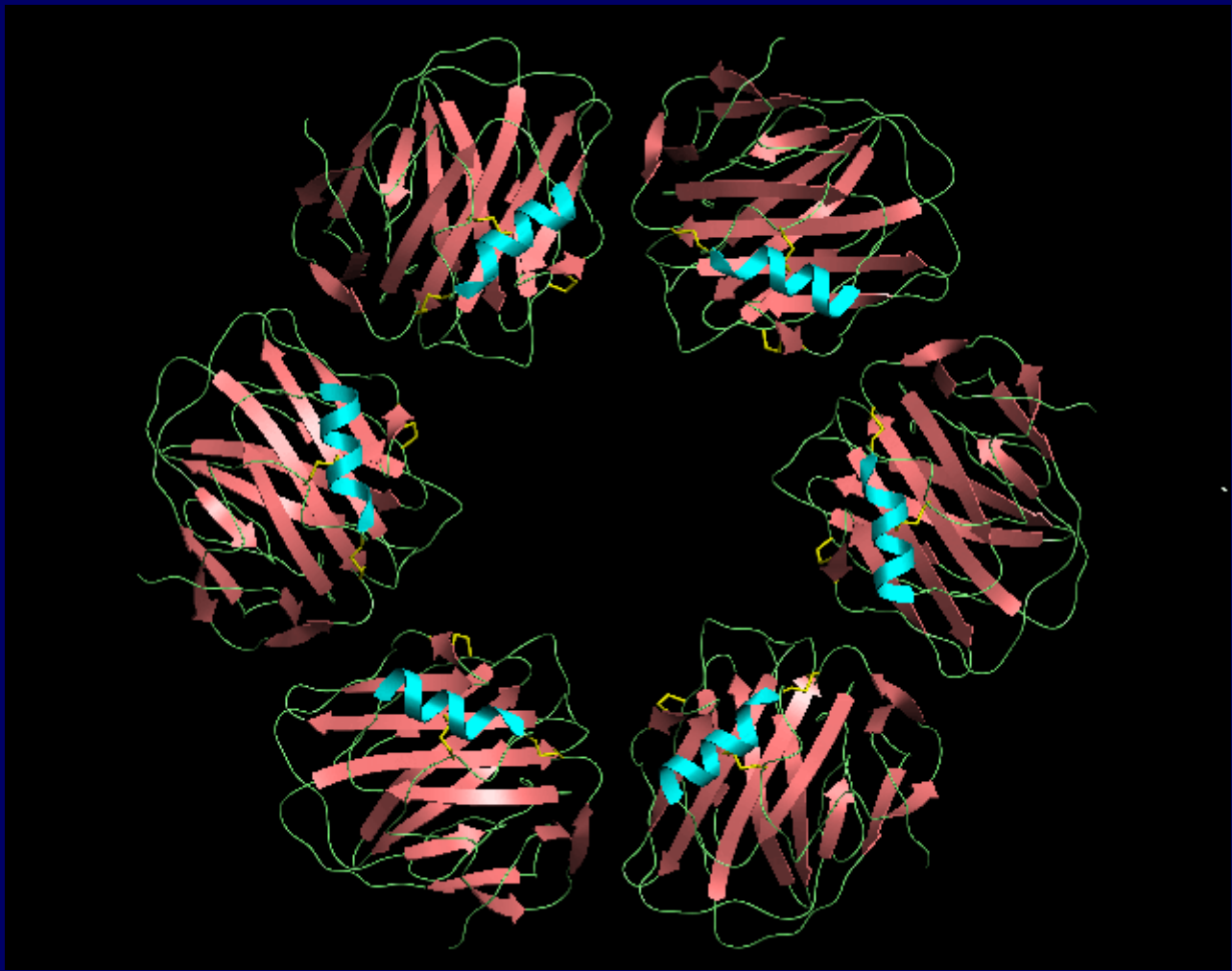


