King's Fund Forum

CONSENSUS AND CONTROVERSY IN MEDICINE

Blood Cholesterol and Coronary Heart Disease:

SOME PRELIMINARY QUESTIONS

AND ANSWERS

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BLOOD CHOLESTEROL AND CORONARY HEART DISEASE: SOME PRELIMINARY QUESTIONS AND ANSWERS.

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Introduction

Cholesterol testing in the prevention of coronary heart disease raises many complex technical and other issues. Without pre-empting the discussions at the Consensus Conference, this booklet aims to provide a simple, introductory guide to some of the technical issues for conference participants. We hope that its question and answer format will help to clarify some of the confusion surrounding terminology in this field.

Although this conference will focus on one of the major factor implicated in heart disease : high blood cholesterol levels , other factors - such as cigarette smoking and high blood pressure - have also been shown to play a major causal role.

Question: What Is Coronary Heart Disease?

Coronary Heart Disease results from a 'furring up' and blocking of the arteries that feed the heart with essential oxygen and other nutrients. A key part of this process which starts in childhood leads to a slow build-up of abnormal, cholesterol containing plugs or *Plaques* being deposited on the walls of the arteries feeding the heart.

Coronary Heart Disease (chd), also known as **Ischaemic Heart Disease Coronary Atherosclerosis; Atheroma Or Coronary Artery Disease,** can manifest itself in many different ways. **Angina,** the chest pain which occurs on exertion in people whose coronary arteries are furred, but not completely blocked, is a common feature. Others may experience a heart attack, or **Myocardial Infarction,** or may die suddenly due to an associated disturbance in the heart's rhythm. Many have no overt symptoms, but show evidence of CHD on an ECG test which measures the electric patterns coming from the heart. Studies into the prevention on **CHD** use this spectrum of features to measure the **Outcomes** or **End Points** of interventions to reduce **CHD**.

Question: What Is Blood Cholesterol?

Cholesterol is a fat, or **Lipid,** that circulates in the bloodstream encased in a package, proteins known as **Lipoproteins.** Overall blood cholesterol is known as **Total Cholesterol.** Lipoproteins can be separated into four sub-groups, each containing different proportions of cholesterol:

1 LDL, Or Low Density Lipoprotein:

This contains the highest proportion - about 60% - of the blood's cholesterol and is considered by many to be the sub-group of cholesterol most closely linked with CHD).

2 HDL, or High Density Lipoprotein

This contains up to 25% of the blood's circulating cholesterol. High levels of this sub group cholestorol are associated with a low risk of CHD.

3 VLDL , or Very Low Density Lipoprotein

This contains about 20% of the total blood cholesterol.

4 Triglycerides

This sub-group contains very little cholesterol - about 2%.

Question: How Can Blood Cholesterol Be Measured?

Total blood cholesterol - and its subfractions - is usually measured from a fraction of the blood known as **Serum** or **Plasma**. The simplest blood cholesterol test will measure **Total Blood Cholesterol**. This can be measured either by sending a full blood sample to the hospital laboratory, or by a simple fingerprick test from which an immediate reading can be obtained. The sub-fractions of blood cholesterol can only be measured in the laboratory.

Question: What Is The Relationship Between Dietary And Blood Cholesterol?

While the conference will consider detailed evidence on the relationship between dietary fats, of which cholesterol is one, and CHD, it is important to note that it is cholesterol levels in the *blood* and not primarily in the *diet* that have been linked to CHD.

Question: How Are High Blood Cholesterol Levels Defined?

Low, moderate and high blood cholesterol levels have been defined on the basis of international population studies which have examined the relationship between blood cholesterol levels and the risk of CHD. A number of expert reports have subsequently identified cut-off points for total blood cholesterol which attempt to define these risk categories: The reports provide guidelines for further intervention for individuals in each category (See Table). The first set of recommendations came from a Consensus Panel convened by the US National Institute of Health (NHI) in 1984. This has been followed by revised US guidelines from NIH's National Cholesterol Education Programme (NCEP) in 1988; the European Atherosclerosis society (1987) and the British Hyperlipidaemia Association (1987)

Recent expert recommendations for defining CHD risk categories and guidelines for subsequent interventions

Category of risk	NHI (1) Consensus Conference (USA, 1984)	NCEP (2) (USA, 1988)	European Athero-sclerosis Society (3) (1987)	British Hyperlipidae mia Assoc. (1988)
	(Total cholesterol levels in m.mol/litre)			
LOW	Below 5.2	Below 5.2	Below 5.2	Below 5.2
ACTION recommended	Re-test yearly	Re-test 5 yearly	-	-
MODERATE/ BORDERLINE HIGH	Above 6.2	5.2 - 6.2	5.2 - 6.2 (and to 7.8)	5.2 - 6.5
ACTION recommended	Dietary advice	Dietary advice Re-check cholesterol	Assess other risk factors. Dietary advice. Give drugs if diet fails. Monitor.	Advice on diet and other risk factors
HIGH	Above 6.7	Above 6.2 (or 5.2 - 6.2 with 2 other risk factors)	Above 7.8	Above 6.5
ACTION recommended	Dietary advice. Drugs for familial hypercholesterol aemias and very high levels	Obtain full lipid profile. Dietary advice followed by drugs if cholesterol still above 4.9 at 3.6 months	Referral to specialist hospital lipid clinic for dietary and for drug treatment	Referral to specialist hospital lipid clinic for dietary and for drug treatment

