Pathophysiology of Acute Coronary Syndrome

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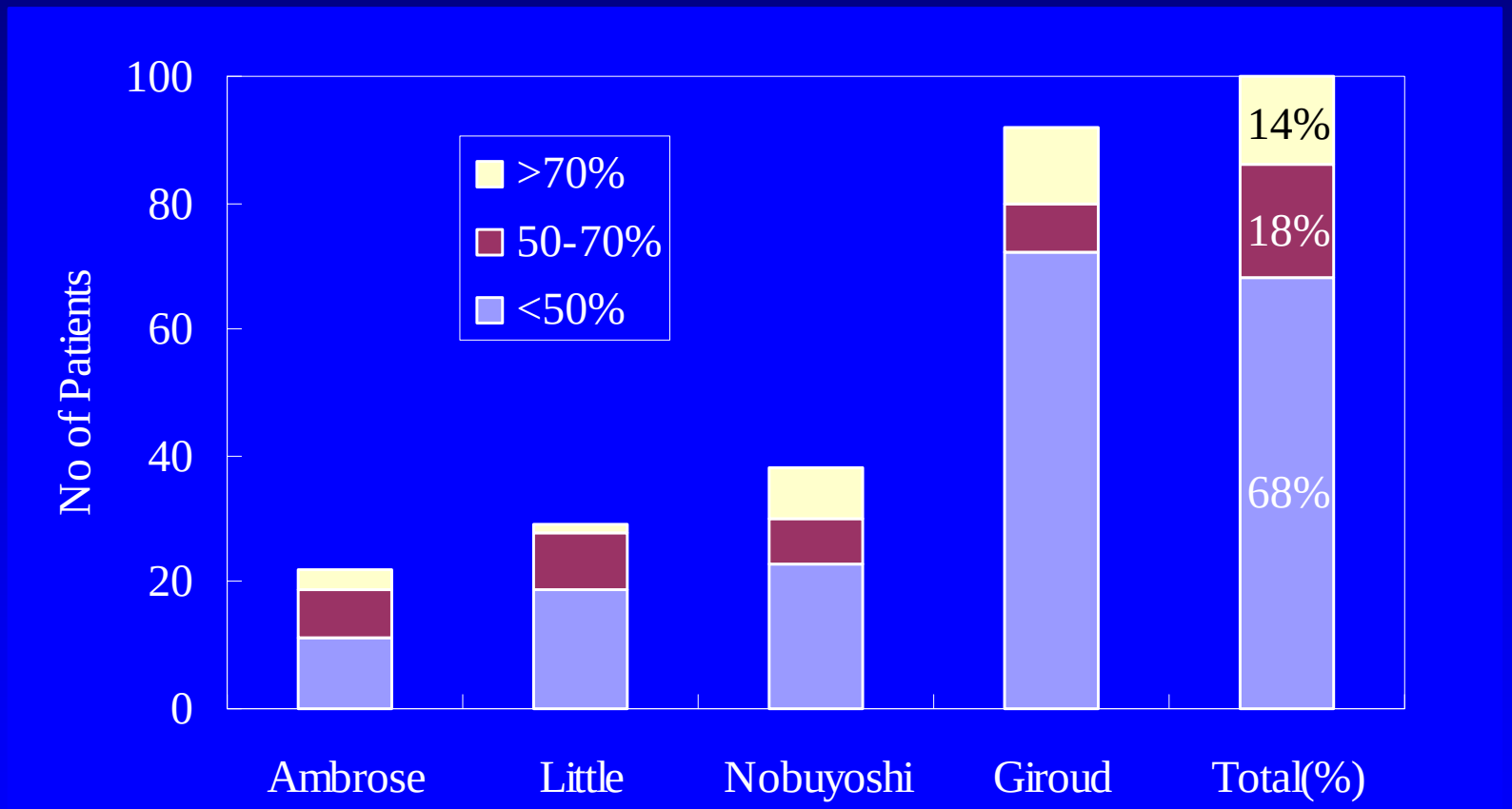
김 치 정

Summary of Angiographic Evolution in Acute Coronary Syndrome

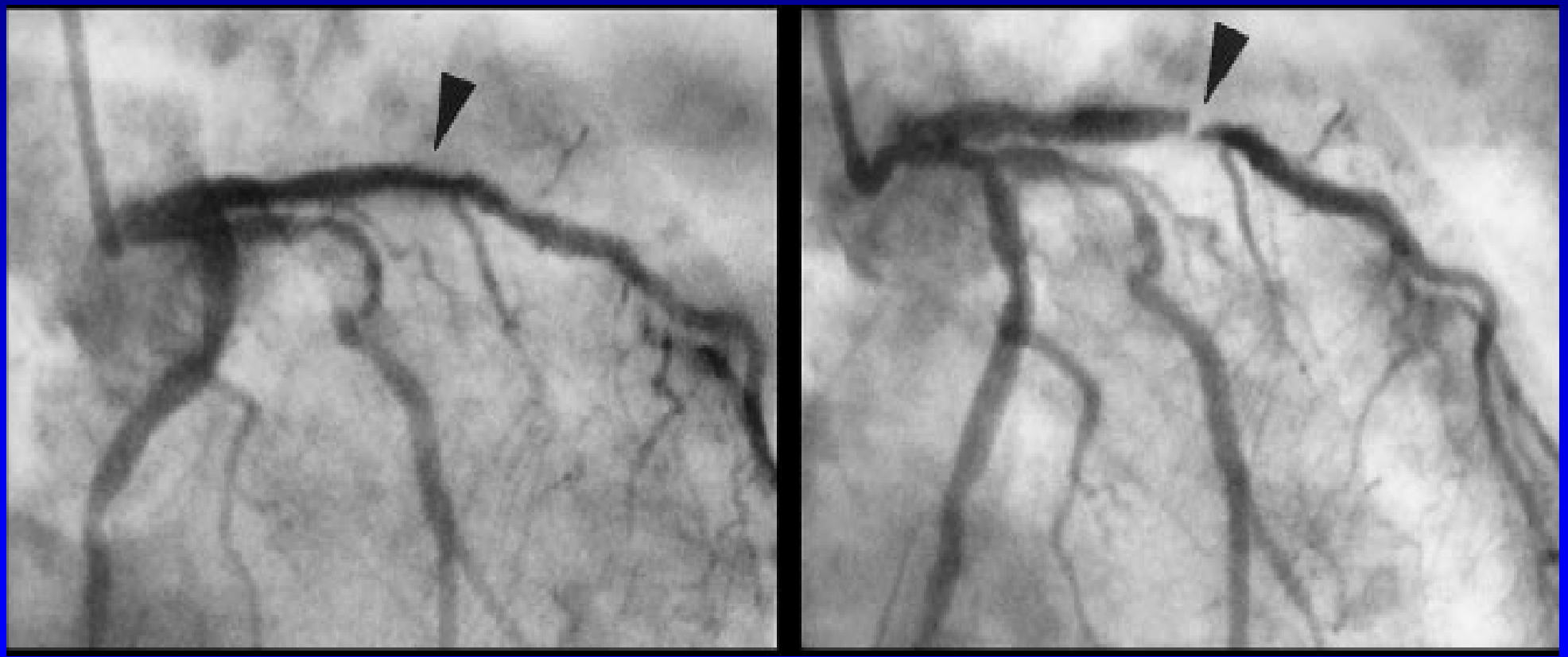


Falk. Circulation 1995;92:657-71

Progression of Coronary Artery Lesions

Yokoya. Circulation. 1999;100:903

Progression of Coronary Artery Lesions

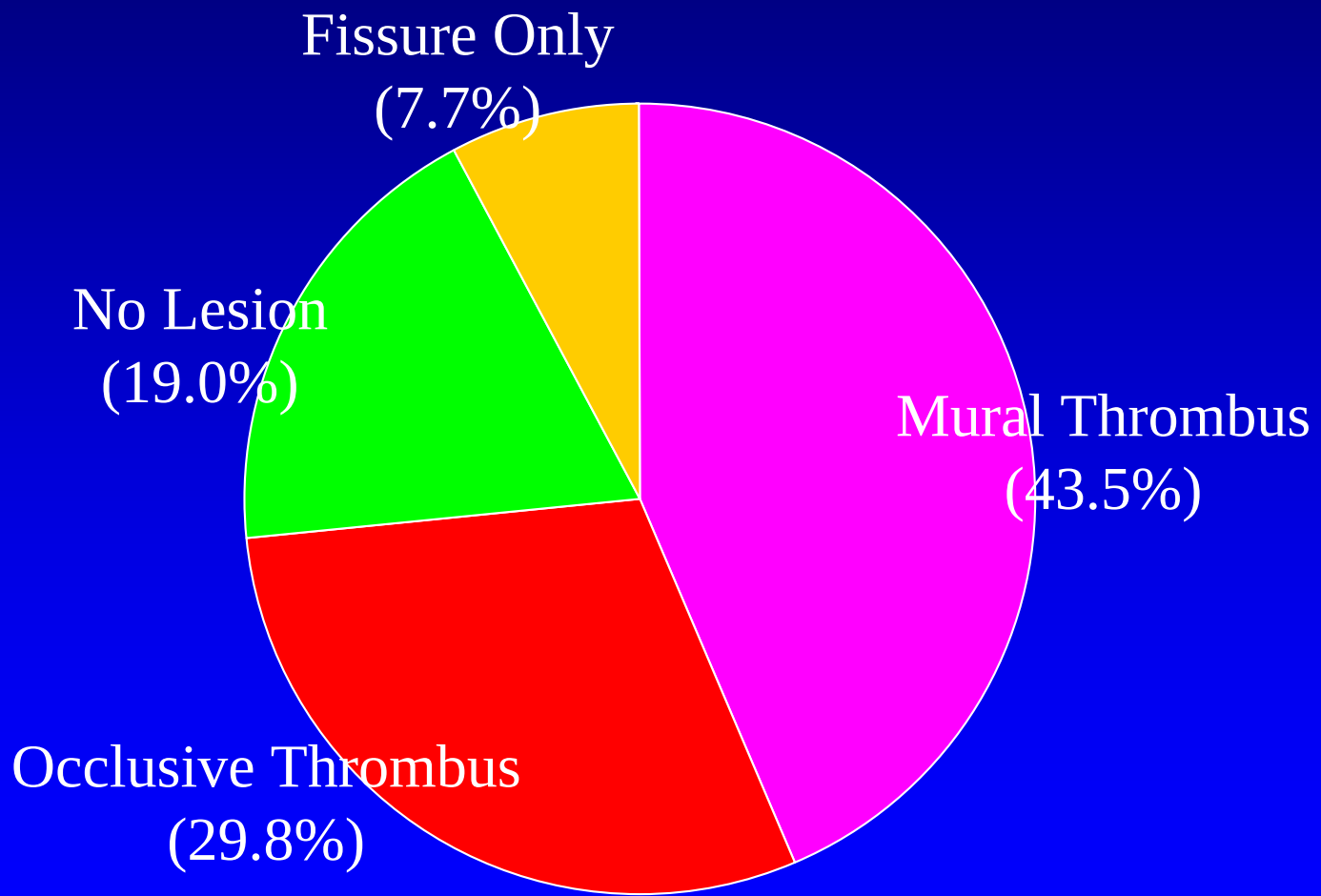


Yokoya. Circulation. 1999;100:903

Frequency of Plaque Rupture in Acute Coronary Syndrome

Author	Rupture/Total Cases	Percent
Horie(1978)	69/76	91%
Falk(1983)	40/49	82%
Davies(1984)	67/74	90%
Forrester(1987)	22/23	95%
Davies(1992)	123/168	73%
Farb(1996)	28/50	56%
Virmani(2000)	74/125	59%

