Serum Paraoxonase After Myocardial Infarction

Aamir Ayub, Michael I. Mackness, Sharon Arrol, Bharti Mackness, Jeetesh Patel, Paul N. Durrington

Abstract—HDL has been shown to prevent the oxidative modification of LDL. The antioxidant activity of HDL is believed to reside in its enzymes, particularly paraoxonase. Human serum paraoxonase (PON1) is closely associated with a specific HDL subfraction containing apoA1 and clusterin. Recently PON1 has been implicated in the pathogenesis of atherosclerosis. We have examined the activity, concentration, and specific activity of PON1 in 50 patients on admission to hospital immediately after acute myocardial infarction (MI) and in 48 age- and gender-matched controls. Serum PON1 activity and concentration were significantly lower in patients with MI than in controls (activity, 221.5 [99.3 to 303.2] nmol · min⁻¹ · mL⁻¹ in controls and 130.1 [78.9 to 230.3] nmol · min⁻¹ · mL⁻¹ in MI patients [P<0.05]; concentration, 95.7 [73.2 to 135.5] µg/mL in controls and 35.4 [21.6 to 51.3] µg/mL in MI patients [P<0.001]). PON1-specific activity was significantly higher in patients with MI than in controls (1.5 [0.9 to 2.9] versus 3.4 [2.0 to 8.5] nmol · min⁻¹ · µg⁻¹ [P<0.001]) due to the much lower PON1 concentration. PON1 activity had risen significantly (P<0.05) to 158.1 (85.4 to 282.0) nmol · min⁻¹ · mL⁻¹ at day 42 but was still significantly less than that of controls. No significant variation in PON1 concentration occurred in the days after MI or at 6 weeks. Also, no significant variation in specific activity was seen after MI. When the patients were divided into subgroups based on whether or not they received thrombolytic therapy on admission to hospital, no significant difference in PON1 levels was observed. Serum HDL cholesterol in patients with MI on admission was not significantly different than in controls, and the decrease that occurred by the fifth day after MI did not explain the lower PON1 levels. We conclude that low serum PON1 activity in patients with MI may be a consequence of the coronary event itself or could have been present before MI. The low PON1 activity was also not explicable on the basis of PON1 genotypes because the prevalence of genotypes associated with low activity was not sufficient to explain fully the difference in activity levels between patients and controls. The explanation for the low PON1 activity was most likely a decrease in serum PON1 concentration. The importance of PON1 as a predictive risk factor for MI should be assessed in future studies. (Arterioscler Thromb Vasc Biol. 1999;19:330–335.)

Key Words: paraoxonase ■ myocardial infarction ■ lipoproteins, HDL ■ atherosclerosis

Paraoxonase (EC.3.1.8.1, aryldialkylphosphatase) has been extensively studied in the field of toxicology.1,2 Paraoxonases as a group hydrolyze organophosphate compounds, which are widely used as insecticides and nerve gases.3,4 Human serum paraoxonase (PON1) is synthesized in the liver and is closely associated with HDL. The serum concentration of HDL has long been known to have an inverse correlation with the development of atherosclerosis.5 The mechanism by which HDL renders its protective effect against atherosclerosis continues to be the subject of considerable debate. The initial focus of attention was on the role of HDL in reverse-cholesterol transport (RCT). However, recent studies have suggested more diversity in the role of HDL in atherogenesis. Several laboratories have reported that HDL protects against LDL oxidative modification,6–9 which is believed to be central to the initiation and progression of atherosclerosis.10 We previously showed that the antioxidant activity of HDL may relate, at least in part, to the enzymes associated with HDL.11 Further studies indicated that PON1 could prevent lipid-peroxide accumulation on LDL12–14 and may act in tandem with platelet-activating factor acetylhydrolase and lecithin-cholesterol acyltransferase to protect LDL from oxidative modification.11 Studies have shown that serum PON1 activity is reduced in diabetes and familial hypercholesterolaemia,15,16 diseases that are associated with accelerated atherogenesis.

