Oral cavity status and cigarette smoking in patients with coronary disease and its exacerbation

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Introduction
Inflammatory processes play an important role in the pathogenesis of coronary heart disease (CHD). Surface of a periodontal membrane is approximately 75 cm² which can be colonized by a large variety of bacteria. Most of them are anaerobic and carry out fermentative degradation of carbohydrates. An increase in the number of these bacteria results in the formation of the dental plaque which is the first stage of dental caries. 

Materials and methods
A study group
We examined 491 patients (216 women) aged between 21–98 years of age, median value – 71, 5 years, who were hospitalized in Warsaw clinical hospitals (internal diseases or cardiologic wards) in 2010 and 2011 year. Patients with C-reactive protein (CRP) concentration which could be significantly influenced by other diseases or treatment such as, patients with tumors, autoimmune or rheumatic diseases, with immunosuppressive drugs, or after surgical procedures in the last month were not included in the study. Therefore, patients with plasma CRP level higher than 40 mg/l were also not included in the study. In our case, after excluding patients with symptoms and signs of infection (in locations other than oral cavity), such level of CRP occurred in patients with periodontium inflammation.

Statistical analysis
The statistical analysis was supported by several tests: Fishers’ test, Wilcoxon’s test, Kruskall-Wallis test, and Spearman’s rank correlation coefficient. Parameters with a normal distribution were presented as an arithmetic mean with a standard deviation. Parameters without a normal distribution were presented as a median value with a lower and upper quartile.

Table 1: Formulas by which dental indicators were obtained – Normal values accepted for the indicators

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<thead>
<tr>
<th>Indicator</th>
<th>Formula</th>
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</tr>
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<tr>
<td>API</td>
<td>Number of interdental spaces covered with a dental plaque / number of evaluated interdental spaces (max. 10) 100%</td>
<td>&lt;30% – Optimum oral hygiene; 30–60% – Average incorrect oral hygiene; 60–100% – Highly incorrect oral hygiene</td>
</tr>
<tr>
<td>mAPI</td>
<td>Number of teeth covered with a dental calculus / number of present teeth 100%</td>
<td>&lt;5 – Low level of caries advancement; ≥5 – Caries with significant advancement</td>
</tr>
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Dental status and smoking in coronary disease or its exacerbation

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Trustee

Disclosures: This article has not received any funding and has no vested commercial interest

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Abstract

Object: Caries, periodontal disease (PD), poor oral hygiene may cause systemic inflammation, which increases the risk of coronary disease (CHD). Moreover, smoking may exacerbate PD. We tried to assess the oral state and the frequency of smoking in patients with CHD and to investigate a potential association between dental state and CHD.

Methods: Dentition state of 491 patients was examined and the plasma C-reactive protein (CRP) concentration of hospitalized patients was obtained. Questionnaire included questions about: smoking frequency, CHD, myocardial infarction (MI). Patients’ dentition state was described by indicators: Decayed-Missing-Filled-Teeth (DMFT), Approximal Plaque Index (API), modified API (mAPI). Patients were divided into groups.

Results: The last visit at dentist: more than 10 years before – 24% of patients; within the last 10 to 2 years – 32%; and during the last 2 years – 24%. Poor oral hygiene was found in 51% of all patients, while caries in 34% of patients. Elevated plasma CRP was associated to higher mAPI and DMFT values. Significant differences in CRP level, API, mAPI and DMFT between patients with and without CHD were noticed. Patients with smoking habit—number of smoked packed-years of hospitalization, occurrence and symptoms of cardiovascular diseases (CVD) including CHD, MI and cigarette smoking habit—number of smoked packed-years were calculated. Results of plasma CRP concentration of the patients during their present hospitalization were obtained from patients’ medical documentation. In patients with MI, pulmonary embolism or infection plasma CRP concentration was measured after at least 14 days after the end of an acute phase of disease.

