Miller, Diane M.

From:
Sent: Wednesday, February 22, 2006 3:15 PM
To: NIOSH Docket Office
Subject: Fire Fatality Investigations
Attachments: Annual Physical Blood Test.doc; Annual Blood Test References.doc

To Whom It May Concern:

I am a Firefighter/paramedic with the Anchorage, Alaska Fire department. On November 21, 2004 I was involved in an inhalation exposure incident to an unknown substance during an ambulance response. Initial symptom was an acute allergic reaction. From the November 21st and culminating on December 29th I continued to have worsening respiratory symptoms. On December 29/30th I experienced an acute myocardial infarction. Presently I have four coronary stents. I was found to have two additional blockages of 80-90 percent after placement of the fourth stent. The two additional blockages were later determined to be caused by coronary spasm. On November 29, 2005 I was diagnosed with endothelial dysfunction, microvascular dysfunction and severe coronary artery spasm at the Mayo Clinic. Presently I am back on full duty as a firefighter/paramedic. I am enclosing research that I have done concerning endothelial dysfunction, C-reactive protein and treatment. I am submitting this research for your consideration to be included into the investigations concerning the Fire Fatality Investigation process.

<<Annual Physical Blood Test.doc>> <<Annual Blood Test References.doc>>

Thank You,

Annual Physical Blood Test Addition

Introduction

Firefighters have one of the highest risk jobs in the world. They are routinely exposed to diesel exhaust, fire gases, infectious agents, chemical exposures, high stress environments both mental and physical. It is well documented that firefighters have a higher risk of premature heart disease and events than other occupations. Anchorage Fire Department provides annual physical examinations to their personnel. This examination has relied on cholesterol testing, blood analysis, 12 lead electrocardiogram and stress treadmill test utilizing the Bruce protocol to evaluate cardiovascular health. It has been recognized that in some instances these test fail to identify personnel who at risk at risk for cardiovascular events. Recent evidence suggests that adding high sensitivity C-reactive protein (hs-CRP) would help to identify at risk personnel. Research has shown that in many cases the development of cardiovascular disease is due to inflammation and elevated hs-CRP. Inflammation may be the result of exposure to agents that firefighters are likely to encounter. Inflammation and elevated hs-CRP levels have been shown to be responsible for the development of endothelial dysfunction. Endothelial dysfunction can cause a rapid development of severe atherosclerosis and coronary spasm independent of the traditional cardiac risk factors. Post exposure employee blood testing should also incorporate hs-CRP. The hs-CRP may be one of the first indications that an exposure has occurred in asymptomatic individuals.

It has been recognized that firefighters have an increased incidence of heart disease. Review of the National Institute of Occupational Safety and Health Firefighter Fatality Reports for 2001 to 2005 does provide clues to underlying heart disease as a cause for some of the deaths. Many reports list underlying traditional risk factors as contributing factors. However, a percentage of the reports fail to explain the cause of the heart attacks. Many of the autopsies performed discover only mild to moderate coronary heart disease or no disease at all. These cases often fail to produce evidence of embolus or thrombus as the occlusive cause of the heart attack. The lack of occlusive evidence points to coronary spasm as a possible cause for the heart attack. These reports developed in 1998 are currently lacking in there investigation procedures. The reports fail to provide insight into the complete medical history. They do not list a complete work history, previous employee exposure reports and recent or past illness of any cause. They rely only on traditional cardiac risk factors for determining cardiac health and fitness.[1] The United States Fire Administration reports that 117 firefighters died in the line of duty in 2004. 52.1 percent of the fatalities listed heart attack as the primary cause of death.[2] The exact cause for the high incidence of heart attack has been elusive. The International Association of Firefighters has pursued the presumption of heart disease on exposure to carbon monoxide on the fire grounds.[3] Carbon monoxide is only one of the substances that firefighters and paramedics are routinely exposed to. Diesel exhaust, high stress environments, infectious agents and chemical exposures have all been linked to the development of heart disease.[4-12] There has been emphasis placed on the prevention and recognition of heart disease risk factors during the annual physical examinations and in physical fitness initiatives. The traditional cardiac risk faetors include sex, heredity and race, age, smoking, high blood pressure, high cholesterol, diabetes, obesity, physical inactivity, stress, anger and excessive alcohol consumption. It has also been recognized that even with modification to these risk factors that the incidence of heart disease continues to be the leading cause of death in the United States and the world.[13]