PON1 contains 2 polymorphisms, both of which are due to amino acid substitutions; one affects amino acid 55 (L→M) and the other affects amino acid 192 (Q→R).17,18 The latter are also termed the A and B isoforms, respectively. More recently, it has been shown that the PON1 genetic polymorphisms may be an independent risk factor for coronary artery disease (CAD); both the 55L and 192B genotype have been shown to be associated with increased susceptibility to CAD.19–21 Recent results from our laboratory have indicated that HDL from PON-BB homozygotes is less efficient at protecting LDL against oxidation than HDL from PON-AA homozygotes, suggesting that the activity of the B alloenzyme of PON1 in metabolizing lipid peroxides is less than that of the A alloenzyme. This is similar to the effect of the
isoforms on diazoxon hydrolysis, although with respect to paraoxon hydrolysis the differential activities are reversed,\textsuperscript{22–24} which was a source of some earlier confusion.\textsuperscript{22–24}

Watson et al\textsuperscript{14} and Navab et al\textsuperscript{25} have reported that PON1 in HDL may block inflammatory responses by preventing the oxidation of LDL. The same groups went on to demonstrate that during an acute phase reaction, there is a significant loss of the PON1 activity, thus accounting for the failure of HDL to protect LDL fromoxidation.\textsuperscript{26} More recently, Navab and colleagues reported a failure of HDL to protect LDL from oxidation in patients with coronary atherosclerosis, which they proposed was due to their low serum PON1 activity despite relatively normal HDL levels.\textsuperscript{25} It was suggested that the decreased serum PON1 activity in survivors of myocardial infarction.\textsuperscript{27} In these studies, however, it was not known whether the low activity was due to the coronary event itself or whether it preceded the myocardial infarction (MI). Furthermore, the studies were done before immunoassay methods were available for PON1, and it is not known whether the low activity was due to low specific activity or low PON1 concentration.

In the current study, we report on serum PON1 activity and concentration in the acute phase after myocardial infarction and also later at 6 weeks when the acute phase response has ended.

**Methods**

**Subjects**

Patients included in the study were admitted to the Coronary Care Unit in Stepping Hill Hospital, Stockport, UK, with acute MI. Patients who did not survive for 6 weeks from the day of admission were not included in the study. The diagnosis of acute MI was made on the basis of typical chest pain, ECG criteria (ST-segment elevation of at least 2 mm and/or Q waves), and serum creatinine kinase elevation >800 U/L. The upper limit of our creatinine kinase reference range is 90 U/L. Fifty patients (38 men) who fulfilled the inclusion criteria and were admitted sequentially were studied. All patients were aged \( \leq \) 65 years. Patients with diabetes or renal and hepatic disease were excluded from the study. None of the patients included were on any lipid-lowering dietary or drug therapy; only patients in whom the first blood sample was obtained within 2 hours of the onset of chest pain were included. Fully informed consent was obtained, and the study was approved by the Stockport Acute Services Unit in Stepping Hill Hospital, Stockport, UK, with acute MI.

**Sample Collection**

Nonfasting venous blood was collected from the patients on days 1, 2, 5, and 42 after acute MI. Day 1 was defined as the day on which patients were admitted to hospital with the diagnosis of acute MI. The average time between the onset of chest pain and the first blood sample was 30 minutes (maximum 2 hours). Serum and plasma were isolated by low speed centrifugation. White cells were removed from the buffy coat of the plasma tube. Samples were stored at \(-20^\circ\text{C}\) for no more than 2 months before analysis.

**Analytical Methods**

**Analysis of PON1 Activity**

PON1 activity was measured by adding serum to Tris buffer (100 mmol/L, pH 8.0) containing 2 mmol/L CaCl\(_2\) and 5.5 mmol/L paraoxon (O,O-diethyl-O-p-nitrophenylphosphate; Sigma Chemical Co). The rate of generation of p-nitrophenol was determined at 405 nm and 25°C with the use of a continuously recording spectrophotometer (Beckman DU-68) as described previously.\textsuperscript{15} PON1 activity was also assessed by use of phenylacetate (arylesterase) as substrate in the same buffer as above, and the increase in absorbance at 270 nm was recorded with the use of a recording spectrophotometer (Beckman DU-68).\textsuperscript{28}

**Determination of PON1 Concentration**

PON1 concentration was determined using our in-house competitive ELISA using rabbit antihuman PON1 monospecific antibodies, as described previously.\textsuperscript{16}