Dental examination

A dental examination was performed by medical students who were hospitalized in Warsaw clinical hospitals (internal diseases wards) in 2010 and 2011 year. Patients with C-reactive protein (CRP) concentration which could be significantly influenced by other diseases or treatment such as, patients with tumors, autoimmune or rheumatic diseases, with immunosuppressive drugs, or after surgical procedures in the last month were not included in the study. Therefore, patients with plasma CRP level higher than 40 mg/l were also not included in the study. In our case, after excluding patients with symptoms and signs of infection (in locations other than oral cavity), such level of CRP occurred in patients with periodontium inflammation. Patients were divided into subgroups like:

• With documented CHD
• Without clinical data confirming CHD who were hospitalized because of other cardiologic or internal causes
• After myocardial infarction (MI) before at least last 6 months
• Without clinical data confirming MI
• After MI passed once or more

Statistical analysis

The statistical analysis was supported by several tests: Fisher’s test, Wilcoxon’s test, Kruskall-Wallis test, and Spearman’s rank correlation coefficient. Parameters with a normal distribution were presented as an arithmetic mean with a standard deviation. Parameters without a normal distribution were presented as a median value with a lower and upper quartile.

Results

Over 76% of the examined patients had not visited a dentist for over previous 2 years from which almost 25%—over 10 years. Median value of the time from the last visit at the dentist was approximately 3 years.

In more than one third (169 patients; 34%) of patients dental caries was confirmed. In more than a half of the examined patients (246 patients; 51%) features of an incorrect oral hygiene were found.

The indicators which represent periodontal status and caries indicator, for a significant group of patients were significantly influenced by other diseases or treatment such as: elevated values of API indicator, which represents dental plaque severity was attained in 403 patients (82%). mAPI indicator, which shows dental hygiene but also in healthy people with a correct hygiene.

In the last ten years reports have indicated the possibility of an essential link between poor condition of oral hygiene and development of CHD. We decided to evaluate oral cavity status of patients and to estimate a potential relation between indices of oral hygiene and the presence or severity of CHD.

Materials and methods

A study group

We examined 491 patients (216 women) aged between 21–98 years of age, median value – 71, 5 years, who were assigned to three groups divided into groups.

Results

Caries, periodontal disease (PD), poor oral hygiene may cause systemic inflammation, which increases the risk of coronary disease (CHD). Moreover, smoking may exacerbate PD. We tried to assess the oral state and the frequency of smoking in patients with CHD and to investigate a potential association between dental state and CHD.

Methods: Dentition state of 491 patients was examined and the plasma C-reactive protein (CRP) concentration of hospitalized patients was obtained. Questionnaire included questions about: smoking frequency, CHD, myocardial infarction (MI). Patients’ dentition state was described by indicators: Decayed-Missing-Filled-Teeth (DMFT), Approximal Plaque Index (API), modified API (mAPI). Patients were divided into groups.

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Dental examination

A dental examination was performed by medical students under the supervision of trained doctors at the Department of Internal Medicine and Cardiology of Dentistry Institute of Medical University of Warsaw in accordance with the standard of dental examination.

On that basis patients’ oral hygiene status was evaluated by the usage of two well-known indicators in dentistry which illustrate caries progress and status of periodontium. These are: DMFT index (caries indicator; number of decayed, missing and filled teeth) and an approximal Plaque Index (API). Another indicator, modified approximal Plaque Index (mAPI), created by the authors of this study is also used. The indicators were obtained by using of the formulas presented in Table 1.

Table 1: Formulas by which dental indicators were obtained – Normal values accepted for the indicators

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<td>DMFT</td>
<td>(number of decayed teeth + number of missing teeth + number of filled teeth) / number of present teeth</td>
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In patients after MI, we have more frequently found increased levels of mAPI and DMFT than in patients without such event in their life. A mildly higher level of plasma CRP, on the verge of significance, was also revealed for the group of patients after MI (Table 2).

A statistical significant and positive correlation between elevated plasma CRP level and values of all dental indicators (API, mAPI, DMFT) are shown in Table 3. An increase of dental indicators values was correlated to an increase of plasma CRP level.

A median value of plasma CRP concentration among examined patients as well as in patients who were hospitalized because of ACS was 4 mg/l. Median values of plasma CRP levels for particular groups of patients are shown by Table 1. No difference in plasma CRP concentration between groups of patients was observed. A correlation between the plasma CRP levels and values of indicators which represent dental and periodontal status in particular groups of patients shows Table 2.

