровню подготовки выпускника вуза по специальности 040100 «Лечебное дело», типовой и рабочей программами по дисциплине «Пропедевтика внутренних болезней» (2003). В учебно-методическом пособии подробно освещается содержание занятий, даны теоретические и справочные материалы, описываются практические умения в четкой последовательности действий у постели больного. Пособие предназначено для иностранных студентов медицинских вузов.

CONTENTS

PART VII

DIAGNOSTICS OF CARDIOVASCULAR DISEASES

HYPERTENSION AND ATHEROSCLEROSIS

Theme 27. HYPERTENSION. ESSENTIAL HYPERTENSION (HYPERTENSIVE DISEASE) AND SECONDARY (SYMPTOMATIC) HYPERTENSIONS. DIFFERENTIAL DIAGNOSTICS.

Goal: to get a notion about the main cardiovascular diseases, their symptoms and signs, diagnostic meanings of additional diagnostic methods data; instrumental diagnostics of cardiovascular diseases; to master skills.

Knowledge objectives:

- to know symptoms and signs of main cardiovascular diseases, appropriate changes of physical examination data, diagnostic meaning of additional diagnostic methods and their findings in these diseases.

Skill objectives:

- to collect interviewing data, to perform physical examination of patients with cardiovascular diseases (inspection, palpation, percussion and auscultation), to interpret data of additional diagnostic methods, to establish diagnosis of main cardiovascular diseases.

Subject-matter:

1. complaints of patients with hypertension
2. etiology and pathogenesis of primary hypertension
3. risk factors of hypertension
4. estimation of absolute cardiovascular risk in hypertensive patients
5. hemodynamics changes in essential hypertension
6. classification of hypertension and hypertensive disease
7. physical examination data in patients with hypertension
8. signs of target organs damage in hypertension
9. instrumental diagnostics of hypertension
10. laboratory diagnostics of target organs damage
11. instrumental diagnostics of target organs damage
12. differential diagnostics of primary and secondary hypertension

Equipment required: stethoscope.

EDUCATIONAL MATERIAL

HYPERTENSION

Arterial hypertension is elevation of systolic (systolic BP >= 140 mm Hg) and/or diastolic BP (>= 90 mm Hg,), either primary or secondary, which can damage the walls of arteries, arterioles and the left ventricle of the heart with serious consequences, chiefly affecting the brain, heart, kidneys and eyes.

Prevalence

It is one of the most common disorders in the Western world, with a prevalence of about 15%.

It is estimated that there are nearly 50 million hypertensives in the USA and about 27 % of all patients with cardiovascular disease in Russia. Hypertension occurs more often in black adults (32%) than in white (23%) adults, and morbidity and mortality are greater in blacks. Diastolic BP increases with age until age 55 or 60.

Prevalence of isolated systolic hypertension (ISH-- >= 140 mm Hg systolic, < 90 mm Hg diastolic) increases with age until at least age 80. If persons with ISH and diastolic hypertension are considered, > 50% of black and white men and > 60% of women over age 65 have hypertension. ISH is more prevalent among women than men in both races. Between 85 and 90% of cases are primary (essential); in 5 or 10%, hypertension is secondary to bilateral renal parenchymal disease or endocrinopathy , and only 1 or 2% of cases are due to a potentially curable condition.

Etiology and Pathogenesis

Primary hypertension: Primary (essential) hypertension is of unknown etiology; its diverse hemodynamic and pathophysiologic derangements are unlikely to result from a single cause. The term “hypertensive disease” is used in Russia.

Heredity is a predisposing factor, as shown by the relevance of a family history of hypertension and by racial variations in prevalence. but the exact mechanism is unclear.

Environmental factors (eg, dietary Na, obesity, stress) seem to act only in genetically susceptible persons.

The pathogenic mechanisms must lead to increased total peripheral vascular resistance (TPR) by inducing vasoconstriction, to increased cardiac output (CO), or to both because BP equals CO (flow) times resistance. Although expansion of intravascular and extravascular fluid volume is widely claimed to be important, such expansion can only raise BP by increasing CO (by increasing venous return to the heart), by increasing TPR (by causing vasoconstriction), or by both; it frequently does neither.

Abnormal Na transport across the cell wall due to a defect in or inhibition of the Na-K pump (Na+,K+-ATPase) or due to increased permeability to Na+ has been described in some cases of hypertension. The net result is increased intracellular Na, which makes the cell more sensitive to sympathetic stimulation. Because Ca follows Na, it is postulated that the accumulation of intracellular Ca (and not Na per se) is responsible for the increased sensitivity. Na+,K+-ATPase may also be responsible for pumping norepinephrine back into the sympathetic neurons to inactivate this neurotransmitter. Thus, inhibition of this mechanism could conceivably enhance the effect of norepinephrine. Defects in Na transport have been described in normotensive children of hypertensive parents.

Stimulation of the sympathetic nervous system raises BP, usually more in hypertensive or prehypertensive patients than in normotensive patients. Whether this hyperresponsiveness resides in the sympathetic nervous system itself or in the myocardium and vascular smooth muscle that it innervates is unknown, but it can often be detected before sustained hypertension develops. A high resting pulse rate, which can be a manifestation of increased sympathetic nervous activity, is a well-known predictor of subsequent hypertension. Some hypertensive patients have a higher-than-normal circulating plasma catecholamine level at rest, especially early in clinical development.

In the ***renin-angiotensin-aldosterone system***, the juxtaglomerular apparatus helps regulate volume and pressure. Renin, a proteolytic enzyme formed in the granules of the juxtaglomerular apparatus cells, catalyzes conversion of the protein angiotensinogen to angiotensin I. This inactive product is cleaved by a converting enzyme, mainly in the

lung but also in the kidney and brain, to angiotensin II, which is a potent vasoconstrictor that also stimulates release of aldosterone. Also found in the circulation, the angiotensin III is as active as angiotensin II in stimulating aldosterone release but has much less pressor activity.

Renin secretion is controlled by at least four mechanisms that are not mutually exclusive: A renal vascular receptor responds to changes in tension in the afferent arteriolar wall; a macula densa receptor detects changes in the delivery rate or concentration of NaCl in the distal tubule; circulating angiotensin has a negative feedback effect on renin secretion; and the sympathetic nervous system stimulates renin secretion via the renal nerve mediated by receptors.

The mosaic theory states that multiple factors sustain elevated BP even though an aberration of only one was initially responsible; eg, the interaction between the sympathetic nervous system and the renin-angiotensin-aldosterone system. Sympathetic innervation of the juxtaglomerular apparatus in the kidney releases renin; angiotensin stimulates autonomic centers in the brain to increase sympathetic discharge. Angiotensin also stimulates production of aldosterone, which leads to Na retention; excessive intracellular Na enhances the reactivity of vascular smooth muscle to sympathetic stimulation.

Hypertension leads to more hypertension. Other mechanisms become involved when hypertension due to an identifiable cause (eg, catecholamine release from a pheochromocytoma, renin and angiotensin from renal artery stenosis, aldosterone from an adrenal cortical adenoma) has existed for some time. Smooth muscle cell hypertrophy and hyperplasia in the arterioles resulting from prolonged hypertension reduce the caliber of the lumen, thus increasing TPR. In addition, trivial shortening of hypertrophied smooth muscle in the thickened wall of an arteriole will reduce the radius of an already narrowed lumen to a much greater extent than if the muscle and lumen were normal. This may be why the longer hypertension has existed, the less likely surgery for secondary causes will restore BP to normal.

Deficiency of a vasodilator substance rather than excess of a vasoconstrictor (eg, angiotensin, norepinephrine) may cause hypertension. The kallikrein system, which produces the potent vasodilator bradykinin, is beginning to be studied. Extracts of renal medulla contain vasodilators, including a neutral lipid and a

prostaglandin; absence of these vasodilators due to renal parenchymal disease or bilateral nephrectomy would permit BP to rise. Modest hypertension sensitive to Na and water balance is characteristic for anephric persons (renoprival hypertension).

Endothelial cells produce potent vasodilators (nitric oxide, prostacyclin) and the most potent vasoconstrictor, endothelin. Therefore, dysfunction of the endothelium could have a profound effect on BP. The endothelium's role in hypertension is being investigated. Evidence that hypertensive persons have decreased activity of nitric oxide is preliminary.

Secondary hypertension: Secondary hypertension is associated with **renal parenchymal disease** (eg, chronic glomerulonephritis or pyelonephritis, polycystic renal disease, collagen disease of the kidney, obstructive uropathy) or **pheochromocytoma, Cushing's syndrome**, **primary aldosteronism**, **hyperthyroidism, myxedema, coarctation of the aorta, or renovascular disease**. It may also be associated with the use of excessive alcohol, oral contraceptives, sympathomimetics, corticosteroids, cocaine, or licorice.

Hypertension associated with ***chronic renal parenchymal disease*** results from combination of a renin-dependent mechanism and a volume-dependent mechanism. In most cases, increased renin activity cannot be demonstrated in peripheral blood, and careful attention to fluid balance usually controls BP.

Pathologic anatomy.

No early pathologic changes occur in primary hypertension.

Large and medium-sized arteries respond to high blood pressure by thickening of the media and disruption of the elastic tissue within their walls. The vessels may become tortuous and dilated and may rupture because of the high pressure in the lumen. If this occurs in the brain, cerebral haemorrhage usually leaves the patient dead or paralysed from a ‘stroke’. Hypertension also promotes the formation of atheroma in medium-sized and large arteries, so a stroke may also be caused by occlusion of a cerebral artery by thrombus formed on an atheromatous plaque, or by embolization of atheromatous material from plaques in the extracranial segments of the carotid arteries or aorta. Atheroma formation in the coronary arteries renders hypertensive patients susceptible to angina pectoris, myocardial infarction and sudden death.

In smaller arteries and arterioles, hypertension causes prominent thickening of the intima, in addition to medial hypertrophy. In cases of ‘accelerated’ or ‘malignant’ hypertension, in which the blood pressure is very high or has risen quickly, these intimal changes can occlude the vessels, producing distal tissue ischemia. This particularly affects the kidneys, causing renal failure. The walls of the small arteries in the brain may be damaged so that their permeability is increased and cerebral edema results, causing ‘hypertensive encephalopathy’ characterized by headache, confusion, fits and coma. There may also be visual disturbances due to retinal arterial damage, which may be seen on examination of the fundi.

The left ventricle responds to high blood pressure by hypertrophy. Initially, this increases its force of contraction and maintains a normal cardiac output, but eventually the hypertrophied muscle outgrows its oxygen supply and angina and cardiac failure result.

Ultimately, generalized arteriolar sclerosis develops; it is particularly apparent in the kidney (nephrosclerosis) and is characterized by medial hypertrophy and hyalinization. Nephrosclerosis is the hallmark of primary hypertension.

Damage of target organs.

Hypertension, particularly long-term existing, leads to viscera damage, called target organs, - heart, vessels, brain and kidneys.

The heart damage in hypertension may declare itself by left ventricular hypertrophy and affecting of coronary vessels with angina pectoris, myocardial infarction development, and also sudden cardiac death. In heart damage progressing the heart failure develops.

Myocardial ischemia may appear not only due to coronary arteries affection (their epicardiac parts), but due to relative coronary insufficiency (unchanged coronary arteries inability to supply with blood hypertrophied myocardium), and due to microvasculopathy.

Vessels damage. Vessels, directly participating in high BP maintenance due to TPR, are themselves one of target organs. Vascular damage is characterized by involving in process retinal vessels, carotids, aorta (aneurysms), and also affecting of small vessels: damage of cerebral vessels (occlusions or microaneurysms) may lead to stroke, renal arteries – to renal functions alteration. Fundi investigation allows physician to assess directly vessels changes (Fig.) (ophtalmoscopy).

In hypertension vessels narrow, then expose to sclerosis, that is accompanied by microaneurysms and microhemorrhages formation, and also by ischemic damage of blood supplying organs. All these changes may be stage by stage observed on patient's fundus of eye.

Brain damage is characterized by thrombosis and hemorrhages, hypertensive encephalopathy and lacunae formation in brain tissues. Cerebral vessels damage may lead to changes of their walls (atherosclerosis). In various stages of disease these changes may be complicated by stroke due to thrombosis or cerebral vessels rupture with hemorrhage.

Kidneys damage. As early as initial stage of disease there is inclination to renal vessels changes, at first, with some increase, and then decrease of glomerular filtration. Long-term course of hypertension leads to nephroangiosclerosis with significant impairment of renal functions and chronic renal failure development.

Renal functions reflect changes of glomerular filtration rate (GFR). If on initial stage of hypertension GFR is usually normal, on later stages (or in malignant hypertension) it progressively decreases. Furthermore, creatinine blood level and protein urine concentration (microalbuminuria is typical) are the indicators of kidneys involvement in pathologic process.

Hemodynamics

Not all patients with primary hypertension have normal CO and increased TPR. CO is increased, and TPR is inappropriately normal for the level of CO in the early labile phase of primary hypertension. TPR increases and CO later returns to normal, probably because of autoregulation. Patients with high, fixed diastolic pressures often have decreased CO. The role of the large veins in the pathophysiology of primary hypertension has largely been ignored, but venoconstriction early in the disease may contribute to the increased CO.

Plasma volume tends to decrease as BP increases, although some patients have expanded plasma volumes. Hemodynamic, plasma volume, and PRA variations are evidence that primary hypertension is more than a single entity or that different mechanisms are involved in different stages of the disorder.

Renal blood flow gradually decreases as the diastolic BP increases and arteriolar sclerosis begins. GFR remains normal until late in the

disease, and, as a result, the filtration fraction is increased. Coronary, cerebral, and muscle blood flow are maintained unless concomitant severe atherosclerosis is present in these vascular beds.

In the absence of heart failure, CO is normal or increased, and peripheral resistance is usually high in hypertension due to pheochromocytoma, primary aldosteronism, renal artery disease, and renal parenchymal disease. Plasma volume tends to be high in hypertension due to primary aldosteronism or renal parenchymal disease and may be subnormal in pheochromocytoma.

Systolic hypertension (with normal diastolic pressure) is not a discrete entity. It often results from increased CO or stroke volume (eg, labile phase of primary hypertension, thyrotoxicosis, arteriovenous fistula, aortic regurgitation); in elderly persons with normal or low CO, it usually reflects inelasticity of the aorta and its major branches (arteriosclerotic hypertension).

Hypertension and risk of cardiovascular complications.

According to accumulation of epidemiological data about natural course of hypertension permanent rise of risk of cardiovascular disease appearance and also steady rise of mortality become evident. It is too difficult to draw a clear distinction between normal and pathologic BP, since complications incidence increases just in its elevation within normal range. Moreover, absolute majority of cardiovascular complications are registered in patients with insignificant BP elevation, and their part significantly exceeds amount of patients with high BP.

Risk factors. Prognosis in patients with hypertension depends not only on BP level. Important meaning have risk factors, divided on main (basic) and additional (Table 1).

Table 1

Main (basic) risk factors	Additional risk factors
1. men and menopause women 2. smoking 3. cholesterol >6,5mmol/L 4. family history of premature cardiovascular disease (women<65y., men - <55 y)	1. reduced HDL cholesterol level 2. raised LDL cholesterol level 3. diabetes mellitus 4. impaired glucose tolerance 5. obesity 6. sedentary life-style 7. raised fibrinogen

	8. endogenous tissular plasminogen activator 9. inhibitor of plasminogen activator type I 10. hyperhomocysteinemia 11. D- dimmer 12. raised C-reactive protein 13. oestrogens deficiency 14. Chlamydia pneumoniae 15. social-economic state 16. ethnicity

On risk evaluation main factors are usually used, among additional factors - cholesterol fractions, obesity, impaired glucose tolerance - are chosen.

Stratification of patients by absolute level of cardiovascular risk

Decisions about the management of patients with hypertension should not be based on the level of blood pressure alone, but also on the presence of other risk factors, concomitant diseases such as diabetes, target organ damage, and cardiovascular or renal disease, as well as other aspects of the patient's personal, medical and social situation (Table 2).

Four categories of absolute cardiovascular disease risk are defined (low, medium, high and very high risk) (Table 3). Each category represents a range of absolute disease risks. Within each range, the risk of any one individual will be determined by the severity and number of risk factors present. So, for example, individuals with very high levels of cholesterol or a family history of premature cardiovascular disease in several first-degree relatives will typically have absolute risk levels that are at the higher end of the range provided. Similarly, individuals with other risk factors listed in Table 2 may also have absolute risk levels that are towards the higher end of the range for the category.

How well these estimates predict the absolute risk of cardiovascular disease in Asian, African or other non-Western populations is uncertain. In those countries CHD incidence is relatively low and heart failure or renal disease is more common.

Table 2. Factors Influencing Prognosis (according to WHO guidelines,1999).

Risk Factors For Cardiovascular Diseases	Target Organ Damage[1]	Associated Clinical Conditions[2]

I. Used for risk stratification -Levels of systolic and diastolic blood pressure (Grades 1-3) -Men >55 years -Women >65 years -Smoking -Total cholesterol >6.5 mmo/l (250 mg/dl) -Diabetes -Family history of premature cardiovascular disease II. Other factors adversely influencing prognosis -Reduced HDL cholesterol -Raised LDL cholesterol -Microalbuminuria in diabetes -Impaired glucose tolerance -Obesity -Sedentary lifestyle -Raised fibrinogen -High risk socioeconomic group -High risk ethnic group -High risk geographic region	-Left ventricular hypertrophy (electrocardiogram, echocardiogram or radiogram) -Proteinuria and/or slight elevation of plasma creatinine concentration (1. 2 - 2.0 mg/dl) -Ultrasound or radiological evidence of atherosclerotic plaque (carotid, iliac and femoral arteries, aorta) -Generalised or focal narrowing of the retinal arteries	<u>Cerebrovascular disease</u> -ischaemic stroke -cerebral haemorrhage -transient ischaemic attack <u>Heart disease</u> -myocardial infarction -angina -coronary revascularisation -congestive heart failure <u>Renal disease</u> -diabetic nephropathy -renal failure (plasma creatinine concentration >2.0 mg/dl) <u>Vascular disease</u> -dissecting aneurysm -symptomatic arterial disease <u>Advanced hypertensive retinopathy</u> -haemorrhages or exudates -papilloedema

[1] - "Target Organ Damage" corresponds to previous WHO Stage 2 hypertension

[2] "Associated Clinical Conditions" corresponds to previous WHO Stage 3 hypertension.