**Determination of PON1 Genotype**

DNA was extracted from the white cells and PON1 genotype for the 192 and 55 polymorphisms determined by PCR amplification and restriction-enzyme digestion, as described.\textsuperscript{17,18}

**Serum Lipids**

HDL was isolated by precipitating lower density lipoproteins with calcium channel blocker before their admission with myocardial infarction. The control population consisted of 48 healthy subjects (matched by age and gender) who either attended a routine health check at a general practice or were members of the hospital staff. Patients were matched with controls of the same sex and age \( \pm 4 \) years. The demographic details of the patients and controls are given in Table 1.

**C-Reactive Protein**

Serum C-reactive protein was measured using the Roche Immuno- turbidimetric assay on the Cobas Fara.

**Creatine Kinase**

Serum creatine kinase was measured using hexokinase and the rate of formation of NADPH, which is directly related to the creatine kinase activity, was measured spectrophotometrically at 340 nm (Olympus AU 5200) in the routine Clinical Biochemistry Laboratory.

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**Table 1.** Characteristics of the Patients and Controls Studied

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Controls</th>
<th>MI Subjects</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>49 ± 8.0</td>
<td>55.7 ± 7.8</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>Sex, m/f</td>
<td>37/11</td>
<td>38/12</td>
<td>...</td>
</tr>
<tr>
<td>BMI</td>
<td>26.3 ± 3.7</td>
<td>27.9 ± 3.98</td>
<td>0.08</td>
</tr>
<tr>
<td>Smoker</td>
<td>5 (10%)</td>
<td>36 (72%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>0</td>
<td>3 (6%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>IHD</td>
<td>0</td>
<td>13 (26%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Angina</td>
<td>...</td>
<td>7</td>
<td>...</td>
</tr>
<tr>
<td>AMI</td>
<td>...</td>
<td>4</td>
<td>...</td>
</tr>
<tr>
<td>CABG</td>
<td>...</td>
<td>2</td>
<td>...</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>...</td>
<td>42 (84%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Sk</td>
<td>...</td>
<td>34</td>
<td>...</td>
</tr>
<tr>
<td>tPA</td>
<td>...</td>
<td>5</td>
<td>...</td>
</tr>
<tr>
<td>SK+ tPA</td>
<td>...</td>
<td>3</td>
<td>...</td>
</tr>
<tr>
<td>None</td>
<td>...</td>
<td>8</td>
<td>...</td>
</tr>
</tbody>
</table>

Values expressed as mean ± SD or percentages (%).
Serum C-reactive protein concentration after myocardial infarction. C-reactive protein was determined as described in Materials and Methods. Points are median (interquartile range). Significantly different from day 1 *P<0.05; **P<0.01.

Statistical Analysis
A paired nonparametric test (Wilcoxon signed rank test) was used to test for differences in variables with a non Gaussian frequency distribution, namely PON1 activity toward both paraoxon and phenylacetate and PON1 concentration plus triglyceride and C-reactive protein concentrations. Student’s paired t test was used for total cholesterol, LDL-C, and HDL-C estimations. Comparisons between controls and the subjects were made by the Mann-Whitney U test. Probabilities of <0.05 were considered statistically significant. Spearman’s correlation coefficient was used to test the strength of any associations between different variables. Differences in gene frequency were sought by the χ² test.

C-Reactive Protein
The plasma concentration of this acute phase reactant showed the typical abrupt rise after myocardial infarction, reaching a peak by day 3 and returning to normal by day 5 (Figure).

Serum Lipids
The serum total cholesterol on the first day of myocardial infarction was 5.5±1.2 mmol/L (mean±SD). This was significantly lower than the value in the control population of 6.2±1.1 mmol/L (P<0.05). However, no significant variation in cholesterol was seen the subsequent days up to day 42 versus day 1 (Table 2). The mean serum HDL cholesterol on day 1 was 1.27±0.44 mmol/L. There was a decline from day 2 onward, and statistical significance was reached on day 5 versus day 1 (P<0.05). By day 42, however, the decline in HDL had apparently recovered, with no significant difference from day 1. The mean HDL-C values in MI patients at day 1 were not significantly different from those of the control population (Table 2). The mean apo AI concentration in the MI patients at day 1 was 141.1±62.4 mg/dL, which was significantly higher than in the controls (113.8±34.3 mg/dL; P<0.005). The concentration of apo AI in the MI patients did not significantly change between days 1 and 42. The mean LDL-C concentration in the MI patients at day 1 was 4.0±1.1 mmol/L, which was significantly lower than in the controls (4.94±1.08 mmol/L; P<0.001).

