

Ministry of Defence

Synopsis of Causation

Coronary Heart Disease

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Disclaimer

This synopsis has been completed by medical practitioners. It is based on a literature search at the standard of a textbook of medicine and generalist review articles. It is not intended to be a meta-analysis of the literature on the condition specified.

Every effort has been taken to ensure that the information contained in the synopsis is accurate and consistent with current knowledge and practice and to do this the synopsis has been subject to an external validation process by consultants in a relevant specialty nominated by the Royal Society of Medicine.

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1. Definition

- 1.1. Atherosclerosis is the main disease process that affects arteries in the body. It is an inflammatory process within the arterial wall, which is fuelled by fats or lipids in the blood stream. This produces a protrusion from within the wall called a plaque, which results in narrowing of the artery with impaired blood supply to the target organ supplied by that artery. Atherosclerosis within the main arteries in the body can lead to the development of diseases, notably coronary heart disease and cerebrovascular disease, which are the leading causes of death in the developed world.
 - 1.1.1. The process of atherogenesis¹ is complex and may take 20 years or longer before causing any symptoms. Specific clinical features usually begin after the fifth decade of life. All arteries are involved to a greater or lesser extent, the important arterial circulations being the coronary, cerebral, peripheral renal and mesenteric circulation. As the process advances, particular patterns evolve and point towards the diagnosis. Changes in the artery walls may be present from a very early age and may be well established from puberty. As they do not cause any symptoms at this time, they are usually detected only because of premature death from some other cause and subsequent post-mortem examination.
 - 1.1.2. Atherosclerosis is the subject of a separate synopsis, which should be read in conjunction with this synopsis. One of the commonest manifestations of atherosclerosis results from disease affecting the coronary arteries.
- 1.2. Coronary artery disease (CAD) is the common term for disorders affecting the coronary arteries. Atherosclerosis, which is the most frequent cause of CAD, produces the formation of plaques which are the result of gradual deposition of fatty deposits beneath the inner layer or intima of the artery. This process is usually diffuse but localised plaques are often large enough to decrease blood flow along the artery. This results in angina when the supply of blood to the heart muscle is insufficient to meet the increase in the demand when the heart responds to exercise. Plaques can rupture and expose their fatty core to the blood stream, which leads to a complex series of reactions resulting in platelets and plasma proteins forming a thrombus. This may produce partial or complete blockage of the coronary artery resulting in the interruption of blood flow and loss of nutrition to the heart muscle which it supplies (myocardial ischaemia or myocardial infarction [MI]). This causes anginal pain at rest and is described as acute coronary syndrome. If there is infarction or death of tissue, there is damage to the heart muscle which, if severe, will reduce the pumping action of the heart.
- 1.3. Coronary heart disease (CHD) is the result of the effects of CAD on the heart muscle. CHD causes approximately 117,000 deaths per year in the UK and is the cause of death in 1 in 5 men and 1 in 6 women, and the commonest cause of premature death.² There is variation in mortality with rates being higher in Scotland than in the south of England. The incidence is higher in men, the socially deprived, and the elderly, as well as among certain ethnic groups. Although mortality is falling in the UK, especially among the 55-64 years age group, the UK still has one of the highest mortality rates from CHD in Western Europe.