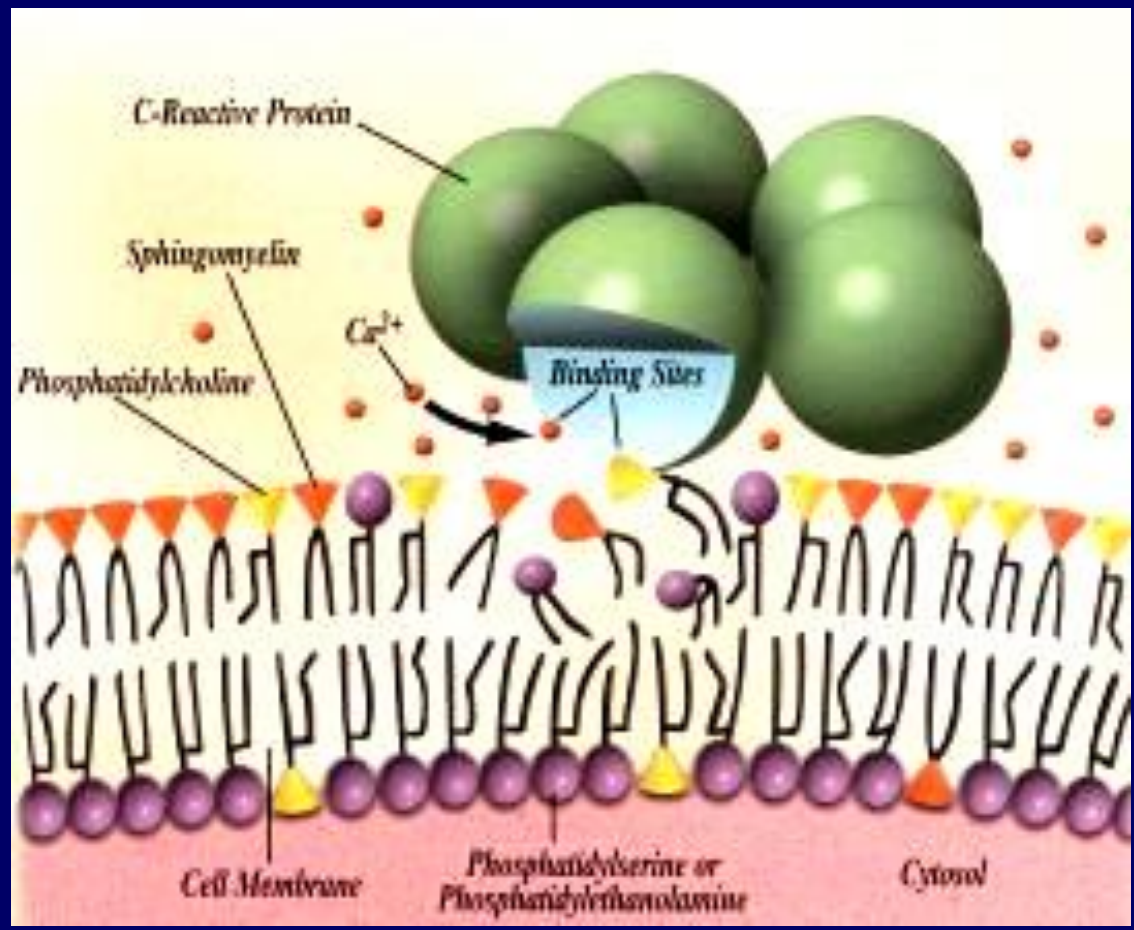
CRP & Acute Coronary Syndrome(ACS)