A statistical significance and positive correlation between plasma CRP levels and values of dental indicators API, mAPI, DMFT were observed. A statistically significant differences considering level of mAPI between patients who have never smoked cigarettes, patients who have already ceased smoking and patients who still actively smoke were observed. Values of the above mentioned parameters were steadily increasing in consecutive groups of patients. Also a statistically significant difference in plasma CRP concentration between smokers and former-smokers was observed (Table 4). A statistically significant relation between a number of smoked packed-years and the value of mAPI was shown. The level of mAPI was increasing with growth of number of smoked packed-years (Table 4).
In patients with CHD, we frequently found significantly increased levels of all dental indicators comparing to patients who did not suffer from that disease. Majority of patients in the group with CHD are characterized by a serious negligence of oral cavity hygiene, which is connected with a severe dental plaque and calculus as well as dental caries (Table 2).

In patients after MI, we have more frequently found increased levels of mAPI and DMFT than in patients without such event in their life. A mildly higher level of plasma CRP, on the verge of significance, was also revealed for the group of patients after MI (Table 2).

A statistical significance and positive correlation between values of dental indicators and age were proved (pAPI=0.039; pDMFT<0.0001; rAPI=0.17; rDMFT<0.0001). An increase of plasma CRP level was correlated to an increase of dental indicators values was correlated to an elevated plasma CRP level and values of all dental indicators which represent dental and periodontal status in particular groups of patients shows Table 2.

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### Discussion

Oral cavity diseases and their relation with cardiovascular diseases

In 2002, World Health Organization placed teeth diseases (caries) at the 7th place on the list of chronic, non-infectious diseases which are the most common causes of death in developed countries.

### Table 2: CRP and dental indicators in individual groups of patients (pts) with and without a coronary heart disease (CHD), after and not after a myocardial infarction (MI), after one or more MI.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CHD (342 pts)</th>
<th>Without a CHD (149 pts)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP (mg/l)</td>
<td>4.1 (2 – 10.4)</td>
<td>4 (2 – 9)</td>
<td>0.38</td>
</tr>
<tr>
<td>API</td>
<td>1 (0.6 – 1)</td>
<td>0.9 (0.2 – 1)</td>
<td>0.002</td>
</tr>
<tr>
<td>mAPI</td>
<td>0.86 (0.47 – 1)</td>
<td>0.57 (0.23 – 1)</td>
<td>0.001</td>
</tr>
<tr>
<td>DMFT</td>
<td>2.79 (1.8 – 6.4)</td>
<td>1.68 (1.19 – 4.57)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

### Table 3: Correlations between CRP and dental indicators API, mAPI and DMFT

<table>
<thead>
<tr>
<th>Indicator</th>
<th>CRP</th>
<th>API</th>
<th>mAPI</th>
<th>DMFT</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>API</td>
<td>0.18</td>
<td>0.18</td>
<td>&lt;0.0001</td>
<td>0.03</td>
</tr>
<tr>
<td>mAPI</td>
<td>0.35</td>
<td>0.34</td>
<td>&lt;0.0001</td>
<td>0.4</td>
</tr>
<tr>
<td>DMFT</td>
<td>0.14</td>
<td>0.14</td>
<td>&lt;0.0001</td>
<td>0.3</td>
</tr>
</tbody>
</table>

### Table 4: Dependence of tobacco smoking and CRP and dental indicators. Dependence of smoked packed-years and CRP and dental indicators. For particular parameters there were given median values and in brackets lower and upper quartile values.

<table>
<thead>
<tr>
<th>Smoking</th>
<th>CRP (mg/l)</th>
<th>&lt;0.0001</th>
<th>DMFT</th>
<th>&lt;0.0001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smokers</td>
<td>8.4 (2 – 15)</td>
<td>4 (2 – 9)</td>
<td>4 (2 – 10.5)</td>
<td>p= 0.03</td>
</tr>
<tr>
<td>Former-smokers</td>
<td>1 (0.5 – 1)</td>
<td>1 (0.5 – 1)</td>
<td>1 (0.33 – 1)</td>
<td>0.175</td>
</tr>
<tr>
<td>Never-smokers</td>
<td>0.96 (0.56 – 1)</td>
<td>0.62 (0.34 – 1)</td>
<td>0.56 (0.13 – 1)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Figure 1: Dental characteristics of examined patients.

