

# PREVENTIVE CARE RECOMMENDATIONS ADULT- AGES 19 AND ABOVE

## INTERMOUNTAIN CARDIOVASCULAR RISK PROFILE

INTERMOUNTAIN CARDIOVASCULAR CLINICAL PROGRAM  
August 20, 2003

### Intermountain Cardiovascular Risk Profile

1. hsCRP
2. Fasting lipid profile
3. Homocysteine level
4. Fasting glucose

### Reports

Risk prediction for patients without known CAD based on the chart below:

### Cardiovascular Risk Table Based on hsCRP and Lipid Parameters

		TC/HDL Ratio				
		> 5.8	4.8-5.7	4.1-4.7	3.4-4.1	< 3.3
hsCRP (mg/L) <sup>***</sup>	≥ 3.9	30.5%* (8.7x)**	21% (6.0x)	14.5% (4.2x)	10.5% (3.0x)	7.5% (2.2x)
	2.0-3.8	25% (7.2x)	18% (5.1x)	12.5% (3.5x)	9% (2.5x)	6% (1.7x)
	1.2-1.9	21% (6.0x)	14.5% (4.2x)	10% (2.9x)	7.5% (2.1x)	5% (1.4x)
	0.7-1.1	17.5% (5.0x)	12.5% (3.5x)	9% (2.5x)	6% (1.7x)	4% (1.2x)
	≤ 0.6	14.5% (4.2x)	10% (2.9x)	7% (2.0x)	5% (1.4x)	3.5% (1.0x)

\*Predicted % risk over 10 years of a cardiovascular event (MI, revascularization, CVA, death).

\*\*Relative risk over 10 years of a cardiovascular event

\*\*\*If hsCRP is initially >5 mg/L, recommend repeat testing, ideally in 2 weeks. If hsCRP is verified to be >10 mg/L, also consider other inflammatory or infectious etiologies

Ref: : Nader Rifai, Paul M. Ridker, "Proposed Cardiovascular Risk Assessment Algorithm Using High-Sensitivity C-Reactive Protein and Lipid Screening," *Clinical Chemistry* 47, No. 1, 2001

**PRIMARY PREVENTION--Who should be tested with Intermountain Cardiovascular Risk Profile?**

1. People with two or more traditional risk factors for CAD (traditional risk factors = smoking, hypertension, family history of CAD, men >35 years, postmenopausal women, known hyperlipidemia) or
2. People with borderline lipid results not meeting ATP III criteria for lipid lowering therapy or
3. Framingham risk profile of >5% risk of CV event in 10 years
4. Not necessary—people with known CAD or equivalent, diabetes peripheral vascular disease, or already meeting ATP III standards for therapy

**PRIMARY PREVENTION--Who should be treated based on Intermountain CV Risk Profile and NCEP III Guidelines?**

1. Statin Treatment (without known CAD) (Red Zone)
  - a. Men >35 years or post-menopausal women, with predicted 10 year risk of CV event of > 15% (not corrected by lifestyle changes)
  - b. Target treatment to achieve 10 year predicted risk of <10% (statins reduce CRP levels)
2. Consider Statin Treatment (Yellow Zone)
  - a. 10 year CV risk of 10-15%, as above, if person has 2 or more traditional risk factors for CAD
3. All people should address lifestyle changes to reduce cardiac risk (esp. regular moderate-intensity exercise, smoking cessation, healthy diet, control of HBP, weight management)
4. Treat elevated fasting glucose or homocysteine levels appropriately

**SECONDARY PREVENTION--Treatment guidelines**

1. All patients with CAD, diabetes mellitus, or other clinical forms of atherosclerotic disease (i.e., peripheral arterial disease, AAA, symptomatic carotid artery disease) should be on a lipid-lowering medication (usually, a statin)
2. Target Rx to achieve an LDL of <100

Intermountain Health Care now offers the diagnostic enhancement a cluster of 4 laboratory chemistry tests called “**The Intermountain Cardiovascular Risk Profile**”. Together, these tests provide complementary, evidence-based information for assessing the risk of coronary heart disease (CHD) and cardiovascular disease (CVD) in appropriate patients without known CHD (primary prevention). (These tests also can still be ordered separately.) Until recently, the fasting lipid profile was the single test used for risk assessment. However, a substantial proportion of risk (up to 2/3) is accounted for by non-lipid-related factors. The addition of **high sensitivity C-reactive protein (hs-CRP)**, **fasting plasma glucose**, and **plasma homocysteine** levels to fasting plasma lipid profile allows for a more complete assessment of risk and the discovery of additional metabolic targets for prevention and treatment. It should be emphasized that the physician must supplement clinical chemistry tests with clinical information (hypertension, smoking, family history, etc.) to complete the assessment of CHD/CVD risk.