The high mortality rate has prompted numerous studies and research into the pathogenesis of heart disease. Through this research new and novel risk factors are emerging.[14-16] Research has shown that dysfunction of the endothelial cells and the nitric oxide system may be responsible for the pathogenesis of heart disease. The endothelial cells of the vascular system are responsible for dilation and constriction and the health of the vascular system. Endothelial dysfunction has been implicated in the earliest stages in the development of coronary artery disease. [17-21] The endothelial cells may become damaged and dysfunctional by inflammation, elevated C-reactive protein (CRP), elevated cholesterol, high blood pressure, infection, allergic reaction, mental stress, irritants such as nicotine, certain diseases such as diabetes, and chemical exposures. [11,14,15,17,21,22,23] It has been shown that even one high fat meal can produce a transient endothelial dysfunction. Endothelial dysfunction can cause coronary artery spasm resulting in an acute myocardial infarction independent of age, traditional risk factors or blood cholesterol levels.[5,6,17,24,25,26,27,28] Specific testing for endothelial dysfunction requires a cardiac catheterization and the administration of acetylcholine in conjunction with an intravascular ultrasound catheter. This technology is unavailable in Alaska. There is current research being conducted on non-invasive testing but it is unavailable at this time. Presently, there is no cure for endothelial dysfunction. In some

cases it may resolve spontaneously or it may become a chronic condition. Prevention of endothelial dysfunction must be made a priority over treatment. Medications and vitamins can help to restore the health and function of the endothelial cells. It has been shown that starting on anticholesterol medications offered cardiac protection within one day of starting the medication. This protection was seen prior to any reduction in the blood cholesterol levels. Other pharmacologic treatments may include calcium channel blockers, ACE inhibitors, aspirin, nitrates, vitamins B6, B12 and folic acid. Life style changes are also critical in the prevention of endothelial dysfunction. Life style changes include balanced low fat and low salt diet, routine exertional physical activity, smoking and tobacco cessation, disease recognition and treatment for high blood pressure and diabetes, recognition and treatment of inflammation and infection, chemical and irritant exposure prevention.[5,6,13,17,21]

The present blood tests performed are adequate for cholesterol levels and blood chemistry. One low cost addition to the blood test that should be considered is the addition of high sensitivity C-reactive protein (hs-CRP). CRP is recognized as a marker of inflammation occurring in the body. Elevated hs-CRP has been recognized as a strong predictor of future cardiovascular events. CRP has been identified not only as a marker for inflammation but also as a causative agent in endothelial dysfunction and heart disease. Inflammation and CRP has been implicated in the earliest stages of cardiac disease, hypertension, acute myocardial infarction, adverse events after percutaneous coronary interventions, sudden cardiac death, cerebrovascular disease, atrial fibrillation and endothelial dysfunction.[14,15,16,29,30,31,32,33,34] The test cannot specifically determine where the origin of the inflammation is but is indicative of it occurring. The normal blood level for hs-CRP is 0-1.0 mg/L. The American Heart Association considers <1, 1-3, >3 mg/L to correspond to low, moderate and high risk for future cardiovascular events. Individuals with LDL cholesterol below 130 mg/dl who have hs-CRP >3 mg/L are considered to represent a high risk group. The cardiac reference range for hs-CRP is 0-10mg/L. Levels above 10 reflect a need to investigate for an underlying chronic inflammatory disease.[35,36] Clinical applications for use of the hs-CRP test are presently being developed. It must be stressed that proper application of this test must take into account the traditional cardiac risk factors. Elevated cholesterol levels, decreased levels of HDL, high blood pressure, diabetes, tobacco use must be addressed and treated irrespective of the hs-CRP level. A low blood level of hs-CRP does not eliminate the need to correct other modifiable risk factors. Presently, the hs-CRP test is to be used as an adjunct to the normal cardiac and cholesterol testing and is not intended to replace them. Proper use of hs-CRP will reinforce healthy lifestyle habits and warn of potential cardiovascular events which may occur acutely even in asymptomatic individuals. Elevated blood levels of 1-10 mg/L should be investigated for underlying cardiac disease irregardless of age. This includes people presently asymptomatic with normal cholesterol levels or an absence of the traditional risk factors. Standards for treating elevated CRP levels are being investigated. Certain cholesterol medications have been found to lower the CRP levels even in persons with normal cholesterol levels. Aspirin, angiotensin converting enzyme (ACE) inhibitors and the HMG coA reductase inhibitors (statins) reduce serum levels of CRP. Healthy lifestyle habits, weight loss, routine exertional physical activity, balanced diets rich in omega 3 oils and 15-30 minute