Thrombosis in Sudden Cardiac Death



Pathogenesis of Acute Coronary Syndrome

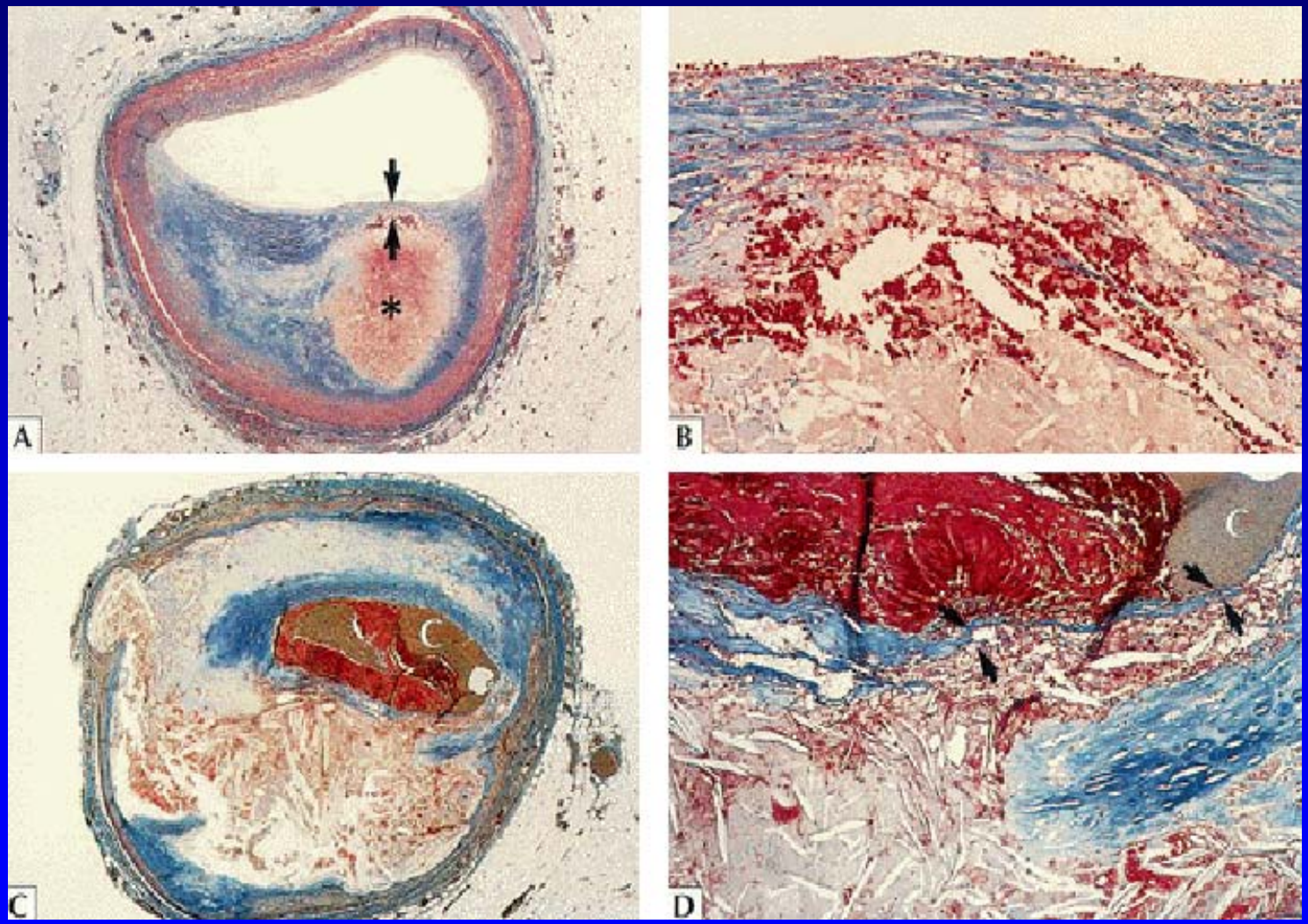
- Rupture, erosion or fissuring of atheromatous plaque
- Exposure of procoagulants
- Platelet adhesion and aggregation
- Thrombus formation
- Narrowing or occlusion of lumen

* Spasm, Intramural hemorrhage, Embolism

Characteristics of Ruptured Plaque
-Unstable or Vulnerable Plaque-

- Thin fibrous cap
  * Less smooth muscle cells - apoptosis
  * Low matrix and collagen - less production & more degradation by high MMP and low TIMP
- Large lipid pool
- Numerous macrophages and foam cells
- More remodeling
- Neovascularization

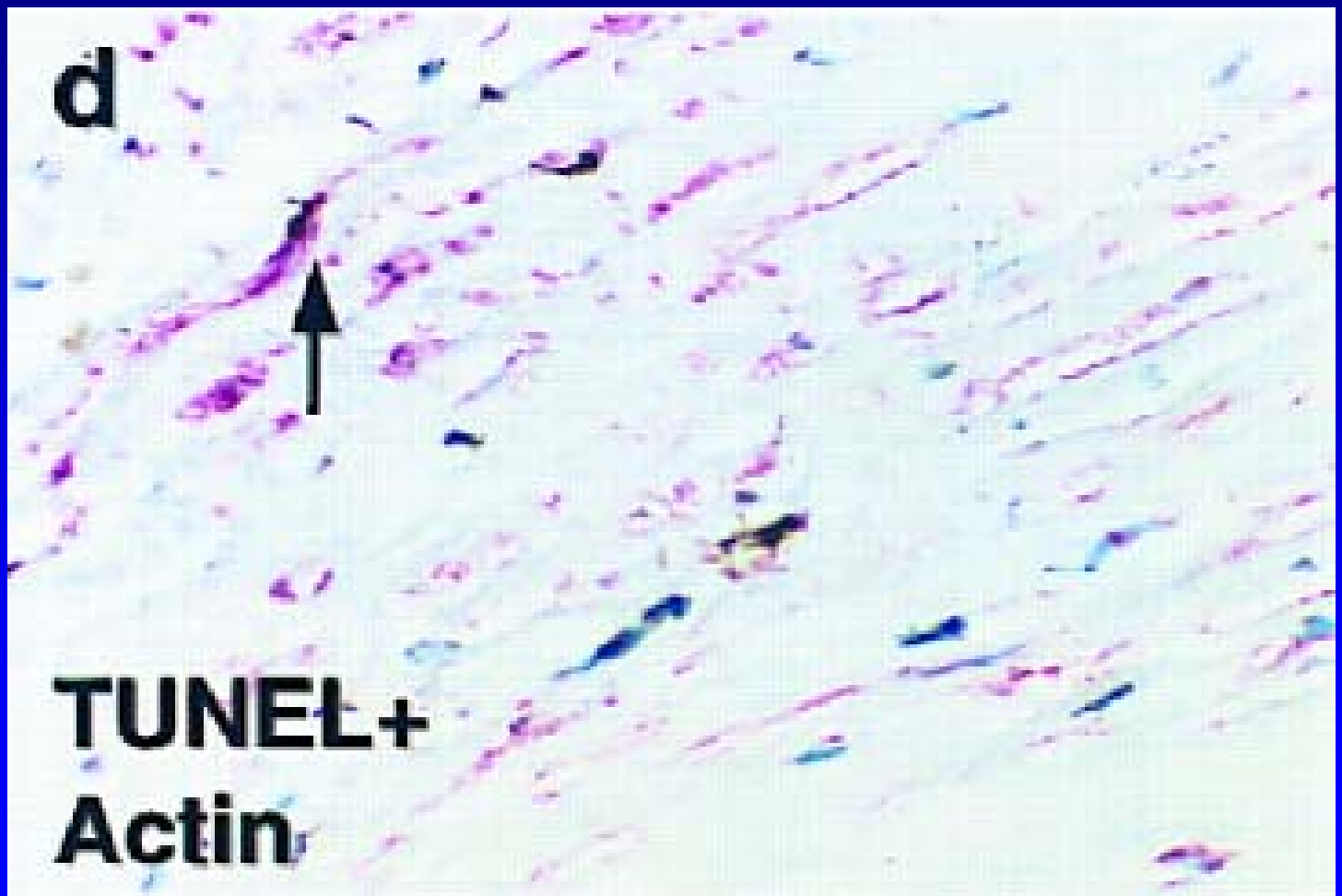
Unstable Atheroma and Thrombosis with Rupture



Falk. Circulation 1995;92:657-71

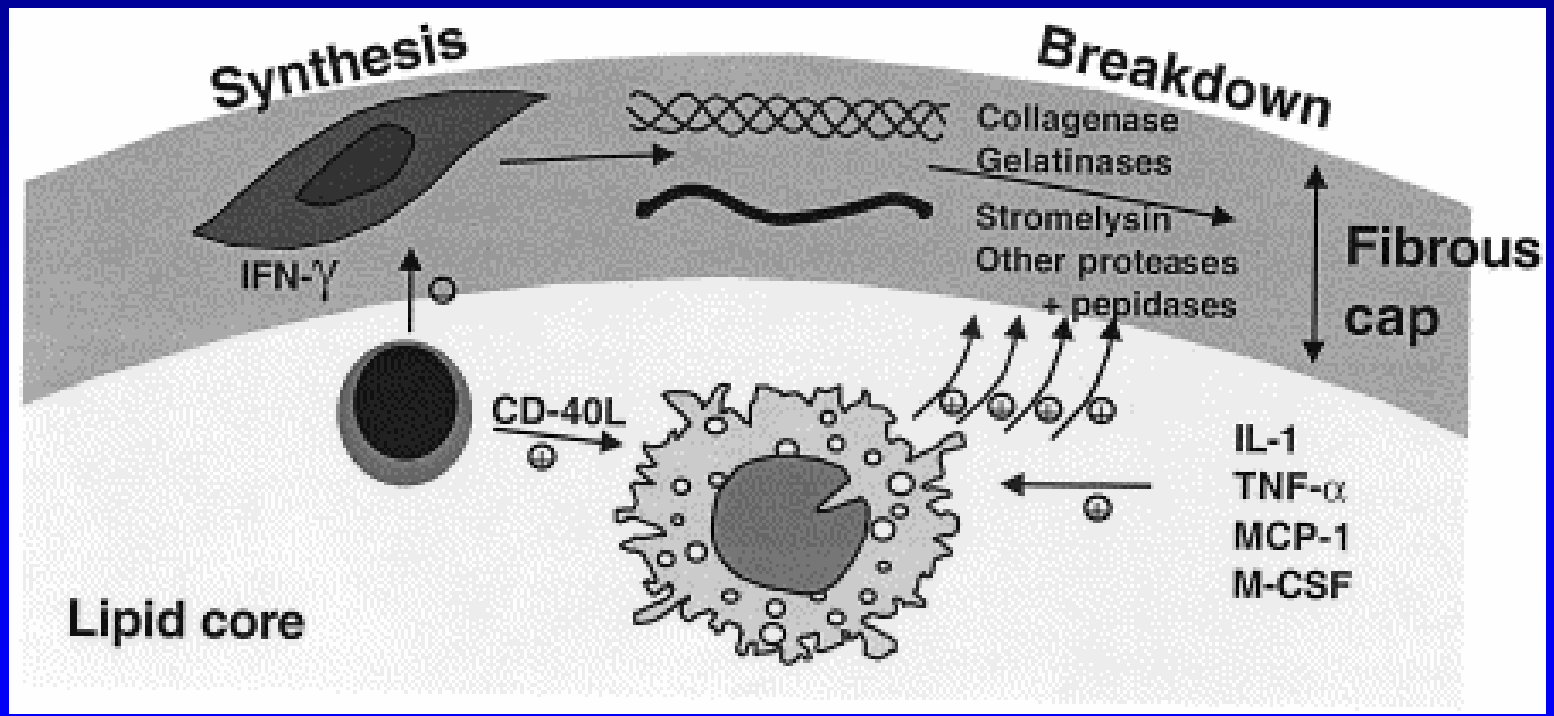
Apoptosis of SMC in Atherosclerosis

-Carotid Endarterectomy-



Geng. ATVD1997;17:2200

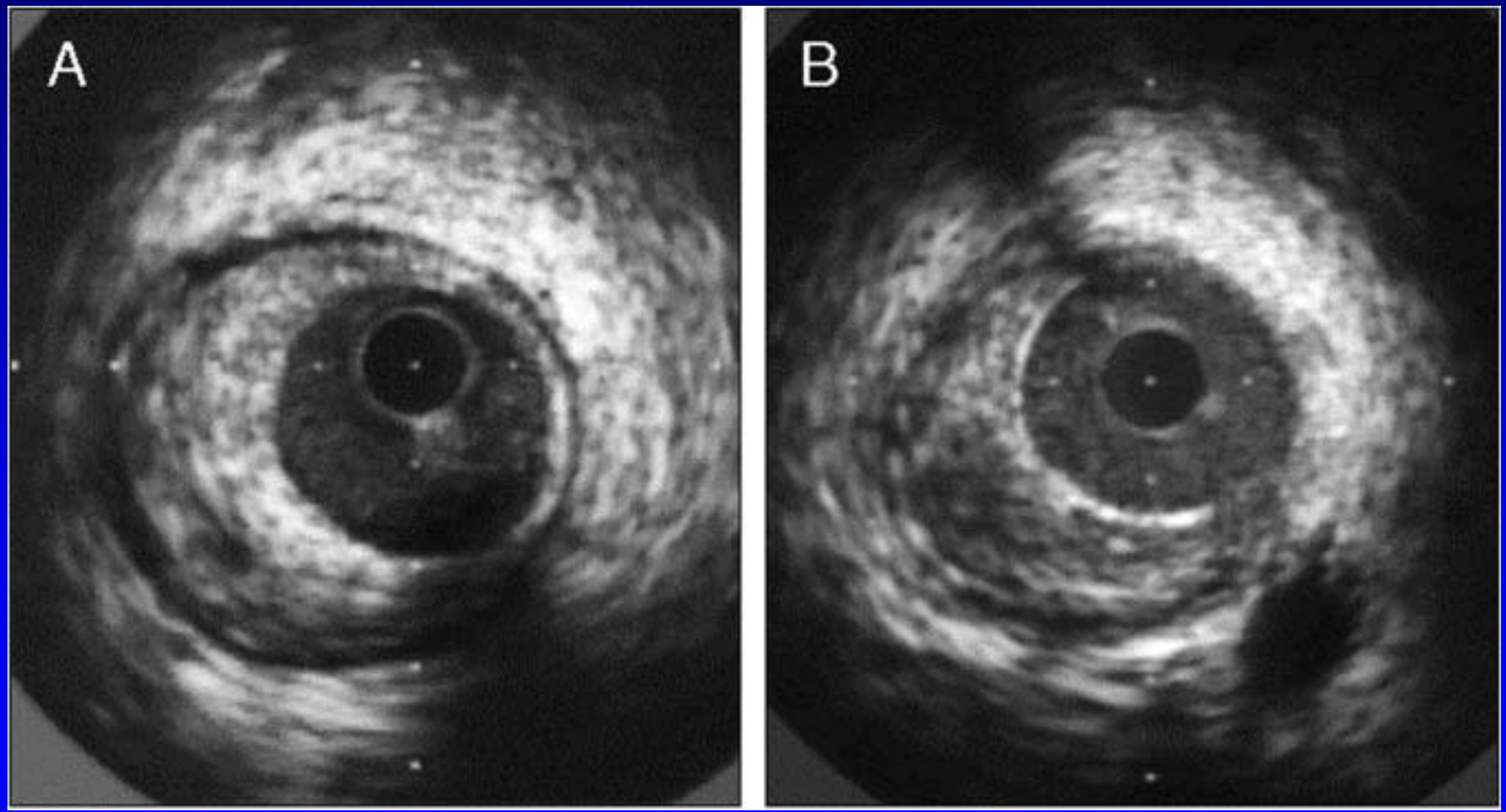
Regulation of Collagen Amount in Atheroma



