Treatment—Therapeutic Lifestyle Modification

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Therapeutic lifestyle modification is the basis for the prevention of the occurrence and development of atherosclerotic diseases, regardless of whether the prevention is primary or secondary. This guideline describes methods to modify lifestyle with primary attention to serum lipids, but also in consideration of hypertension, impaired glucose tolerance, and the accumulation of visceral fat. The following 4 items comprise the core of lifestyle change. Appropriate guidance and practice of lifestyle modification can lead to reduction of metabolic risk factors and as the result prevent the progression of the atherosclerotic vascular disease:

1. Smoking Cessation
   Smoking is a major independent risk factor of all atherosclerotic diseases and significantly increases the risk of cardiovascular death and total death. Smoking cessation, in contrast, leads to decrease in mortality and the cardiovascular risk with or without a history of coronary artery disease (CAD) regardless of age or gender. In addition, the positive effect of smoking cessation is known to appear rapidly and increase with prolongation of the non-smoking period. Therefore, patients of all ages should be advised to stop smoking for the prevention of atherosclerotic diseases. However, the guidance for smoking cessation is not easy to be performed at a general outpatient clinic, and therefore long-term and well-designed counseling including psychological support is often required. Nicotine-replacement therapy using nicotine patches or nicotine chewing gum may be effective for the treatment of nicotine dependence, and the former, in particular, began to be covered by medical insurance in Japan in 2006.

2. Diet Improvement
   Whether or not there is a history of atherosclerotic disease, dietary modification is the basis for the modification of lifestyle in patients with dyslipidemia, and its usefulness has been demonstrated by many studies.

   Excessive energy intake causes obesity and invites various metabolic risk factors including dyslipidemia and impaired glucose tolerance. Restriction of the total energy intake causes amelioration of insulin resistance and decreases in TG and TC levels, and thus prevent the progression of CAD. As an increase in the intake of saturated fatty acids, which are contained at high levels in animal fat, also increases the TC level and incidence of CAD. Therefore, the restriction of not only total fat but also saturated fatty acid intake is effective. Indeed, it has been reported that the progression of atherosclerosis could be prevented and the coronary artery risk could be reduced by controlling the intake of saturated fatty acids and increasing the intake of mono-unsaturated fatty acids, which are contained at high levels in vegetable oils such as olive oil. Moreover, an appropriate intake of n-3 polyunsaturated fatty acids, which are contained at high levels in fish, has been reported to improve not only serum lipid levels but also blood pressure, antiagulation effect, and endothelial function, and thus, to be beneficial for the prevention of CAD and cere-
bral infarction. The negative correlation between fish consumption and mortality due to coronary artery disease supports this notion. Moreover, soybean protein reduces the LDL-C level and increases the HDL-C level and has been shown to be effective for the prevention of atherosclerotic diseases.

Oxidative stress is considered to be involved in the occurrence of atherosclerosis. In fact, various observational studies have suggested that the intake of antioxidant vitamins (vitamins C, E, etc.) is effective for the prevention of atherosclerotic diseases. However, as many of the large-scale clinical studies performed recently presented negative views on a significant preventive effect of high-dose administration of vitamins C and E on atherosclerotic diseases, there are no solid grounds for recommending the intake of antioxidant vitamins in addition to regular meals for the prevention of the progression of atherosclerosis. Similarly, as hyperhomocysteinemia is closely related to an increased cardiovascular risk, the intake of folic acid, vitamins B6 and B12, which are known to reduce homocysteine levels, was expected to be effective for the prevention of atherosclerotic diseases. However, the results of large-scale clinical studies have rejected this view. A negative correlation has also been reported between the intake of polyphenols, which are contained in green tea and red wine, and the morbidity and mortality of CAD. However, further evaluation is necessary before the establishment of their clinical usefulness because of the lack of randomized intervention studies.

Table 1 shows the basic principles of dietary therapy based on current scientific evidence. Since it is more practical to conduct guidance step by step rather than introducing complicated dietary therapy all at once, 2-step dietary therapy is recommended. In the first step, correction of the total energy intake, nutritional balance, and cholesterol intake are intended. Obese, elderly, female, and inactive patients should be instructed to maintain a lower energy intake per standard body weight/kg than indicated by the table. Meat intake is reduced, and fish and soybean products are increased, as protein sources, and the intake of foods high in dietary fiber and vegetables and fruits with high antioxidant contents is encouraged.