The median serum triglyceride value on day 1 was 1.85 (range, 1.2 to 2.4) mmol/L (Table 2). There was a transient, but significant, rise on day 2 (P<0.05) (Table 2). By day 5, there was no significant difference in serum triglyceride levels compared with day 1. No further significant variation was seen at day 42. No significant difference in the median triglyceride level was observed between the MI patients and the control population (Table 2).

PON1 Activity
PON1 activity toward paraoxon on the first day of myocardial infarction was 130.1 (median) (interquartile range, 78.9 to 230.3) mmol·min⁻¹·mL⁻¹ (Table 3). No significant variation in activity was seen in the subsequent days 2 and 5. At day 42, PON1 activity was 158.1 (85.4 to 282) mmol·min⁻¹·mL⁻¹, which was significantly higher from day 1 (P<0.05). In the control group, serum PON1 activity was 221.5 (99.3 to 303.2) mmol·min⁻¹·mL⁻¹, which was significantly greater than in patients at all times after MI (P<0.05).

PON1 activity toward phenylacetate (arylesterase activity) was 59.4 (median) (interquartile range, 48.3 to 80.1) μmol·min⁻¹·mL⁻¹ on the first day of myocardial infarction. This was significantly lower (P<0.05) than the value in the control population at 74.8 (54.9 to 87) μmol·min⁻¹·mL⁻¹. No significant variation in the PON1 activity toward phenylacetate was seen from the first day of MI to day 42 (Table 3).

A comparison was also made between a group of subjects who received thrombolytic therapy and those who were not given any form of thrombolytic therapy. No significant difference in the pattern of serum PON1 activity was seen between the two groups with either of the substrates (results not shown), nor could any difference be found in PON1 parameters between smokers and nonsmokers (result not shown).

PON1 Concentration
The median PON1 concentration on the first day of MI was 35.4 median (interquartile range, 21.6 to 51.3) μg/mL (Table

### Table 2. Serum Lipids in Control and MI Subjects

<table>
<thead>
<tr>
<th>MI Subjects</th>
<th>Controls</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 5</th>
<th>Day 42</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>6.2±1.1</td>
<td>5.4±1.2*</td>
<td>5.4±1.1</td>
<td>5.3±1.0</td>
<td>5.6±1.3</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.5 (1.1–2.3)</td>
<td>1.8 (1.2–2.4)</td>
<td>2.2 (1.6–2.5)**</td>
<td>1.9 (1.5–2.5)</td>
<td>1.9 (1.3–2.4)</td>
</tr>
<tr>
<td>HDL-cholesterol, mmol/L</td>
<td>1.3±0.34</td>
<td>1.27±0.44</td>
<td>1.21±0.34</td>
<td>1.1±0.33**</td>
<td>1.3±0.35</td>
</tr>
</tbody>
</table>

Values expressed as mean±SD and except triglycerides which are median with IQR.

Statistical comparisons were made between parameters in controls and MI subjects at day 1 and between day 1 and all other time points in the MI subjects.

*P<0.05, significantly different from control subjects; **P<0.01, significantly different from day 1.
weeks later only a small increase in PON1 activity and no concentration occurred in the immediate post-MI period. Six controls. No significant further decline in PON1 activity or activity and concentration were profoundly lower than in within 2 hours of the onset of acute MI; both serum PON1 activity and concentration in patients with MI were present disease. Our current findings were that low serum PON1 ing a role of PON1 in atherogenesis and coronary heart disease. The last decade has seen accumulation of evidence suggest-

The ratio of LDL-C to PON1 mass was 0.13±0.07 in the MI patients at day 1 and 0.05±0.03 in the controls (P<0.001). The ratio of LDL-C to PON1 activity was 0.051±0.012 in the MI patients and 0.033±0.003 in the controls (P<0.001). The ratio of apo AI to PON1 mass was 4.38±2.67 in the MI patients at day 1 and 1.31±0.92 in the controls (P<0.001).