Table 3. Stratification of Risk to Quantify Prognosis

	BLOOD PRESSURE (mmHg)		
Other Risk Factors & Disease History	Grade 1 SBP 140-159 or DBP 90-99	Grade 2 SBP 160-179 or DBP 100-109	Grade 3 SBP i 180 or DBP i 110
I. no other risk factors	LOW RISK	MED RISK	HIGH RISK
II. 1-2 risk factors	MED RISK	MED RISK	V HIGH RISK
III. 3 or more risk factors or TOD[1] or diabetes	HIGH RISK	HIGH RISK	V HIGH RISK
IV. ACC[2]	V HIGH RISK	V HIGH RISK	V HIGH RISK

Risk strata (typical 10 year risk of stroke or myocardial infarction): Low risk = less than 15%; medium risk = about 15-20% risk; high risk = about 20-30%; very high risk = 30% or more

[1]. TOD – Target Organ Damage (Table 2)

[2]. ACC – Associated Clinical Conditions, including clinical cardiovascular disease or renal disease (Table 2)

Classification of essential hypertension (hypertensive disease)

According to great attention to cardiovascular risk evaluation in hypertensive patients there is designed transition to classifications with distinction of BP elevation grades with simultaneous risk assessment (low, medium, high, very high). This approach was stipulated in WHO and ISAH experts recommendations (1999) and was supported in Russian national recommendations on AH (2000). Recently used in Russia classifications are presented below (Table 4 &5). Until now classification of essential hypertension (hypertensive disease) by WHO (1962) is widespread in Russia.

Table 4. Classification of essential hypertension (hypertensive disease) by WHO (1962).

I stage — BP elevation >160/95 mmHg without organic changes of cardiovascular system; II stage — BP elevation > 160/95 mmHg in combination with changes of target organs (heart, kidneys, brain, fundal vessels), caused by hypertension, but without their functional alterations; III stage — hypertension, combined with target organs damage (heart, kidneys, brain, fundal vessels) with their functional alterations.

Table 5. Definitions and Classification of Blood Pressure Levels

CATEGORIES OF BP	SYSTOLIC BP (mmHg)	DIASTOLIC BP (mmHG)
Categories of normal BP		
Optimal	<120	<80
Normal	<130	<85
High normal	130-139	85-89
Categories of high BP		
AH of the 1st grade	140-159	90-99
AH of the 2nd grade	160-179	100-109
AH of the 3d grade	≥ 180	≥ 110
Isolated systolic hypertension	≥ 140	≤ 90

Recently both classifications are recommended in Russia; it is necessary to indicate stage of disease as well as BP grade.

Clinical manifestations depend on damage of target organs.

Many of patients are asymptomatic, and frequently hypertension is detected occasionally. There may be neurosis signs, headaches, particularly in the mornings; nausea, flashing of “midges” in front of eyes; pains in precordium, palpitation, rapid fatigability, epistaxis (nasal bleedings), hyperexcitability, irritability, sleep disturbance. In later stages coronary events may appear. Severity of these symptoms, in particular, headaches, not always corresponds to BP elevation grade.

On medical history analysis it is necessary to obtain information about family history of hypertension as well as other conditions, worsening prognosis in their presence – diabetes mellitus, coronary heart disease, stroke, dyslipidemia. Information about duration and level of BP arising, previous drug and non-pharmaceutical therapy effectiveness are important. It is necessary to elicit patient's lifestyle peculiarities, including diet (fats, excessive salt and alcohol consumption), smoking, physical activity level, excessive body mass or obesity.

On examination one attracts attention on excessive body mass. A face hyperemia as well as pallor due to peripheral arteriolar spasm are noticed.

On heart examination sign of left ventricular hypertrophy (apical impulse shift to the left) - key syndrome in hypertension - is detected, that confirmed by ECG, X-ray and, especially, ECO examinations. On elevated BP there is typical pulse strain increase, due to grade of which may be approximately assessed level of BP. Moreover, elevated BP is characterized by accent of S_2 at the aorta appearance.

ECG changes are initially characterized by decrease of T-wave amplitude in the left chest leads. Left ventricular hypertrophy is revealed by high-amplitude R-wave with oblique depression of ST segment in V_{4-6}. Left bundle-branch block may develop.

On ECO hypertrophy of interventricular septum and left ventricular posterior wall is verified. Sometimes these changes are accompanied by dilatation, increase of end-systolic and end-diastolic left ventricular dimensions. Appearance of hypokinetic and even dyskinetic zones in the myocardium is the sign of left ventricular contractile capacity decline.

Different metabolic disorders: hyperinsulinemia, impaired glucose tolerance (in some cases – diabetes mellitus, type II), dyslipidemia (reduced HDL cholesterol, raised LDL cholesterol), obesity were frequently marked during last years.

Hypertensive crisis. Clinical course of hypertension may be complicated by hypertensive crisis. It is fast, additional, significant BP rise. It may be provoked by different physical and mental loading, excessive dietary sodium, water, alcohol intake; cessation of drug therapy. Very high BP is detected in patient (diastolic BP may exceed 130—140 mmHg). In the majority of cases on the background of such BP elevation cerebral signs (nausea, vomiting, vision reduction) appear.

Simultaneously or later other signs and complications of hypertension may increase: coronary heart disease (CHD) exacerbation, acute left-sided heart failure occurrence and stroke. On severe crisis fundal hemorrhages, papilledema may appear.

Kidneys damage. During the late stage of hypertension due to arteriolosclerosis development the signs of kidneys damage appear: impaired concentrative capacity, decrease of urine relative density, proteinuria, hematuria, and in the terminal stage – azotic wastes retention. Parallel signs of eyes fundum damage develop: increasing retinal arteries narrowing and tortuosity, especially in comparison with veins; veins dilation, may be fundal hemorrhages, and later degenerate foci in retina.

Central nervous system damage determines various signs, concerned with intensity and location of vascular disorders. Vascular narrowing (due to their spasm) leads to focal brain ischemia with partial fall-out of its functions and in more severe cases is accompanied by brain hemorrhages. In sharp BP elevation there may be arterial wall ruptures with massive hemorrhage.

Primary hypertension is asymptomatic until complications in target organs develop (eg, left ventricular failure, atherosclerotic heart disease, cerebrovascular insufficiency with or without stroke, renal failure). Dizziness, flushed facies, headache, fatigue, epistaxis, and nervousness are not caused by uncomplicated hypertension.

A fourth heart sound and broad, notched P-wave abnormalities on the ECG are among the earliest signs of hypertensive heart disease. Echocardiographic evidence of left ventricular hypertrophy may appear later. Chest x-ray is often normal until the late dilated phase of hypertensive heart disease. Aortic dissection or leaking aneurysm of the aorta may be the first sign of hypertension or may complicate untreated hypertension. Polyuria, nocturia, diminished renal concentrating ability, proteinuria, microhematuria, cylindruria, and nitrogen retention are late manifestations of arteriolar nephrosclerosis.

Retinal changes may include retinal hemorrhages, exudates, papilledema, and vascular accidents. On the basis of retinal changes, Keith, Wagener, and Barker classified hypertension into groups that have important prognostic implications: group 1--constriction of retinal arterioles only; group 2--constriction and sclerosis of retinal arterioles;

group 3--hemorrhages and exudates in addition to vascular changes; group 4 (malignant hypertension)--papilledema.

Diagnosis

Diagnosis of primary hypertension depends on repeatedly demonstrating higher-than-normal systolic and/or diastolic BP and excluding secondary causes (Fig.1).

CAUSES OF SECONDARY HYPERTENSION

Renal disease
- Bilateral: Chronic glomerulonephritis; Chronic pyelonephritis (reflux nephropathy); Polycystic kidneys; Analgesic nephropathy
- Unilateral: Chronic pyelonephritis (reflux nephropathy); Renal artery stenosis

Endocrine disorders
- Conn's syndrome
- Cushing's syndrome
- Phaeochromocytoma
- Acromegaly
- Hyperparathyroidism

Cardiovascular disorders
- Coarctation of the aorta

Pregnancy
- Pre-eclampsia and eclampsia

Drugs
- Oral contraceptives
- Corticosteroids
- Carbenoxolone
- Monoamine oxidase inhibitors (interaction with tyramine)

Fig.1. Causes of secondary hypertension.

It is important to look for signs of 'end-organ' damage (renal failure, cerebrovascular disease, cardiac failure) and to 'stage' any changes in the fundi (Fig.2-5).

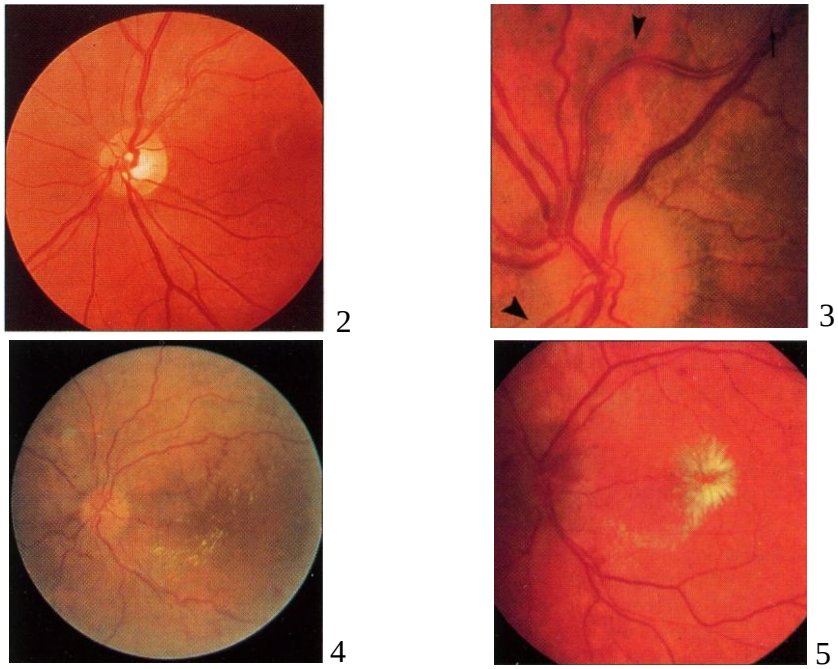


Fig.2-5. Hypertensive retinopathy is traditionally divided into four grades. Grade 1 (2) shows very early and minor changes in a young patient: increased tortuosity of a retinal vessel and increased reflectiveness (silver wiring) of a retinal artery, are seen at 1 o'clock in this view. Otherwise, the fundus is completely normal. Grade 2 (3) again shows increased tortuosity and silver wiring (coarse arrows). In addition there is 'nipping' of the venules at arteriovenous crossings (fine arrow). Grade 3 (4) shows the same changes as grade 2 plus flame- shaped retinal haemorrhages and soft 'cotton-wool' exudates. In Grade 4 (5) there is swelling of the optic disc (papilloedema), retinal edema is present, and hard exudates may collect around the fovea, producing a typical 'macular star'.

At least two BP determinations should be taken on each of 3 days before a patient is diagnosed as hypertensive. More BP determinations are desirable for patients in the low hypertension range and especially for patients with markedly labile BP. Sporadic higher levels in patients who have been resting for > 5 min suggest an unusual lability of BP that may precede sustained hypertension. For example, office or white coat hypertension refers to BP that is consistently elevated in the physician's office but normal when measured at home or by ambulatory BP monitoring.

The basic or minimal evaluation recommended for patients with hypertension includes history and physical examination, CBC, urinalysis, serum analysis (K; Na; glucose; total, high density, and low density lipoprotein cholesterol). Investigations should usually include an ECG for signs of left ventricular hypertrophy and ischemia (Fig.6),

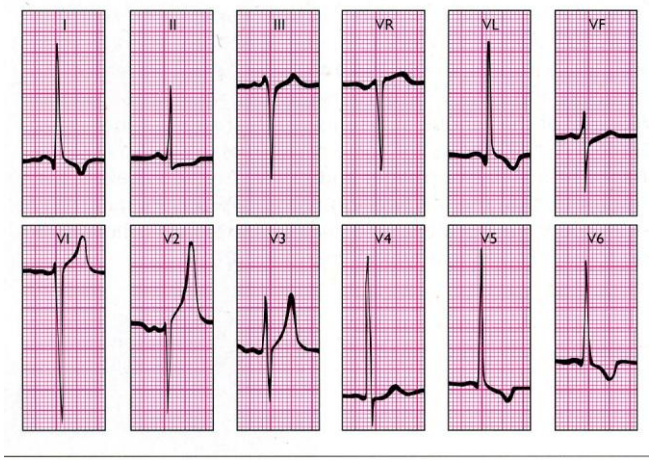


Fig.6 Left ventricular hypertrophy. This ECG shows severe hypertrophy. Left ventricular hypertrophy (LVH) is present when the R wave in V_5 or V_6 or the S wave in V_1 or V_2 exceeds 25 mm in an adult of normal build. This ECG also shows T-wave inversion over the left ventricle ($V_{5–6}$) and, as the heart is relatively horizontally placed, in I and aVL.

and a chest X-ray for cardiac size (Fig.7) and (rarely) signs of coarctation of the aorta (Fig.8).

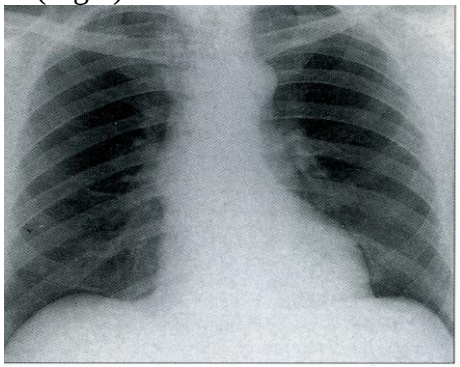


Fig.7.Hypertension. The chest X-ray is usually normal in mild to moderate hypertension, but cardiac enlargement associated with left ventricular hypertrophy (as here) may occur in the later stages. There is no evidence of cardiac failure in this patient.

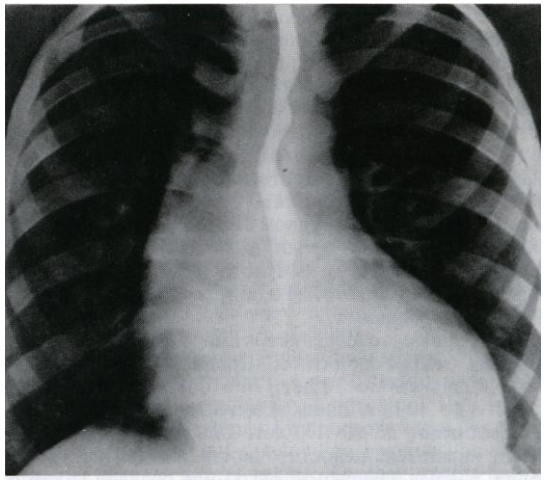
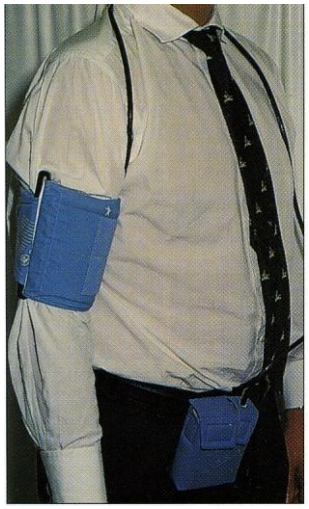


Fig.8. X-ray film of patient with coarctation of the aorta (posteroanterior view). Heart transverse size is significantly enlarged, heart waist is pronounced, there is contrasted esophagus shift on the level of pre- and poststenotic aortic dilatation (“reverse 3” sign).

Echocardiography can also provide an accurate assessement of the severity of ventricular hypertrophy.

The extent and severity of hypertension can often be usefully clarified by ambulatory blood pressure monitoring (Fig.9 & 10).



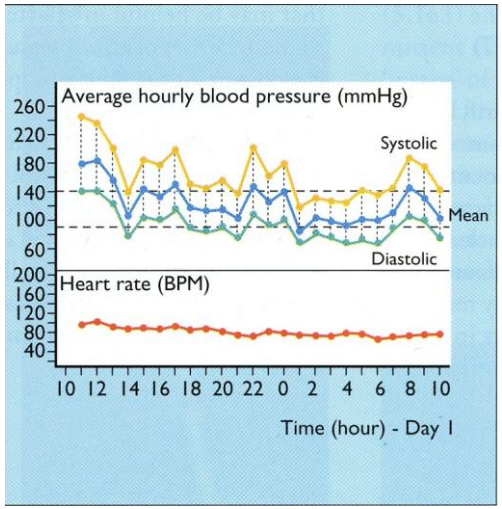


Fig. 9 & 10. Ambulatory blood pressure monitoring was developed to record blood pressure over a 24—48 hour period, to take account of changes due to sympathetic overactivity, posture, muscle activity and state of hydration. These lightweight monitoring devices consist of a cuff applied to the upper arm, connected to a monitor attached to the belt (9). The air pressure cuff is inflated automatically and the Korotkoff sounds are recorded electronically with the heart rate and time. A typical tracing is shown in 10. In the initial part of the trace the blood pressure has fallen dramatically after the patient left the clinic (indicative of 'white-coat' hypertension), but the blood pressure was also elevated several times over the next 24 hours. It is important to obtain a proper baseline value for BP before starting therapy with hypotensive agents.