If the lipid management goals are not achieved even after practicing the 1st-step dietary therapy for 3 months, the 2nd-step dietary therapy should be considered. In the 2nd step, attention must be paid to the individual types of dyslipidemia, for example, to high-LDL-cholesterol, hypertriglyceridemia, their concurrence, or chylomicronemia, and dietary guidance in more detail should be given according to the type of dyslipidemia. A diet restricting the total fat intake to 20% or less and appropriate saturated/unsaturated fatty acid ratio should be considered.

In addition, it is important to correct inappropriate dietary pattern as well as the dietary contents. Generally, instruction on the principles alone is ineffective, and guidance based on a consideration of indi-
Principles of dietary therapy for dyslipidemia

More precisely, if lipid management goal cannot be achieved after performing 1st step, dietary therapy should be advanced to the 2nd step.

1st step (Correction of the total energy intake, nutritional balance, and cholesterol intake)

1) Correction of total energy intake
   Appropriate energy intake = Standard body weight $^*$ $\times$ 25-30 (kcal)
2) Correction of nutritional balance
   Carbohydrates: 60% of total energy
   Protein: 15-20% of total energy (More fish- and soybean-derived protein than that from animals and fowl should be eaten.)
   Fat: 20-25% of total energy (Animal- and fowl-derived fat should be reduced, and that from plants and fish should be increased.)
   Cholesterol: $\leq$ 300 mg/day
   Dietary fiber: $\geq$ 25 g/day
   Alcohol: $\leq$ 25 g/day (Guidance must be made in consideration of other complications.)
   Others: Intake of foods such as vegetables and fruits with high vitamin (C, E, B6, B12, folic acid, etc.) or polyphenol contents should be increased (except that the intake of fruits should be limited to 80-100 kcal/day because of their high monosaccharide contents).

If lipid management goal cannot be achieved after performing 1st step, dietary therapy should be advanced to the 2nd step.

2nd step (Disease-type-adjusted dietary therapy and appropriate fatty acid intake)

1) If the high LDL-cholesterol persists
   Intensification of lipid restriction: Fat-derived energy $\leq$ 20% of the total energy intake.
   Restriction of cholesterol intake: $\leq$ 200 mg/day
   Saturated /mono-unsaturated/polyunsaturated fatty acid intake ratio: About 3/4/3
2) If hypertriglyceridemia persists
   Alcohol: Abstention
   Restriction of carbohydrate intake: Carbohydrate-derived energy $\leq$ 50% of the total energy intake
   Monosaccharides: Reduced as much as possible. If possible, restricted to seasonings alone except $\leq$ 80-100 kcal/day from fruits.
3) If both hypercholesterolemia and hypertriglyceridemia persist
   Dietary restrictions 1) and 2) are combined.
4) If hyperchylomicronemia is present
   Restriction of fat intake: $\leq$ 15%

*: Standard body weight = [Height (m)]^2 $\times$ 22

An increase in physical activities causes improvements in serum lipid levels, a decrease in the blood pressure, improvement of insulin resistance, correction of impaired glucose tolerance, improvement of endothelial function, and alleviation of thrombogenic tendency and is effective for primary and secondary prevention of CAD$^{37-40}$. Exercise, primarily aerobic exercise, should be performed for 30 minutes or longer per day 3 or more times a week (every day if possible) or for 180 minutes per week or more in total. Mild resistance (muscle strength) training is also effective in elderly people with reduced muscle mass$^{41}$.

There is, however, the risk of musculoskeletal injuries in exercising, particularly if the person is not used to, and the vigorous exercise may also lead to sudden death or myocardial infarction in patients with cardiovascular disorders$^{41, 42}$. With sufficient consideration of these risks, candidates for exercise therapy must be examined in advance for asymptomatic atherosclerotic diseases. Table 2 shows a simplified guideline for exercise therapy.