**PON1 Specific Activity**

The PON1-specific activity in the control population was 1.5 median (interquartile range, 0.9 to 2.9) nmol · min⁻¹ · µg⁻¹, which was significantly less than the specific activity in MI patients on day 1, which was 3.4 (2 to 8.5) nmol · min⁻¹ · µg⁻¹ (P<0.05). There was no change in the specific activity in the subsequent postinfarction period up to day 42.

**PON1 Genotype**

The distribution of PON-192 genotypes in the MI patients was 43% AA, 51% AB, and 6% BB, giving a gene frequency of A=0.69, B=0.31. In the controls the distribution was 64% AA, 29% AB, and 7% BB (gene frequency, A=0.78, B=0.22). The distribution of PON-55 genotypes in the MI patients was 53% LL, 34% LM, and 13% MM (gene frequency, L=0.70, M=0.30). In the controls the distribution was 35% LL, 54% LM, and 11% MM (gene frequency, L=0.62, M=0.38). None of the differences in either gene frequency were statistically significant.

**Discussion**

The last decade has seen accumulation of evidence suggesting a role of PON1 in atherogenesis and coronary heart disease. Our current findings were that low serum PON1 activity and concentration in patients with MI were present within 2 hours of the onset of acute MI; both serum PON1 activity and concentration were profoundly lower than in controls. No significant further decline in PON1 activity or concentration occurred in the immediate post-MI period. Six weeks later only a small increase in PON1 activity and no increase in concentration had occurred. It is possible either that PON1 declined as an acute reaction to the acute MI or that the decrease in its concentration and activity had occurred before the acute MI. Typical changes in an acute-phase reactant C-reactive protein were found. The low PON1 activity in acute MI was certainly not due to a preponderance of the low-activity A genes in the MI group, which in this study were present at a much higher frequency in the control group than in the MI group. This finding is consistent with previous case-control studies in which the B allele was reported to be associated with coronary heart disease.19,20 In the general population, the B allele PON1 is associated with higher paroxonase activity indicating an even more profound decrease in activity in patients who sustain acute MI.1-3

The low serum PON1 activity in survivors of MI in the current study was probably a consequence of the remarkably low PON1 concentration in survivors of myocardial infarction versus controls. This conclusion was reached because the decrease in serum PON1 concentration in MI patients was relatively greater than the decrease in activity suggesting that the low concentration of PON1 was the primary factor. Indeed the PON1 specific activity was higher in patients versus controls. The factors modifying serum PON1 concentration are not yet clear. One study conducted in non-insulin dependent diabetes has suggested that polymorphism at position 55 is a major determinant of variable PON1 concentration.21 However, we have found no effect of the 55 polymorphism on PON1 concentration in nondiabetic, healthy people.24 The low PON1 concentration in the current study was likely to have been due to decreased synthesis and/or enhanced catabolism. The possibility of a circulating inhibitory factor is less likely unless it interfered with our immunoassay for PON1. PON1 activity has been shown to be reduced in atherosclerosis-susceptible mice fed an atherosclerotic diet, as a result of decreased hepatic synthesis of PON1.26 PON1 mRNA levels in human hepatic (HEP G2) cells have also been shown to decrease on incubation with oxidized phospholipids.25 Although our MI patients were normolipidaemic, it remains a possibility that a previous high fat intake leading to the generation of oxidized phospholipids has inhibited hepatic synthesis and secretion. While the majority of our patients (72%) were smokers, we could not find any significant difference in either the PON1 concentra-