saunas have been found to reduce CRP levels and improve endothelial dysfunction.[36,37,38,39]

Recommendations:

Testing

1. Include hs-CRP levels in the blood test conducted during annual physicals.
2. Include hs-CRP levels in post exposure testing. Suggested schedule would be at initial blood draw, day 3, week1.
3. hs-CRP included in all post exposure testing whether chemical or infectious agent is involved.

References

1. National Institute Occupational Safety and Health. Fire Fighter Fatality Investigation and Prevention Program. http://www2a.cdc.gov/NIOSH-fire-fighter-face
2. United States Fire Administration. Firefighter Fatalities in the United States in 2004. http://www.usfa.fema.gov
3. International Association of Firefighters. http://www.iaff.org/safe/health/facts/.html
4. Mills N, Hakan T, Robinson S, et al. Diesel Exhaust Inhalation Causes Vascular Dysfunction and Impaired Endogenous Fibrinolysis. Circulation 2005; 112: 3930-36
5. Rackley C. Pathogenesis of atherosclerosis. http://patients.uptodate.com/topic.asp?file=chd/21090
6. Charakida M, Donald AE, Terese M, et al. Endothelial dysfunction in childhood infection. Circulation 2005 Apr; 111(13): 1568-70
7. Oshima T, Ozono R, Yano Y, et al. Association of Helicobacter pylori infection with systemic inflammation and endothelial dysfunction in healthy male subjects. J Am Coll Cardiol. 2005 Apr 19; 45(8): 1219-22
8. Mittermayer F, Pleiner J, Schaller G, et al. Tetrahydrobiopterin corrects Escherichia coli endotoxin induced endothelial dysfunction. Am J Physiol Heart Circ Physiol. 2005 Oct; 289(4): H1752-7
9. Prasad A, Zhu J, Halcox J, et al. Predisposition to Atherosclerosis by Infections: Role of Endothelial Dysfunction. http://circ.ahajournals.org/cgi/content/full/106/2/184
10. Ross R. Atherosclerosis-An Inflammatory Disease. N Engl J Med 1999; 340:115-126
11. Mayo Clinic. Arteriosclerosis/Atherosclerosis. http://www.mayoclinic.com/health/arteriosclerosis-atherosclerosis
12. Mayo Clinic. Risk Factors for Coronary Artery Disease. Http://www.mayoclinic.org/coronaryartery-rst/risks.html
13. American Heart Association. Heart disease and Stroke Statistics-2006 update. http://americanheart.org
14. Verma S, Szmitko PE, Ridker PM. C-reactive protein comes of age. Nat Clin Pract Cardiovasc Med 2005 Jan; 2(1): 29-36
15. Wilson AM, Ryan MC, Boyle AJ. The novel role of C-reactive protein in cardiovascular disease: Risk marker or pathogen. Int J Cardiol 2006 Jan 26; 106(3):291-7
16. Mayo Clinic. C-Reactive Protein (CRP) Seen as Key Indicator of Heart Disease Risk. http://www.mayoclinic.org/news2004-sct/2386.html
17. Mohler E. Endothelial dysfunction. http://patients.uptodate.com/topic.asp?file=chd/57702
18. Szmitko P, Wang C, Weisel R, et al. Biomarkers of Vascular Disease Linking Inflammation to Endothelial Activation, part ll. Circulation 2003; 108:2041-2048
19. Szmitko P, Wang C, Weisel R, et al. New Markers of Inflammation and Endothelial Cell Activation, part l. Circulation 2003;108:1917-1923