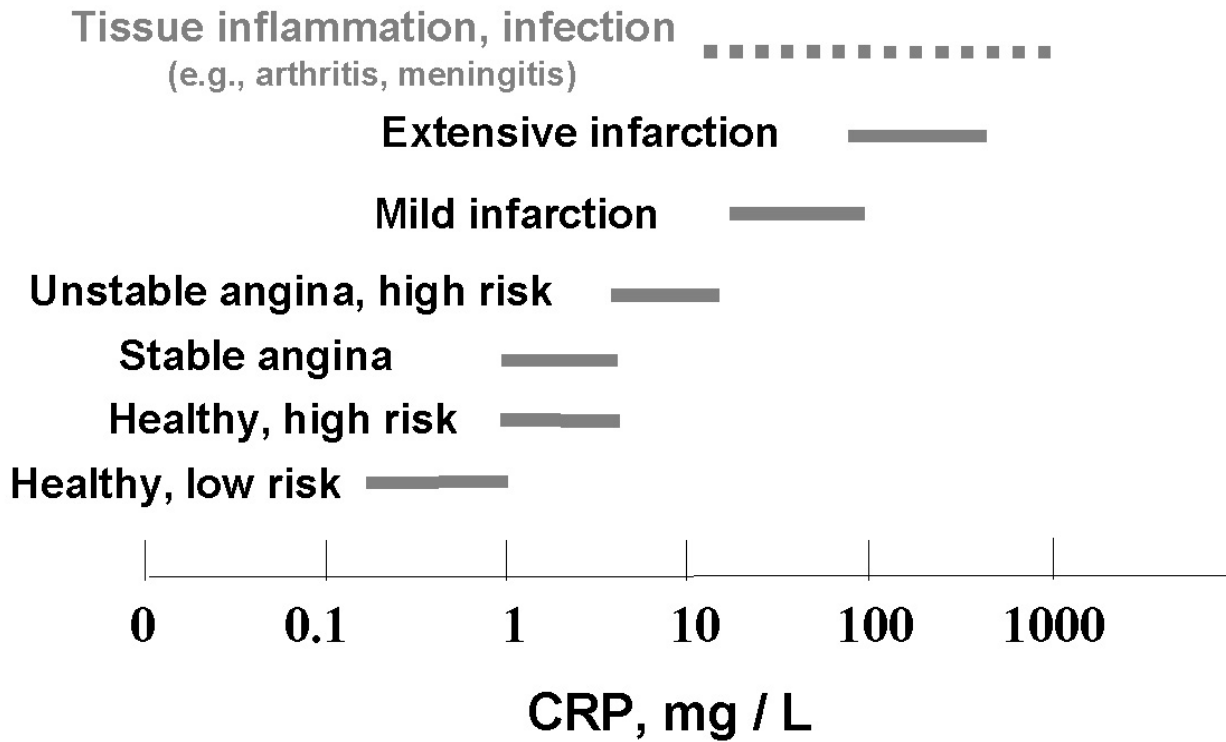
- 1- CRP: Structure & Function
- 2- ACS & Inflammation
- 3- CRP & ACS
- 4- Conclusion
- 5- Perspective

CRP

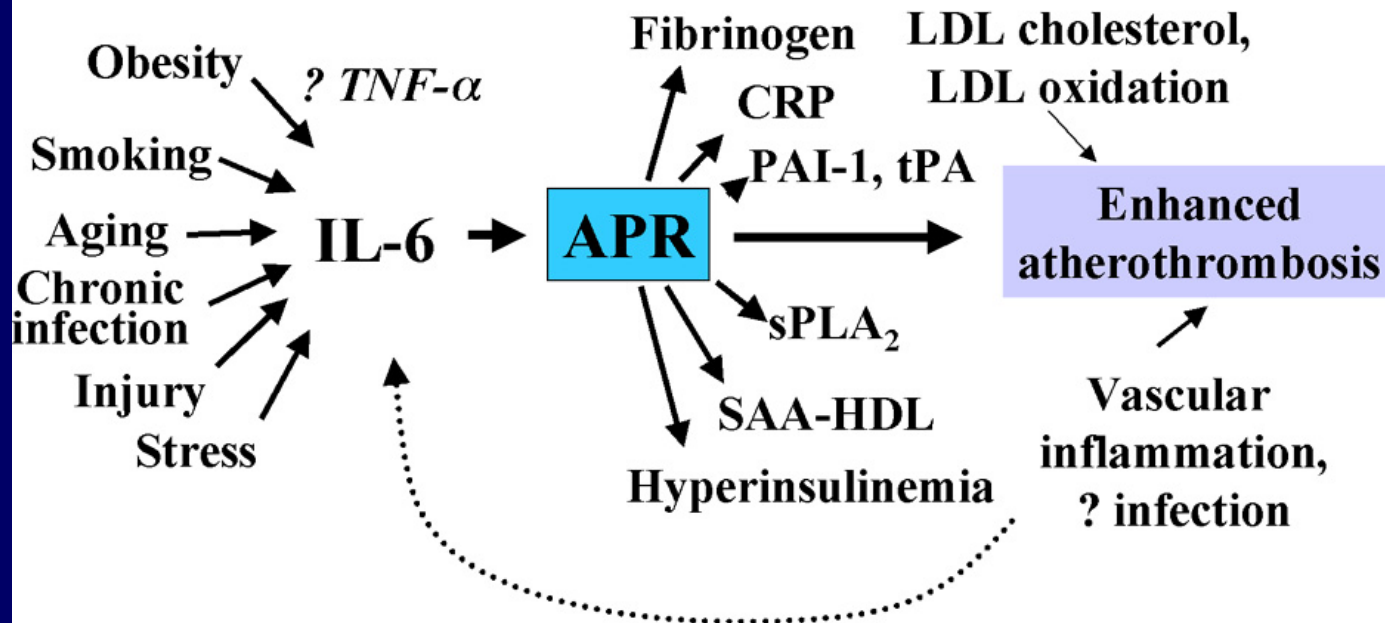
- 1- 1930: Pneumococcal c-polysaccharide
- 2- Flocculation & Purification of CRP
- 3- Pentamere with similar monomeres
- 4- Stable & Calcium-dependent
- 5- Range: 0.1mg/L at birth, 0.17 in child, 0.43-1.37 in adult (mean)
- 6- Synthesis by Liver, gene on chromosome 1
- 7- Gamma band in electrophoresis
- 8- No deficiency & No specific inhibitor (except 1,6 bisphosphocoline)