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In adults, periodontium inflammation is one of the most frequently observed inflammatory diseases of the oral cavity. It is usually a consequence of an incorrect oral hygiene. Dental plaque which is formed by Gram-positive and Gram-negative bacteria such as Streptococcus viridans (S. mitis, S. oralis, S. sanguis, S. salivarius, S. mutans), Chlamydia pneumoniae, Porphyromonas gingivalis, Treponema denticola constitutes an important point of an inflammatory process beginning. The transient bacteria is also in relation with everyday actions (tooth brushing) and some medical procedures (periodontal probing, scaling). The longer lasting (30–60 minutes) bacteremia occurs after tooth extraction.

A healthy organism with an efficient immune system can easily render bacteria and produce negative outcomes of its presence in the bloodstream. However, especially in the elderly or subjects with metabolic diseases the gingival bleeding index and percentage of deep gingival pockets are increased and promoting a subsequent bacteremia. An interrelationship of periodontium inflammation and CHD has been widely discussed.

A summary of the so far known relations linking these diseases were presented recently by P. B. Lockhart et al. Authors summarize several studies and analyzed the relationship between a periodontium and systemic inflammation, increased concentration of acute-phase markers and endothelium function. Authors of cohort studies and randomized clinical trials have mentioned that non-surgical therapy of periodontium diseases leads to an improvement of endothelial function and to a reduction of inflammatory markers. A relationship between periodontium inflammation and endothelial dysfunction, atherosclerosis, increased risk of myocardial infarction as well as a stroke was also emphasized in the newest European Guidelines on cardiovascular disease prevention in clinical practice of the European Society of Cardiology (ESC).

Studies from recent years using a polymerase chain reaction (PCR) technique have shown a presence of bacteria on a dental plaque in an atherosclerotic plaque. We, therefore, acknowledge that a problem of bacteria that forms a dental plaque in an atherosclerotic plaque. This process is also worth of paying attention to the relationship between tobacco smoking and periodontium diseases as well as caries. Patients after MI when compared to patients without MI presented more advanced dental calculus and caries. Furthermore a great majority of patients who were hospitalized due to ACS were characterized by a serious negligence of oral hygiene and caries which was accompanied by an increased concentration of plasma CRP. A large difference between the general health state of patients with a correct and incorrect oral hygiene was noticed. An occurrence of periodontium diseases as well as caries is often correlated with CHD and its exacerbation. Among examined women, a significantly higher percentage of toothless patients were noticed than among men. Furthermore, in women an essentially higher level of DMFT was observed. It testifies to a faster progress of caries in the female population.

In our study, we have found significant differences in oral cavity status between patients with or without history of CHD or MI. Reason for these differences should be searched in the pathophysiologic influence of inflammatory markers on the organism. It is correlated with its prothrombotic and destabilizing effect on the atherosclerotic plaque. The factor that starts an inflammatory cascade is a nuclear factor NF-kB, which is a product of gene transcription, for example: for proinflammatory cytokines. As a result of damaged endothelium NF-kB is released. In consequence it induces the release of chemokines from endothelial cells and exposition of adhesion molecules on the bloodarterial cells which turn cause the attraction of monocytes. These cells phagocytize oxidized LDL molecules and are the source of proteolytic enzymes, which belong to the metalloproteinases group responsible for consuming the connective tissue framework of the cap on the atherosclerotic plaque. Besides this effect, proinflammatory cytokines influence the progress of the autoimmune response for a human heat shock protein HSP90 which is located on the endothelial cells of arteries. It is as a result of the presence of a very similar heat shock protein on the bacteria wall surface forming the dental plaque, and also the following immune cross reactions.

Inflammatory markers also allow the accumulation of calcium and oxLDL in atherosclerotic plaques by the process of lymphocytes and monocytes activation.