| TABLE 3. PON1 Activity, Concentration, and Specific Activity in Control and MI Subjects |
|--------------------------------|------------|------------|------------|------------|
|                                | Controls   | Day 1      | Day 2      | Day 5      | Day 42     |
| PON1 activity, nmol · min⁻¹ · mL⁻¹ | 221.5 (99.3–303.2) | 130.1* (78.9–230.3) | 148.1 (79.2–247.5) | 133.2 (80.5–225) | 158.1† (85.4–282) |
| PON1 concentration, µg/mL        | 95.7 (73.2–135.5) | 35.4** (21.6–51.3) | 29.4 (22.6–54.7) | 39.3 (24.9–63) | 44.6 (24.5–60) |
| PON1 specific activity, nmol · min⁻¹ · mg⁻¹ | 1.5 (0.9–2.9) | 3.4** (2.0–8.5) | 3.6 (2.0–8.4) | 3.9 (1.2–8.4) | 3.3 (1.6–10.9) |
| Arylesterase activity, nmol · min⁻¹ · mL⁻¹ | 74.8 (54.9–87) | 59.4* (48.3–80.1) | 65.2 (46.2–78) | 62.1 (47.4–75.4) | 56.3 (45.8–73.4) |

Values expressed as median with IQR.
Statistical comparisons were as described in Table 2.
*P<0.05, **P<0.001 significantly different from control subjects; †P<0.05, significantly different from day 1.
tion or activity between smokers and nonsmokers. Thrombolytic therapy for MI did not explain the initial low PON1 concentration because, blood was obtained before this therapy was instituted. Later, we found no significant difference in serum PON1 concentration or activity in patients who had been treated with thrombolytic therapy and those who had not, and furthermore, the first blood sample in our series was obtained before thrombolytic therapy.

The low PON1 concentration and activity in patients presenting with acute MI was evident within the first 2 hours of the onset of symptoms. This suggests either that the decline followed the onset of the acute MI or that it was already present before the onset of symptoms. If the former is true, the decrease would have to have been exceptionally rapid and to have occurred fully in virtually all cases within the 2 hours after the onset of symptoms, because there is no subsequent further decline. Perhaps this makes it more likely that PON1 concentration was already low at the time of the MI, but to answer this question is beyond the scope of the current investigation.

The relatively greater decrease in PON1 concentration as opposed to activity in survivors of acute MI appears to be different from the explanation for the low PON1 activity in diabetes mellitus, in which the decrease in activity is more profound than the decrease in concentration and that we have speculated may be due to changes in the lipid environment that HDL affords PON1 in diabetes. PON1 present in serum is located on HDL, being tightly bound to a HDL subfraction containing apo AI and clusterin. Low concentrations of HDL increase susceptibility to atherosclerosis and consequently CHD. The PON1-containing HDL particles constitute a very small fraction of the total plasma HDL. Low serum PON1 levels occur when HDL concentrations are profoundly low in, for example, fish eye and Tangier diseases. However, when serum HDL levels are only moderately decreased, as in, for example, insulin-dependent diabetes mellitus and familial hypercholes-
terolemia, the decrease in PON1 is independent of changes in HDL. In the current study, patients who sustained MI did not on average have markedly decreased HDL concentrations, but PON1 activity and PON1 concentration were profoundly decreased. Under most circumstances, including in the acute-MI survivors studied here, the serum PON1 activity is therefore likely to depend on the number of PON1 molecules in HDL rather than the serum HDL concentration. The greatly increased ratio of apo AI to PON1 mass found in the MI patients would tend to support this argument.

PON1 has been suggested as the factor largely responsible for the antioxidant role of HDL. Several studies have shown an increase in the products of lipid peroxidation in the plasma of patients with coronary artery disease. Furthermore, LDL isolated from the plasma of patients with diabetes and coronary artery disease has been reported to be more susceptible to oxidation in vitro than LDL from normal subjects, and autoantibodies to oxidized LDL are increased in patients with coronary artery disease. The significantly elevated LDL-C to PON1 mass and activity ratios in MI patients in this investigation indicates an increased lipid-burden to protective capacity that may have rendered the patients LDL more susceptible to oxidation in vivo.

From the evidence presented here, a low PON1 activity is very likely to be present at the time of acute MI, although we cannot exclude the possibility that the event itself lowered PON1. Earlier evidence suggests that it may predispose to coronary heart disease. The major question to be answered in future studies is therefore, whether the decrease in PON1 concentration and activity occurs immediately preceding an acute MI or whether it is low for sufficiently long before the event for it to have value in predicting the MI and whether intervention aimed at increasing its concentration would have the potential to prevent the MI. There is a cogent need for prospective epidemiological studies of PON1.

Acknowledgments

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References


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