Libby. Circulation 1995;91:2844-50

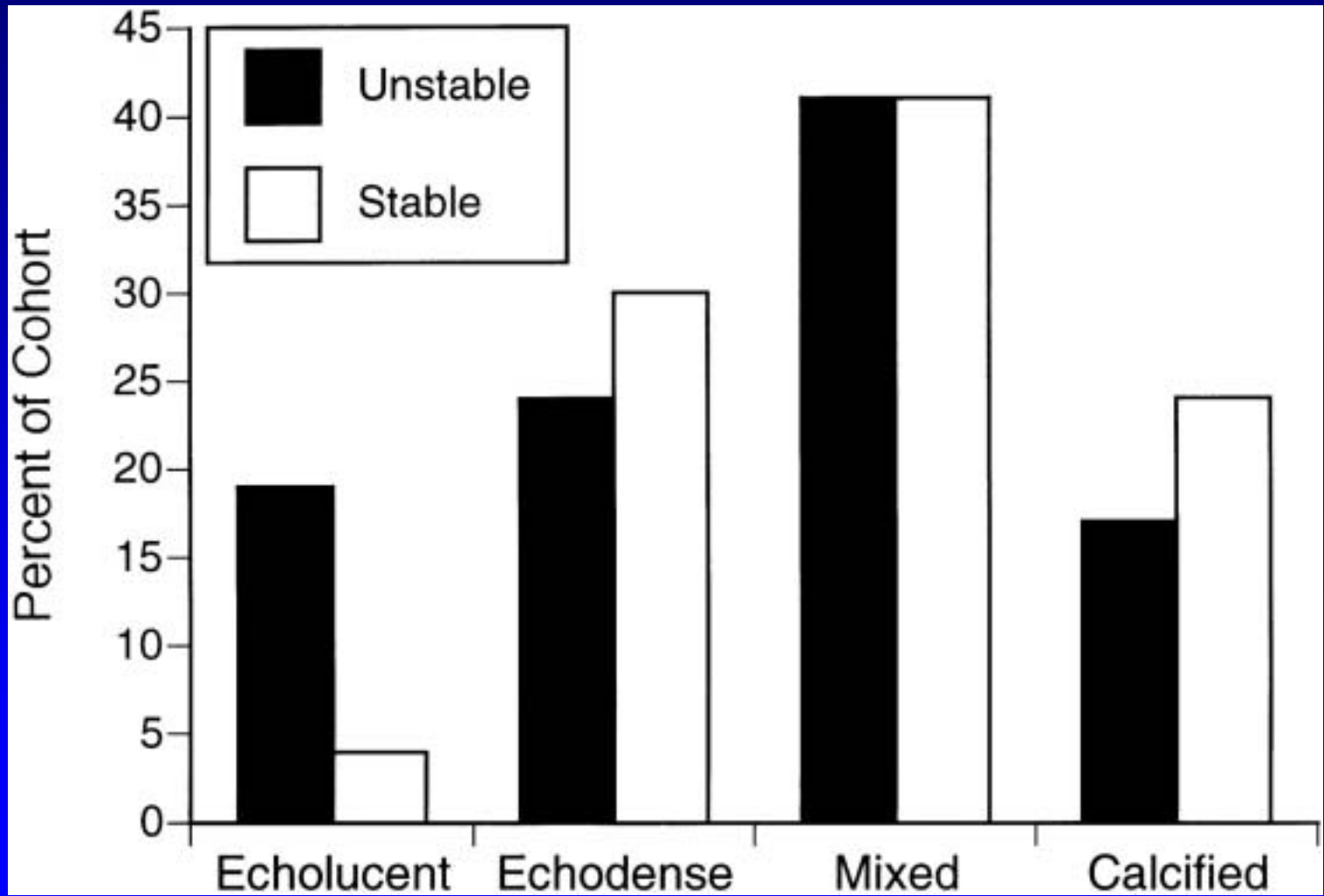
Stable and Unstable Plaque

-IVUS -



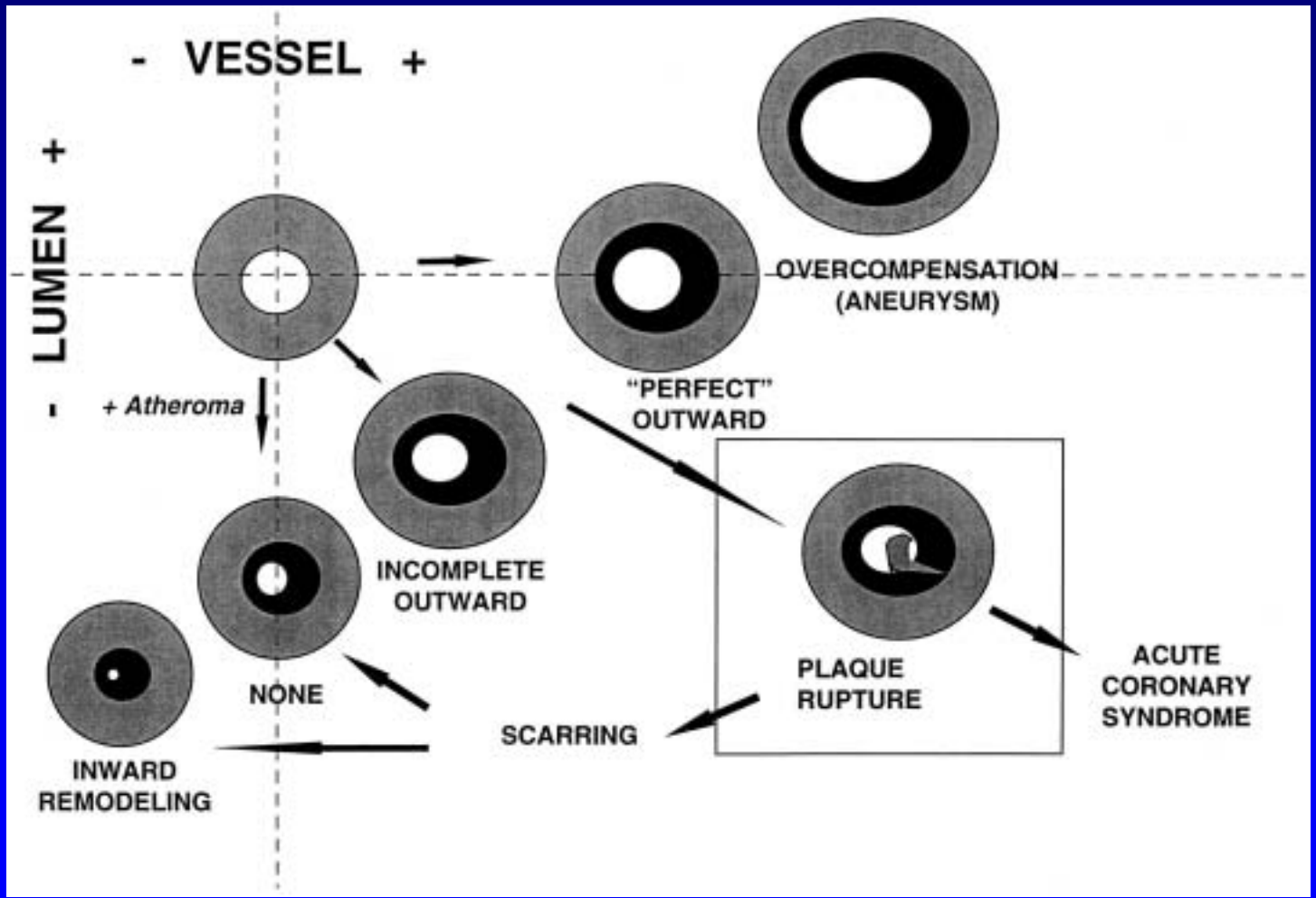
Nissen. Circulation 2001;103:604

Plaque Morphology in Unstable and Stable Angina
-IVUS-



Schoenhagen. Circulation 2000;101:598

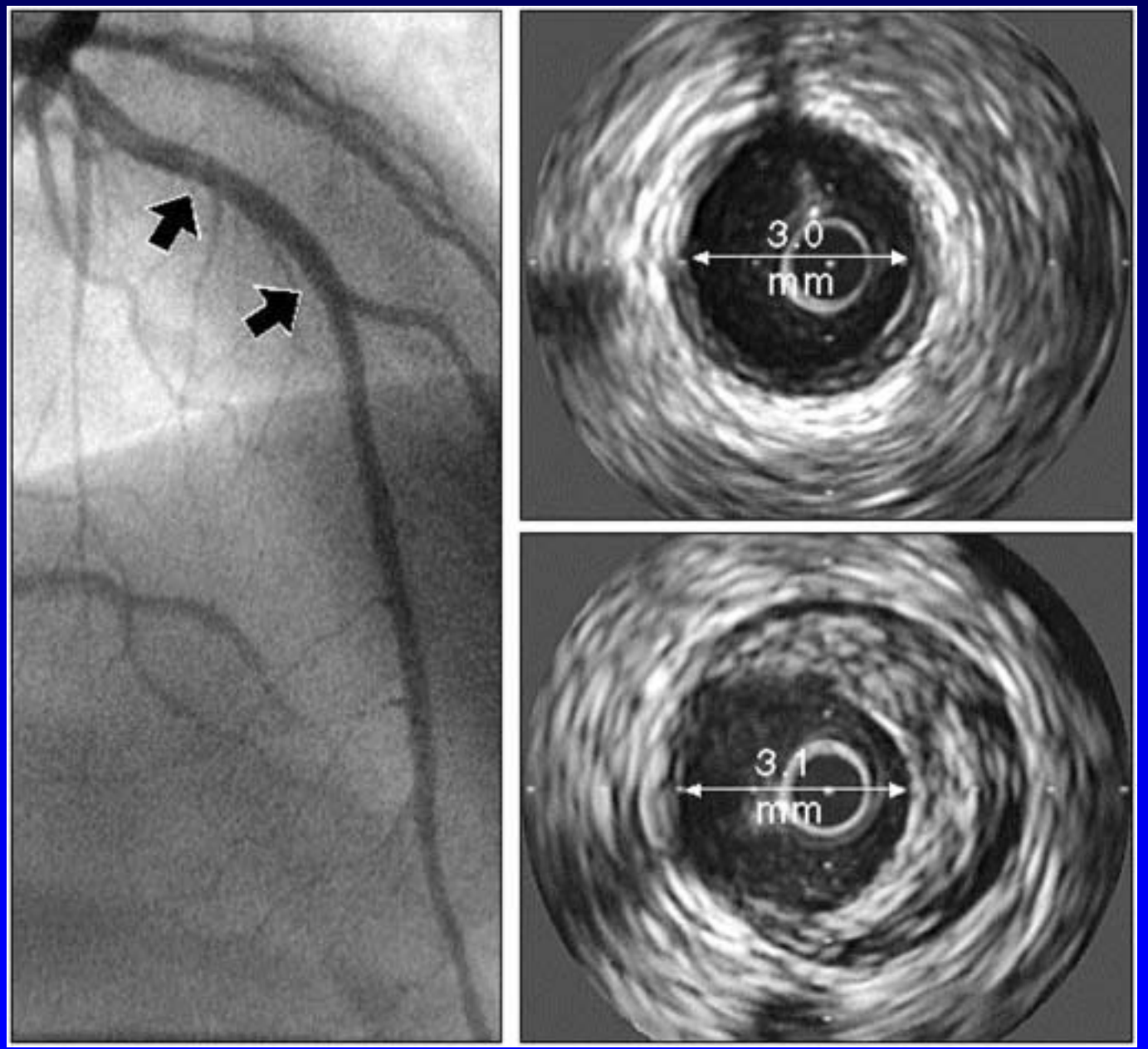
Scheme of Remodeling



Ward. Circulation 2000;102:1186

Positive Remodeling

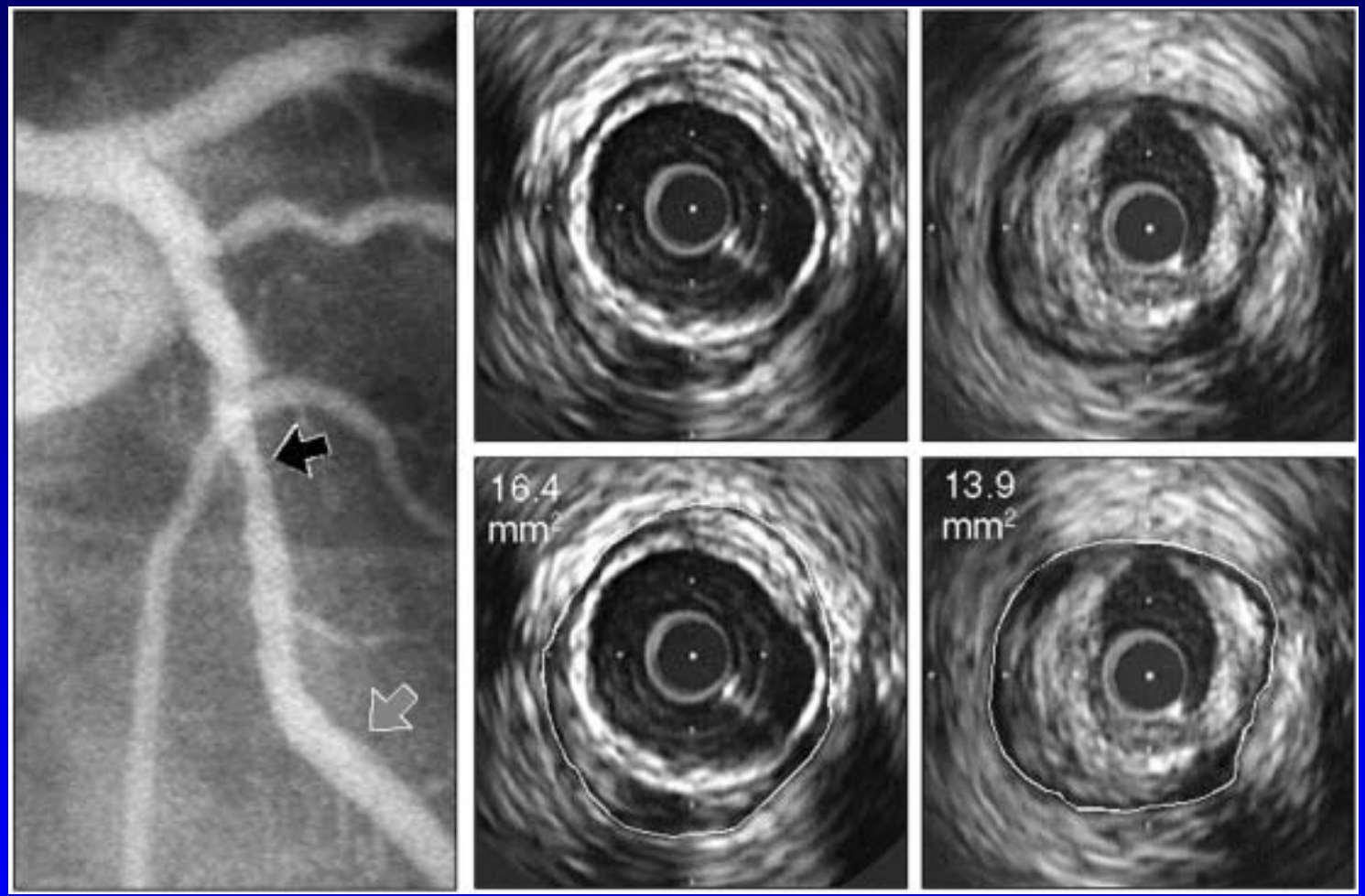
CAG vs IVUS



Nissen. Circulation 2001;103:604

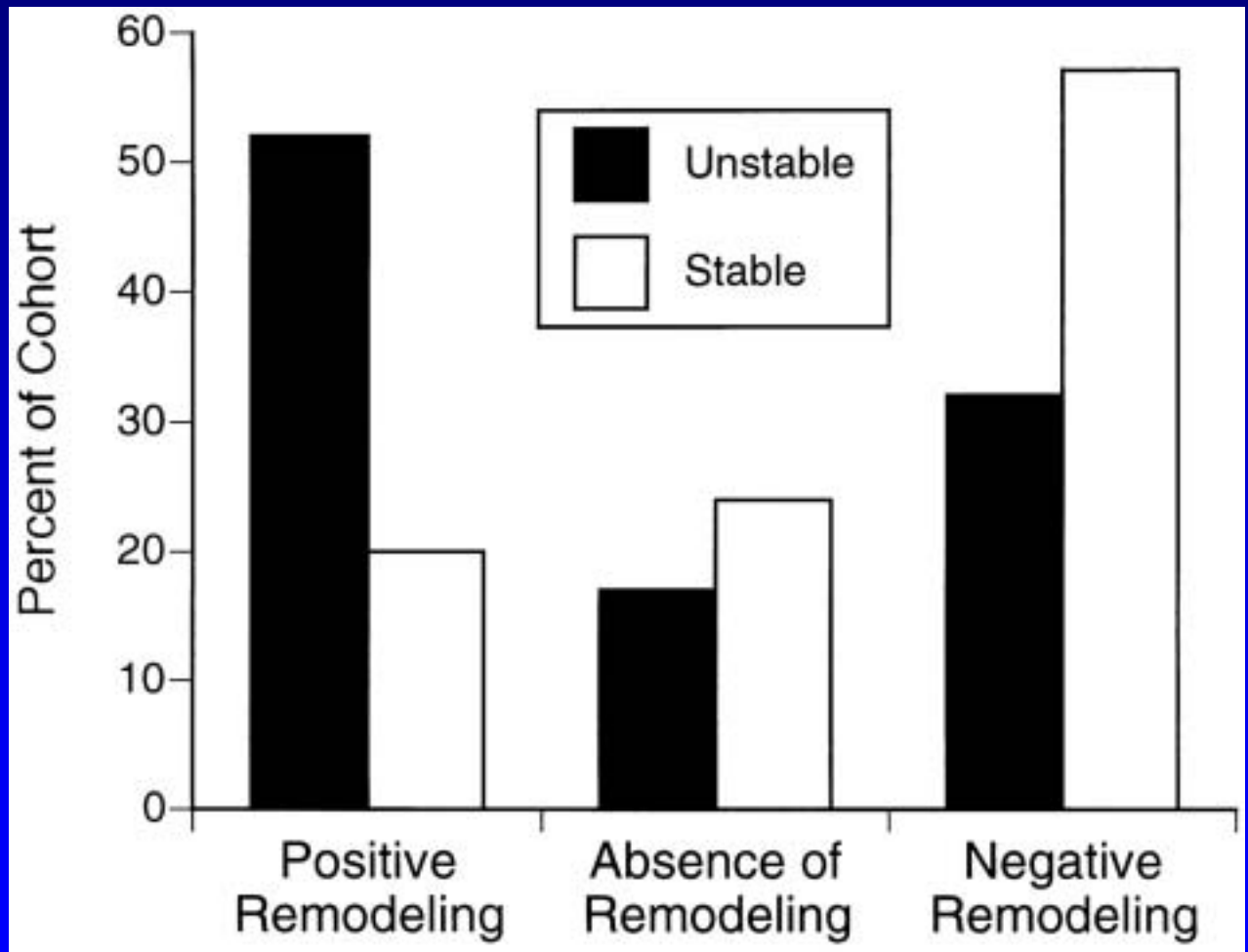