Proteinuria is an indicator of possible renal disease. Plasma electrolytes, urea and creatinine will show changes if there is renal failure and these and other specific investigations may be required in patients with renal disease and to exclude other causes of secondary hypertension.

The more severe the hypertension and the younger the patient, the more extensive the evaluation should be. Ambulatory BP monitoring, renal scintigraphy, chest x-ray, screening tests for pheochromocytoma, and renin-sodium profiling are not routinely necessary. Peripheral plasma renin activity has not been helpful in diagnosis or drug selection, but it may be an independent risk factor for coronary disease (but not for stroke or total cardiovascular mortality).

Pheochromocytoma secretes catecholamines, which, besides elevating BP, usually produce symptoms (various combinations of headache, palpitations, tachycardia, excessive perspiration, tremor, and pallor) that should alert the physician to this possibility. Catecholamines (eg, epinephrine, norepinephrine) are eventually metabolized in the body to a common product, 3-methoxy-4-hydroxymandelic acid, often called vanillylmandelic acid (VMA). Diagnosis depends on demonstrating increased urinary or plasma concentrations of catecholamine or increased urinary concentrations of metanephrines and VMA.

Hypokalemia not due to diuretics should suggest primary aldosteronism. Proteinuria, cylindruria, or microhematuria with or without nitrogen retention early in the course of hypertension is strong evidence of underlying primary renal disease. Absent or markedly reduced and delayed femoral arterial pulses in a hypertensive patient aged < 30 yr are presumptive evidence of coarctation of the aorta.

Cushing's syndrome, collagen disease, toxemia of pregnancy, acute porphyria, hyperthyroidism, myxedema, acromegaly, some CNS disorders, and primary aldosteronism must be excluded.

Prognosis

An untreated hypertensive patient is at great risk of disabling or fatal left ventricular failure, MI, cerebral hemorrhage or infarction, or renal failure at an early age. Hypertension is the most important risk factor predisposing to stroke. It is one of three risk factors (along with cigarette smoking and hypercholesterolemia) predisposing to coronary atherosclerosis. The higher the BP and the more severe the changes in the retina, the worse the prognosis. Fewer than 5% of patients with group 4 or malignant hypertension characterized by papilledema and < 10% of patients with group 3 changes in the fundus survive 1 yr without treatment. Effective medical control of hypertension will prevent or forestall most complications and will prolong life in patients with ISH or diastolic hypertension. Coronary artery disease is the most common cause of death among treated hypertensive patients. Systolic BP is a more important predictor of fatal and nonfatal cardiovascular events than diastolic BP. In a follow-up of men screened for the Multiple Risk Factor Intervention Trial, overall mortality was related to systolic BP, regardless of diastolic BP.

Treatment

Primary hypertension has no cure, but treatment can modify its course. It is estimated that only 24% of hypertensive patients in the USA have their BP controlled to < 140/90 mm Hg, and 30% are unaware that they have hypertension.

Lifestyle modifications: Extra rest, prolonged vacations, moderate weight reduction, and dietary Na restriction are not as effective as antihypertensive drug therapy. Patients with uncomplicated hypertension need not restrict their activities as long as their BP is controlled. Dietary restrictions can help control diabetes mellitus, obesity, and blood lipid abnormalities. In stage 1 hypertension, weight reduction to ideal levels, modest dietary Na restriction to < 2 g/day, and alcohol consumption to < 1 oz/day may make drug therapy unnecessary. Prudent exercise should be encouraged. Smoking should be unambiguously discouraged.

Antihypertensive drug therapy: Most authorities would agree that patients with systolic BP averaging 140 to 159 mm Hg and/or diastolic

BP of 90 to 94 mm Hg should receive antihypertensive drugs if lifestyle modifications do not normalize BP. The benefit of drug therapy for patients with stage 1 hypertension is unequivocal. There are no data on the efficacy of antihypertensive therapy for borderline hypertension. When target organ damage or other risk factors are present, or when the systolic BP is >= 160 mm Hg and/or diastolic BP is >= 100 mm Hg, drug therapy should not be deferred to await the uncertain results of lifestyle modifications. Heart failure, symptomatic coronary atherosclerosis, cerebrovascular disease, and renal failure require urgent and judicious antihypertensive therapy.

Drug therapy should be initiated with a diuretic or a β-blocker, unless these drugs are contraindicated or another class of drugs is indicated. If these drugs are ineffective, alternative classes suitable for initial therapy include Ca blockers, ACE inhibitors, angiotensin II receptor blockers, α_1-adrenergic blockers, and α - β-blockers. However, none of these except nitrendipine, a dihydropyridine Ca blocker, has been shown to reduce cardiovascular morbidity and mortality in prospective, randomized trials, whereas diuretics or β-blockers as initial therapy have shown beneficial effects on cardiovascular and cerebrovascular morbidity and mortality. Nitrendipine significantly reduced fatal and nonfatal strokes but not coronary events in elderly patients with isolated systolic hypertension.

Selection of the initial drug should be guided by age and race of the patient and by coexisting diseases or conditions that may represent a contraindication for certain drugs (eg, asthma and β-blockers) or a special indication for certain drugs (eg, angina pectoris and β-blockers or Ca blockers).

If the initial drug is ineffective or causes intolerable adverse effects, another can be substituted (sequential monotherapy). Alternatively, if the original drug is only partially effective but well tolerated, the dose may be increased or a second drug can be added, which should be of a different class (stepped care). The central-acting sympathetic inhibiting drugs are not recommended for initial therapy because of their high adverse effect profile. However, they are effective and can be used in small doses in combination regimens. A direct vasodilator (hydralazine or minoxidil) may be used with a diuretic to prevent fluid retention and with a - β-blocker to prevent reflex tachycardia.

Preferably, treatment is started with only one drug unless hypertension is severe. However, combinations of a diuretic with a - β-blocker or an ACE inhibitor are available in single tablets in subtherapeutic doses of each compound that together have an antihypertensive effect with minimal adverse effects.

RENOVASCULAR HYPERTENSION

Acute or chronic elevation of systemic BP caused by partial or complete occlusion of one or more renal arteries or their branches, often correctable by surgery or percutaneous transluminal angioplasty.

Stenosis or occlusion of one or both main renal arteries or their branches or an accessory renal artery or its branches can cause hypertension by inciting release of the enzyme renin from juxtaglomerular cells of the affected kidney. The area of the lumen must be decreased by >= 70% before the stenosis is hemodynamically significant.

In patients > 50 yr old (usually men), the most frequent cause of renal arterial stenosis is atherosclerosis; in younger patients (usually women), it is one of the fibrous dysplasias. Rarer causes of renal arterial stenosis or obstruction include emboli, trauma, inadvertent ligation during surgery, and extrinsic compression of the renal pedicle by tumors.

Although renovascular disease is the most frequent cause of curable hypertension (with the possible exceptions of oral contraceptive therapy in women and excessive alcohol intake), it accounts for < 2% of all cases of hypertension.

Symptoms, Signs, and Diagnosis

Renovascular hypertension should be suspected when diastolic hypertension first develops in a patient < 30 or > 55 yr old or when previously stable hypertension abruptly accelerates. Rapid progression to malignant hypertension within 6 months of onset suggests renal artery disease. A systolic-diastolic bruit in the epigastrium, usually transmitted to one or both upper quadrants and sometimes through to the back, is an almost pathognomonic physical finding, but unfortunately it is absent in about 50% of patients with fibrous disease and is rarely heard in patients with atherosclerotic renovascular disease. Trauma to the back or flank, or acute pain in this region with or without hematuria, should alert the physician to the possibility of renovascular hypertension, but these

historic features are rare. Renovascular hypertension is characterized by high cardiac output and high peripheral resistance.

Renovascular and primary hypertension are usually asymptomatic, and only the history, the presence of an epigastric bruit, or abnormalities on intravenous urography (IVU) or technetium ^{99}-pentetic acid (^{99}Tc-DTPA) scintiscan will distinguish them. The main justification for diagnostic evaluation is to find a surgically curable lesion.

No available test is ideal. All give false-positive and false-negative results, all are expensive, and some are hazardous. The most widely used screening test, replacing the rapid-sequence IVU, is the ^{99}Tc-DTPA scintiscan. Delayed perfusion or decreased function of one kidney on the ^{99}Tc-DTPA scintiscan suggests ischemia. The sensitivity and specificity can be enhanced by comparing scans done before and after the oral administration of captopril.

Doppler ultrasonography (duplex scan) is a reliable noninvasive method for determining the presence or absence of significant stenosis (eg, > 60%) in the main renal arteries. The sensitivity and specificity of this technique approach 90% in experienced hands. Unfortunately, the presence of > 60% stenosis in one or both renal arteries does not per se indicate that it is the cause of the hypertension, but this finding, combined with the typical clinical scenario, is highly suggestive of renovascular hypertension.

Before intervention is planned (i.e., surgery, angioplasty), arteriography should be performed.

Prognosis and Treatment

Without treatment, the prognosis is similar to that in untreated primary hypertension.

Oral captopril will also stimulate disproportionate renin production from the ischemic kidney and will therefore enhance the predictability of renal vein renin activity ratios.

Revascularization of the involved kidney with percutaneous transluminal angioplasty is recommended for younger patients with fibrous dysplasia of the renal artery.

Compared with fibrous disease, atherosclerotic lesions respond less well to surgery and angioplasty, presumably because the patients are older and have more extensive vascular disease within the kidneys and throughout the vascular system. Hypertension may persist, and surgical

complications are more common. Their surgical mortality is higher than in young patients with fibrous dysplasia of the renal artery. Restenosis within 2 years of percutaneous transluminal angioplasty occurs in up to 50% of patients with atherosclerotic renal vascular disease, especially when the plaque is located at the ostium of the renal artery. Placement of a stent has reduced the risk of restenosis. The decision to perform surgery must be based on the patient's overall status, age, and prior response to medical therapy and the type and location of renal arterial disease and its threat to renal function. When possible, surgery should involve repair and revascularization instead of nephrectomy.

RENAL PARENCHYMAL DISEASE

Although an entire kidney may be removed without obvious effect and no rise in blood pressure, hypertension may be associated with unilateral and bilateral renal parenchymal diseases in the absence of significant renal insufficiency. Although such hypertension may reflect other unrecognized processes, most likely it is caused by activation of the renin-angiotensin-aldosterone mechanism. However, in some patients whose hypertension has been relieved by correction of a renal defect, the levels of renin have not been high.

UNILATERAL PARENCHYMAL RENAL DISEASE. A number of unilateral kidney diseases may be associated with hypertension, and in some of these the affected kidney may appear shrunken. Nonetheless, most small kidneys do not cause hypertension, and when they are indiscriminately removed from patients with hypertension, the condition is relieved in only about 25 per cent. Of that 25 per cent, most have arterial occlusive disease, either as the primary cause of the renal atrophy or secondary to irregular scarring of the parenchyma.

POLYCYSTIC KIDNEY DISEASE. Although patients with adult polycystic kidney disease usually progress to renal insufficiency, some retain reasonably normal glomerular filtration rates(GFR) and display no azotemia. Hypertension, although more common in those with renal failure, is present in perhaps half of those with a normal GFR and probably reflects variable degrees of both renin excess and fluid retention.

CHRONIC PYELONEPHRITIS. The relationship between pyelonephritls and hypertension is multifaceted: Pyelonephritis, either unilateral or bilateral, may cause hypertension; hypertensive individuals may be more susceptible to renal infection. In pyelonephritic patients with hypertension, and fairly normal renal function, renin levels are high, probably from interstitial scarring with obstruction of intrarenal vessels.

ADRENAL CAUSES OF HYPERTENSION

Adrenal causes of hypertension include primary excesses of aldosterone, cortisol, and catecholamines; more rarely, excess deoxycorticosterone (DCC) is present along with congenital adrenal hyperplasia. Together these cause less than 1 per cent of all hypertensive diseases, each can usually be recognized with relative ease, and patients suspected of having these disorders can be screened by means of readily available tests. The greater problem than the diagnosis of these adrenal disorders is the need to exclude their presence because of the increasing identification of incidental adrenal masses when abdominal computed tomography (CT) is done to diagnose intraabdominal pathology. Unsuspected adrenal tumors have been found in from 1 to 2 per cent of abdominal CT scans obtained for reasons unrelated to the adrenal gland. Most of these “incidentalomas” appear to be nonfunctional on the basis of normal basal adrenal hormone levels. The threat of malignancy probably can be best excluded by adrenal scintigraphy with the radioiodinated derivative of cholesterol, NP-59. Benign lesions almost always take up the isotope, while malignant ones almost always do not. Most tumors larger than 4 cm are resected, since a significant number of them are malignant.

Pheochromocytoma.

Pheochromocytoma. — tumour of adrenal medulla, producing catecholamines. This disease is characterized by the wild fluctuations of blood pressure, but in a half of patients the hypertension may be persistent. Spells with paroxysmal hypertension may occur with a number of stresses, and a large number of conditions may involve transient catecholamine release. A pheochromocytoma should be suspected in patients with hypertension that is either paroxysmal or persistent and accompanied by sudden spells with headache, sweating, palpitations with tachycardia, nervousness, nausea and vomiting; pain in

the chest or abdomen, with associated signs such as pallor, weight loss. Those whose tumors secrete predominantly epinephrine are prone to postural hypotension from a contracted blood volume and blunted sympathetic reflex tone. Suspicion should be heightened if activities such as bending over, exercise, palpation of the abdomen, smoking, or dipping snuff cause repetitive spells that begin abruptly, advance rapidly, and subside within minutes.

To establish diagnosis it is important to disclose high catecholamines blood level, particularly during the spell (onset), and also to examine daily urine catecholamines, and visualize tumour by using CT, MRI and ultrasonography.

Primary Aldosteronism

Primary aldosteronism (Cohn's syndrome) is caused by adrenal cortical tumour, releasing aldosterone excess. Besides BP elevation, it is characterized by paroxysmal general weakness, paresthesia and paralyses, hypokalemia, renal function alteration with polyuria. To establish diagnosis it is important, besides hypokalemia, to find increased urine excretion of aldosterone, defining by radioimmunoassay technique. At the same time plasma renin is low. Radologic visualization techniques are analogous the same in pheochromocytoma.

Cushing's syndrome.

Cushing's syndrome develops due to excess glucocorticoids secretion by adrenal cortex. Blood pressure may increase for a number of reasons. The secretion of mineralocorticoids also may be increased along with cortisol. The excess cortisol may overwhelm the renal enzyme’s ability to convert it to the inactive cortisone so that it activates renal mineralocorticoid receptors to retain sodium and expand fluid volume. Cortisol stimulates the synthesis of renin substrate and the expression of angiotensin II receptors, which may be responsible for enhanced pressor effects.

Besides hypertension it is characterized by obesity with peculiar crescent-shaped face, striae on trunk lateral surfaces. Cushing's syndrome (in addition to hypercortisonism) may develop as a result of tumours, producing AKTH and analogous substances, and also adrenal and other organs tumours. The same manifestations appear in prolong glucocorticoid therapy.

COARCTATION OF THE AORTA

This congenital heart disease is characterized by deformation and local narrowing of the aorta. Coarctation region is usually located below left subclavia artery origin (95 per cent of cases). Above the coarctation level systolic as well as diastolic BP is elevated, whereas in underlying regions arterial hypotension is observed. At that anastomoses dilatation develops (intercostals arteries, chest wall arteries), and also left ventricular overload and hypertrophy as a compensatory reaction. It is noticed frequent combination of the coarctation with double-flap aortic valve (also congenital heart anomaly).

The main clinical manifestation of coarctation is hypertension, occurred usually between 15 and 30 years at that BP in brachial artery is elevated, and in femoral – normal or even decreased. BP and pulse filling on the left and right arms may differ. On quite lingering course of hypertension left ventricular hypertrophy signs appear: apical impulse increase and lateral shifting, corresponding changes on ECG.

Symptoms may appear late and may be caused by inadequate blood supply of the legs: foot coldness, quick fatigue and pains in gastrocnemius muscles on walking. Headaches, epistaxis (nosebleed) may be connected with hypertension. Systolic murmur in the right 2nd intercostals space close to the sternum, transmitted to neck arteries and interscapular area, may be listened. It is necessary to draw attention on intercostals arteries pulsation, through which collateral circulation is provided. It correlates with lower ribs contour usurpation by dilated intercostals arteries, revealed on X-ray. In late stage of disease such complications as heart failure, dissecting aortic aneurysm, bacterial endocarditis or endarteritis, brain hemorrhage may develop. Evidence and location of aortic narrowing is specified on aortography, which is performed on solving question of surgery treatment.

CONTROL QUESTIONS

1. Complaints of patients with hypertension
2. Etiology and pathogenesis of primary hypertension
3. Risk factors of hypertension
4. Estimation of absolute cardiovascular risk in hypertensive patients
5. Hemodynamics changes in essential hypertension
6. Classification of hypertension and hypertensive disease
7. Physical examination data in patients with hypertension
8. Signs of target organs damage in hypertension
9. Instrumental diagnostics of hypertension
10. Laboratory diagnostics of target organs damage
11. Instrumental diagnostics of target organs damage
12. Differential diagnostics of primary and secondary hypertension

Theme 28. ATHEROSCLEROSIS AND ITS MANIFESTATIONS. CORONARY HEART DISEASE: ANGINA PECTORIS, MYOCARDIAL INFARCTION. INSTRUMENTAL AND LABORATORY DIAGNOSTICS, ECG

Goal: to get a notion about the main cardiovascular diseases, their symptoms and signs, diagnostic meanings of additional diagnostic methods data; instrumental diagnostics of cardiovascular diseases; to master skills.