### 3. Increase in Physical Activities

In order to increase the physical activities exercise appropriate for each individuals should be incorporated in their daily life. An increase in physical activities causes improvements in serum lipid levels, a decrease in the blood pressure, improvement of insulin resistance, correction of impaired glucose tolerance, improvement of endothelial function, and alleviation of thrombogenic tendency and is effective for primary and secondary prevention of CAD$^{37-40}$. Exercise, primarily aerobic exercise, should be performed for 30 minutes or longer per day 3 or more times a week (every day if possible) or for 180 minutes per week or more in total. Mild resistance (muscle strength) training is also effective in elderly people with reduced muscle mass$^{41}$.

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### 4. To Maintain an Appropriate Body Weight and Reduce Visceral Fat

Attaining an appropriate body weight and maintaining it are important elements of lifestyle modification. Obesity, particularly the excess accumulation of visceral fat, is considered to be an independent risk factor of cardiovascular diseases, and it promotes atherosclerosis indirectly via dyslipidemia, impaired glucose tolerance, hypertension, etc., or directly by the actions of adipocytokines, etc$^{43-46}$.

The appropriateness of body weight is evaluated according to the body mass index (BMI):

$$
BMI = \frac{Body \ weight \ (kg)}{[Height \ (m)]^2}
$$

In Japan, a BMI of 22 is regarded as the standard body weight, a BMI $\geq$ 25 is regarded as overweight$^{47}$, and a diagnosis of obesity is made when being overweight is, or is expected to be, accompanied by health damage (JAT, 2008; 15:1-5, Reference 1). Caution to avoid the accumulation of visceral fat is necessary even if the BMI is within the normal range. For screening in daily clinical practice, a waist girth at the umbilical level of $\geq$ 85 cm in males and $\geq$ 90 cm in females is a criterion for visceral fat obesity$^{47, 48}$. More precisely, the visceral fat area at the umbilical level is measured by abdominal CT scan, and a visceral fat area of $\geq$ 100 cm$^2$ is defined as visceral fat-type obesity. These are core factors of metabolic syndrome as mentioned earlier (JAT, 2008; 15:1-5), and a decrease in visceral fat is expected to lead to improvements in not only dys-
lipidemia but also hypertension and impaired glucose tolerance \(^{49}\). For treatment focused on the visceral fat area, the Japan Society for the Study of Obesity recommends a 5% decrease in waist girth at the umbilical level or body weight as an initial weight control target, as well as periodic checks to assess whether the target is being attained \(^{50}\).

Reference

7) Qiao Q, Tervahauta M, Nissinen A, and Tuomilehto J: Mortality from all causes and from coronary heart disease related to smoking and changes in smoking during a 35-year follow-up of middle-aged Finnish men. Eur Heart J, 2000; 21:1621-1626
17) Katzel LI, Blecker ER, Colman EG, Rognes EM, Sorkin

### Table 2. Guideline for exercise therapy

<table>
<thead>
<tr>
<th>Exercise intensity*</th>
<th>Approximately 50% of the intensity which requires the maximum oxygen uptake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration and frequency</td>
<td>≥ 30 minutes/day (everyday if possible), ≥ 180 minutes/week</td>
</tr>
<tr>
<td>Kinds</td>
<td>Fast walking, ball-room dancing, swimming, cycling, etc.</td>
</tr>
</tbody>
</table>

*Exercise intensity
1) Estimation based on the heart rate during exercise
   (1) Karvonen formula (heart rate during exercise)
      Heart rate (beats/minutes) = ((220-age) – resting heart rate) × exercise intensity + resting heart rate
   (2) Simplified method (when the exercise intensity is 50% of the maximum)
      Heart rate (beats/minutes) = 138 – (age/2)
2) Estimation based on subjective feelings
   11-13 according to the Borg’s scale for the rating perceived exertion (“light” to “relatively hard”)

Maximum oxygen uptake: An index of endurance exercise capacity

Borg’s scale\(^{51}\) (The rating of perceived exercise intensity)