Negative Remodeling

CAG vs IVUS



Nissen. Circulation 2001;103:604

Comparison of Remodeling between Unstable and Stable Angina



Schoenhagen. Circulation 2000;101:598

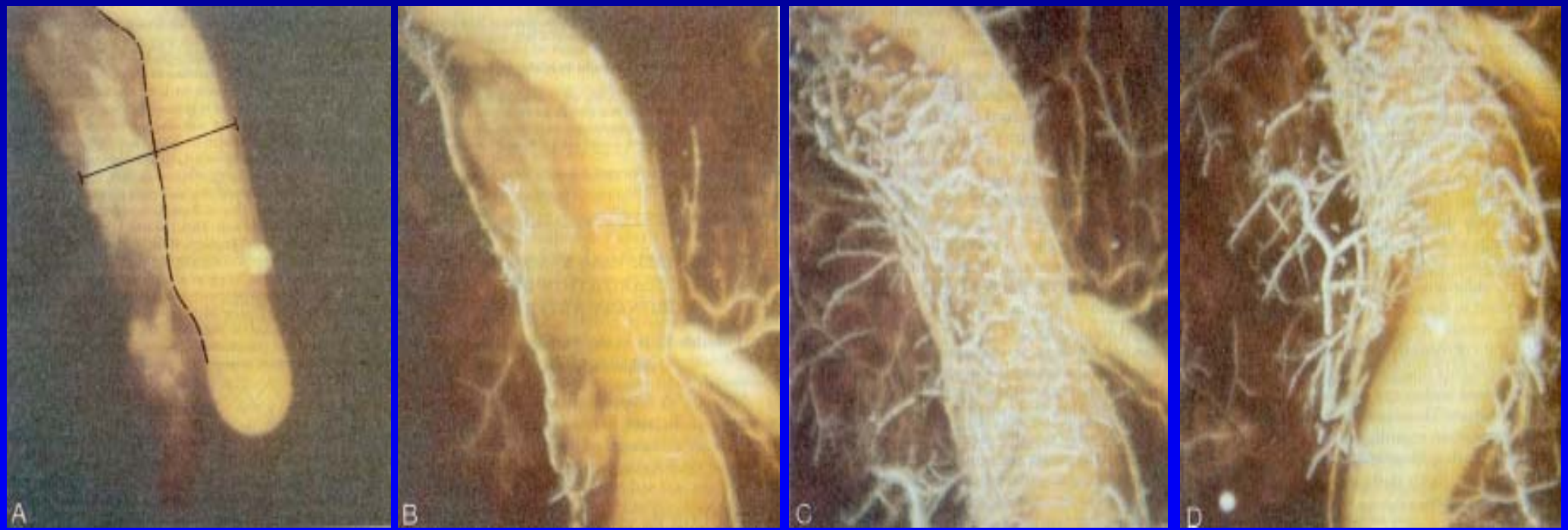
Effect of Local Stress on Rupture

- Circumferential wall stress (σ)

  = Pressure (P) X Radium (r) / Wall thickness (h)

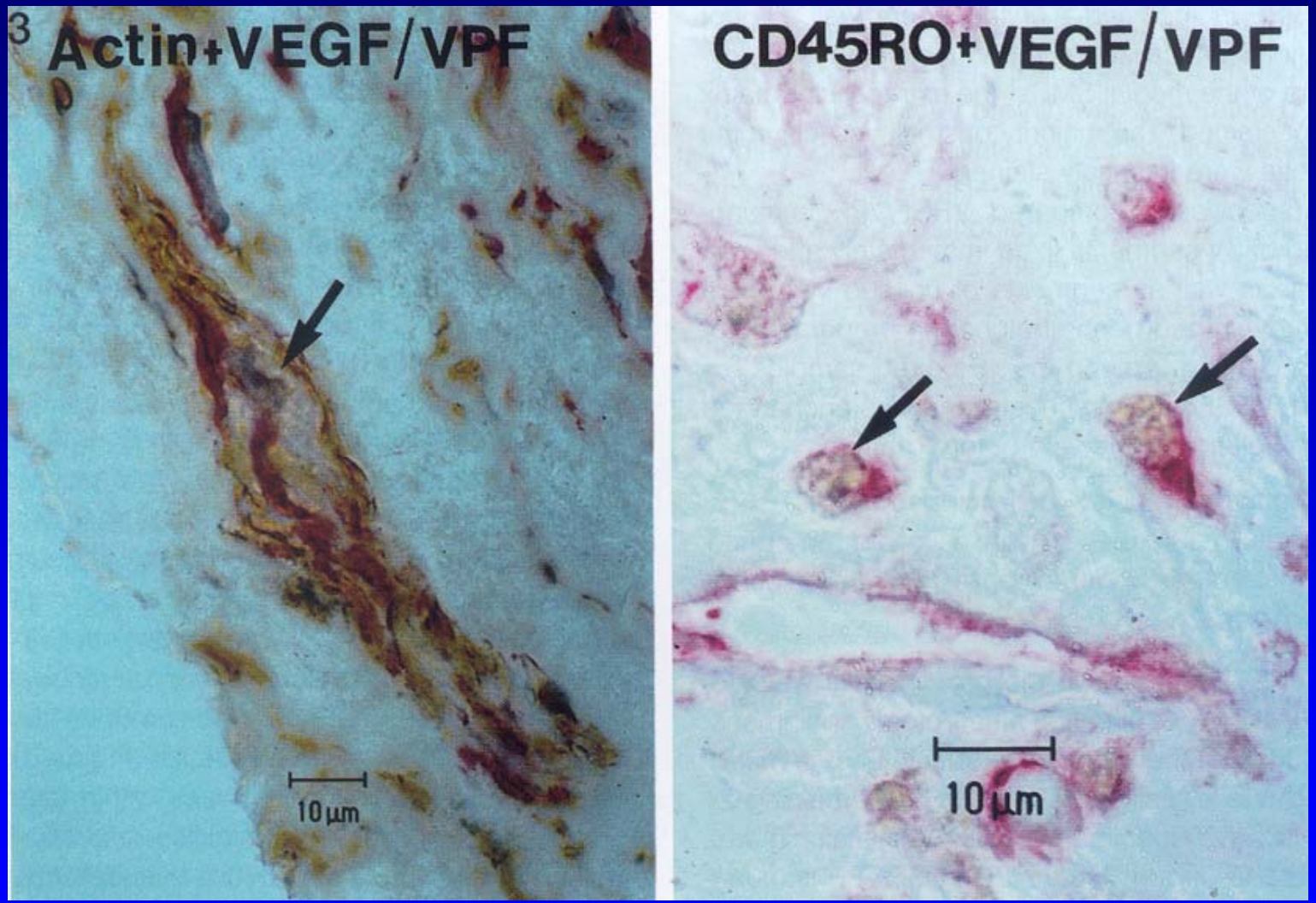
- Structural configuration of plaque
  - Thin fibrous cap and soft lipid core displaces the stress to the overlying fibrous cap and more particularly to the lateral edge.