Knowledge objectives:

- to know symptoms and signs of main cardiovascular diseases, appropriate changes of physical examination data, diagnostic meaning of additional diagnostic methods and their findings in these diseases.

Skill objectives:

- to collect interviewing data, to perform physical examination of patients with cardiovascular diseases (inspection, palpation, percussion and auscultation), to interpret data of additional diagnostic methods, to establish diagnosis of main cardiovascular diseases.

Subject-matter:

1. complaints of patients with coronary heart disease
2. pathology and pathogenesis atherosclerosis
3. reversible and irreversible risk factors for atherosclerosis

4. hemodynamics changes in coronary artery disease
5. classification of coronary artery disease
6. physical examination data in patients with angina pectoris
7. instrumental diagnostics of angina pectoris
8. physical examination data in patients with myocardial infarction
9. instrumental diagnostics of myocardial infarction
10. laboratory diagnostics of myocardial infarction
11. complications of myocardial infarction

Equipment required: stethoscope.

EDUCATIONAL MATERIAL

Invasive Cardiovascular Procedures

CARDIAC CATHETERIZATION

Cardiac catheterization (Fig.11) is usually used to determine the technical feasibility of a mechanical intervention in patients with coronary artery disease, congenital anomalies, heart failure, acute myocardial infarction (MI), or conduction disturbances.

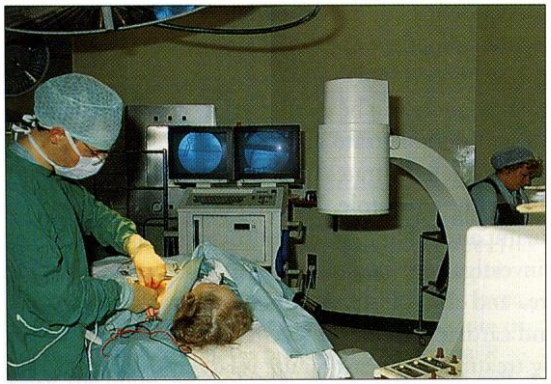


Fig.11. The cardiac catheter laboratory. Catheters may be advanced to the left and right heart in aseptic conditions and under X-ray control. Angiography and an increasing number of interventional techniques, including ablation of abnormal conduction pathways, may be performed, in addition to pressure and oxygen saturation studies.

It provides anatomic information on the heart chambers, coronary arteries, valves, myocardium, and the great vessels. Angiograms can be taken using the catheter to insert radiopaque dye. The flow of blood through the heart and across the valves is recorded, and valvular gradients, cardiac output, and vascular resistance are calculated. Endomyocardial biopsy and evaluation of intracardiac electrical activity can also be performed. Blood gas measurements allow localization of cardiac shunts.

ANGIOCARDIOGRAPHY

This radiopaque technique is carried out during cardiac catheterization to define any heart chamber, major vessel, or coronary vessel.

Procedure For suspected anomalies, contrast material (usually iodinated compounds) is injected into the lesion or into the chamber with the higher pressure. Thus, in valvular incompetence, the contrast material is injected into the chamber with the higher pressure adjacent to the valve.

Biplanar angiocardiography gives a three-dimensional perspective of the chambers and great vessels. Unlike static films, cinecardiograms can be monitored during the injection, and the sequence can be simultaneously recorded on videotape and instantly replayed. Digital subtraction angiography is used for nonmoving arteries and for chamber cineangiography.

Right ventricle and pulmonary valve: Direct injection of contrast material into the apex of the right ventricle records tricuspid valve competence and shows the pulmonary valve, subvalvular region, and proximal pulmonary arteries. The right ventricular outflow tract is best seen with the patient in a steep lateral position, which also reveals the relationship of the pulmonary artery to the aorta. Occasionally, a ventricular septal defect or communication between the right ventricle and the aorta can be seen.

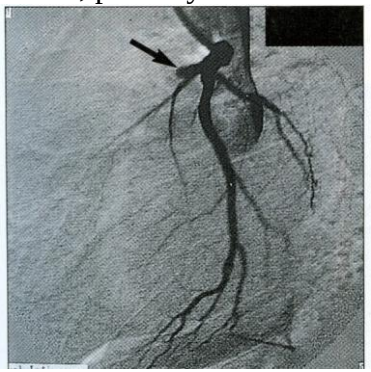
Pulmonary artery: Pulmonary angiography is the definitive technique for diagnosing acute pulmonary embolism; intraluminal filling defects or arterial cutoffs are diagnostic. Contrast material is injected into the main pulmonary artery or right ventricular outflow tract, but selective injection into one or both pulmonary arteries may achieve better definition with less contrast material.

Left atrium: Space-occupying lesions (eg, myxomas, clots) are the usual reason for opacification of the left atrium, although echocardiography is the procedure of choice for diagnosing these lesions. Direct injection for opacification of the left atrium may be hazardous in such cases; instead, the levo phase of a pulmonary angiogram (ie, as dye fills the left atrium from the pulmonary veins) can be safely used.

Left ventricle: A 30 to 45° right anterior oblique projection best demonstrates the long axis of the left ventricle and ventricular aneurysms or areas of asynergy of the anterior wall and separates the left atrium from the left ventricle so that mitral regurgitation can be seen. The left anterior oblique projection defines the left ventricular outflow tract and subvalvular aortic areas as well as the motion of the interventricular septum and left ventricular posterior wall. Cineangiography assesses left ventricular volume, wall motion, and performance. After left ventricular mass and volume are determined from single plane or biplane angiocardiograms, end-systolic and end-diastolic volumes and ejection fraction can be calculated.

Aorta: Aortic regurgitation is best seen by injecting contrast material into the ascending aorta in a 60° left anterior oblique or left lateral projection. Coarctation of the aorta, patent ductus arteriosus, and aortic dissection also are diagnosed from aortic angiograms.

Coronary arteries: Indications for coronary angiography (Fig.12 &13) include unstable angina (including post-MI angina unresponsive to or incompletely relieved by proper medical therapy); atypical chest pain; valve disease that might be corrected by valve replacement, especially in patients with a history of angina or syncope; and unexplained heart failure, possibly due to a left ventricular aneurysm.



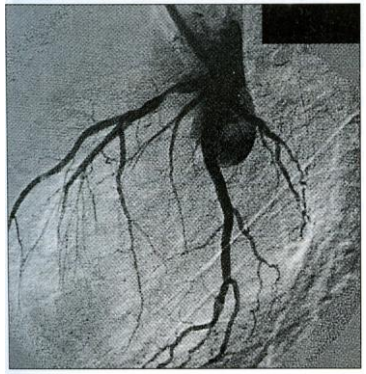
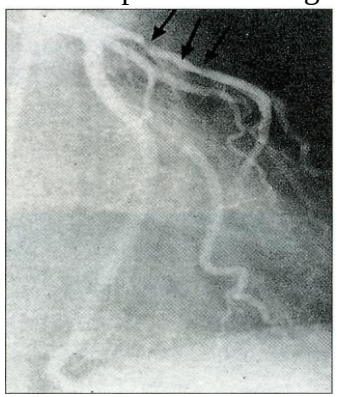


Fig.12 &13. Coronary angiography and angioplasty. The coronary angiogram in left lateral projection shows complete occlusion of the left anterior descending coronary artery. Only a stump is seen (12, arrow). After coronary angioplasty, there is good perfusion of the left anterior descending artery, although a residual stenosis is seen (13). This can, if necessary, be dealt with electively at a later stage by further angioplasty, stenting or surgery.

PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY

Percutaneous transluminal coronary angioplasty (PTCA) is indicated for the revascularization of coronary arteries narrowed by atheroma (Fig.14-17). Immediate PTCA may be superior to and more cost effective than thrombolytic therapy as initial treatment of MI. Finally, elective PTCA may be performed on post-MI patients who have recurrent or provokable angina before hospital discharge.



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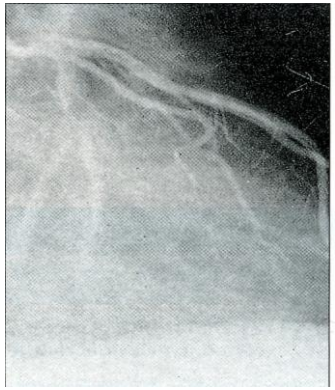

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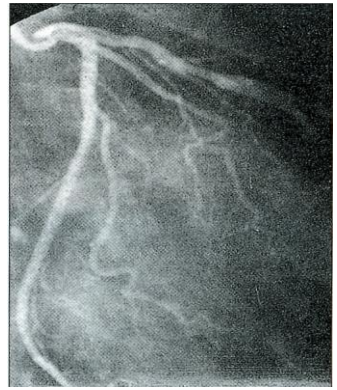

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Fig.14-17. Percutaneous transluminal coronary angioplasty of a left anterior descending coronary stricture: 14 is the preangioplasty coronary arteriogram — a long stricture is

arrowed; 15 shows the balloon of the angioplasty catheter inflated in situ across the stricture; 16 shows the coronary arteriogram taken immediately after the angioplasty catheter had been removed. The stricture has been successfully dilated; 17 shows the appearance 1 month after angioplasty. There is a slight residual narrowing, which is a normal finding at this stage and does not indicate re-stenosis. The patient's angina was dramatically improved by the manoeuvre.

Procedure

The appropriate coronary ostium is catheterized with a guiding catheter, allowing the passage of a balloon-tipped catheter distally into the coronary artery. The balloon is aligned within the stenosis and then inflated to dilate the vessel. Angiography is repeated at the completion of the procedure to document any changes.

Various anticoagulation regimens are used during and after angioplasty to reduce the incidence of thrombosis at the site of balloon dilation. Ca blockers and nitrates may also reduce coronary spasm.

The incidence of restenosis is highest in the first 6 mo after angioplasty, with rates as high as 35%. Repeat angioplasty is required in most patients with restenosis, with fewer requiring surgical revascularization.

Coronary artery stents are being used with increased frequency to decrease the need for repeat revascularization procedures. In short nonrestenotic lesions with large native coronary arteries, coronary stenting has reduced the need for repeat revascularization in the short term. The use of stents for restenotic lesions, acute MI, long lesions, diffuse disease, and acute occlusions is still under investigation.

ATHEROSCLEROSIS

A form of arteriosclerosis characterized by patchy subintimal thickening (atheromas) of medium and large arteries, which can reduce or obstruct blood flow.

The prevalence of clinical manifestations of atherosclerosis in general increases in postmenopausal women and begins to approach that in age-matched men.

Pathology and Pathogenesis

Atherosclerotic plaque consists of accumulated intracellular and extracellular lipids, smooth muscle cells, connective tissue, and glycosaminoglycans. The earliest detectable lesion of atherosclerosis is

the fatty streak (consisting of lipid-laden foam cells, which are macrophages that have migrated as monocytes from the circulation into the subendothelial layer of the intima), which later evolves into the fibrous plaque (consisting of intimal smooth muscle cells surrounded by connective tissue and intracellular and extracellular lipids) (Fig.18).

Atherosclerotic vessels have reduced systolic expansion and abnormally rapid wave propagation. Arteriosclerotic arteries of hypertensive persons also have reduced elasticity, which is further reduced when atherosclerosis develops.

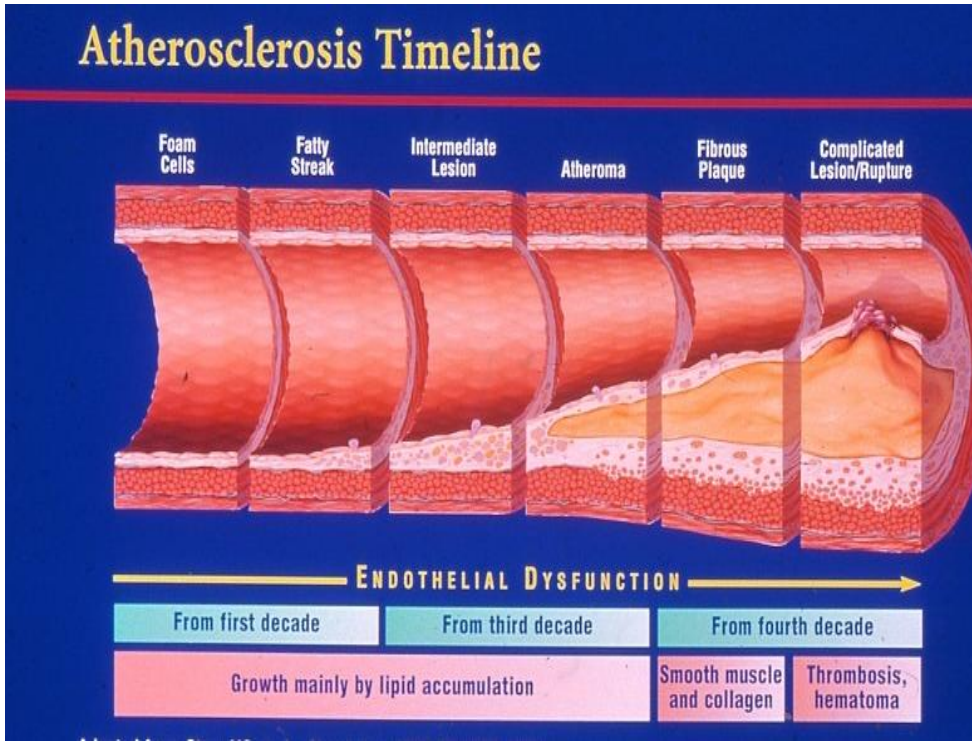


Fig.18. Atherosclerosis timeline.

Two main hypotheses have been proposed to explain the pathogenesis of atherosclerosis: the lipid hypothesis and the chronic endothelial injury hypothesis. They are probably interrelated.

The lipid hypothesis postulates that an elevation in plasma low density lipoproteins (LDL) levels results in penetration of LDL into the arterial wall, leading to lipid accumulation in smooth muscle cells and in macrophages (foam cells). LDL also augments smooth muscle cell hyperplasia and migration into the subintimal and intimal region in response to growth factors. LDL is modified or oxidized in this environment and is rendered more atherogenic. Small dense LDL cholesterol particles are also more susceptible to modification and oxidation. The modified or oxidized LDL is chemotactic to monocytes, promoting their migration into the intima, their early appearance in the fatty streak, and their transformation and retention in the subintimal compartment as macrophages. Scavenger receptors on the surface of macrophages facilitate the entry of oxidized LDL into these cells, transferring them into lipid-laden macrophages and foam cells. Oxidized LDL is also cytotoxic to endothelial cells and may be responsible for their dysfunction or loss from the more advanced lesion.

Proliferating smooth muscle cells also accumulate lipid. As the fatty streak and fibrous plaque enlarge and bulge into the lumen, the subendothelium becomes exposed to the blood at sites of endothelial retraction or tear, and platelet aggregates and mural thrombi form. Release of growth factors from the aggregated platelets may increase smooth muscle proliferation in the intima. Alternatively, organization and incorporation of the thrombus into the atherosclerotic plaque may contribute to its growth.

The chronic endothelial injury hypothesis postulates that endothelial injury by various mechanisms produces loss of endothelium, adhesion of platelets to subendothelium, aggregation of platelets, chemotaxis of monocytes and T-cell lymphocytes, and release of platelet-derived and monocyte-derived growth factors that induce migration of smooth muscle cells from the media into the intima, where they replicate, synthesize connective tissue and proteoglycans, and form a fibrous plaque. Other cells (eg, macrophages, endothelial cells, arterial smooth muscle cells) also produce growth factors that can contribute to smooth muscle hyperplasia and extracellular matrix production.

These two hypotheses are closely linked and not mutually exclusive. Modified LDL is cytotoxic to cultured endothelial cells and may induce endothelial injury, attract monocytes and macrophages, and stimulate

smooth muscle growth. Modified LDL also inhibits macrophage mobility, so that once macrophages transform into foam cells in the subendothelial space they may become trapped. In addition, regenerating endothelial cells (after injury) are functionally impaired and increase the uptake of LDL from plasma.

The atherosclerotic plaque may grow slowly and over several decades may produce a severe stenosis or may progress to total arterial occlusion. With time, the plaque becomes calcified. Some plaques are stable, but others, especially those rich in lipids and inflammatory cells (eg, macrophages) and covered by a thin fibrous cap, may undergo spontaneous fissure or rupture, exposing the plaque contents to flowing blood. These plaques are deemed to be unstable or vulnerable and are more closely associated to the onset of an acute ischemic event. The ruptured plaque stimulates thrombosis; the thrombi may embolize, rapidly occlude the lumen to precipitate a heart attack or an acute ischemic syndrome, or gradually become incorporated into the plaque, contributing to its stepwise growth.

Risk Factors

Major nonreversible risk factors for atherosclerosis include age, male sex, and family history of premature atherosclerosis. Major reversible risk factors are discussed below. Evidence also strongly suggests that physical inactivity is associated with an increased risk of coronary artery disease (CAD). Although personality type has been proposed as a risk factor, its role is controversial.

Abnormal serum lipid levels: Elevated levels of low density lipoprotein (LDL) and reduced levels of high density lipoprotein (HDL) predispose to atherosclerosis. The association of total serum cholesterol and LDL cholesterol levels with the risk of CAD is direct and continuous. HDL levels are inversely correlated with CAD risk. The main causes of reduced HDL are cigarette smoking, obesity, and physical inactivity. Low HDL is also associated with the use of androgenic and related steroids (including anabolic steroids), β-blockers, hypertriglyceridemia, and genetic factors.