Relation between oral cavity diseases, coronary diseases, myocardial infarction and gender among examined patients

Our study directly confirms a great need of cooperation between doctors of different specialties who manage patients with CVD. Such teamwork is of great significance in the prophylaxis of these illnesses. First of all, it was revealed that the scale of negligence of oral hygiene is very high. A great majority of patients seldom visited a dentist for a prophylactic examination. Every fourth of them meet the dentist even more rarely than once in ten years. An incorrect oral hygiene and caries are very common among hospitalized patients, as well as in whole society. Hygiene negligence was observed in over half of the examined patients while caries was related to over one third of them. As a result of a high dependence between an increased concentration of CRP and severe dental calculus, dental plaque or advanced caries was shown. It had a great influence on the health of patients examined by us, especially in the group of patients with CHD or after MI. Patients with CHD when compared to a group of patients without CHD frequently presented highly advanced dental plaque, calculus and caries. Patients after MI when compared to patients without MI presented more advanced dental calculus and caries. Furthermore a great majority of patients who were hospitalized due to ACS were characterized by a serious negligence of oral hygiene and caries which was accompanied by an increased concentration of plasma CRP. A large difference between the general health state of patients with a correct and incorrect oral hygiene was noticed. An occurrence of periodontium diseases as well as caries is often correlated with CHD and its exacerbation.

Among examined women, a significantly higher percentage of toothless patients were noticed than among men. Furthermore, in women an essentially higher level of DMFT was observed. It testifies to a faster progress of caries in the female population.

Conclusion

Dental status of patients hospitalized on internal medicine and cardiological wards indicates a substantial negligence of oral hygiene. This result is in elevation of plasma CRP levels, periodontium inflammation and caries. Our study confirms an important relationship of dental and periodontium illnesses with CVD. Pathological processes concerning the oral cavity potentially contribute to the development of CHD and its exacerbation.

References

In adults, periodontium inflammation is one of the most frequently observed inflammatory diseases of the oral cavity. It usually is a consequence of an incorrect oral hygiene. Dental plaque which is formed by Gram-positive and Gram-negative bacteria such as: Streptococcus viridans (S. mitis, S. oralis, S. sanguins, S. salivarius, S. mutans), Chlamydia pneumoniae, Porphyromonas gingivalis, Treponema denticola constitutes an important point of an inflammatory process beginning. The transient bacteria is also in relation with everyday actions (tooth brushing) and some medical procedures (periodontal probing, scaling). The longer lasting (30-60 minutes) bacteriaemia occurs after tooth extraction.

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Studies from recent years using a polymerase chain reaction (PCR) technique have shown a presence of bacteria from dental plaque in an atherosclerotic plaque. We, therefore, acknowledge that a problem of caries and periodontium disease is particularly important for prophylaxis and treatment of CVD.

**Relation of inflammation markers in cardiovascular diseases promotion**

CRP has a remarkable significance in pathogenesis of CVD. It makes oxidized LDL phagocytosis easier for macrophages and is an inhibitor of nitric oxide synthesis. That protein has been regarded as an independent risk factor of cardiovascular incidents. Guidelines of ESC pay attention to the important role of increased concentration of CRP in the pathogenesis of these diseases. Cut-off point at level 40 mg/l for the plasma CRP level was accepted on the basis of literature which states that generally, plasma CRP concentration is found in cases of mild inflammation. Plasma CRP declines with a half-life of 19 hours. Patients who in a period shorter than 14 days before the day of our examination fell ill used to show increased concentration of plasma CRP level were not included to the study. Such safety margin was considered proper for security and essential correctness of the study.

In our study, we have found significant differences in oral cavity status between groups of patients with or without CHD or MI. For proinflammatory cytokines. As a result of damaged endothelium NF-kB is released. In conclusion it induces the release of chemokines from endothelial cells and exposition of adhesion molecules which in turn cause the attraction of monocytes. These cells phagocyte oxidized LDL molecules and are the source of proteolytic enzymes, which belong to the metalloproteinases group responsible for consuming the connective tissue framework of the cap on the atherosclerotic plaque. Besides this effect, proinflammatory cytokines contribute to the progress of the autoimmune response for a human heat shock protein HSP90 which is located on the endothelial cells of arteries. It is as a result of the presence of a very similar heat shock protein on the bacteria wall surface forming the dental plaque and also, and the following immune cross reactions.