The acute phase response and atherothrombosis (hypothesis)



Traditional Risk Factors

- Tobacco Exposure
- Hypertension
- Diabetes Mellitus
- Lipid Disorders

Table 10.3 Major Risk Factors for Atherosclerosis

Nonmodifiable (Constitutional)

Genetic abnormalities
Family history
Increasing age
Male gender

Modifiable

Hyperlipidemia
Hypertension
Cigarette smoking
Diabetes
Inflammation

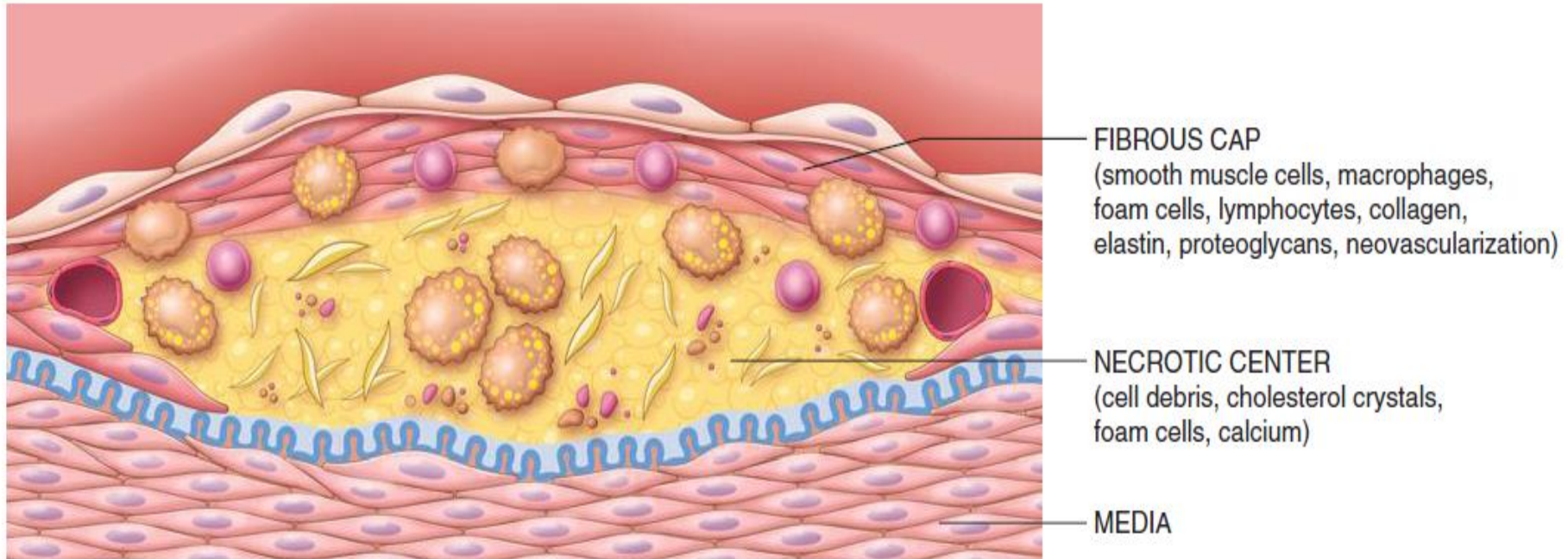
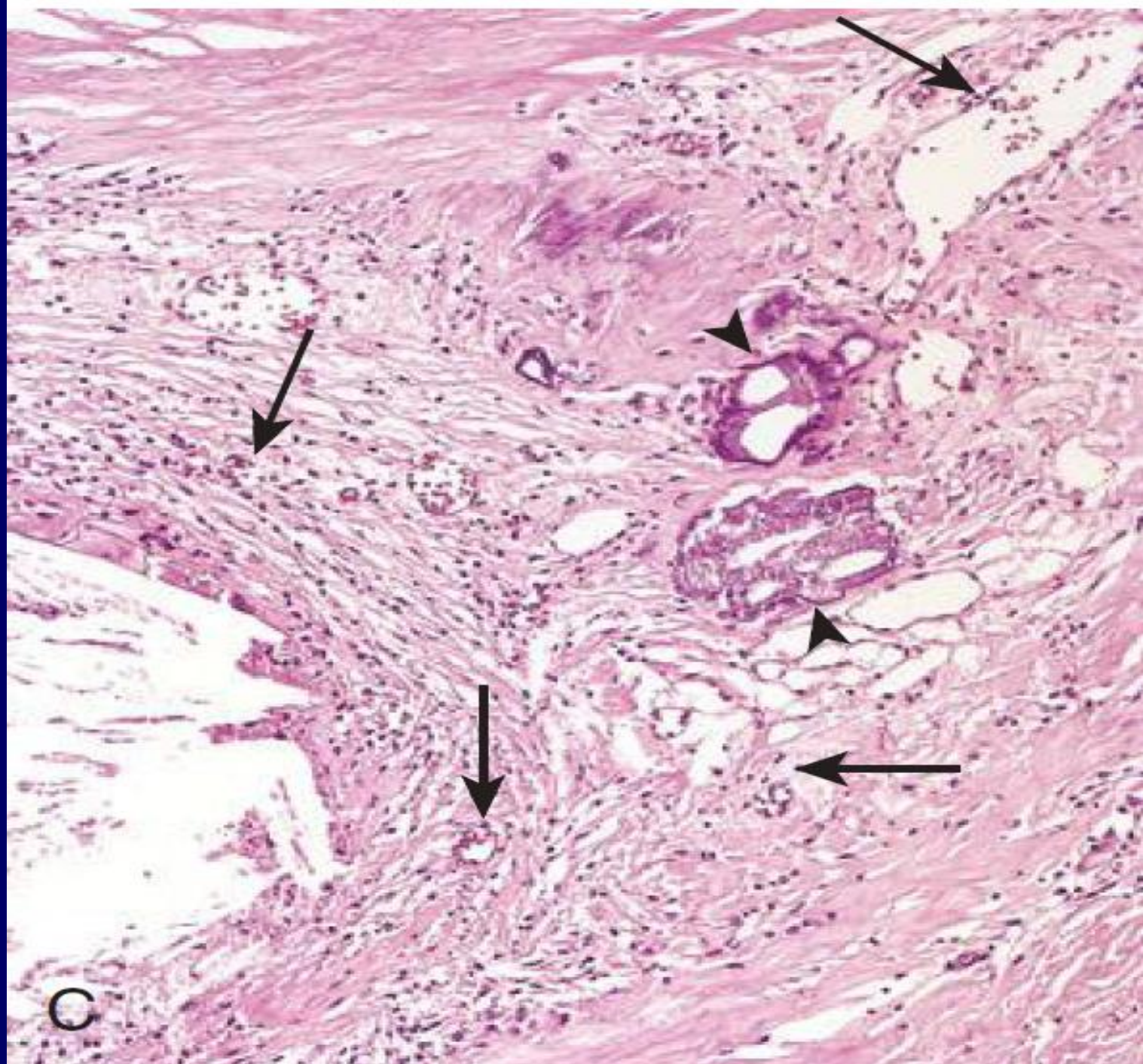
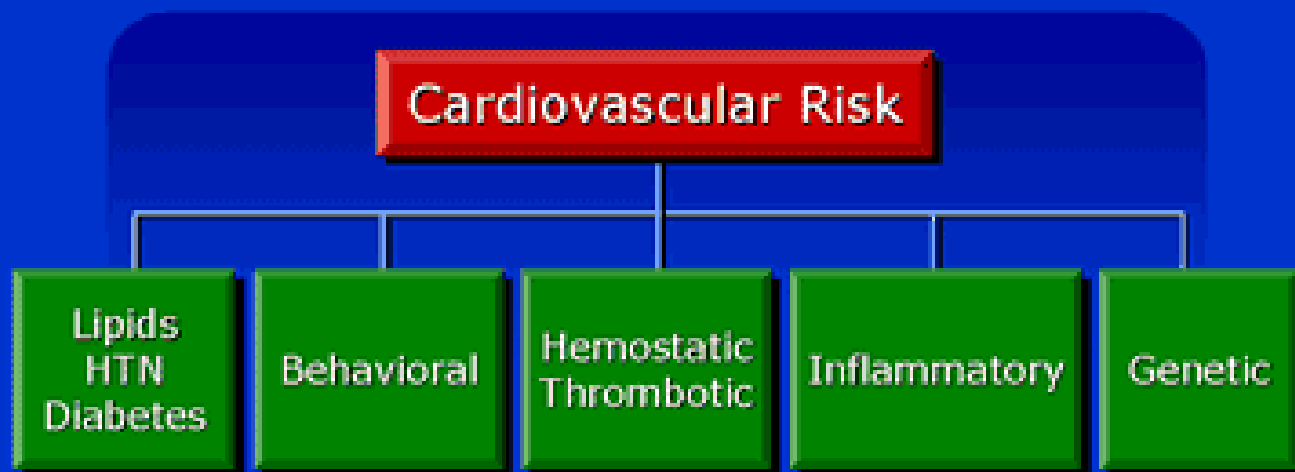