2. Clinical Features

- 2.1. Coronary heart disease can present in several ways:
 - Angina pectoris
 - Acute coronary syndrome
 - Heart failure and sudden death, which may complicate either of the above but may also be the presenting feature of CAD
- 2.2. **Angina pectoris** is typically felt as a discomfort of varying severity, often a sensation of tightness or burning in the chest, which may radiate to the neck, jaw, to either or both arms, back, or upper abdomen. On occasions the chest is not the major site of the pain. Exercise, emotion, stress or fear often provoke the onset of an attack.
 - 2.2.1. Stable angina is usually predictable and is precipitated by exertion and relieved by a short period of rest or by the use of sublingual glyceryl trinitrate, either as a spray or tablets. There are many other conditions, which may present as chest pain, for example, inflammation of the upper abdominal organs, of the lungs, pleura, heart or chest wall. The history of the pain is the most important aspect in the diagnosis of cardiac pain. Physical examination enables the exclusion of valvular disease, which may cause angina without CHD. Occasionally there are physical manifestations of hyperlipidaemia.
 - 2.2.2. Angina can be provoked by a graded exercise test on a bicycle or a treadmill, and changes on the ECG during the exercised induced chest pain may indicate myocardial ischaemia and confirm the diagnosis. The exercise test is a sensitive test to diagnose angina in a population of patients with chest pain but false-positive tests can occur, particularly in women. For patients suspected of having a false-positive exercise test or if the patient cannot exercise sufficiently, other tests such as myocardial perfusion scintigraphy of the heart or coronary angiography may be required to diagnose the presence of CAD. Newer tests such as coronary angiography with computer tomographic or magnetic resonance imaging need to be evaluated further before their availability becomes more widespread.
- 2.3. By definition, **acute coronary syndrome** is diagnosed when angina-like symptoms occur more frequently on exertion or at rest, and ranges from unstable angina without any myocardial damage to a heart attack with extensive myocardial damage or infarction. It results from the rupture of a plaque within the coronary artery and thrombus formation on the plaque, with varying degrees of obstruction and embolisation of thrombus down the artery.³
 - 2.3.1. The degree of myocardial damage will depend on a number of factors including the size of the artery affected, the degree of obstruction, and the amount of collateral circulation to the vulnerable muscle. When a

major artery is occluded, this will produce ST elevation on the ECG. If the artery is small, or there is incomplete occlusion of the artery, or good collateral circulation to the threatened muscle, the ECG often shows ST depression.

- 2.3.2. When there is damage to the muscle, there is release of enzymes into the blood stream, which can be detected in the biochemistry laboratory. There are several such markers that can be measured, but troponin T is both sensitive and specific in detecting myocardial injury.
- 2.4. Myocardial infarction may be complicated by **cardiac arrest**, which if not corrected expeditiously will result in sudden death. If there is extensive myocardial damage the heart will be unable to pump blood efficiently, the patient will develop heart failure, and severe shock will result
- 2.5. **Heart failure.** There are many causes of heart failure, which is a clinical syndrome and not a specific diagnosis. CHD is the cause of approximately 2 out of 3 cases, with heart failure most often due to death or infarction of myocardial tissue, which reduces the pumping action or systolic contraction of the heart. This results in an increase in pressure within the heart which is transmitted back into the lungs and, when acute, causes fluid to leak out into the small sacs or alveoli, producing pulmonary oedema. As a result the patient is acutely breathless and can cough up frothy sputum.
 - 2.5.1. Left heart failure can exert increased pressure through the lungs to produce right heart failure with venous congestion, liver enlargement and ankle swelling.
 - 2.5.2. Not every patient with a heart attack will have acute heart failure and the myocardial damage may be asymptomatic or produce chronic symptoms such as breathlessness on exertion and fatigue. In heart failure the body tries to rectify the loss of output of blood from the heart by increasing activity of the sympathetic nervous system resulting in an increase in heart rate and constriction of small arteries. As a result of reduced blood flow through the kidney, hormones are secreted which cause further vascular constriction (angiotensin) and act on the kidney to retain sodium and water (aldosterone). These compensatory mechanisms paradoxically further reduce the output of the heart and worsen the patient's condition.
 - 2.5.3. Echocardiography remains the most useful test to diagnose reduction of the pumping action of the heart (left ventricular ejection fraction [LVEF]).
 - 2.5.4. There is a marked increase in incidence of heart failure in the elderly and it carries a poor prognosis.²
- 2.6. **Sudden cardiac death.** Sudden cardiac death (SCD), that is death within one hour of the onset of symptoms, is the cause of death in over half of all mortality due to CHD.⁴ It can be the presenting feature of CHD and is due to plaque rupture which causes myocardial damage and precipitates ventricular fibrillation (VF), a chaotic heart rhythm which results in a loss of output from the heart. Prompt defibrillation can correct the VF, while cardiopulmonary resuscitation increases the chances of survival if any delays occur before defibrillation.