Cholesterol level and CAD prevalence are influenced by genetic and environmental factors (including diet). Persons with low serum cholesterol levels who move from a country with a low CAD prevalence to a country with a high CAD prevalence and who tend to alter their

eating habits accordingly develop higher serum cholesterol levels and an increased risk of CAD.

Hypertension: High diastolic or systolic BP is a risk factor for stroke, MI, and cardiac and renal failure. The risk associated with hypertension is lower in societies with low average cholesterol levels.

Cigarette smoking: Smoking increases the risk of peripheral artery disease, CAD, cerebrovascular disease, and graft occlusion after reconstructive arterial surgery. Smoking is particularly hazardous in persons at increased cardiovascular risk. There is a dose relationship between the risk of CAD and the number of cigarettes smoked daily. Passive smoking may also increase the risk of CAD. Men and women are both susceptible, but the risk for women may be greater. Nicotine and other tobacco-derived chemicals are toxic to vascular endothelium.

Cigarette smoking increases LDL and decreases HDL levels, raises blood carbon monoxide (and could thereby produce endothelial hypoxia), and promotes vasoconstriction of arteries already narrowed by atherosclerosis. It also increases platelet reactivity, which may favor platelet thrombus formation, and increases plasma fibrinogen concentration and Hct, resulting in increased blood viscosity.

Diabetes mellitus: Both insulin-dependent and non-insulin-dependent diabetes mellitus are associated with earlier and more extensive development of atherosclerosis as part of widespread metabolic derangement that includes dyslipidemia and glycosylation of connective tissue. Hyperinsulinemia damages vascular endothelium. Diabetes is a particularly strong risk factor in women and significantly negates the protective effect of female hormones.

Obesity: Some studies have found that obesity, particularly truncal obesity in men, is an independent risk factor for CAD. Hypertriglyceridemia is commonly associated with obesity, diabetes mellitus, and insulin resistance and appears to be an important independent risk factor in persons with lower LDL or HDL levels and in the nonelderly. Not all triglyceride elevations are likely to be atherogenic. Smaller, denser very low density lipoprotein particles may carry greater risk.

Physical inactivity: Several studies have associated a sedentary lifestyle with increased CAD risk, and others have shown that regular exercise may be protective.

Hyperhomocysteinemia: Elevated blood homocysteine due to a genetically determined decrease in its metabolism may cause vascular endothelial injury, which predisposes the vessels to atherosclerosis.

Chlamydia pneumoniae infection: Chlamydia pneumoniae infection or viral infection may play a role in endothelial damage and chronic vascular inflammation that may lead to atherosclerosis.

Symptoms and Signs

Atherosclerosis is characteristically silent until critical stenosis, thrombosis, aneurysm, or embolus supervenes. Initially, symptoms and signs reflect an inability of blood flow to the affected tissue to increase with demand (eg, angina on exertion, intermittent claudication).

Symptoms and signs commonly develop gradually as the atheroma slowly encroaches on the vessel lumen. However, when a major artery is acutely occluded, the symptoms and signs may be dramatic.

Diagnosis

Atherosclerosis is suspected based on the risk factors and on its symptoms and signs, of which there may be few. Atheromatous obstruction is commonly confirmed by arteriography or Doppler ultrasonography.

Hyperlipidemia commonly presents with symptoms and signs of premature obliterative atherosclerosis affecting the brain (cerebral transient ischemic attacks or stroke), heart (angina pectoris or MI), intestine, and lower extremities (intermittent claudication). Xanthomas (in the creases of hands and elbows and along tendon sheaths) and xanthelasmas are sometimes associated with hyperlipidemia, particularly of the familial type. Recurrent attacks of acute pancreatitis, with or without alcoholism, suggest hypertriglyceridemia. A family history of hyperlipidemia or onset of cardiovascular disease before age 60 is further reason to look for premature atherosclerosis.

Prevention

The most effective way to prevent the cardiovascular and cerebrovascular complications of atherosclerosis and the associated arterial thrombosis is to prevent atherosclerosis itself. Reversible risk factors for atherosclerosis are

- abnormal serum lipid levels,
- hypertension,
- cigarette smoking,

- diabetes mellitus,
- obesity,
- physical inactivity,
- hyperhomocysteinemia, and possibly
- *C. pneumoniae* infection.

Increased understanding of these risk factors and their role in the etiology, pathogenesis, and course of atherosclerosis will lead to more focused intervention for preclinical or overt atherosclerotic disease and will thereby contribute to further declines in morbidity and mortality.

Treatment

Treatment of established atherosclerosis is directed at its complications (eg, angina pectoris, MI, arrhythmias, heart failure, kidney failure, ischemic stroke, and peripheral arterial occlusion).

CORONARY ARTERY DISEASE

Most coronary artery disease (CAD) is due to subintimal deposition of atheromas in the large and medium-sized arteries serving the heart. Less often, CAD is due to coronary spasm, which is usually idiopathic (with or without associated atheroma) or may be due to drugs such as cocaine. Rare causes include an embolus to the coronary artery, Kawasaki syndrome, and vasculitis.

Coronary atherosclerosis is characteristically insidious in onset, is often irregularly distributed in different vessels, and can abruptly interfere with blood flow to segments of the myocardium, most often due to rupture of an eccentric atheromatous plaque with consequent intraluminal thrombosis.

The major complications of CAD are angina pectoris, unstable angina, MI, and sudden cardiac death due to arrhythmias. In the USA, CAD is the leading cause of death in both sexes, accounting for about one third of deaths each year.

Although the precise pathogenesis of CAD is unclear, the risk factors are well known: high blood levels of low density lipoprotein cholesterol (LDL-C) and lipoprotein a, low blood levels of high density lipoprotein cholesterol (HDL-C) and serum vitamin E, and poor physical fitness.

RISK FACTORS FOR ISCHAEMIC HEART DISEASE (IHD)

Fixed risks
- Male sex
- Family history of IHD
- Increasing age
- Social class V
- Race

Modifiable risks
- Cigarette smoking
- High blood cholesterol level (total and LDL); low HDL
- High blood triglyceride
- Hypertension
- Obesity
- 'Western' diet
- Diabetes mellitus
- Physical inactivity
- Use of oral contraceptive pill
- High plasma fibrinogen level
- Unemployment
- Stress
- Personality

Other factors still await identification

High blood levels of triglycerides and insulin reflecting insulin resistance may be risk factors, but the data are less clear. CAD risk is increased by tobacco use; diets high in fat and calories and low in phytochemicals (found in fruits and vegetables), fiber, and vitamin E and C or, at least in some persons, diets with relatively low levels of omega-3 polyunsaturated fatty acids (PUFAs); poor stress management; and inactivity. Several systemic diseases (eg, hypertension, diabetes, hypothyroidism) are also associated with increased CAD risk.

Homocysteine has recently been identified as a risk factor for coronary, peripheral, and cerebral vascular disease. Patients with homocystinuria, a rare recessive disease, have plasma homocysteine levels 10 to 20 times above normal (hyperhomocysteinemia) and accelerated, premature vascular disease. Homocysteine has a direct toxic effect on endothelium and promotes thrombosis and oxidation of LDL. Normal values range from about 4 to 17 μmol/L. Modest elevations of total plasma homocysteine have multiple causes, including low levels of folic acid, vitamins B6 and B12, renal insufficiency, certain drugs, and

genetically controlled variations in homocysteine metabolic enzymes. Patients with homocysteine values in the top 5% have a 3.4 greater risk of MI or cardiac death than those in the lower 90% after adjustment for other risk factors. Increased homocysteine levels are associated with increased risk regardless of etiology. Recent studies suggest a graded risk even in normal-range homocysteine; thus, reduction of normal plasma levels may be advantageous. The most simple and effective way to reduce plasma homocysteine is administration of folic acid 1 to 2 mg/day, which has essentially no side effects except in untreated vitamin B12 deficiency. Many authorities recommend that patients with CAD be screened for plasma homocysteine levels and, unless the values are in the lower normal range, treatment be initiated with folic acid.

Patients with CAD undergoing atherectomy have biologic markers suggesting coronary artery localization of Chlamydia infection. The role of this and other putative infectious agents in the genesis of CAD is being investigated

Ischemic heart disease (IHD; also known as coronary heart disease — CHD) is usually caused by structural disorder of the coronary arteries (coronary artery disease — CAD), although disorders of small coronary vessels may occasionally lead to similar symptomatology.

Ischemic heart disease produces five clinical syndromes:

1. angina pectoris — stable or unstable, and variant;
2. myocardial infarction.
3. постинфарктный кардиосклероз
4. heart failure
5. arrhythmias
6. sudden cardiac death.

ANGINA PECTORIS

A clinical syndrome due to myocardial ischemia characterized by precordial discomfort or painflul constricting sensation of pressure, which may radiate to the arms, the throat, back and epigastrium. It is usually provoked by activity that increases heart rate and blood pressure, thereby increasing myocardial oxygen demand, for example exercise, emotion, stress, fear or sexual intercourse. The pain or tightness of ‘stable’ angina typically starts while walking and is relieved in a few minutes by rest or sublingual nitroglycerin.

Etiology

The cause is usually critical coronary artery obstruction due to atherosclerosis. Spasm (idiopathic or due to cocaine) or, rarely, a coronary embolism may be causative. Disease other than atherosclerosis (eg, calcific aortic stenosis, aortic regurgitation, hypertrophic subaortic stenosis) can cause angina directly (by increasing cardiac work) or in combination with CAD.

Pathology and Pathogenesis

Usually, patients with long-standing angina are found at autopsy to have extensive coronary atherosclerosis and patchy myocardial fibrosis. There may be gross or microscopic evidence of old MI.

Angina pectoris occurs when cardiac work and myocardial O_2 demand exceed the ability of the coronary arteries to supply oxygenated blood. Heart rate, systolic tension or arterial pressure, and contractility are the major determinants of myocardial O_2 demand. An increase in any of these factors in a setting of reduced coronary blood flow may induce angina. Thus, exercise in the patient with a critical degree of coronary stenosis induces angina relieved by rest.

As the myocardium becomes ischemic, coronary sinus blood pH falls, cellular K loss occurs, lactate production replaces lactate use, ECG abnormalities appear, and ventricular performance deteriorates. Left ventricular (LV) diastolic pressure frequently rises during angina, at times to levels inducing pulmonary congestion and dyspnea. The discomfort of angina pectoris is believed to be a direct manifestation of myocardial ischemia and the resultant accumulation of hypoxic metabolites.

Symptoms and Signs The discomfort of angina pectoris is not usually perceived as pain. It may be a vague, barely troublesome ache, or it may rapidly become a severe, intense precordial crushing sensation. It has a variable location but is most commonly felt beneath the sternum. It may radiate to the left shoulder and down the inside of the left arm, even to the fingers; straight through to the back, into the throat, jaws, and teeth; and occasionally down the inside of the right arm. It may also be felt in the upper abdomen. Because discomfort seldom occurs in the region of the cardiac apex, the patient who points to this precise area or describes fleeting, sharp, or hot sensations usually does not have angina.

Between and even during attacks of angina, signs of heart disease may be absent. However, during the attack, heart rate may increase modestly, BP is often elevated, heart sounds become more distant, and the apical impulse is more diffuse. Palpation of the precordium may reveal localized systolic bulging or paradoxical movement, reflecting segmental myocardial ischemia and regional dyskinesia. The second heart sound may become paradoxical because of more prolonged LV ejection during the ischemic episode. A fourth heart sound is common. A midsystolic or late-systolic apical murmur--shrill but not especially loud due to localized papillary muscle dysfunction secondary to ischemia--may occur.

Angina pectoris is typically triggered by physical activity and usually persists no more than a few minutes, subsiding with rest. Response to exertion is usually predictable, but in some persons a given exercise that is tolerated one day may precipitate angina the next. Angina is worsened when exertion follows a meal. Also, symptoms are exaggerated in cold weather: walking into the wind or first contact with cold air on leaving a warm room may precipitate an attack.

Angina may occur at night (nocturnal angina) preceded by a dream that is accompanied by striking changes in respiration, pulse rate, and BP. Nocturnal angina may also be a sign of recurrent LV failure, an equivalent of nocturnal dyspnea. Attacks may vary from several days to occasional episodes with symptom-free intervals of weeks, months, or years. They may increase in frequency (crescendo angina) to a fatal outcome or may gradually decrease or disappear if adequate collateral coronary circulation develops, if the ischemic area becomes infarcted, or if heart failure or intermittent claudication supervenes and limits activity.

Angina may occur spontaneously at rest (angina decubitus), usually accompanied by modest increases in heart rate and a rise in BP that may be marked. If the angina is not relieved, the higher BP and fast heart rate increase unmet myocardial O_2 need and make MI more likely.

Because the characteristics of angina are usually constant for a given patient, any deterioration in the pattern of symptoms-- increased intensity, decreased threshold of stimulus, longer duration, occurrence when the patient is sedentary or waking from sleep--should be considered serious. Such changes are termed ***unstable angina.***

Classification.

Canadian functional classification (1976) of stable angina is used in clinical practice.

I functional class — Ordinary physical activity does not cause symptoms. Angina does not occur on walking or stair climbing. Attacks appear during hard, fast or long-term exertion.

II functional class — Comfortable at rest, ordinary physical activity causes symptoms. Angina appears on walking or fast stair climbing, going uphill, after meals, in cold weather, against the wind, emotional exertion. Walking on distance more than 100—200 m on flat place or stair climbing more than 1 stair-well at a normal pace and in normal conditions.

III functional class — Comfortable at rest, less than ordinary activity causes symptoms. Walking on flat place or stair climbing more than 1 stair-well at a normal pace and in normal conditions provoke angina attack appearance.

IV functional class — Symptoms present at rest, inability of any kind of physical ability without discomfort. Angina attack appearance is possible at rest.

Diagnosis

Diagnosis is based on a characteristic complaint of chest discomfort brought on by exertion and relieved by rest. Diagnosis may be confirmed if reversible ischemic ECG changes are seen during a spontaneous attack (Fig.19).

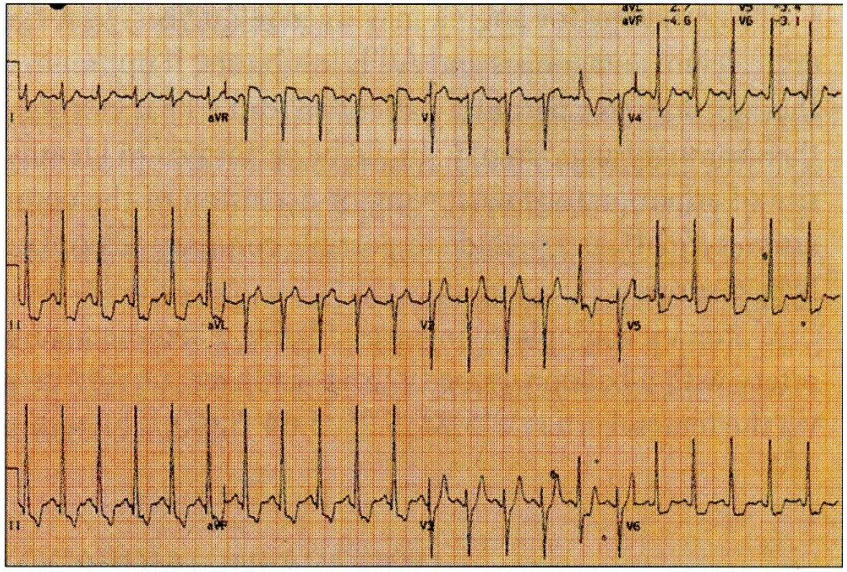


Fig.19. Angina pectoris associated with ECG changes. During anginal pain, there are usually ST-segment changes on the ECG. This ECG was taken during an episode of exercise-induced angina, and it shows ST-segment depression (4 mm) in leads V4—6, standard leads II and Ill and lead aVF.

A wide variety of changes may appear: ST segment depression (typically), ST segment elevation, decreased R-wave height, intraventricular or bundle branch conduction disturbances, and arrhythmia (usually ventricular extrasystoles). Between attacks, the ECG (and usually LV function) at rest is normal in about 30% of patients with a typical history of angina pectoris, even with extensive three-vessel CAD (an abnormal resting ECG alone does not establish or refute the diagnosis). Alternatively, diagnosis can be confirmed by a test dose of sublingual nitroglycerin, which characteristically should relieve the discomfort in 1.5 to 3 min.

Exercise stress ECG testing: Because the diagnosis of angina is usually primarily based on the patient's history, exercise testing in a patient with typical symptoms is generally used to determine functional and ECG response to graded stress.

The patient exercises to a predetermined goal (eg, 80 to 90% of maximal heart rate, which can be approximated as 220 less the age in

years), unless distressing cardiovascular symptoms (dyspnea, reduced endurance, fatigue, hypotension, or chest pain) supervene (Fig.20).

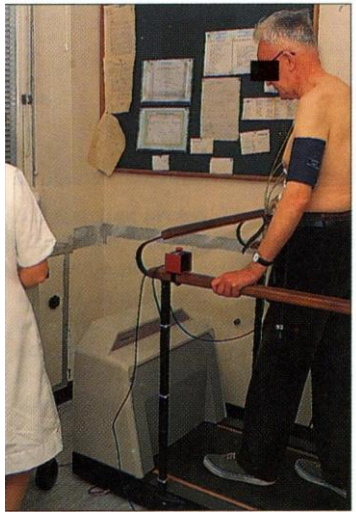


Fig.20. The exercise treadmill test may reveal signs of ischemia on the ECG when the resting trace is normal.

The ischemic ECG response during or after exercise is characterized by a flat or downward-sloping ST segment depression >= 0.1 millivolts (1 mm on the ECG when properly calibrated) lasting >= 0.08 sec (Fig.21).