Fig. 10.7 The basic structure of an atheromatous plaque.



Beyond Cholesterol: *Predicting Cardiovascular Risk In the 21st Century*



CRP relation to ACS

- 1- Cause of ACS effect ?
- 2- Consequence of ACS effect ?
- 3- Both Cause & Consequence ?
- 4- Association ?

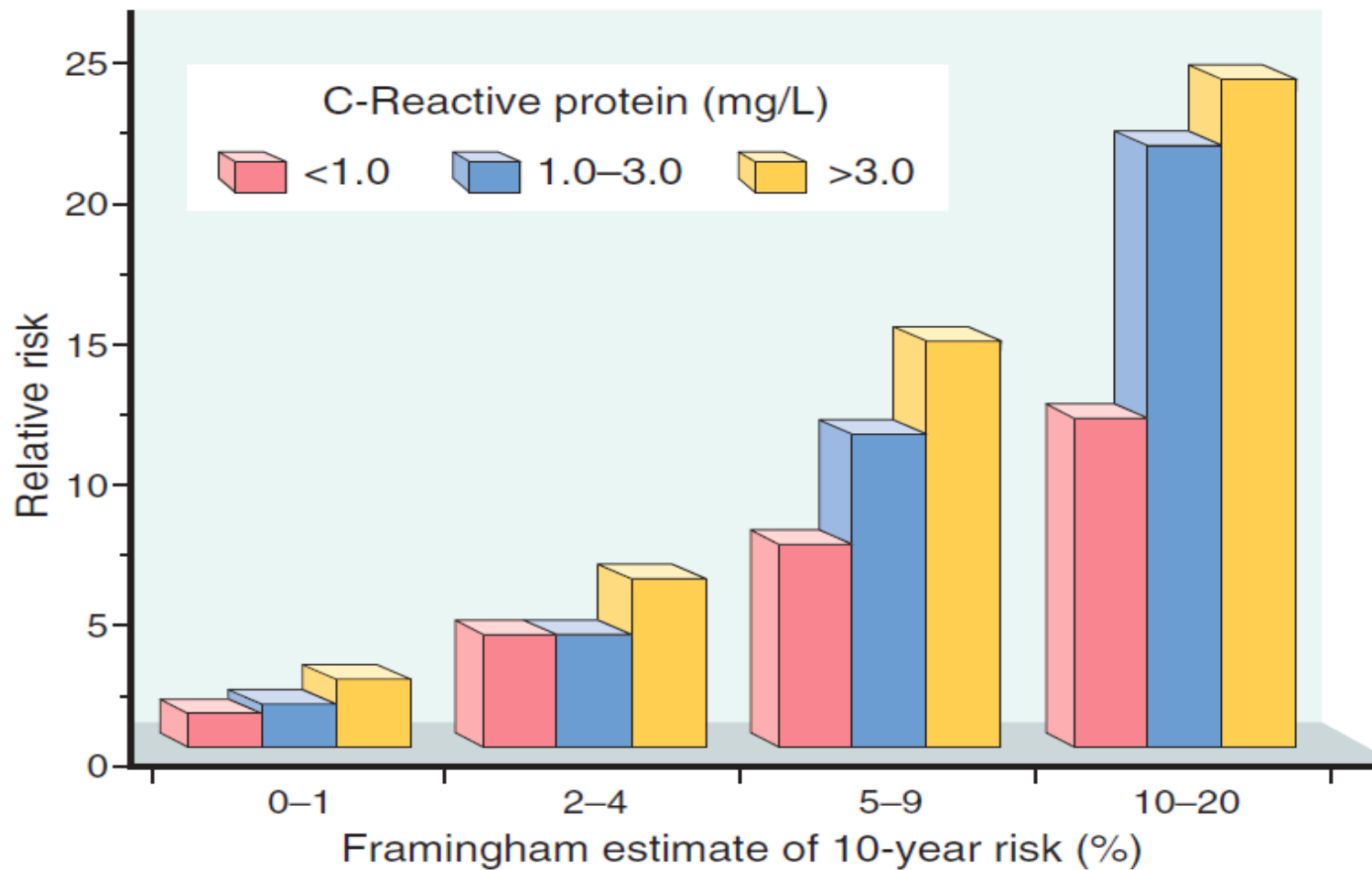


Fig. 10.9 Prognostic value of C-reactive protein (CRP) in coronary artery disease. Relative risk (y-axis) reflects the risk for a cardiovascular event (e.g., myocardial infarction). The x-axis shows the 10-year risk for a cardiovascular event calculated from the traditional risk factors identified in the Framingham Study. In each risk group, CRP levels further stratify the patients. (Data from Ridker PM, et al: Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. *N Engl J Med* 347:1557, 2002.)

CRP & ACS

1- Epidemiologic: Association

Nissen S., et al 2005: Statin on CRP

JUPITER study (17802, Rosuvastatin): LDL<130
& CRP

2- Genetic: Polymorphism (>200000), No causal effect

3- Experimental: Interspecies variation

In mice, not-related

In rat, related (Pepys, 2006)

Conclusion (Principles) of CRP

- 1- No direct causal effect
- 2- No pathophysiologic effect for circulating CRP
- 3- Innocent Bystander (marker rather than maker), with limitations
- 4- Linked to inflammation with probably better novel markers

Limitations of CRP

- 1- A single plasma CRP estimation in an individual subject has a high risk of misclassification and cannot accurately determine whether they are at future risk of atherosclerotic events
- 2- In order to reduce the intra-individual variation sufficiently, each subject is likely to require blood samples collected on multiple occasions”