<table>
<thead>
<tr>
<th>Rating</th>
<th>Borg’s Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Very light</td>
</tr>
<tr>
<td>7</td>
<td>Very light</td>
</tr>
<tr>
<td>8</td>
<td>Very light</td>
</tr>
<tr>
<td>9</td>
<td>Very light</td>
</tr>
<tr>
<td>10</td>
<td>Fairly light</td>
</tr>
<tr>
<td>11</td>
<td>Somewhat hard</td>
</tr>
<tr>
<td>12</td>
<td>Hard</td>
</tr>
<tr>
<td>13</td>
<td>Very hard</td>
</tr>
<tr>
<td>14</td>
<td>Very hard</td>
</tr>
<tr>
<td>15</td>
<td>Very hard</td>
</tr>
</tbody>
</table>

\(^{51}\) (Borg GA: Med Sci Sports, 1973; 5:90-93)
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Reference 1. 5A Approach

Step 1: Ask (Identify all smokers systematically at each examination.)
Step 2: Advise (Clearly, strongly, and individually advise all smokers to stop smoking.)
Step 3: Assess (Assess the desire to smoking cessation.)
Step 4: Assist (Assist patients in smoking cessation.)
Step 5: Arrange (Arrange a schedule of follow-up examinations.)

Strategies for implementation

Step 1
• Prepare a system within the medical organization to ensure that all patients are asked about smoking at each examination and the answers are recorded.
• Add a space for smoking (to distinguish current, former, and non-smokers) to the section of vital signs such as the blood pressure, heart rate, body temperature, and body weight. Alternatively, attach a sticker indicating the smoking status to all charts.

Step 2
• Clearly: “It is important for you to stop smoking now. I am ready to help you.” or “It is not enough to cut back on smoking only when you are sick.”
• Strongly: “As your attending physician, I must let you know that smoking cessation is the most important step you can take to protect your health. I and the hospital staff are ready to help you.”
• Individually: Relate smoking with the current state of health/disease, social and economic cost, motivation/desire to quit smoking, and impact on children and family.

Step 3
• Ask all smokers if they are willing to stop smoking now (within 30 days).
  If they are, support them in cessation.
  If they are not, motivate them to cessation.

Step 4
Assist patients to make a plan of smoking cessation.
• Set a date to start smoking cessation (preferably within 2 weeks)
• Tell family, friends, and colleagues about smoking cessation and ask for their understanding and support.
• Mentally prepare for problems that will arise in smoking cessation (particularly during the first few weeks) in advance. They include nicotine-withdrawal symptoms.
• Eliminate tobacco from the environment on smoking cessation. Before smoking cessation, avoid smoking in places where you spend prolonged periods of time such as the office, home, and car.

Counsel the patients (training in problem-solving skills)
• It is important not to smoke even a single cigarette: Not even a puff is permitted after the day you start to quit.
• History of smoking cessation: Look back on what helped and interfered with smoking cessation during past attempts.
• Alcohol: Since alcohol consumption may lead to a resumption of smoking, patients should reduce or give up drinking during smoking cessation.
• Smokers in the family: Smokers in the family make smoking cessation difficult. Persuade these family members to quit smoking at the same time or not to smoke in the patient’s presence.

Provide social support in medical activities
• Say, “I and my staff are always ready to help you.”
• Help the patients to receive social support from people other than medical professionals.
• Say, “Ask your spouse/partner, friends, and colleagues for social support.”

Recommend undergoing drug therapy
• Recommend the use of drugs with established efficacy. Explain how these drugs increase the success rate of smoking cessation and alleviate withdrawal symptoms.
• Use a nicotine-replacing agent and bupropion hydrochloride SR (not approved in Japan) as the first choices.

Provide supplementary study materials
• Select study materials appropriate for the characteristics of the patient from those published by the government or NPOs.

Step 5
• Timing: The first follow-up examination should be scheduled immediately after the beginning of smoking cessation, within 1 week if possible.
  The second should be scheduled within 1 month. Make a schedule for subsequent follow-ups.
• What should be done in follow-up examinations: Congratulate the patient on smoking cessation. If the patient has started smoking again, study the situation, and advise them to try again. Advise the patient to regard the failure as a chance to learn for future success. Anticipate problems that have actually arisen and those expected to arise.
• Assess the use of drug therapy and its problems. Evaluate the possibility of the use of, or suggestion to use, stronger treatments.