Vasa Vasorum in Atherosclerotic Plaque of Human Coronary Artery



Barger NEJM 1984;310:175

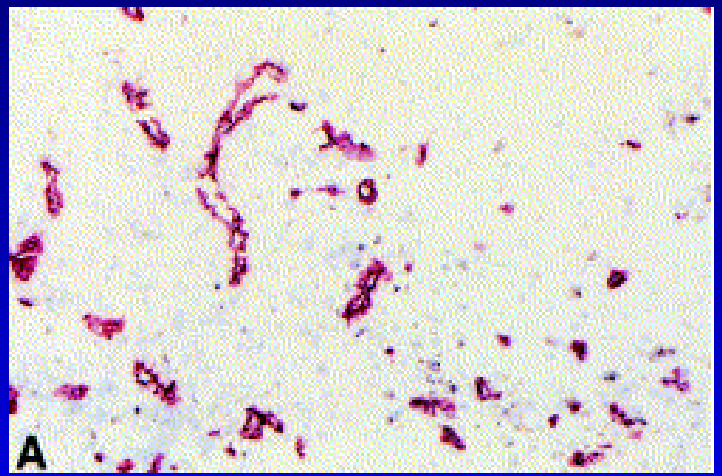
Expression of VEGF in Atheosclerotic Plaque



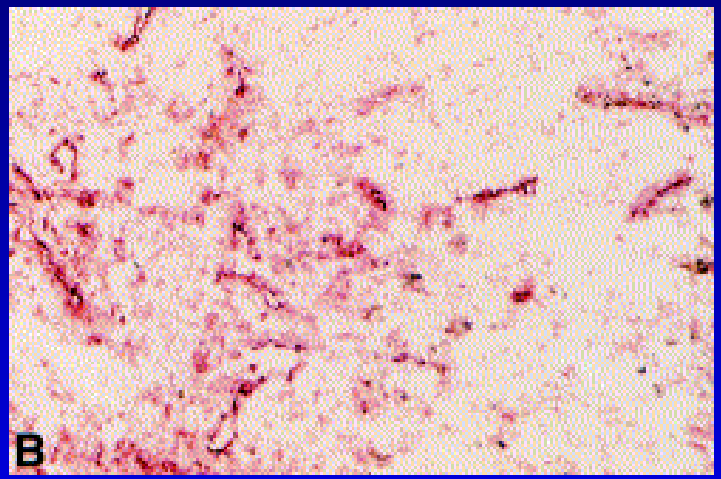
Couffinhal AJC 1997;150:1673

Expression of Adhesion Molecules in Vessels of Atheosclerotic Plaque

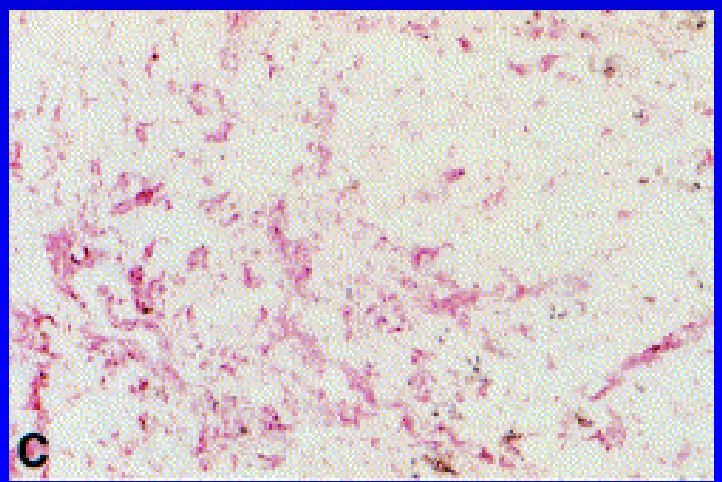
EC



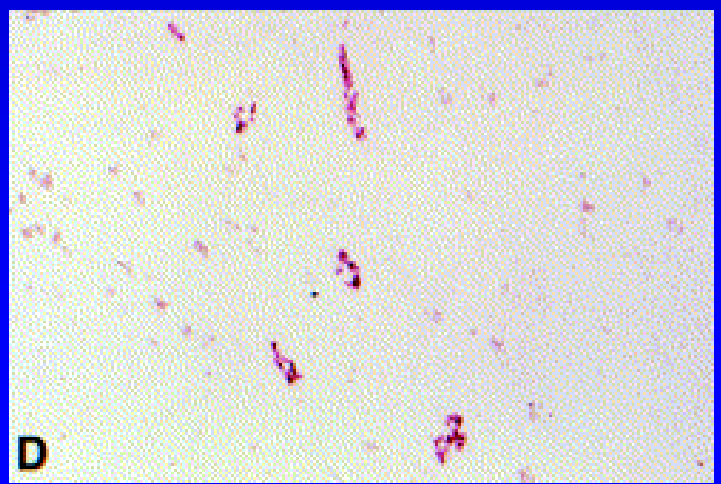
ICAM-1



VCAM-1

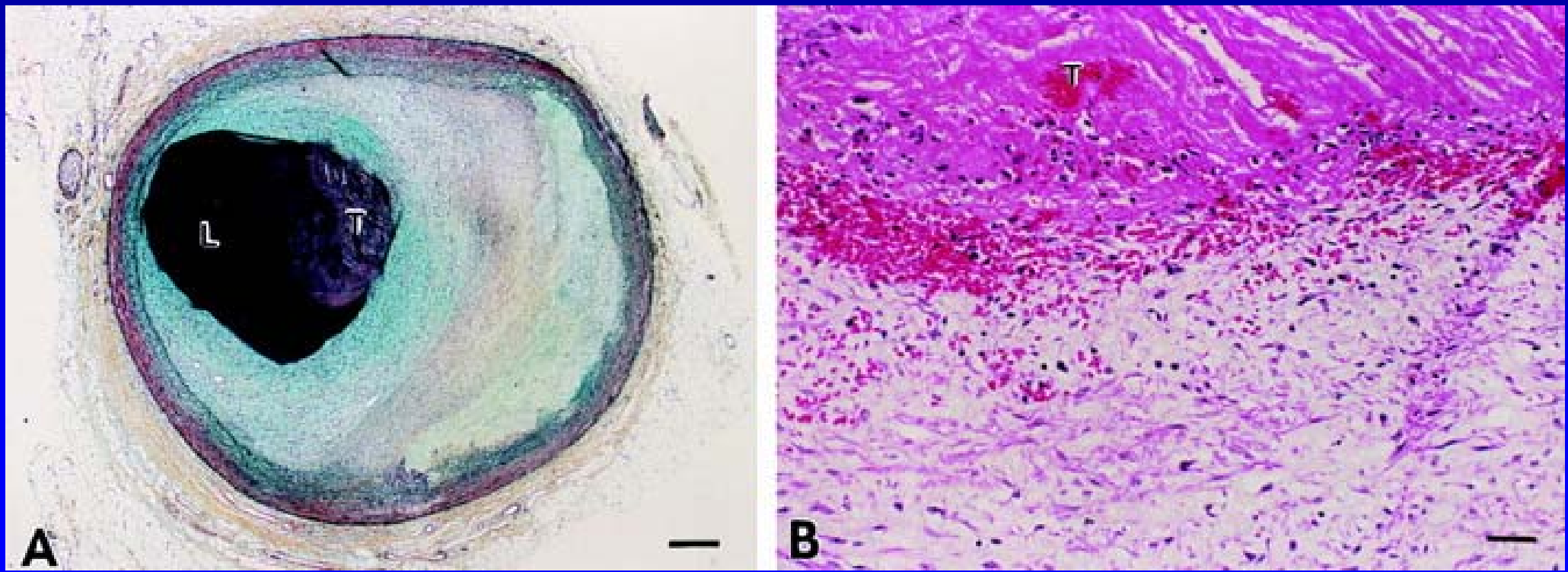


E-selectin



deBore CV Res 1999;41:443

Plaque Erosion and Thrombosis



Comparison between Ruptured and Eroded Plaques in SCD Patients

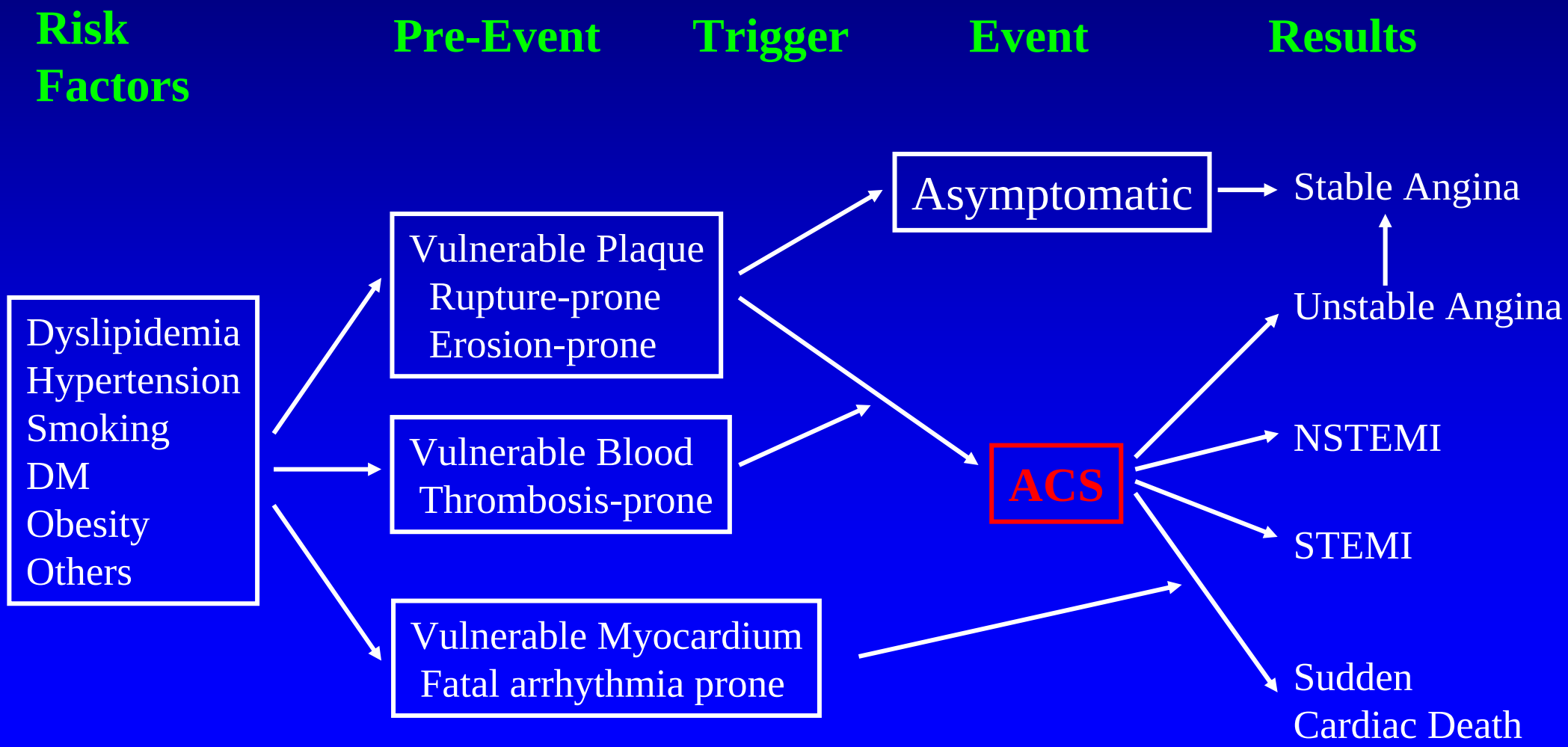
	Rupture (n=28)	Erosion (n=22)	P
Male:female	23:5	11:11	.03
Age, y	53±10	44±7	<.02
% Stenosis	78±12	70±11	<.03
Calcified plaque	19 (69)	5 (23)	.002
Occlusive thrombus	12 (43)	4 (18)	.08
Concentric	13 (46)	4 (18)	.07
Macrophages	28 (100)	11 (50)	<.0001
T cells	21 (75)	7 (32)	<.004
Smooth muscle cells	11 (33)	21 (95)	<.0001
HLA-DR positive	25 (89)	8 (36)	.0002