Conclusion (Practice) of CRP

based on joint committee of AHA & CDC in 2003

- 1- hs-CRP should be averaged from at least two specimens drawn about 2wks apart.
- 2- CRP > 10mg/L should be discarded
- 3- Risk: <1=Low, 1-3=Intermediate, >3=High
- 4- Primary prevention: Additional information in moderate risk estimate by traditional risk factors
- 5- Secondary Prevention: not likely to change management (not recommended, but maybe revised)
- 6- Universal hs-CRP screening is not warranted

Conclusions:

The Canakinumab Anti-Inflammatory Thrombosis Outcomes Study (CANTOS)

1. Overall, CANTOS demonstrates that targeting the IL-1b to IL-6 pathway of innate immunity with canakinumab reduces cardiovascular event rates and potentially reduces rates of incident lung cancer and lung cancer mortality.
2. CANTOS thus provides critical proof-of-concept that inflammation inhibition, in the absence of lipid lowering, can improve atherothrombotic outcomes. It has been uncertain, however, if there are patient groups where the benefits of treatment clearly outweigh potential hazards.
3. The current analysis suggests that the magnitude of hsCRP reduction following a single dose of canakinumab may provide a simple clinical method to identify individuals most likely to accrue the largest cardiovascular and cancer benefits from continued treatment.

Perspective

- 1- In-situ studies in atheromatous plaque
- 2- CRP monomere: insoluble & neoantigen
- 3- Other markers of inflammation: IL-1, IL-6, TNF- α & Serum Amyloid A
- 4- CRP & Other disorders (Stroke, ...)