20. Abbate A, Bonanno E, Mauriello A, et al. Widespread Myocardial Inflammation and Infarct-Related Artery Patency. Circulation 2004; 110: 46-50
21. Bove A, Management of Patients with Endothelial Dysfunction and/or Early Atherosclerosis in Clinical Practice. http://cardiosource.com/rapidnewssummaries/
22. Guzik TJ, Korbut R, Adamek-Guzek T. Nitric oxide and superoxide in inflammation and immune regulation. J Physiol Pharmacol. 2003 Dec; 54(4): 469-87
23. Verghese M. Nitric oxide in coronary artery disease. http://patients.uptodate.com/topic.asp?file=chd/69237
24. Athanasiadis A, Sechtem U. Rest angina caused by coronary spasm. Dtsch Med Wochenschr. 2004 Dec 3; 129(49): 2648-50
25. Kawano H, Ogawa H. Endothelial function and coronary spastic angina. Intern Med. 2005 Feb; 44(2): 91-9
26. Katayama N, Nakao K, Horiuchi K, et al. Disease activities and serum C-reactive protein levels in patients with vasospastic angina pectoris. J Cardio. 2005 Aug; 46(2): 63-70
27. Saitoh S, Muto M, Osugi T, et al. Repeated epicardial coronary artery endothelial injuries lead to a global spontaneous coronary artery spasm. Coron Artery Dis. 2004 May; 15(3): 137-45
28. Kostner KM, Fahti RB, Case C, et al. Inflammation, complement activation and endothelial function in stable and unstable coronary artery disease. Clin Chim Acta 2005 Oct 15
29. Becker R. Vascular endothelial function and the mechanisms of thrombolysis. http://patients.uptodate.com/topic.asp?file=chd27476
30. Rackley C. The role of plaque rupture in acute coronary syndromes. http://patients.uptodate.com/topic.asp?file=chd/22746
31. Mineo C, Gormley AK, Yuhanna IS, et al. FcgammaRIIB mediates C-reactive protein inhibition of endothelial NO synthase. Circ Res 2005 Nov 25; 97(11): 1124-31
32. Kushner I. Acute phase proteins. http://patients.uptodate.com/topic.asp?file=bas_imm/4838
33. American Heart Association. Inflammation, heart disease and Stroke: The Role of C-Reactive Protein. Dec 17, 2005 http://www.americanheart.org
34. Verma S, Buchanan M, Anderson T. Endothelial Function testing as a Biomarker of Vascular Disease. http://circ.ahajournals.org/cgi/content/full/108/17/2054
35. WebMD. A-Z Health Guide from WebMD: Medical tests. C-Reactive Protein (CRP). http://www.webmd.com/hw/health_guide_atoz/tu6309.asp
36. Ridker P. Clinical Application of C-Reactive Protein for Cardiovascular Disease detection and Prevention. http://circ.ahajournals.org/cgi/content/full/107/3/363
37. Podrid P. C-reactive protein in cardiovascular disease. http://patients.uptodate.com/topic.asp?file=chd/24795
38. Rosenson R. Mechanisms of benefit of lipid lowering in patients with coronary heart disease. http://patients.uptodate.com/topic.asp?file=lipiddid/10410
39. Mayo Clinic. Treatment of Coronary Artery Disease at Mayo Clinic in Rochester. http://mayoclinic.org/coronaryartery-rst/index.html