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**Relation of tobacco smoking and periodontium diseases or cardiovascular diseases**

Scientific reports from recent years point at an important relationship between tobacco smoking and new risk factors of CVD in the general population. Confirmation of the influence of tobacco smoking on the development of systemic inflammatory processes has been an important discovery. These researches have shown a higher concentration of markers such as CRP, fibrinogen or homocysteine among tobacco smoking patients than among those who quit smoking or who have never smoked. Results obtained in our study confirm these conclusions. It is also worth of paying attention to the relationship between tobacco smoking and periodontium diseases. In the last 15 years, numerous reports have shown that habitual tobacco smoking is an important risk factor of periodontium disease development. Results obtained in our study are in unison with previous studies.

It seems to be obvious that further evaluation on the influence of teeth and periodontium diseases on development and exacerbations of CVD is necessary. Interdisciplinary studies at the level of plasma CRP levels, periodontium inflammation and caries. Our study confirms an important relationship of periodontium and dental caries with CVD. Pathological processes concerning the oral cavity potentially contribute to the development of CHD and its exacerbation.

**References**

Statins in CVD prevention

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Abstract
Cardiovascular diseases are one of the leading causes of mortality and morbidity worldwide. Dyslipidemia, particularly LDL cholesterol, being an important major risk factor, plays a robust role in the pathogenesis of atherosclerosis. Different drugs have shown variable efficacy in clinical trials in treating dyslipidemia. Statins have been the most effective and best tolerated agents amongst them. Statins have proved their significant beneficial effects in primary prevention trials, e.g., AFCAPS/TexCAPS, ASCOT-LA, CARDOS and more recent trials like JUPITER showing reduced cardiovascular events. Hence advocating statins to healthy, normocholesterolemic, intermediate- to high-risk individuals as a primary prevention strategy would probably save more lives than expected. Landmark primary prevention trials like CARE, LIPID, TNT, MIRACL, PROVE IT-TIMI 22, etc. have proved the beneficial effects of statins in mortality and morbidity reduction following AMI, ACS and also in chronic stable CAD. These benefits are observed in all subsets of population and irrespective of blood lipid levels. Trials like REVERSAL, ASTEROID, SATURN, etc. have shown plaque regression with statins by advanced imaging techniques. High dose of statins have better efficacy in certain clinical scenarios. Current recommendations have clearly mentioned the appropriate use of statins in different group of patients on a target to treat basis. However, routine combination of statins with drugs for lowering triglycerides/raising HDL should be done with caution.

Key Words
- Dyslipidemia
- Statins
- Primary prevention
- Secondary prevention

Introduction
Today, cardiovascular diseases (CVD) are the leading cause of mortality as well as morbidity worldwide. In 2001, CVD was responsible for 29% of all deaths. By 2020, the world population is likely to reach 7.8 billion and 33% of all deaths will be caused by CVD. By 2030, WHO predicts that worldwide, CVD will be responsible for 24.2 million deaths.

Lipids and atherosclerosis
Dyslipidemia is among the most important and major risk factor of cardiovascular diseases and has been addressed continuously for decades. Hypercholesterolemia was linked to atherosclerosis long back in 1940s and this was soon followed by discovery of abnormal lipoprotein fractions (low HDL and high LDL levels) as culprit agents. In the late 1970s, the Framingham Study demonstrated the cardioprotective role of HDL, noting that it was inversely related to CVD risk independent of LDL levels.

Lowering lipids with drugs specifically targeting cholesterol was initially attempted with fibrates. Clofibrate was studied in a World Health Organisation initiated randomized controlled primary prevention trial and it was found that 9% reduction in cholesterol level resulted in 25% decrease in myocardial infarction and 20% decrease in CVD events after more than 5 years of follow-up. It was soon followed by another, the Coronary Drug Project using clofibrate, niacin, estrogen, or dextrothyroxine or placebo. This study, however, failed to demonstrate any mortality.