**Hs-CRP:** Atherosclerosis is not simply a passive process of lipid infiltrating into arterial walls, but an active, inflammatory process involving cellular elements (monocytes/macrophages, T-lymphocytes, and vascular smooth muscle and endothelial cells) and signaling and effector molecules (cellular adhesion molecules, pro-inflammatory cytokines, matrix degrading enzymes, and procoagulants). The activity of this vascular inflammatory process now can be assessed by certain circulating factors, including soluble adhesion molecules, cytokines, white blood cell count, and acute phase reactants, of which CRP is the first to be approved for clinical application. CRP rises non-specifically in response to infection, injury, or to other pro-inflammatory stimuli. In their absence, serum or plasma CRP levels are low but detectable using high-sensitivity assays (hs-CRP). These chronic, “stable” levels, below the previous limits of detection (“normal range”) using older, standard assays, have proven strongly predictive of the relative risk of incident CHD and other CVD events independent of lipids and other standard risk factors. A recent workshop, sponsored by the American Heart Association and Centers for Disease Control, has made recommendations for the initial clinical application of hs-CRP (Circulation 2003; 107:499). Hs-CRP thresholds are defined as: normal (<1 mg/L), average (1-3 mg/L), and high (>3 mg/L). Very high levels (>5-10 mg/L) should be repeated within 2 weeks and, if still elevated, evaluated for the presence of a non-cardiovascular inflammatory process. The chemistry laboratory is able to more precisely determine hs-CRP risk thresholds by using quintiles and automatically computes the associated relative risk for the ordering physician.

The AHA/CDC guidelines recommend (Class IIa) that hs-CRP be applied at the discretion of the physician, together with standard risk factors, for assessing primary CVD risk and assisting in directing preventive and treatment measures in those judged to be at least at “intermediate risk” (10-20% ten-year risk of an incident cardiovascular event). Optionally (Class IIb recommendation), hs-CRP may be used more generally at the discretion of the physician as part of a global coronary risk assessment in adults without known CVD. Two additional suggested hs-CRP applications include improving prognostication in patients either with stable coronary disease or with acute coronary syndromes and in motivating patients to improve lifestyle behaviors. Perhaps the greatest therapeutic impact of hs-CRP might be on patients at intermediate risk who haven’t reached a threshold for lipid-lowering therapy or in whom lipid lowering is optional based on lipids alone (NCEP-ATP III guidelines). In these patients, the finding of an elevated hs-CRP might lead to lowering of the threshold for initiation of lipid lowering (e.g., with a statin). The clinical chemistry report now integrates hs-CRP with lipids to provide a combined risk estimate and recommends who should be considered for initiation of therapy.

**Impaired glucose metabolism** (dysglycemia), even without overt diabetes, has emerged as an important additional CVD risk factor. Impaired glucose metabolism takes two forms:

1. **Impaired Fasting Glucose** (IFG) is defined as a fasting blood (plasma) glucose of >110 mg/dL. (Some younger individuals may have abnormal glucose metabolism with even lower fasting glucose values).
2. **Impaired Glucose Tolerance** (IGT) is defined as a 2 hour post-prandial glucose of >140 mg/dL and <200 mg/dL. Both of these conditions are “pre-diabetic” and significantly increase the risk of progression to Type 2 diabetes.
  - 25% of those with IGT also have IFG
  - 40% of those with IFG also have IGT
  - 20% of those with IFG have undiagnosed **Type 2 Diabetes** (defined as FBG >125 mg/dL or post-prandial glucose >200 mg/dL).

Impaired fasting glucose (IFG) is one of the components of the **Metabolic Syndrome**, a CVD risk-associated cluster that also includes low HDL, high triglycerides, hypertension, and increased abdominal girth. As many as 67% of patients with IGT also have Metabolic Syndrome. In the Intermountain CV database, IFG increased CVD risk by 4-fold in patients with known CHD; other studies have shown increased risk in those without known CHD. **Recognition that impaired glucose metabolism is present should lead to aggressive lifestyle interventions (diet, exercise) and careful follow-up for possible progression to diabetes (FG>125 mg/dl). All patients with overt DM (w or w/o known CHD) should be treated for secondary CHD prevention, including statins and ACEI.**

**Homocysteine** is a vasculo-toxic amino acid by-product of methionine metabolism. High levels of homocysteine (i.e., over 15 micromoles/L) have been associated with increased primary and secondary CV risk in several population-based studies. In the Intermountain database, CHD patients with increased homocysteine were at 64% increased CV risk (death/MI). Folic acid with or without B vitamins (B6, B12) can lower homocysteine inexpensively and safely. Outcomes trials to demonstrate a reduction in risk with folic acid supplements are underway but have not yet been completed, however.