- 2.6.1. SCD may also occur weeks to years after a heart attack due to the resulting scar within the heart muscle. Sometimes SCD is preceded by arrhythmias (ventricular tachycardia [VT]), which do not result in death and appear to be more common in those patients who have sustained a large amount of heart damage resulting in a lower LVEF.⁴
- 2.6.2. In epidemiological studies age, pre-existing CHD, systolic hypertension, elevated cholesterol, smoking, and physical inactivity were risk factors for SCD.⁵

3. Aetiology

Fixed risks	Modifiable risks
Male sex Family history Advancing age Lower socioeconomic group Ethnicity	Cigarette smoking High blood cholesterol High triglycerides Hypertension Central obesity “Western” diet Diabetes mellitus Physical inactivity Unemployment Stress Personality Excessive alcohol intake

Table 1: Fixed and modifiable risks of coronary artery disease

- 3.1. **Risk factors for coronary artery disease.** While the exact cause of coronary artery disease is not known, a variety of different risk associations have been identified which may interact together and may be considered as risk factors. These include the fixed risks - male sex, family history, advancing age, and lower socio-economic group - as well as the modifiable risks listed in Table 1. Further details on individual risk factors are given below. However, there is increasing recognition that estimation of the total risk and not just individual risk factors is important, as coexistent risk factors have a synergistic effect.
- 3.1.1. There are various graphs or tables available to help compute the overall risk for cardiovascular disease by taking into account the presence of several risk factors. Risk assessment should commence in adults aged over 40 years, and in younger patients with a family history of premature coronary artery disease. Formal risk estimation is not required for certain groups of patients who are known to have pre-existing conditions that already place them at a high total risk for cardiovascular disease. This includes patients with known atherosclerotic cardiovascular disease, diabetes, hypertension with target organ damage, or familial lipid disorders.⁶
- 3.2. **Physical activity.** Over the last 20 years there has been increasing inactivity in the adult population and this has been shown to be an independent risk factor.⁷ Not only do increased levels of physical activity reduce other risk factors such as obesity, diabetes, and hyperlipidaemia, but are also protective against death from CHD. At least, moderate intensity levels of activity are protective, with increasing protection as the intensity and duration of the exercise increases. Physical activity needs to be maintained if benefit is to be sustained as this is lost during periods of inactivity.
- 3.3. **Smoking.** Smoking increases the risk of cardiovascular disease including coronary artery disease, stroke, and peripheral vascular disease as well as cardiovascular mortality.^{8,9} The risk is increased in the presence of diabetes and

hypertension. Passive smoking also increases the risk of coronary heart disease. The total burden of cigarette smoking should be assessed as well as whether the patient is a current smoker or not. Stopping smoking reduces the risk of developing coronary heart disease and reduces mortality in patients with established disease.¹⁰

- 3.4. **Alcohol.** People who drink alcohol in moderate amounts e.g. up to 3 units/day for men and up to 1 unit/day for women have a lower mortality than non-drinkers due to a lower mortality from CHD.¹¹ Binge drinking above these levels can result in hypertension, high blood cholesterol, and increased incidence of sudden death. High alcohol intake can also have a deleterious effect on the liver and nervous system.¹²
- 3.5. **Hypertension.** The cause of high blood pressure in most hypertensive patients is unknown. High blood pressure increases the risk of developing coronary artery disease, heart failure, stroke, and kidney failure, with the risk of developing any of these complications increasing with the degree of high blood pressure.⁶ Lifestyle modifications are important for all patients and these include weight reduction and dietary restriction of fat, salt and alcohol, as well as increased physical activity.⁷ Drug therapy is effective in reducing the risk and in those patients with diabetes and renal impairment the threshold to start treatment is lower.¹³ Table 2 indicates the grades of hypertension and whether therapy is required.⁶

Blood pressure (BP) category	Systolic BP mm HG	Diastolic BP mm Hg	Lifestyle Intervention	Drug therapy
Normal	<120	<80	-	-
High-normal	135-139	85-89	Yes	Consider
Mild hypertension (grade 1)	140-159	90-99	Yes	Consider
Moderate hypertension (grade2)	160-179	100-109	Yes	Yes
Severe hypertension (grade 3)	>180	>110	Yes	Yes