(1)   Cholesterol levels given for those aged 40+

(2)   NCEP = National Cholesterol Education Programme of the NIH, USA

(3)   Risk groups here are defined A,B,C,D and include triglyceride measurements

Question: What Is Familial Hypercholesterolaemia And How Is It Connected To Chd?

Familial Hypercholesterolaemia is the name given to a group of rare, inherited diseases which result in very high blood cholesterol levels, CHD, and premature death, early in adult life. Unlike familial hypercholesterolamia, the main causes of the vast majority of CHD lie in the environment and not with heredity. The main public health gains for the community therefore, lie in the prevention of environmentally caused CHD.

Question: What Are The Population And High Risk Approaches To The Prevention Of Chd?

The Population Approach to the prevention of CHD argues that in countries like the UK, where CHD is so common, the *whole population* is at risk. For maximum health benefit, it is claimed that interventions must be directed *at the whole community*, and not merely at those sections defined to be at highest risk. By contrast, the **High Risk Approach** to CHD prevention argues that the most effective way forward is to identify a minority of individuals with the greatest risk - such as those with high blood pressure and target interventions at this group rather than the whole population. Although the two approaches are not mutually exclusive, the population approach implies that national policy and planning is required, whereas the high risk approach is more individualistic.

Question: Why Measure Blood Cholesterol Levels?

There are three main purposes for which blood cholesterol testing is claimed to be of value:

1 Population Screening: The main aim here would be to invite the whole population (or selected parts of it) to have their blood cholesterol levels measured in order to identify those people who are at highest risk of CHD. Intervention would then be directed at this 'high risk' group. Subsequent measurement would be for **Monitoring** and not screening purposes. This approach is similar, in principle, to the national breast and cervical screening programmes.

2 Motivational Testing: The aim here is not to *identify* those at highest risk, but to use the result of the test in *individuals* to motivate them towards dietary and other health—related behavioural change. This would be similar to using carbonmonoxide measuring devices as an aid to stopping smoking.

3 Population Surveillance: The aim here is not primarily directed at intervention, but to monitor trends in blood cholesterol levels in representative groups of the population. Such measurements might be used for research and planning purposes.

The Consensus Conference will confine itself to a discussion of the merits of cholesterol measurement for screening and motivational purposes.

Question: What Are The Requirements For A Worthwhile Screening Programme?

The aim of cholesterol screening would be to target interventions at those individuals who are most at risk of developing and dying from CHD.

There are 7 main criteria that should be fulfilled in order to justify any screening programme:

The Disease:

1. Its frequency and its natural history must be known.

2. It must be of public health importance.

3. Effective diagnostic confirmation, intervention or treatment for the disease must be available.

The Facilities

4. The screening test must be simple and safe.

Ethical

5. The screening programme should be acceptable to the public and to the authorities.

Economic

6. The screening programme should demonstrate that the benefits outweigh the costs.

Test Performance

7. The screening test should be able to satisfactorily separate the high risk from the low risk population. This means that the overlap in test values between high and low risk individuals should be small with well defined cut-off points.

8. The distribution of test values in high risk and low risk individuals should be known.

Question: How May Cholesterol Testing Be Organised?

1. Mass Testing: the whole population (in a workplace, or general

practice for eg) is actively invited to be tested.

2. Selective Testing: certain sub—groups of the population — usually those identified as high risk for other reasons — are actively invited to be tested.

3. Opportunistic Testing: the test is offered during the course of a consultation (in a primary care or occupational health setting) for other reasons. In this case, patients are not actively invited to come forward for a test.

Question: What Methods Are Recommended For Reducing Blood Cholesterol?

There are two main approaches to reducing blood cholesterol levels in individuals: dietary advice and drug treatment.

1. Dietary Advice aims to reduce total fat and saturated fat consumption, together with an increase in fibre — especially oat bran — intake and a reduction in sugar intake

2. Drug Treatment can be divided into several groups including:

- Compounds which interfere with the body's bile acid circulation eg cholestyramine and colestipol

- Fibric acid derivatives eg clofibrate and gemfibrozil

- Nicotinic acid

- Compounds which directly inhibit a key enzyme needed for the manufacture of cholesterol (known as HMG CoA Reductase inhibitors) eg simvastatin.

- Probucol