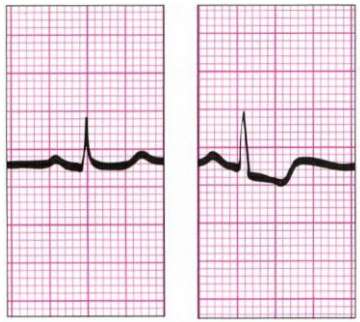


Fig.21 A positive exercise test as shown in lead II. The trace taken before exercise is normal, but the second trace, recorded 2 minutes after the end of exercise, shows ST segment depression with T-wave inversion. Analysis of the full trace may show further evidence of ischemia

Interpretation of exercise testing is further complicated by the increased incidence of CAD with age; tests are falsely positive in >= 20% patients under age 40 but in < 10% over age 60. The frequency of true-positive tests increases with the number of coronary arteries obstructed, and greater degrees of ST segment depression generally correlate with more extensive disease.

Exercise testing is most predictive of CAD in men with chest discomfort suggestive of angina (specificity, 70%; sensitivity, 90%).

Exercise tests are more difficult to interpret in women aged < 55; a high incidence of false-positive responses, probably related in part to a lower pretest incidence of the disease in the younger population, reduces the specificity. However, women are more likely than men to have an abnormal ECG in the presence of disease (32 vs. 23%). The false-negative rate in women is comparable to that in men, suggesting that a negative test is a reliable indicator of absence of disease.

In patients with atypical symptoms, a negative exercise test generally rules out angina pectoris and CAD. A positive test may indicate exercise-induced ischemia but may not explain atypical symptoms, suggesting the need for further investigation.

Patients with unstable angina or those in whom recent MI is suspected should not undergo exercise testing. However, with proper indications and close monitoring, an exercise test in an ischemic patient carries a low risk. The patient's response provides valuable prognostic information and helps to evaluate the need for angiography and possible bypass surgery in those on maximal medical therapy. A complete life support system, including emergency drugs, airway, and defibrillator, should be immediately available for any patient undergoing exercise testing.

Coronary angiography documents the extent of anatomic coronary artery obstruction. Coronary angiography findings parallel postmortem findings, but the extent and severity of disease are usually underestimated. Vessels as small as 1 mm may be visualized with high-quality imaging. CAD is recognized by narrowing, beading, or occlusion of the vessels. Obstruction is assumed to be physiologically significant when the luminal diameter is reduced > 70%, which correlates well with the presence of angina pectoris; lesser degrees of obstruction are unlikely to result in ischemia, unless spasm or thrombosis is superimposed.

Evaluation of wall motion by LV angiography is important if not contraindicated by potential adverse effects of contrast agent on renal or ventricular function.

Echocardiography can be used for anatomic and functional myocardial analysis. Valve anatomy is well depicted, and PA pressure can be reliably estimated. Patients with poor ventricular function, evidence of reduced contractility, have a decreased life expectancy. Yet, if poor function is due to CAD, these patients benefit most from coronary artery bypass grafting, if they survive the operation.

Radionuclide images provide information about cardiac anatomy, cardiac function, myocardial perfusion, and metabolism.

Differential Diagnosis

Many conditions must be considered in the differential diagnosis (eg, abnormalities of the cervicothoracic spine, costochondral separation, nonspecific chest wall pain). However, few truly mimic angina, which is generally so characteristic that errors in diagnosis usually result from careless history taking (Table 6)

Table 6

Major causes of chest pain which is not IHD

Cause	**Features**	**Further investigations**
Esophageal/gall bladder/peptic ulcer	Associated with dyspepsia, waterbrash, related to food, not related to exertion, relieved by antacids	Endoscopy Ultrasound of gall bladder
Lung/pulmonary embolism	Pain is pleuritic, worse on breathing, coughing and sneezing. May have cough, or infected sputum, or blood in sputum. There may be a friction rub.	Chest X-ray Ventilation/perfusion scan
Other cardiac causes	Dissecting aneurysm – very severe pain especially in back. Patient hypotensive and may collapse.	Chest X-ray CT scan

	Pericarditis – sharp pain worse on breathing and lying flat – better it upright. Pericardial rub may be heard.	Echocardiogram
	Mitral valve prolapse – pain is often vague central chest – comes on after exercise – often present in young women.	Echocardiogram
Musculoskeletal	Sharp pain related to position and movement. May be localized to chest wall – perhaps a history of injury (includes costochondritis - Tietze's syndrome).	Chest X-ray Spine and rib X-ray
Functional	Present in anxious young women and men – no apparent cause is found. May be associated with hyperventilation (Da Costa's syndrome).	Rebreathing from bag if hyperventilation. Otherwise diagnose by exclusion.

GI disorders: Diagnostic difficulties arise when the patient has atypical anginal symptoms, especially GI symptoms (eg, bloating; belching, which may give relief; abdominal distress) that are often ascribed to indigestion. Peptic ulcer, hiatus hernia, and gallbladder disease may cause symptoms similar to angina pectoris or may precipitate attacks in persons with preexisting CAD. Nonspecific changes in the T waves and ST segments have been reported in esophagitis, peptic ulcer disease, and cholecystitis, which can further complicate diagnosis.

Dyspnea: Angina may be confused with dyspnea, partly because of the sharp and reversible rise in LV filling pressure that often accompanies the ischemic attack. The patient's description may be imprecise, and whether the problem is angina, dyspnea, or both may be difficult to determine. Recurrent breathlessness on mild exertion may reflect increased LV filling pressure secondary to ischemia, with or without pain.

Silent ischemia: Twenty-four hour Holter monitoring has revealed a surprising incidence (up to 70% of episodes) of T-wave and ST segment abnormalities in the absence of pain in patients with CAD. Such changes are rare in persons without CAD. Radionuclide studies have documented myocardial ischemia in some persons during mental stress (eg, mental arithmetic) and during spontaneous ECG change. Silent ischemia and angina pectoris may coexist. In silent ischemia, the prognosis is defined by the severity of CAD. Revascularization may improve prognosis by reducing the incidence of subsequent MI or sudden death.

Prognosis

The major adverse outcomes are unstable angina, MI, recurrent MI, and sudden death due to arrhythmias. Annual mortality is about 1.4% in men with angina and no history of MI, a normal resting ECG, and normal BP. The rate rises to about 7.5% if systolic hypertension is present, to 8.4% when the ECG is abnormal, and to 12% if both risk factors are present.

Lesions of the left main coronary artery or in the proximal anterior descending vessel indicate particularly high risk. Although outcome correlates with number and severity of coronary vessels involved, in stable patients the prognosis is surprisingly good, even with three-vessel disease, if ventricular function is normal.

Reduced ventricular function, often measured by analysis of ejection fraction, adversely influences prognosis, especially in patients with three-vessel disease.

Prognosis also correlates with symptoms; it is better in patients with mild or moderate angina (class I or II) than in those with severe exercise-induced angina (class III).

Age is a major risk factor in the elderly.

Treatment

The major tenet of treatment is to prevent or reduce ischemia and minimize symptoms. The underlying disease, usually atherosclerosis, must be delineated and the primary risk factors reduced as much as possible. Smokers should quit: Discontinuing smoking for >= 2 yr reduces the risk of MI to the level of those who never smoked. Hypertension should be treated diligently because even mild hypertension increases cardiac work. Angina sometimes improves markedly with treatment of mild LV failure. Paradoxically, digitalis

occasionally intensifies angina, presumably because increased myocardial contractility raises O_2 demand in the presence of fixed coronary blood flow. Aggressive reduction of total and LDL cholesterol (with dietary treatment supplemented by drugs as necessary) in patients at risk retards progression of CAD and may cause some lesions to regress. An exercise program emphasizing walking often improves the sense of well-being, reduces risk, and improves exercise tolerance.

Three classes of drugs are usually effective, alone or in combination, in relieving symptoms: nitrates, β-blockers, and Ca blockers.

Nitroglycerin is a potent smooth-muscle relaxer and vasodilator. Its major sites of action are in the peripheral vascular tree, especially in the venous or capacitance system and on the coronary blood vessels. Even severely atherosclerotic vessels may dilate in areas without atheroma. Nitroglycerin lowers systolic BP and dilates systemic veins, thus reducing myocardial wall tension, a major determinant of myocardial O_2 need. Overall, the drug helps balance myocardial O_2 supply and demand.

Sublingual nitroglycerin 0.3 to 0.6 mg is the most effective drug for the acute episode or for prophylaxis before exertion. Dramatic relief is usual within 1.5 to 3 min, is complete by about 5 min, and lasts up to 30 min. The dose may be repeated after 4 to 5 min three times if initial relief is incomplete. Patients should carry nitroglycerin tablets or aerosol spray with them at all times to use promptly at the onset of an angina attack.

β-Blockers completely block sympathetic stimulation of the heart and reduce systolic pressure, heart rate, contractility, and cardiac output, thus decreasing myocardial O_2 demand and increasing exercise tolerance. Additionally, they increase the threshold for ventricular fibrillation. Because tissue O_2 requirements are met by greater O_2 extraction from capillary blood, systemic arteriovenous O_2 difference is widened. These drugs are extremely useful in reducing symptoms and are well tolerated by most patients.

Ca blockers are the important third arm in the approach to angina pectoris and CAD. These vasodilators are useful in the treatment of angina with hypertension and counter coronary spasm if present. They are often highly effective in variant angina (see below), but their effectiveness may be limited by negative chronotropic and inotropic effects (diltiazem, verapamil).

Antiplatelet drugs are important in opposing platelet aggregation, which is pivotal in the genesis of MI and unstable angina. Aspirin, which binds irreversibly to platelets and inhibits cyclooxygenase and platelet aggregation in vitro, has been shown in epidemiologic studies to reduce coronary events (MI, sudden death) in CAD patients.

Angioplasty involves insertion of a balloon-tipped catheter into an artery at the site of a partially obstructive atherosclerotic lesion. Inflation of the balloon can rupture the intima and media and dramatically dilate the obstruction. About 20 to 30% of obstructions reocclude in a few days or weeks, but most can be redilated successfully. Use of stents significantly reduces the reocclusion rate, which continues to decline with application of newer techniques. Repeat angiography 1 yr later reveals an apparently normal lumen in about 30% of vessels undergoing the procedure. Angioplasty is an alternative to bypass surgery in a patient with suitable anatomic lesions. The risk is comparable with that of surgery: Mortality is 1 to 3%; MI rate is 3 to 5%; emergency bypass for intimal dissection with recurrent obstruction is required in < 3%; and the initial success rate is 85 to 93% in experienced hands. Results continue to improve with advances in technique, catheter and balloon mechanics, and pharmacotherapy to maintain postangioplasty patency.

Coronary arterial bypass surgery is highly effective in selected patients with angina.

UNSTABLE ANGINA

(Acute Coronary Insufficiency; Preinfarction Angina; Crescendo Angina; Intermediate Syndrome)

Angina characterized by a progressive increase in anginal symptoms, new onset of rest or nocturnal angina, or onset of prolonged angina.

Unstable angina is precipitated by an acute increase in coronary obstruction due to rupture of the fibrous plaque covering an atheroma with consequent platelet adhesion. In unstable angina, >= 1/3 of patients studied angiographically have partially occluding thrombi in the vessel subtending the recurrent ischemic area. Because recognition of a thrombus on angiography may be difficult, the incidence is probably underreported.

Compared with stable angina, the pain of unstable angina is generally more intense, lasts longer, is brought on by less effort, occurs spontaneously at rest (angina decubitus), is progressive (crescendo) in nature, or involves any combination of these changes.

About 30% of patients with unstable angina will probably suffer an MI within 3 months of onset; sudden death is less common. Presence of marked ECG changes with chest pain is an important marker for subsequent MI or death.

Unstable angina is a medical emergency to be treated in a cardiac care unit (CCU). Both heparin and aspirin reduce the incidence of subsequent MI. To reduce intracoronary clotting, aspirin 325 mg po and IV heparin should be instituted immediately. If aspirin cannot be tolerated or is contraindicated, ticlopidine 250 mg bid or clopidogrel 75 mg/day is a possible alternative. Ticlopidine requires monitoring of WBC at regular intervals because of the risk of neutropenia.

Cardiac work should be reduced by slowing heart rate and lowering BP with β-blockers and IV nitroglycerin, thus restoring the balance between cardiac O_2 demand and coronary blood flow. Contributing disorders (eg, hypertension, anemia) should be vigorously treated. Bed rest, nasal O_2, and nitrates are useful. Ca blockers may be useful for patients with hypertension and possible coronary artery spasm. Thrombolytic drugs are not useful and may be harmful. Use of the antiplatelet glycoprotein IIb/IIIa receptor antagonist, the humanized chimeric Fab fragment abciximab, has been shown to improve outcome in a randomized trial in patients with refractory unstable angina. Tirofiban has been shown to prevent cardiac ischemic events in unstable angina and non-Q-wave infarction. Other IIb/IIIa receptor antagonists are being evaluated in acute ischemic syndromes.

The patient's symptoms should be brought under control within a few hours of intensive treatment. After 24 to 48 h, if therapy is not effective, more aggressive treatment may be required. The intra-aortic counterpulsating balloon reduces systolic afterload and increases diastolic pressure, the driving force for coronary blood flow. It frequently relieves continuous anginal pain and may be used to support the circulation during diagnostic cardiac catheterization prior to revascularization with coronary bypass surgery or angioplasty. Angiography may be indicated in a patient poorly responsive to medical

therapy in order to identify the culprit lesion and evaluate the extent of CAD and LV function, with a plan for percutaneous transluminal coronary angioplasty or coronary artery bypass grafting if technically feasible.

VARIANT ANGINA
(Prinzmetal's Angina)

Angina pectoris that is usually secondary to large vessel spasm and is characterized by discomfort at rest and by ST segment elevation during the attack.

Most patients have significant fixed proximal obstruction of at least one major coronary vessel. Spasm usually occurs within 1 cm of the obstruction (often accompanied by ventricular arrhythmia). Between anginal attacks, which tend to occur with regularity at certain times of day, the ECG may be normal or may present a stable abnormal pattern. Ergonovine IV has been used as a provocative test to induce spasm, but this should be done only by experienced personnel in an angiographic laboratory. Although the average survival at 5 yr is 89 to 97%, patients with variant angina and severe coronary artery obstruction are at greater risk. Relief of variant angina is usually prompt after sublingual nitroglycerin; Ca blockers appear to be highly effective.

MYOCARDIAL INFARCTION

Ischemic myocardial necrosis usually resulting from abrupt reduction in coronary blood flow to a segment of myocardium.

Etiology and Pathogenesis

In > 90% of patients with acute MI, an acute thrombus, often associated with plaque rupture, occludes the artery (previously partially obstructed by an atherosclerotic plaque) that supplies the damaged area. Altered platelet function induced by endothelial change in the atherosclerotic plaque presumably contributes to thrombogenesis. Spontaneous thrombolysis occurs in about 2/3 of patients so that, 24 h later, thrombotic occlusion is found in only about 30%.

MI is rarely caused by arterial embolization (eg, in mitral or aortic stenosis, infective endocarditis, and marantic endocarditis). MI has been reported in patients with coronary spasm and otherwise normal coronary arteries (Fig.22). Cocaine causes intense coronary arterial spasm, and users may present with cocaine-induced angina or MI.

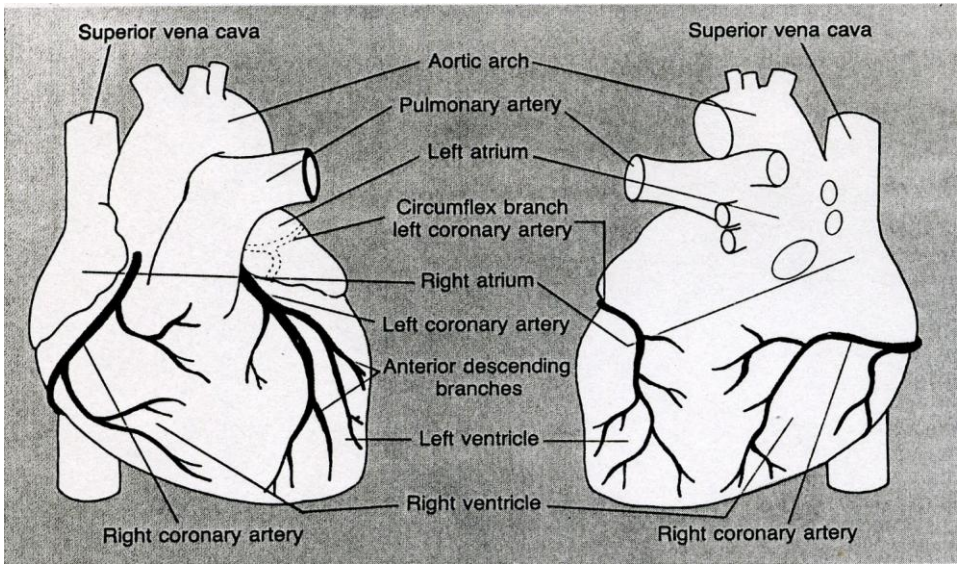


Fig.22. Major coronary arteries and their branches.

MI is predominantly a disease of the LV, but damage may extend into the right ventricle (RV) or the atria. RV infarction usually results from occlusion of the right coronary or a dominant left circumflex artery and is characterized by high RV filling pressure, often with severe tricuspid regurgitation and reduced cardiac output. Some degree of RV dysfunction occurs in about half of patients with an inferior-posterior infarction, producing hemodynamic abnormality in 10 to 15%. RV dysfunction should be considered in any patient with inferior-posterior infarction and elevated jugular venous pressure with hypotension or shock.