Table 2: Grades of hypertension³

- 3.6. **Psychosocial issues.** Stress is a commonly used term but is difficult to define and therefore its estimation as a risk factor for CHD is not possible. Depression and social isolation are independent risk factors for CHD and the risk is related to the severity of the depression.¹⁴ Conversely, the evidence for anxiety as a risk factor is not strong. Early studies suggested that people with type A personality were more likely to develop CHD but recent larger studies have invalidated these claims.¹⁵ There is good evidence that symptomatic CHD can be triggered by acute life events such as bereavement, as well as catastrophic events such as terrorist attacks or earthquakes.¹⁴ However, the role of chronic “stress”, including stress in the work place, as a risk factor for CHD is unclear.¹⁵

- 3.6.1. Depression can affect nearly half of patients after MI with almost one fifth having severe depression. It is an independent risk factor for mortality following MI. However, there is little evidence that

psychological interventions can reduce mortality, although they do decrease anxiety and depression in these patients.^{16,17}

- 3.6.2. Cardiovascular disease risk has a gradient by social status with the socially deprived having the highest risk. This risk is not included in existing risk scores which underestimate risk in these groups and development of new scoring systems to include social status is suggested.¹⁸
- 3.7. **Hyperlipidaemia.** The higher the level of cholesterol in the blood, the higher the risk of CHD.⁶ The level of cholesterol is dependent on genetic factors, diet and exercise, and can rise in certain diseases.
 - 3.7.1. The total cholesterol can be divided into low density lipoprotein (LDL - “bad” cholesterol) and high density lipoprotein (HDL - “good” cholesterol).¹⁹ Patients at risk are those with a high LDL and low HDL and the risk is similar for those with and without CHD. However, the need for treatment of a high LDL level should be considered in the context of a full risk assessment which includes other risk factors. Treatment of high LDL with potent cholesterol lowering drugs e.g. “**statins**” has reduced the incidence of heart attacks and strokes in patients with and without CAD, the middle-aged, the elderly, and both men and women.
- 3.8. **Gender.** The incidence of CHD is lower in women than men especially in the 45 to 54 years age group but the male predominance decreases in later decades.^{2,20} The commonest symptom in women is angina but they often have atypical symptoms and thus tend to be under-diagnosed and under-treated compared to male patients.
 - 3.8.1. While women who undergo premature menopause have an increased risk of CHD, there is no relation between hormone levels and CHD in normal women. Several epidemiological studies suggest a protective role for hormone replacement therapy (HRT) in the prevention of CHD in women but this has not been born out in observational studies which have been carried out in younger peri-menopausal women. More studies are required on HRT and CHD but presently it is not recommended for prevention of CHD.
- 3.9. **Diet and obesity.** There is a relationship between mortality from CHD and a diet high in saturated fats and LDL cholesterol. Reduction in intake of saturated fats and replacement with mono- and polyunsaturated fats reduces the incidence of heart attacks and strokes.²¹ People who eat a regular diet of fish have fewer heart attacks. Eating 5 portions of vegetables and fruit a day is widely advised, and there is evidence that this reduces strokes and heart attacks.
 - 3.9.1 Obesity is often measured as the body mass index (BMI) and as it increases so does the risk of CHD. The abdominal distribution of fat is a better marker of risk, and the hip to waist ratio, calculated from simple clinical measurements, correlates better than BMI with risk of myocardial infarction.²² Waist measurement alone also correlates with other risk factors including elevated LDL, low HDL cholesterol, hypertension, and diabetes. Weight loss reduces these markers of risk and should be advised in patients with increased waist measurement (men ≥ 102 cm; women ≥ 88 cm) or obese BMI ≥ 25 kg/m², and

especially the morbidly obese BMI ≥ 30 kg/m². In addition to diet, these patients must be encouraged to increase their physical activity and may require drug treatment to lose weight.

3.10. **Diabetes mellitus.** Diabetes mellitus (DM) is a condition in which there is too much glucose in the blood due to loss of insulin activity.²³ In its most severe form it can cause dehydration, acidosis and death. Poor control in the longer term, can cause complications such as stroke or heart attack, kidney failure, and blindness. Type I diabetes is due to failure of specialised cells in the pancreas to produce insulin and is usually seen in young people. In Type II diabetes there is a reduction in the amount of insulin and a failure of the insulin to work properly.