Farb. Circulation. 1996;93:1354

Healed Plaque Erosion & Rupture

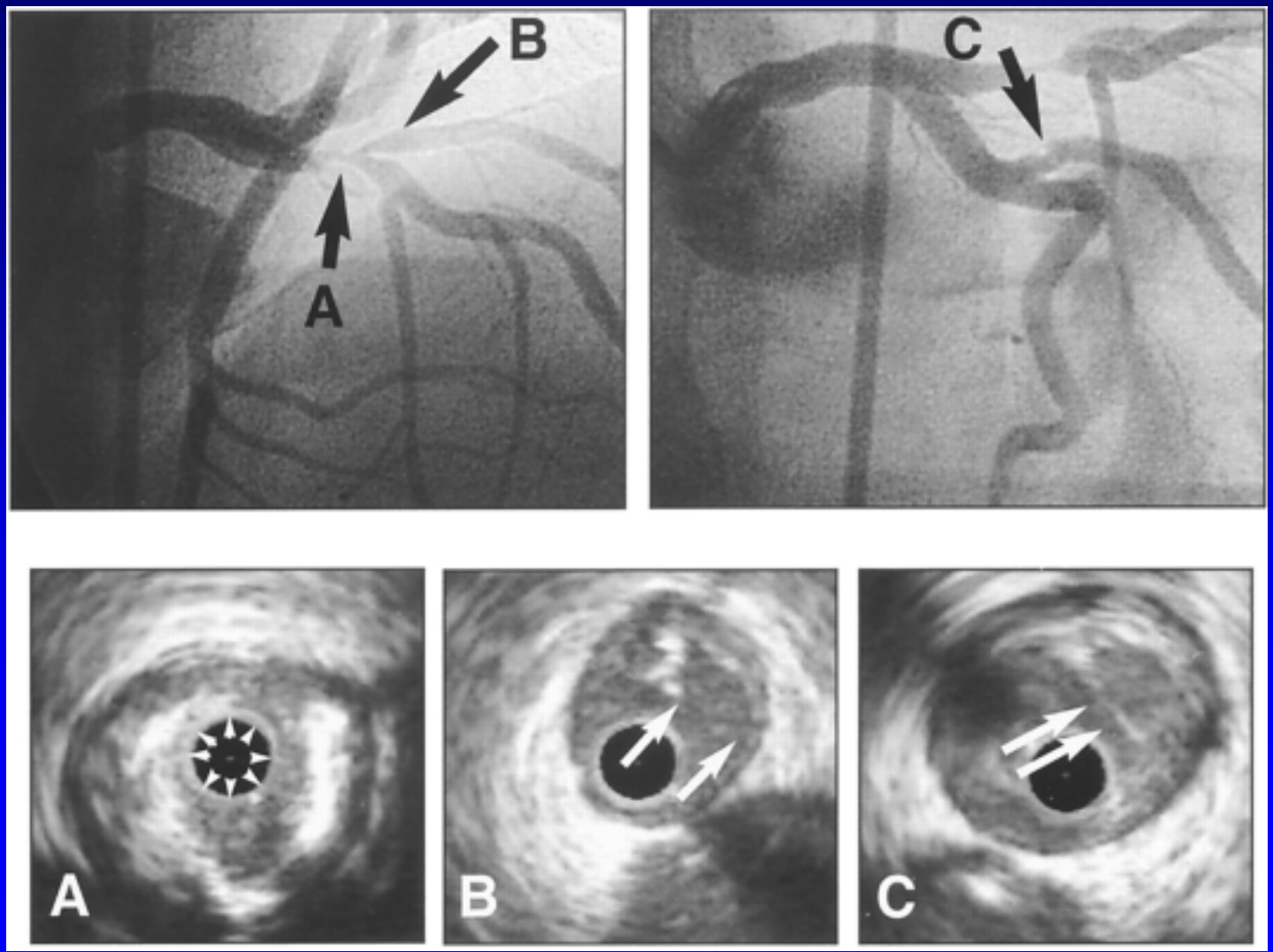
Virmani. ATVD 2000;20:1262

Progression of CAD



Unstable Plaque in Insignificant Areas in CAG

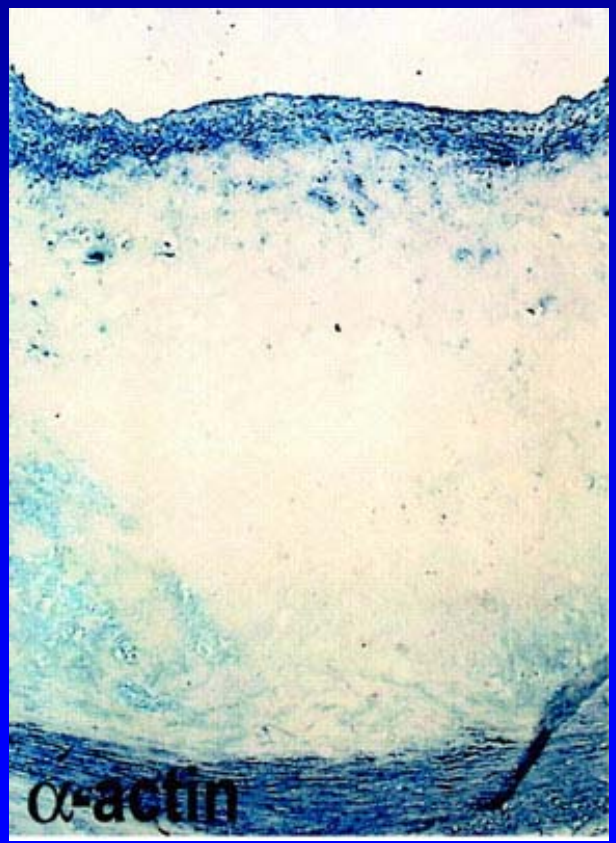
-IVUS-



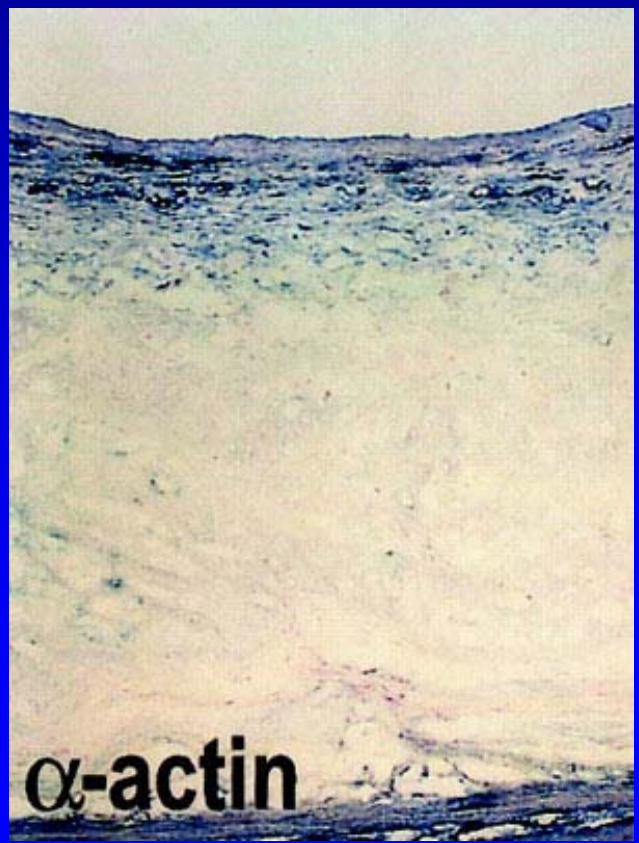
Rioufol. Circulation 2002;106:804

Changes of SMC by Diet in Rabbit

Atherogenic Diet
for 16 Months



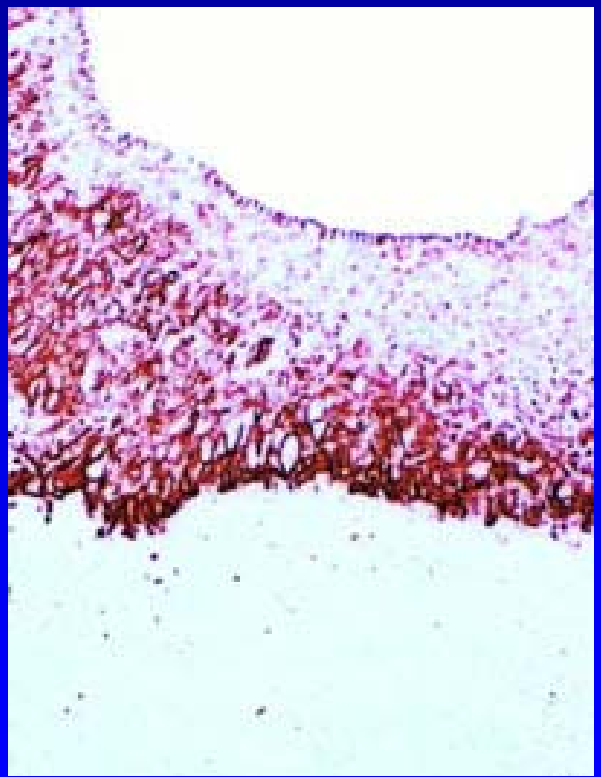
Atherogenic Diet for 4
Months & Chow Diet



