

(about 20% of the population) have one or more types of cardiovascular disease (American Heart Association 2002). For the major diseases within the category of total cardiovascular disease, about 50 million Americans have high blood pressure, 13 million have ischemic (coronary) heart disease, 5 million have heart failure, 4 million have cerebrovascular disease (stroke), and 2 million have rheumatic fever or heart disease.

For the derivation of AEGL-2 values a level of 4% COHb was chosen. At this exposure level, patients with coronary artery disease may experience a reduced time until onset of angina (chest pain) during physical exertion (Allred et al. 1989a,b, 1991).

Characteristic points of an electrocardiogram are the P wave, reflecting atrial depolarization, the QRS complex, representing the ventricular muscle depolarization, and the T wave, reflecting ventricular muscle repolarization. In the normal electrocardiogram, the ST segment is isoelectric, resting at the same potential as the interval between the T wave and the next P wave. Horizontal depression or a downsloping ST segment merging into the T wave occurs as a result of ischemia, ventricular strain, changes in the pattern of ventricular depolarization or drug effects. In chronic ischemic heart disease, there may be moderate degrees of horizontal ST-segment depression or a downward sloping ST segment, flattening or inversion of T waves and prominent U waves. It is difficult to define an abnormal ST-segment depression in precise quantitative terms. However, a myocardial ischemia has to be considered if the beginning of the ST segment is more than 0.5 mm (corresponding to 0.05 mV) below the isoelectric line, and there is an associated T-wave abnormality (Wilson et al. 1991).

According to the practice guidelines for chronic stable angina (Gibbons et al. 1999), an ST-segment depression at rest is a marker for adverse cardiac events in patients with and without known coronary artery disease. Additional exercise-induced ST-segment depression in the patient with  $\geq 1$  mm of rest ST-segment depression is a reasonably sensitive indicator of coronary artery disease. The ST-segment depression is indicative of clinically relevant myocardial ischemia requiring medical treatment. From the ST-segment depression, the Duke treadmill score can be calculated. It equals the exercise time in minutes minus ( $5 \times$  the ST-segment deviation, during or after exercise, in millimeters) minus ( $4 \times$  the angina index, which has a value of 0 if there is no angina, 1 if angina occurs, and 2 if angina is the reason for stopping the test). Among outpatients with suspected coronary artery disease, the two-thirds of patients with scores indicating low risk (score  $\geq 5$ ) had a 4-year survival rate of 99% (average annual mortality rate 0.25%), and the 4% who had scores indicating high risk (score  $\leq 10$ ) had a 4-year survival rate of 79% (average annual mortality of 5%) (Gibbons et al. 1999).

In the available experimental studies, the CO exposure alone (that is, with subjects at rest) did not cause angina, while exercise alone did so. Moreover, the changes in the electrocardiogram (ST-segment depression of 1 mm or greater) as well as the angina symptoms can be considered fully reversible after a single