3.10.1. Type II DM is associated with obesity and physical inactivity. Often other risk factors for CHD are present such as hypertension and hyperlipidaemia. Until recently it was a disease of the middle aged but it is increasingly seen in younger Asians and Afro-Caribbeans and even overweight children. DM is treated with insulin and oral medications, which reduce the blood glucose. Patients with Type II DM who make radical lifestyle changes can reverse their overall risk profile. However, the addition of drug therapy to control hypertension and hyperlipidaemia may be required and both have been shown to decrease the risk of cardiovascular events in diabetic patients.⁶

3.11. **Family history.** CHD can run in certain families and if a first-degree relative develops coronary heart disease (angina or heart attack) at a young age (females under 65 and males under 55 years), this confers an additional risk to close family members. In the minority of cases, this may be related to an inherited elevation of the serum cholesterol but usually the exact mechanism of inheritance is unknown.

3.12. **Prevention.** It is recommended that measures to prevent CHD in clinical practice should focus on patients with established atherosclerotic cardiovascular disease, on those with diabetes, and on apparently healthy individuals who are at high risk of developing symptomatic atherosclerotic disease for the first time. This last group is defined as individuals with a cardiovascular disease risk of $\geq 20\%$ over the next 10 years, as measured by risk prediction charts. It is important to calculate the total risk as the presence of several risk factors is multiplicative, risk factors tend to cluster in one individual, and the pathogenesis of arteriosclerosis cannot be attributed to one risk factor alone. Nevertheless, other people with particularly elevated single risk factors will also require CHD prevention because they too are at high risk, regardless of the presence of other risk factors.⁶

4. Prognosis

- 4.1. Men aged 51-59 years with angina have a higher mortality than those without angina. In a Swedish study, the 16-year survival rate of men with angina was 53% compared to 72% with no angina and 34% in those with a history of heart attack.²⁴ For patients with angina, prognosis is worse in those who are male, have resting ECG abnormalities, or who have had a previous myocardial infarction.
- 4.2. For those patients who undergo coronary angiography, prognosis can be judged by the extent of the disease and the left ventricular ejection fraction (LVEF). Patients with the most extensive disease and reduced LVEF have the worst prognosis. For patients with acute coronary syndrome who survive to reach hospital, there are several risk scores based on clinical criteria to identify high-risk patients.^{25,26} Despite modern therapies the 6-month mortality after myocardial infarction is nearly 20%. Patients diagnosed with heart failure also have a poor prognosis with just under 40% surviving at 5-year follow up.¹

5. Summary

- 5.1. Coronary heart disease causes approximately 117,000 deaths per year in the UK, being the cause of death in 1 in 5 men and 1 in 6 women, and the commonest cause of premature death. There is variation in mortality with rates being higher in Scotland than in the south of England.
- 5.2. Atherosclerosis is the most frequent cause of CHD.
- 5.3. The process of atherosclerosis begins in childhood and progresses throughout adult life, but the specific clinical features usually begin after the fifth decade of life.
- 5.4. The modifiable risk factors are inactive life-style, cigarette smoking, a diet rich in calories and saturated fats, high blood pressure, diabetes mellitus, and hyperlipidaemia.

6. Related Synopses

Stroke

Hypertension

Atherosclerosis

Atrial Fibrillation

Diabetes Mellitus

7. Glossary

angiography	A procedure performed to view blood vessels after injecting them with a radioopaque dye that outlines them on x-ray.
atherogenesis	The process of forming atheromas, plaques in the inner lining (the intima) of arteries.
embolisation	The obstruction or occlusion of a blood vessel by an embolus.
hyperlipidaemia	Presence of excess lipids in the blood.
scintigraphy	A diagnostic test in which a two-dimensional picture of a body radiation source is obtained through the use of radioisotopes.
statins	A class of drugs that lower cholesterol.
tomographic	Any of several techniques for making detailed x-rays of a predetermined plane section of a solid object while blurring out the images of other planes.

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