Aikawa. Circulayion 1999;100:1215-22

Changes of MMP-1 by Diet in Rabbit

Atherogenic Diet
for 16 Months

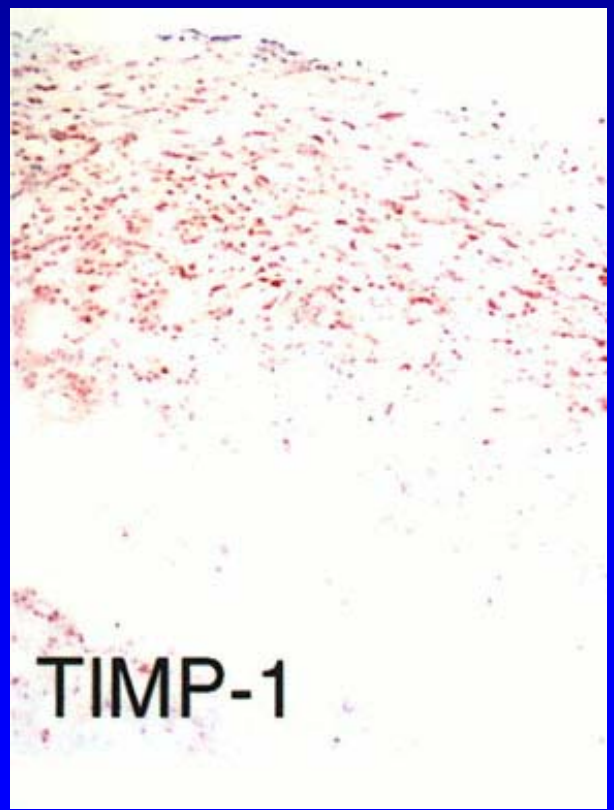


Atherogenic Diet for 4
Months & Chow Diet

Aikawa. Circulayion 1999;100:1215-22

Changes of TIMP-1 by Diet in Rabbit

Atherogenic Diet
for 16 Months

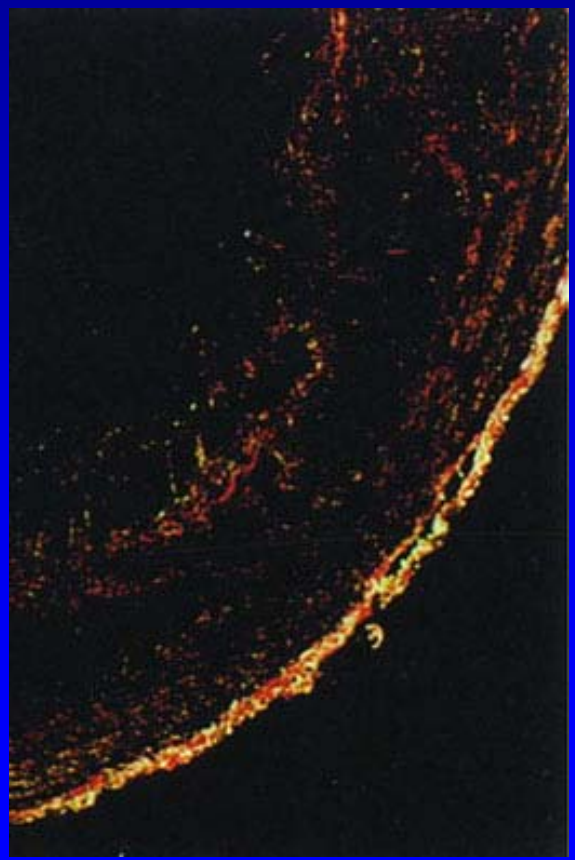


Atherogenic Diet for 4
Months & Chow Diet

Aikawa. Circulayion 1999;100:1215-22

Changes of Collagen by Diet in Rabbit

Atherogenic Diet
for 16 Months



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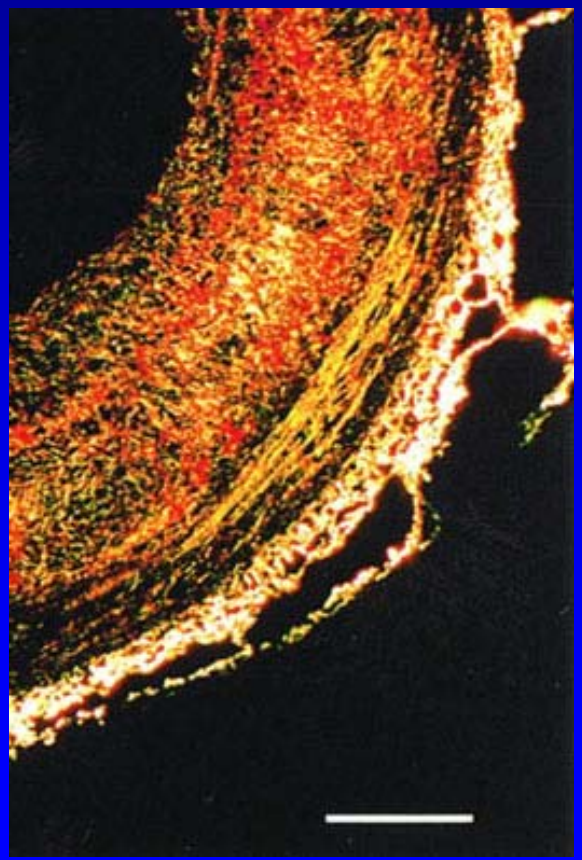
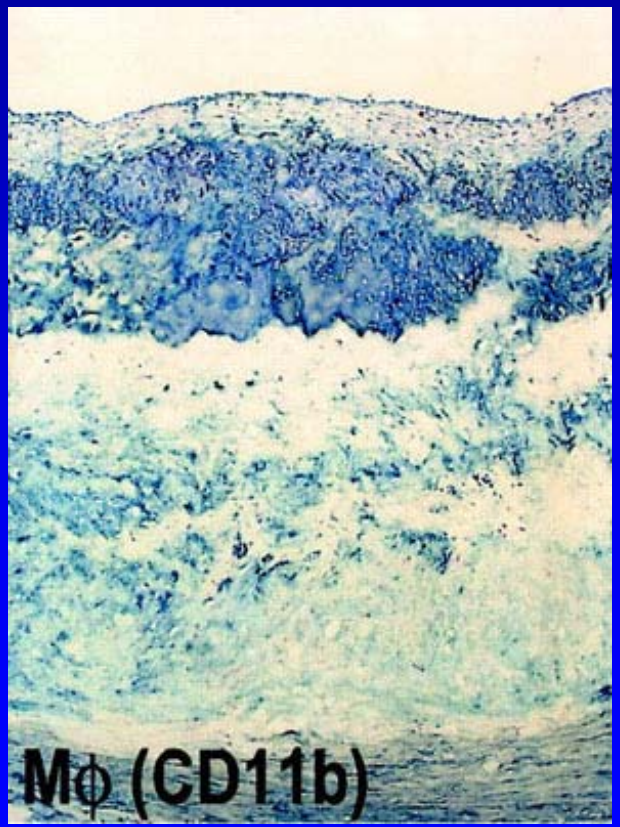


Aikawa. Circulayion 1999;100:1215-22

Changes of Macrophage by Diet in Rabbit

Atherogenic Diet
for 16 Months

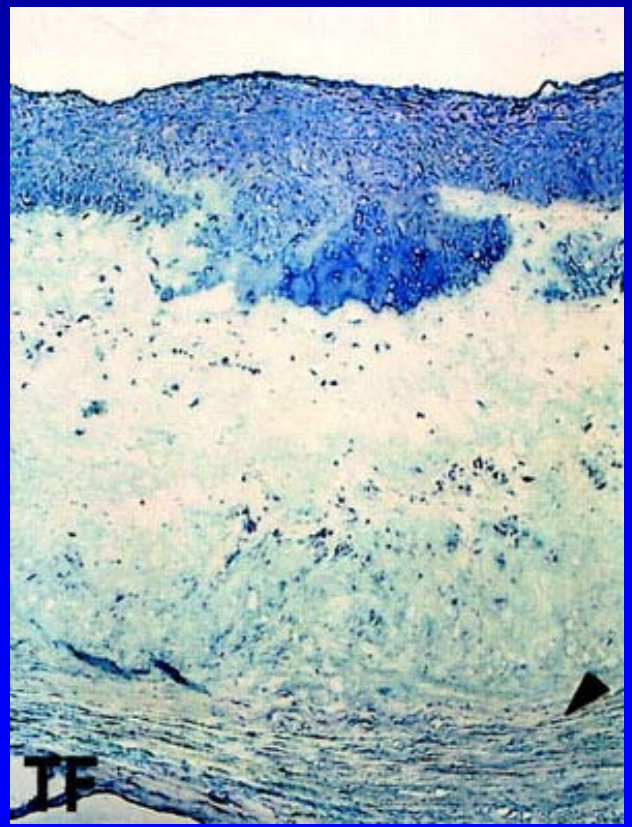


Atherogenic Diet for 4
Months & Chow Diet

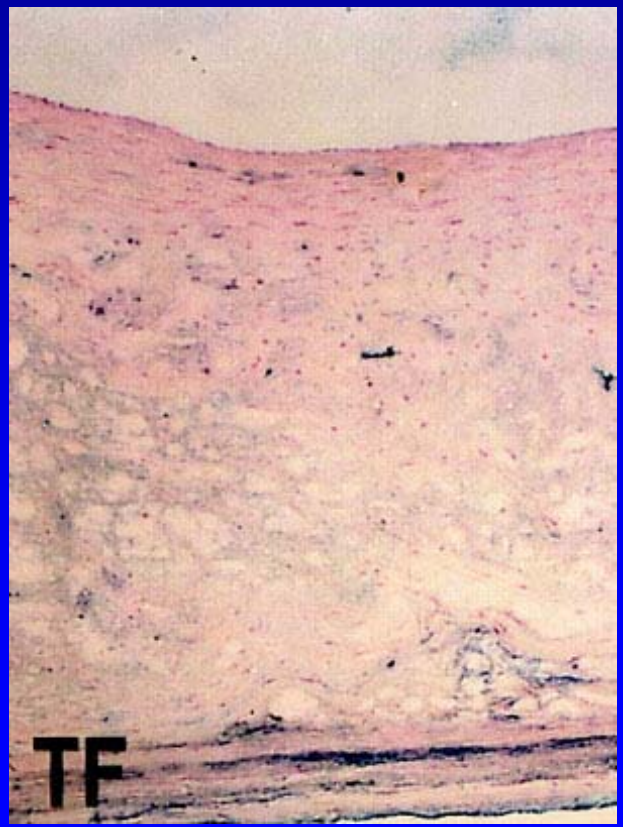
Aikawa. Circulayion 1999;100:1215-22

Changes of Tissue Factor by Diet in Rabbit

Atherogenic Diet
for 16 Months



Atherogenic Diet for 4
Months & Chow Diet



Aikawa. Circulayion 1999;100:1215-22

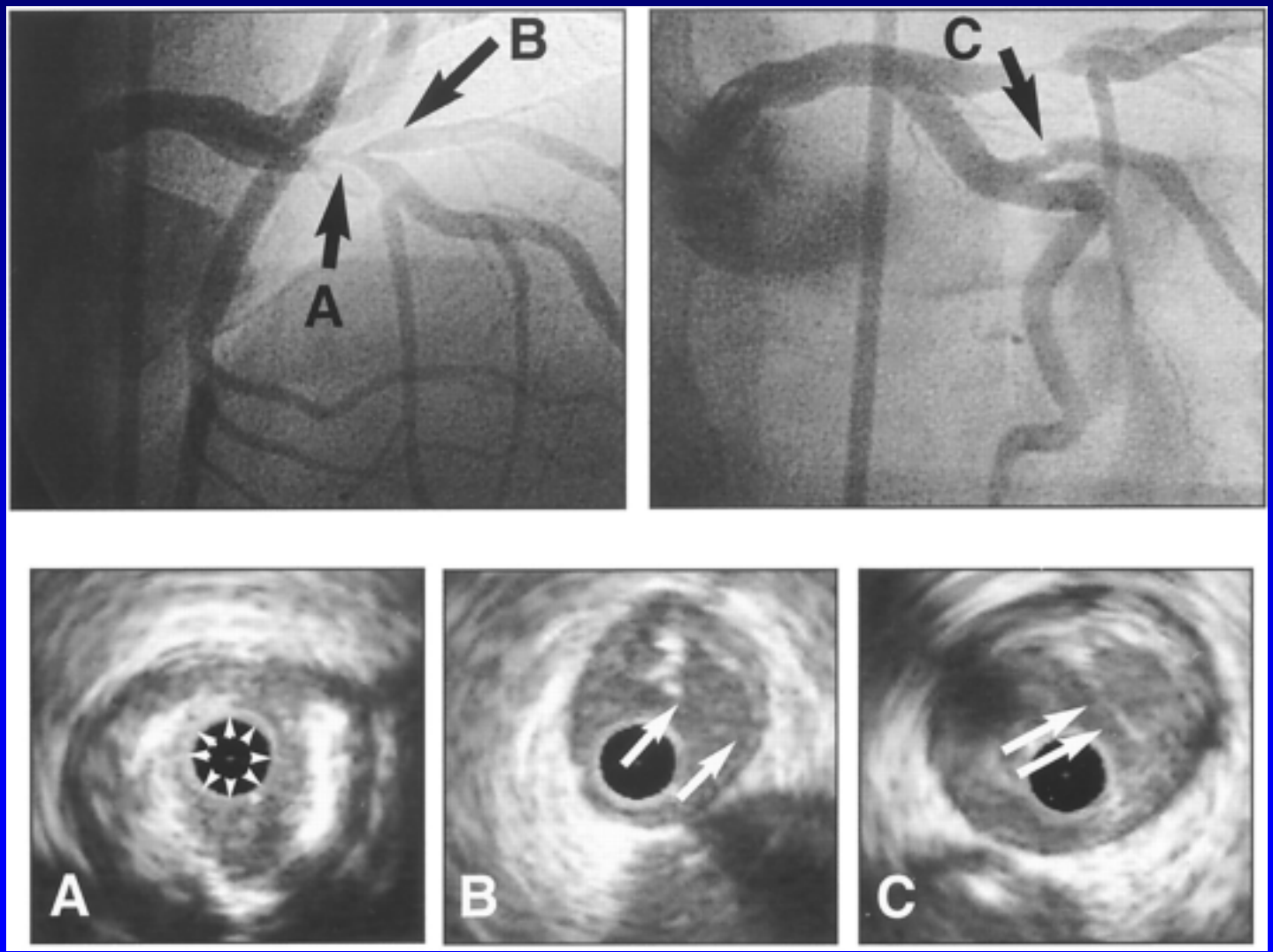
Angiographic and Clinical Outcome in Lipid Lowering Trial

Study	No	Drug	ΔD(%)	Event Reduction
NHLBI	143	R		33%
CLAS	61	R+N		25%
FATS	146	N+C	-0.9*	80%*
		L+C	-0.7*	70%
STARS	46	D	-1.1	69%*
		D+R	-1.9*	89%

R: Resin, N:Niacin, C:Colestipol, L:Lovastatin, D:Diet. *: statistically significant

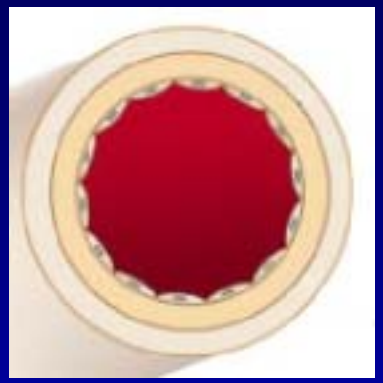
Unstable Plaque in Insignificant Areas in CAG