The ability of the heart to continue functioning as a pump relates directly to the extent of myocardial damage. Patients who die of cardiogenic shock usually have an infarct, or a combination of scar and new infarct, of >= 50% of LV mass. Anterior infarcts tend to be larger and have a worse prognosis than inferior-posterior infarcts. They are usually due to occlusion in the left coronary arterial tree, especially the anterior descending artery, whereas inferior-posterior infarcts reflect right

coronary occlusion or occlusion of a dominant left circumflex artery. Transmural infarcts involve the whole thickness of myocardium from epicardium to endocardium and are usually characterized by abnormal Q waves on ECG. Nontransmural or subendocardial infarcts do not extend through the ventricular wall and cause only ST segment and T-wave abnormalities. Subendocardial infarcts usually involve the inner 1/3 of the myocardium where wall tension is highest and myocardial blood flow is most vulnerable to circulatory changes. They may also follow prolonged hypotension. Because the transmural depth of necrosis cannot be precisely determined clinically, infarcts are better classified by ECG as Q wave and non-Q wave. The volume of myocardium destroyed can be estimated by the extent and duration of creatininkinase (CK) elevation.

Symptoms and Signs

About 2/3 of patients experience prodromal symptoms days to weeks before the event, including unstable or crescendo angina, shortness of breath, or fatigue. The first symptom of acute MI usually is deep, substernal, visceral pain described as aching or pressure, often with radiation to the back, jaw, or left arm. The pain is similar to the discomfort of angina pectoris but is usually more severe, long-lasting, and relieved little, or only temporarily, by rest or nitroglycerin. However, discomfort may be very mild, and perhaps 20% of acute MIs are silent or unrecognized as illness by the patient. Women may have atypical chest discomfort. Older patients may complain of dyspnea more than ischemic-type chest pain. In severe episodes, the patient becomes apprehensive and may sense impending doom. Nausea and vomiting may occur, especially in inferior MI. Symptoms of LV failure, pulmonary edema, shock, or significant arrhythmia may dominate.

On examination, the patient is usually in severe pain, restless, and apprehensive, with pale, cool, diaphoretic skin. Peripheral or central cyanosis may be apparent. The pulse may be thready (*pulsus filiformis*), and the BP is variable, although many patients initially manifest some degree of hypertension unless cardiogenic shock is developing.

Heart sounds are usually somewhat distant (diminished); the presence of a fourth heart sound is almost universal. A soft systolic blowing apical murmur (a reflection of papillary muscle dysfunction) may occur. At initial evaluation, a friction rub or more striking murmurs

suggest preexisting heart disease or another diagnosis. Detection of a friction rub within a few hours after onset of MI symptoms is distinctly unusual and might suggest acute pericarditis rather than MI. Friction rubs, usually evanescent, are common on days 2 and 3 post-MI with Q-wave infarcts.

Complications

Arrhythmia in some form occurs in > 90% of MI patients. Bradycardia or ventricular ectopic beats (VEBs) may be observed early in the course of MI. Conduction disturbances can reflect damage to the sinus node, the atrioventricular node, or specialized conduction tissues. Life-threatening arrhythmias, major causes of mortality in the first 72 h, include tachycardia from any focus rapid enough to reduce cardiac output and lower BP, Mobitz II or second-degree or third-degree heart block, and ventricular tachycardia (VT) and ventricular fibrillation (VF). Complete heart block with wide QRS (atrial impulses fail to reach the ventricle, ventricular rate is slow) is uncommon and usually denotes massive anterior MI. Complete atrioventricular block with narrow QRS usually indicates an inferior or posterior infarct. Asystole is uncommon except as a terminal manifestation of progressive LV failure and shock.

Sinus node disturbances are influenced by the origin of the coronary artery (ie, left or right) to the sinus node, the location of the occlusion, and the possibility of preexisting sinus node disease, especially in the elderly. Sinus bradycardia is generally of no significance unless the rate falls below 50/min. Persistent sinus tachycardia is generally ominous, often reflecting LV failure and low cardiac output. Other causes (eg, sepsis, thyroid excess) should be sought.

Atrial arrhythmias, including atrial ectopic beats (AEBs), atrial fibrillation, and atrial flutter (which is less common than atrial fibrillation), occur in about 10% of MI patients and may reflect LV failure or right atrial infarction. Paroxysmal atrial tachycardia is uncommon and usually occurs in patients who have had previous episodes.

Atrial fibrillation occurring within the first 24 hours is usually transient. Risk factors include age > 70 yr, heart failure, previous history of MI, large anterior infarct, atrial infarction, pericarditis, hypokalemia, hypomagnesemia, chronic lung disease, and hypoxia. Thrombolytic

therapy reduces the incidence. Recurrent paroxysmal atrial fibrillation is a poor prognostic sign and increases the risk of systemic embolus.

In *atrioventricular block,* reversible changes in atrioventricular conduction, Mobitz I conduction abnormalities with prolonged PR time, or Wenckebach phenomenon is relatively common, particularly with an inferior-diaphragmatic infarction involving the blood supply to the posterior wall of the LV with branches to the atrioventricular node. These disturbances usually are self-limited. ECG diagnosis of the type of block is important. Progression to complete heart block is unusual. True Mobitz II with dropped beats or atrioventricular block with slow, wide QRS complexes is usually an ominous complication of massive anterior MI.

Ventricular arrhythmias are common. VEBs occur in most patients with MI but do not warrant treatment. Primary VF occurs in the first few hours after MI. Late VF may be associated with continued or late myocardial ischemia and, when associated with hemodynamic deterioration, is a poor prognostic sign. Ventricular arrhythmia may reflect hypoxia, electrolyte imbalance, or sympathetic overactivity.

Heart failure occurs in about 2/3 of hospitalized patients with acute MI. LV dysfunction usually predominates, with dyspnea, inspiratory rales at the lung bases, and hypoxemia. Clinical signs depend on the size of the infarction, the elevation of LV filling pressure, and the extent to which cardiac output is reduced. In LV failure, PaO_2 before and after response to a rapidly acting diuretic (eg, furosemide 40 mg IV) may help establish a diagnosis: the reduced PaO_2 of LV failure should rise after diuresis. The mortality rate varies directly with the severity of LV failure.

Hypotension in acute MI may be due to decreased ventricular filling or loss of contractile force secondary to massive MI. Decreased LV filling is most often caused by reduced venous return secondary to hypovolemia, especially in patients receiving intensive loop diuretic therapy.

Cardiogenic shock, characterized by hypotension, tachycardia, reduced urine output, mental confusion, diaphoresis, and cold extremities, has a mortality of >= 65%. It is most often associated with massive anterior infarction and > 50% loss of LV functioning myocardium.

Recurrent ischemia may follow MI. The chest pain of MI generally subsides within 12 to 24 h. Any residual or subsequent chest pain may represent pericarditis, pulmonary embolus, or other complications (eg, pneumonia, gastric symptoms, recurrent ischemia). Usually, recurrent ischemia is accompanied on ECG by reversible ST and T-wave changes. BP may be elevated. Silent ischemia (ECG changes without pain) may occur in up to 1/3 of patients without recurrent pain. Evidence of continued post-MI ischemia suggests further myocardium at risk for infarction.

Functional papillary muscle insufficiency occurs in about 35% of patients. In some patients, permanent mitral regurgitation is caused by papillary muscle or free wall scar. Frequent auscultation during the first few hours of infarction often reveals a transient late apical systolic murmur thought to represent papillary muscle ischemia with failure of complete coaptation of the mitral valve leaflets.

Myocardial rupture occurs in three forms: rupture of the papillary muscle, rupture of the interventricular septum, and external rupture.

Rupture of the papillary muscle is most often associated with an inferior-posterior infarct due to right coronary artery occlusion. It produces acute, severe mitral regurgitation and is characterized by the sudden appearance of a loud apical systolic murmur and thrill, usually with pulmonary edema.

Rupture of the interventricular septum, although rare, is 8 to 10 times more common than rupture of the papillary muscle. Sudden appearance of a loud systolic murmur and thrill medial to the apex along the left sternal border in the 3rd or 4th intercostal space, accompanied by hypotension with or without signs of LV failure, is characteristic. Doppler echocardiography is often diagnostic.

External rupture increases in incidence with age and is more common in women. It is characterized by sudden loss of arterial pressure with momentary persistence of sinus rhythm and often by signs of cardiac tamponade. It is almost always fatal.

Pseudoaneurysm is a form of rupture of the free LV wall in which an aneurysmal wall containing clot and pericardium prevent exsanguination.

Ventricular aneurysm is common, especially with a large transmural infarct (most commonly anterior) and good residual

myocardium. Aneurysms may develop in a few days, weeks, or months. They do not rupture but may be associated with recurrent ventricular arrhythmias and low cardiac output. Another hazard of ventricular aneurysm includes mural thrombus and systemic embolization. An aneurysm may be suspected when paradoxical precordial movements are seen or felt, accompanied by persistent elevation of ST segments on the ECG or a characteristic bulge of the cardiac shadow on x-ray. Echocardiography helps establish the diagnosis and determine the presence of a thrombus. Administration of ACE inhibitors during acute MI modifies LV remodeling and may reduce the incidence of aneurysm.

Ventricular asynergy may occur because of the juxtaposition of normal and abnormal myocardium in acute MI. An akinetic segment is noncontracting with no systolic inward motion. A hypokinetic segment has reduced contractile excursion and partial impairment of inward motion. In cases with multiple infarcts, the myocardial hypokinesis is diffuse and termed ischemic myocardiopathy if low cardiac output and heart failure with pulmonary congestion predominate. A dyskinetic segment shows systolic expansion or bulging (paradoxical motion). These changes may be recognized by two-dimensional echocardiography, radionuclide ventriculography, or angiography and may contribute to reduced ventricular function and long-term disability.

Mural thrombosis occurs in about 20% of acute MI patients (60% of patients with large anterior infarcts). Systemic embolism occurs in about 10% of patients with LV thrombus (best diagnosed by echocardiography); risk is highest in the first 10 days but persists at least 3 mo.

Pericarditis may cause a pericardial friction rub in about 1/3 of patients with acute transmural MI. The friction rub usually begins 24 to 96 h after MI onset. Earlier onset is unusual and suggests other diagnoses (eg, acute pericarditis), although hemorrhagic pericarditis occasionally complicates the early phase of MI. Acute tamponade is rare.

Post-MI syndrome (Dressler's syndrome) develops in a few patients several days to weeks or even months after acute MI, although the incidence appears to have declined in recent years. It is characterized by fever, pericarditis with friction rub, pericardial effusion, pleurisy, pleural effusions, pulmonary infiltrates, and joint pains. Differentiation

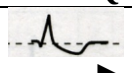
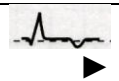
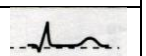
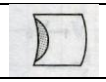
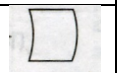
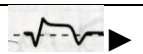
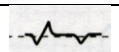
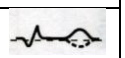
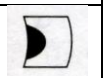
from extension or recurrence of infarction may be difficult, but cardiac enzymes do not significantly rise. This syndrome may be recurrent.

Diagnosis and Laboratory Findings

Typical MI is diagnosed by the history, confirmed by initial and serial ECG, and supported by serial enzyme changes. However, in some cases, definitive diagnosis may not be possible; the clinical findings may be typical or strongly suggestive, but the ECG and enzyme assay are not diagnostic, and patients will be categorized as having had a possible or probable MI. It is likely that some of these patients have suffered a small MI.

MI should be considered in men > 35 yr and women > 50 yr whose major complaint is chest pain, which must be differentiated from the pain of pneumonia, pulmonary embolism, pericarditis, rib fracture, costochondral separation, esophageal spasm, chest muscle tenderness after trauma or exertion, acute aortic dissection, renal calculus, splenic infarction, or a wide variety of abdominal disorders. Patients often interpret MI pain as indigestion, and evaluation may be difficult because coexisting hiatus hernia, peptic ulcer, or gallbladder disease is frequent. Although MI pain is commonly relieved by belching or antacids, such relief is usually brief or incomplete.

ECG: ECG is the most important laboratory procedure in the patient with suspected acute MI (Fig.23).

15-60 min	**Hours**	**1st day**	**To 2-3 weeks**	**To 6 weeks**	**Months, years**
Non-Q-wave MI					
					
					
					
					

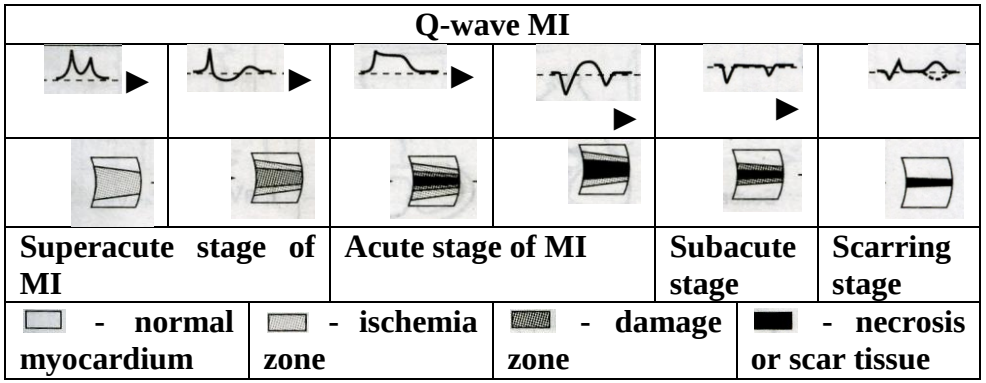


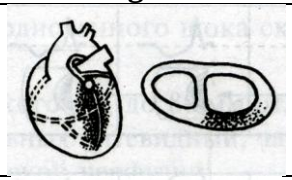
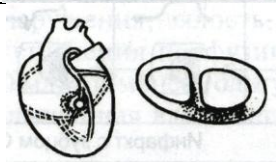
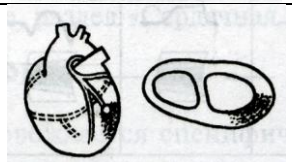
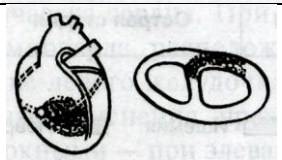
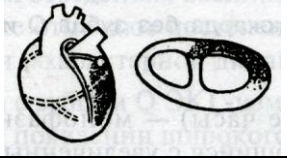
Fig.23. Stages of Q-wave and non Q-wave MI.

In acute transmural MI (Q-wave infarct), the initial ECG is usually diagnostic, showing abnormal deep Q waves and elevated ST segments in leads subtending the area of damage, or the ECG may be strikingly abnormal with elevated or depressed ST segments and deeply inverted T waves without abnormal Q waves. New-onset left bundle branch block may be a sign of recent MI. The 12-lead ECG at first encounter is at the center of the decision pathway (patients with ST segment elevation may benefit from thrombolytic therapy). In the presence of characteristic symptoms, ST segment elevation on ECG has a specificity of 90% and a sensitivity of 45% for diagnosing MI. Serial tracings showing a gradual evolution toward a stable, more normal pattern, or development of abnormal Q waves over a few days tends to confirm the initial impression of acute MI. Because nontransmural (non-Q-wave) infarcts are usually in the subendocardial or midmyocardial layers, they are not associated with diagnostic Q waves on the ECG and commonly produce only varying degrees of ST segment and T-wave abnormalities. In some patients, ECG abnormalities are less striking, variable, or nonspecific and therefore are difficult to interpret. However, acute MI probably cannot be diagnosed when repeat ECGs are normal. A normal ECG when the patient is pain-free does not rule out unstable angina that may culminate in acute MI.

ECG changes according to MI location are presented in Table 7.

Table 7.

ECG changes according to MI location

MI location	Damaged area	ECG leads
Anterolateral		I, II, aVL, V_1–V_6
Anteroseptal		I, aVL, V_1–V_4
Lateral		I, aVL, V_4–V_6
Inferior		II, III, aVF
Inferolateral		II, III, aVF, aVL, V_5–V_6

ECG changes in different MI location are presented on Fig.24-25.

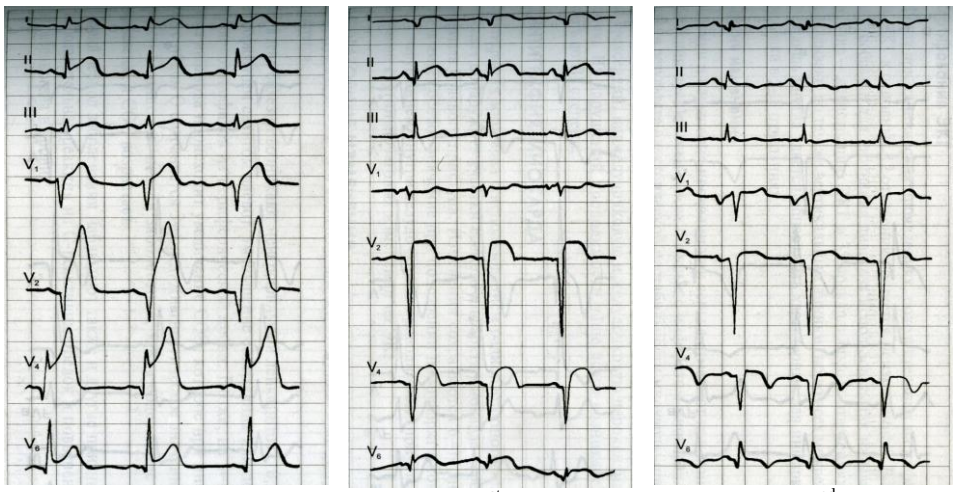


Fig.24. ECG in anterolateral MI: a – at the 1st h after MI onset; b – on the 2nd day; c – 10th day after MI onset. Diffuse transmural infarction.

