atherosclerosis by promoting adhesion of platelets to the endothelial cells of the vasculature, thereby stimulating thrombus formation (134).

CRP is likely to be part of the mechanism for acute damage occurring during a heart attack (135). In this mechanism, CRP contributes to complement activation. During this acute timeframe, CRP levels in the bloodstream can reach 150–200 mg/L (136,137). The highest levels of plasma CRP occur at 2–4 days after myocardial infarction (138). These high values are much greater than CRP levels occurring in chronic timeframes. Ørn et al. (139) provide time-course data on plasma CRP in heart attack patients, and demonstrate that a peak (mean of 35 mg/L) occurs at 2 days.

# IV. BIOMARKERS—SPECIALIZED TOPICS

## a. Introduction

Individual biomarkers, as well as biomarker combinations, are typically used for these purposes.

- Diagnosing a disease,
- Assessing the prognosis of the disease,
- Predicting efficacy of a given drug,
- Predicting safety of a drug.

In using a panel of biomarkers, subgroups of study subjects are identified prior to initiating treatment of subjects in a clinical trial, thus enabling the biomarker panel to identify subgroups of particular interest.

## b. Exploratory Biomarkers

Biomarkers that are used in clinical trials include those that are used as study endpoints, as well as those that are merely exploratory biomarkers. Exploratory biomarkers are used with the goal of arriving at a suitable panel that can subsequently be tested and validated, for use as an endpoint in future clinical trials. In an account of endpoints for clinical trials, Turk et al. (140) distinguished "exploratory endpoints" from biomarkers that are used to define a primary endpoint, multiple primary endpoints, secondary endpoints, and composite endpoints. In using a composite endpoint, multiple endpoints are typically combined to produce a single variable, such as an index or score.

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