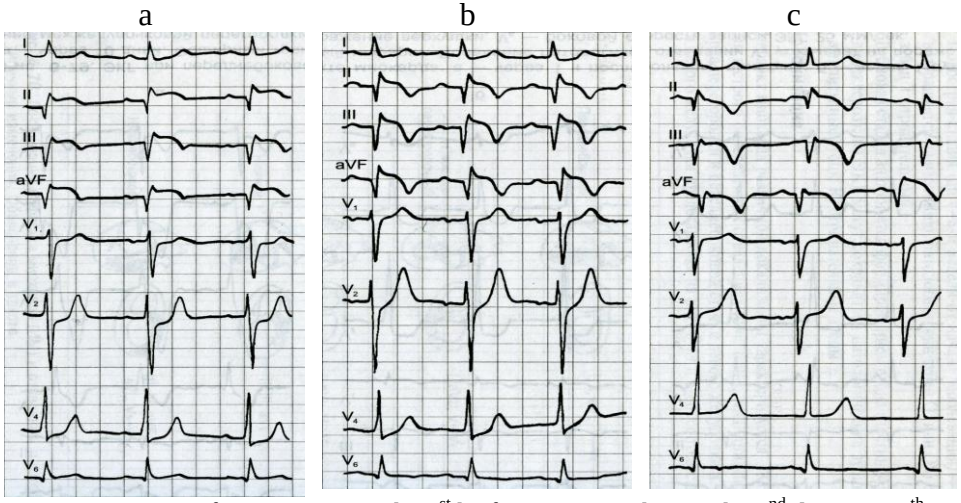


Fig.25. ECG in inferior MI: a – at the 1st h after MI onset; b – on the 2nd day; c – 14th day after MI onset.

Blood tests: Routine laboratory examination reveals abnormalities compatible with tissue necrosis. Thus, after about 12 h, the ESR is increased, the WBC is moderately elevated, and differential WBC count reveals a shift to the left.

Creatinkinase-MB, the myocardial component of CK, is found in blood within 6 h of myocardial necrosis. Levels are elevated for 36 to 48 h. Although small amounts of CK-MB are found in other tissues, elevations of CK with > 4% MB are diagnostic when associated with clinical findings suggestive of MI. Routine measurement of CK-MB on admission and q 6 to 8 h for the first 24 h will confirm or reject the diagnosis. Normal CK-MB for 24 h virtually rules out MI.

Myoglobin and the contractile proteins troponin-T and troponin-I are also released by infarcted myocardium. Troponin-T and troponin-I appear to be highly sensitive markers of myocardial injury and may replace conventional CK-MB analysis in early triage decisions in patients with chest pain and nondiagnostic ECG. Troponins are released in some patients with unstable angina, and activity level predicts future adverse events (Fig.26).

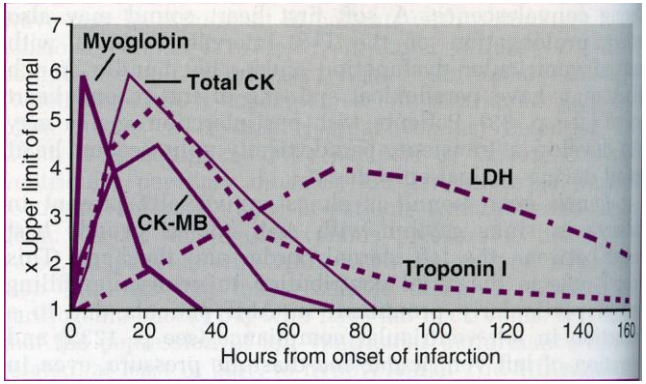


Fig.26. Time course of elevations of serum markers after MI. This figure summarizes the relative timing, rate of rise, peak values, and duration of elevation above the upper limit of normal for multiple serum markers following MI. Although traditionally total CK, CK-MB, and lactic dehydrogenase (LDH [with isoenzymes]) are measured, the relatively slow rate of rise above normal for CK and potential confusion with noncardiac sources of enzyme release for both total CK and LDH have inspired the search for additional serum markers. The smaller molecule myoglobin is released quickly from infarcted myocardium but is not cardiac specific. Therefore, elevation of myoglobin that may be detected quite early after the onset of infarction require confirmation with a more cardiac-specific marker such as CK-MB or troponin I. Troponin I (and troponin T; not shown) rises more slowly than myoglobin and may be useful for diagnosis of infarction even up to 3 to 4 days after the event. Assays for cardiac-specific troponin I and troponin T using monoclonal antibodies are now available.

Myocardial imaging For imaging MI, two techniques are available. Technetium-^{99}m pyrophosphate accumulates in recently (<= 3 to 4 days) infarcted myocardium. Conversely, thallium-201 accumulates intracellularly in viable myocardium in the manner of K and is distributed according to blood flow. However, imaging is slow and expensive, involves exposure to radiation, and is often of only marginal benefit in the diagnosis and treatment of MI.

Echocardiography may be useful in evaluating wall motion, presence of ventricular thrombus, papillary muscle rupture, rupture of the ventricular septum, ventricular function, and presence of intracavitary thrombus in patients with anterior Q-wave infarcts. When the diagnosis of MI is uncertain, recognition of LV wall motion abnormality by echocardiography establishes the presence of myocardial damage presumably due to recent or remote MI.

Right heart catheterization: Management of MI complications (eg, severe heart failure, hypoxia, hypotension) may be aided by measurement of right heart, pulmonary artery, and wedge pressures using balloon-tipped catheters that float into position (Swan-Ganz). Cardiac output can be determined with indicator dilution techniques

Treatment

Treatment is designed to relieve distress, reverse ischemia, limit infarct size, reduce cardiac work, and prevent and treat complications. MI is an acute medical emergency, and outcome is significantly influenced by rapid diagnosis and treatment.

There should be a quiet, calm, restful area. Single rooms are preferred, and privacy consistent with monitoring function should be ensured. Visitors usually are restricted during the first few days of illness, and outside influences (eg, radios, newspapers) are reduced to a minimum. A wall clock, a calendar, and an outside window help to orient the patient and prevent a sense of isolation.

Anxiety, mood changes, and denial are common. A mild tranquilizer is often given. After the acute phase of illness, the most important tasks are often management of depression, rehabilitation, and institution of long-term preventive programs. Overemphasis on bed rest, inactivity, and the seriousness of the illness reinforces depressive tendencies. Thorough explanation of the illness and an outline of a rehabilitation program customized to the patient's situation will be beneficial.

General measures include maintenance of normal bowel function and avoidance of straining at stool by using laxatives. Urinary retention is common in older patients, especially after several days of bed rest and atropine therapy. A catheter may be required but can usually be removed when the patient can stand or sit to void.

Smoking should be prohibited. The physician should devote considerable effort to making smoking cessation permanent.

Acutely ill patients have little appetite, although modest amounts of tasty food are good for morale. Patients usually are offered a soft diet of 1500 to 1800 kcal/day with Na reduction to 2 to 3 g (87 to 130 mEq). Na reduction is not required after the first 2 or 3 days for the patient without evidence of heart failure. Diets low in cholesterol and saturated fats are used to start education about healthy eating.

Initial treatment: Fifty percent of deaths from acute MI occur within 3 to 4 h of onset of the clinical syndrome, and outcome can be influenced by early treatment. The major factor delaying treatment is the patient's denial that the symptoms represent a serious, potentially life-threatening illness. The immediate threat to life is, occasionally, heart block or profound bradycardia with consequent hypotension that initiates cardiac arrest. Optimal early management includes rapid diagnosis, alleviation of pain and apprehension, stabilization of heart rhythm and BP, administration of a thrombolytic drug if possible, and transportation to a hospital with a monitoring unit.

Systems should be in place in every emergency room for immediate triage of the patient with chest pain for rapid assessment and urgent ECG. A reliable IV route must be established, blood drawn for enzyme analysis, and continuous (single-lead) ECG monitoring instituted. The efficacy of emergency medical services, including mobile ECG, early thrombolysis when indicated, and triage to the appropriate hospital depending on initial assessment, influences mortality and complications.

Despite the wide variety of electronic monitoring equipment available, only cardiac rate and rhythm as revealed by the ECG have consistently proved useful to monitor routinely and continuously. Qualified nurses can interpret the ECG for arrhythmia and initiate protocols for arrhythmia treatment. All professional personnel should know how to apply CPR.

Aspirin 160 to 325 mg (if not contraindicated) should be given at presentation and daily indefinitely thereafter. The first dose appears to be absorbed more quickly if chewed. Its antiplatelet effects reduce short-term and long-term mortality.

Oxygen is reasonably administered with 40% mask or nasal prongs at 4 to 6 L/min for the first few hours.

Morphine 2 to 4 mg IV, repeated as needed, is highly effective for the pain of MI, but it can depress respiration, can reduce myocardial contractility, and is a potent venous vasodilator. Hypotension and bradycardia secondary to morphine can usually be overcome by prompt elevation of the lower extremities. Continued pain may also be relieved in some patients by administration of nitroglycerin, initially sublingual followed by continuous IV drip if needed.

Most patients are moderately hypertensive on arrival at the emergency room, and BP gradually falls over the next several hours. Severe hypotension or signs of shock are ominous and must be treated aggressively. Continued hypertension requires aggressive treatment with antihypertensive therapy, preferably IV, to lower BP and reduce cardiac work.

Thrombolytic therapy: Thrombolytic therapy is most effective in the first few minutes and hours after onset of MI, requiring rapid diagnosis. During the acute phase of Q-wave MI, thrombolytic drugs reduce hospital mortality between 30 and 50% when used in conjunction with ASA and improve ventricular function. The earlier therapy begins, the better. Greatest benefit occurs within 3 h, but effectiveness up to 12 h has been demonstrated. ST segment elevation identifies candidates for thrombolysis. Every effort should be made to achieve a "door to needle" time of <= 30 min. About 50% of patients with enzyme-proven MI do not have ST segment elevation or Q waves.

Plaque fissuring, rupture, and intraplaque hemorrhage with subsequent thrombotic occlusion commonly lead to MI. In experimental coronary occlusion, necrosis progresses from subendocardium to subepicardium, with most of the necrosis occurring by 6 h. Major myocardial recovery occurs if the occlusion is released by 2 h.

Thrombolysis should be considered in patients with ST segment elevation in two or more contiguous leads, in patients with typical symptoms in whom bundle branch block obscures evidence of infarction,

in those with strictly posterior MI (presenting with an r or R, and ST segment depression in leads V_1-V_4), and in the occasional patient presenting with giant T waves. Improvement is greatest in patients with anterior MI or bundle branch block. Non-Q-wave infarcts generally do not have a totally occlusive thrombus and are usually not treated with thrombolysis because no therapeutic advantage is evident.

Concomitant antithrombotic therapy: The use and route of heparin therapy depends on the thrombolytic drug used and the thrombolic-embolic risk.

Drugs to reduce cardiac work: Cardiac performance after recovery depends largely on the mass of functioning myocardium surviving the acute episode. Scars from previous infarcts add to the acute damage. When the total damaged myocardium is > 50% of LV mass, survival is unusual. Reduction of myocardial O_2 requirements by decreasing afterload with vasodilators or reducing heart rate and contractility with β -blockers reduces the size of the infarct.

β-Blockers reduce the incidence of VF and are recommended if not contraindicated, especially in high-risk patients. IV β -blockers given within the first few hours after onset of MI improve prognosis by reducing infarct size, recurrence rate, incidence of VF, and mortality. Clinically, β -blockers reduce heart rate, arterial pressure, and contractility, thereby reducing cardiac work and O_2 demand. Usefulness is less well established in non-Q-wave MI. Contraindications include bradycardia, heart block, and asthma.

ACE inhibitors appear to reduce mortality in MI patients, especially in those with anterior infarction, heart failure, or tachycardia. The greatest benefit occurs in the highest risk patients early in and during convalescence. ACE inhibitors should be given > 24 h after thrombolysis stabilization and, because of continued beneficial effect, may be prescribed long-term. Contraindications include hypotension, renal failure, bilateral renal artery stenosis, and known allergy.

Vasodilators may be useful for judicious reduction of myocardial work in selected patients with acute MI. A short-acting IV drug with quick onset and offset of pharmacologic effect is preferable. IV nitroglycerin is recommended for the first 24 to 48 h in patients with acute MI and heart failure, large anterior MI, persistent ischemia, or

hypertension (reduced 10 to 20 mm Hg but not to < 80 to 90 mm Hg systolic).

Primary percutaneous transluminal cardiac angioplasty (PTCA): Using PTCA as initial treatment is at least as effective and, in certain catheterization laboratories, may be modestly better than thrombolysis in reducing infarct size, additional cardiac events, and mortality in patients with elevated ST segment MI or bundle branch block. Favorable PTCA outcomes generally reflect great procedural skill, high volume experience, and a short time to catheterization. However, only a few acute MI patients have access to a skilled cardiac catheterization team. Anecdotal evidence suggests a role for PTCA or coronary bypass surgery in patients with massive recent-onset MI and severe hypotension or shock.

Treatment After Hospital Discharge

Secondary prevention of late recurrent MI and death: Aspirin reduces mortality and reinfarction rates in post-MI patients by 15 to 30%. Enteric-coated aspirin 160 to 325 mg/day is recommended long-term. Warfarin plus aspirin also reduces the incidence of recurrent MI, but when used alone in the absence of an LV thrombus or atrial fibrillation, it is of no benefit.

Timolol, propranolol, or metoprolol reduces post-MI mortality by about 25% for >= 7 yr. High-risk patients should be treated. Whether low-risk patients should be treated is much debated. Because these drugs are generally well tolerated, it seems reasonable to treat all patients who have minimal or no side effects and are willing to continue long-term therapy.

Rehabilitation: Bed rest for the first 1 to 3 days is wise until the clinical course becomes evident. Longer bed rest results in rapid physical deconditioning, with development of orthostatic hypotension, decreased work capacity, and increased heart rate during effort. Feelings of depression and helplessness are intensified. Patients without complications may be permitted chair rest, passive exercise, and use of a commode on day 1. Walking to the bathroom and nonstressful paperwork or reading are allowed shortly thereafter. Hospital discharge after 5 to 7 days is reasonable and without significant hazard in the absence of complications.

Physical activity is gradually increased during the next 3 to 6 wk. Resumption of sexual activity is often of great concern and, with other moderate physical activities, may be encouraged. If cardiac function is well maintained 6 weeks after acute MI, most patients can return to their full range of normal activity. A regular exercise program consistent with lifestyle, age, and cardiac status is protective and enhances general well-being.

The impact of acute illness and treatment provides strong motivation to both physicians and patients to analyze and manage risk factors. Discussion and evaluation of the patient's physical and emotional status with advice about smoking, diet, work and play habits, and exercise, combined with treatment of risk factors, may improve the patient's prognosis. Recent evidence of slower progression and even regression of atherosclerotic lesions with treatment of hypercholesterolemia by diet and hydroxymethylglutaryl coenzyme A reductase inhibitors (statins) should motivate an aggressive therapeutic approach .

CONTROL QUESTIONS

1. Complaints of patients with coronary heart disease
2. Pathology and pathogenesis atherosclerosis
3. Reversible and irreversible risk factors for atherosclerosis
4. Hemodynamics changes in coronary artery disease
5. Cassification of coronary artery disease
6. Physical examination data in patients with angina pectoris
7. Instrumental diagnostics of angina pectoris
8. Physical examination data in patients with myocardial infarction
9. Instrumental diagnostics of myocardial infarction
10. Laboratory diagnostics of myocardial infarction
11. Complications of myocardial infarction

Theme 29. CONTROL SUMMING-UP

Goal: to check-up knowledge and practical skills of the main pulmonary syndromes and diseases diagnostics.

Knowledge objectives:

- to know educational materials to themes 24-28.

Skill objectives:

- to perform inspection, auscultation, percussion and palpation of patients; to interpret data of additional diagnostic methods.

Equipment required: stethoscope.

Classes include control tests according to themes 24-28 and work-up with patients on bedside. Physical examination skills will be assessed.

REFERENCES

1. Основы семиотики заболеваний внутренних органов. Атлас./ А.В.Струтынский, А.П.Баранов, Г.Е.Ротберг, Ю.П.Гапоненков.- М.; РГМУ, 1997, 222 с.
2. Пропедевтика внутренних болезней. /Под редакцией В.Х.Василенко, А.Л.Гребенева, Н.Д.Михайловой.- М., Медицина, 1974, 528с.
3. Cecil essentials of medicine. Third edition/ T.E.Andreoli, J.C.Bennett, C..J.Carpenter et al. – W.B.Saunders Company, Philadelphia, 1996, 921p.
4. Ferri's clinical advisor: instant diagnosis and treatment. First edition/Edited by F.F.Ferri – Mosby, St. Luis, 1998, 1124 p.
5. Forbes C.D. Color Atlas and text of clinical medicine / C.D. Forbes, W.F. Jackson. - 2nd ed. - London: Mosby-Wolfe, 1997. - 534 p.: ill.
6. A Guide to physical examination. Third Edition./B. Bates, R. A. Hoekelman.- J.B. Lippincott Company, Philadelphia, 1983, 561p.
7. Heart disease: a textbook of cardiovascular medicine. Fifth edition/Edited by E.Braunwald.- W.B.Saunders Company, Philadelphia, 1997, 1996 p.

8. Manual of Introductory Clinical Medicine./R.M.Maclis, M.E.Mendelson, G.H.Mudge.- Little. Brown and Company, Medical division, Waltham, 1997, 251p.
9. The 17th Edition of The Merck Manual of Diagnosis and Therapy/ http://www.merck.com./mrkshared/mmanual. a public service by Merck & Co., Inc