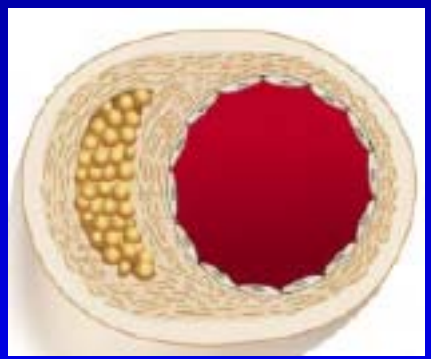
-IVUS-

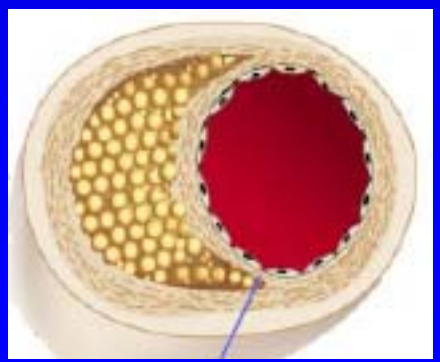


Rioufol. Circulation 2002;106:804

Life History of Atheroma

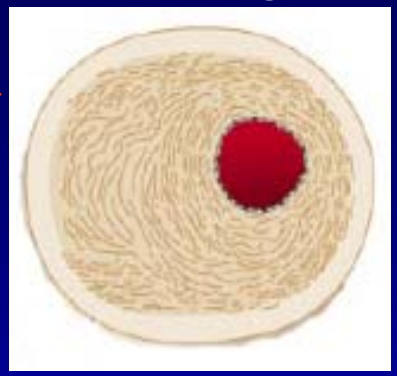


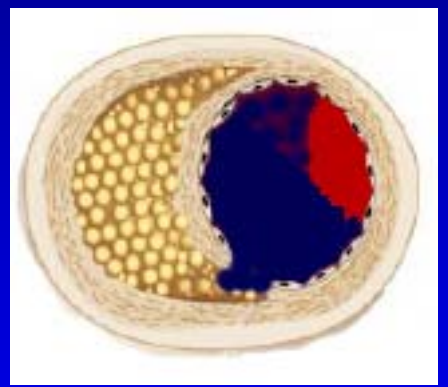




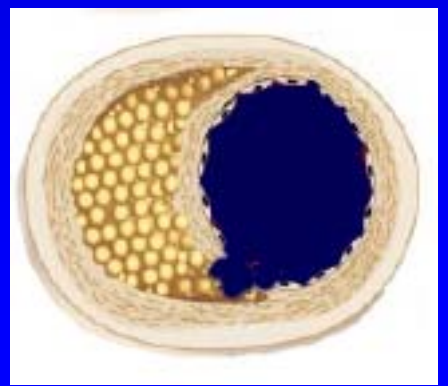
Fibrous Cap

Stable Angina

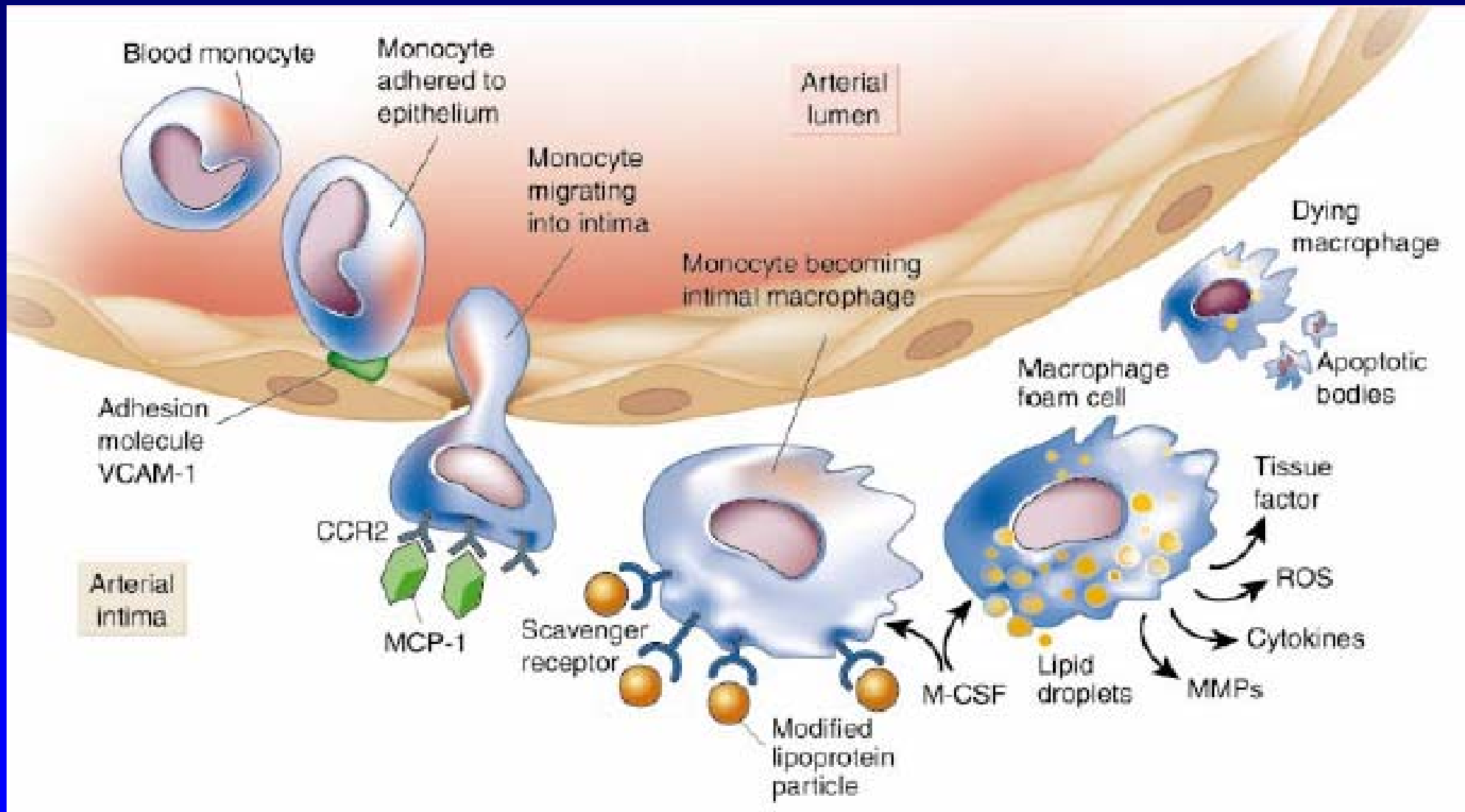


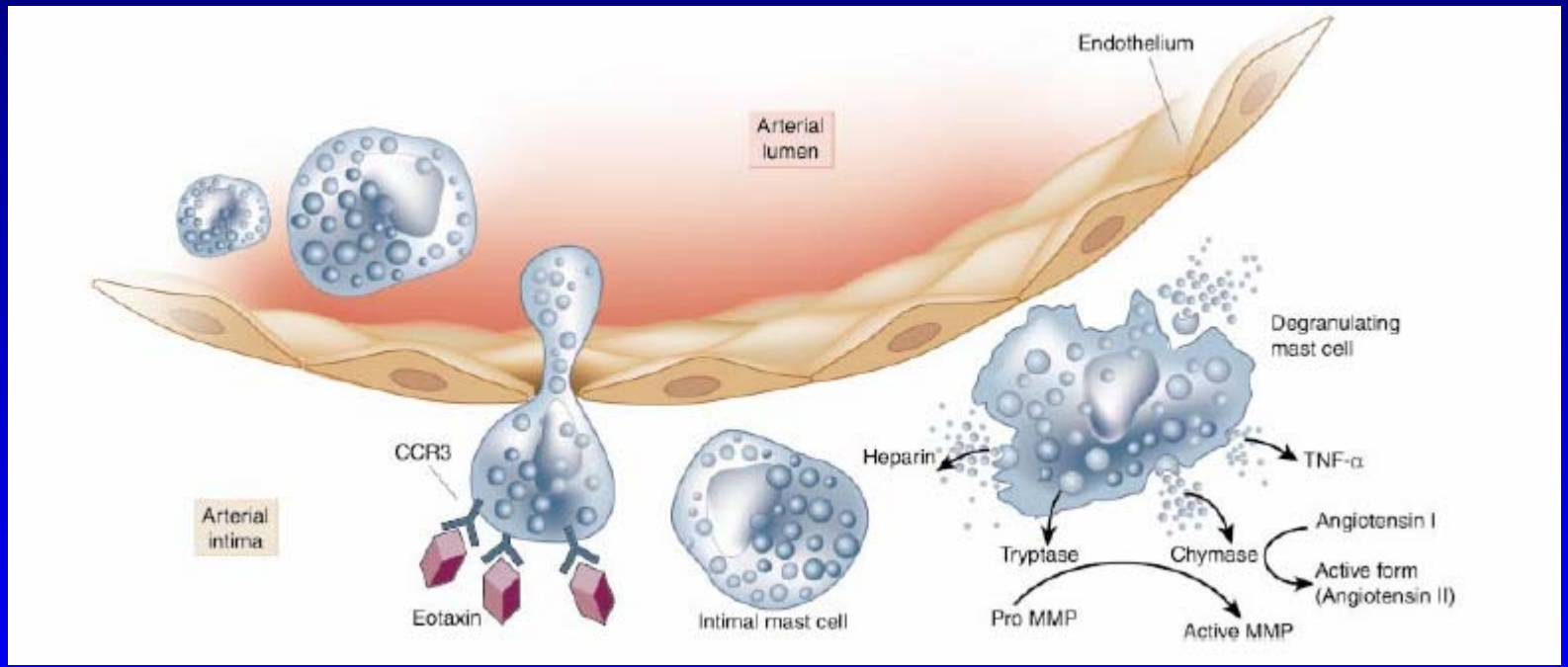


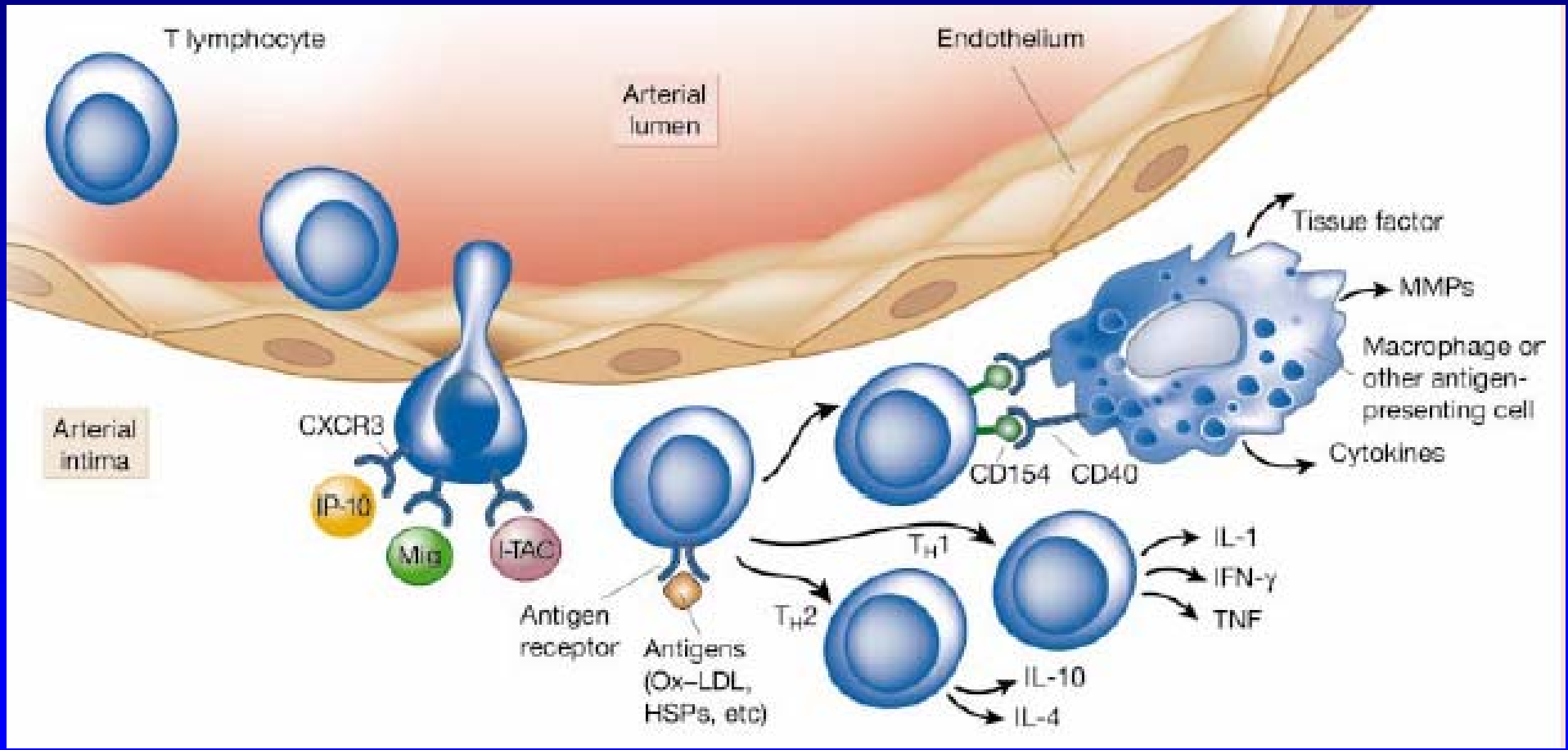
Unstable Angina

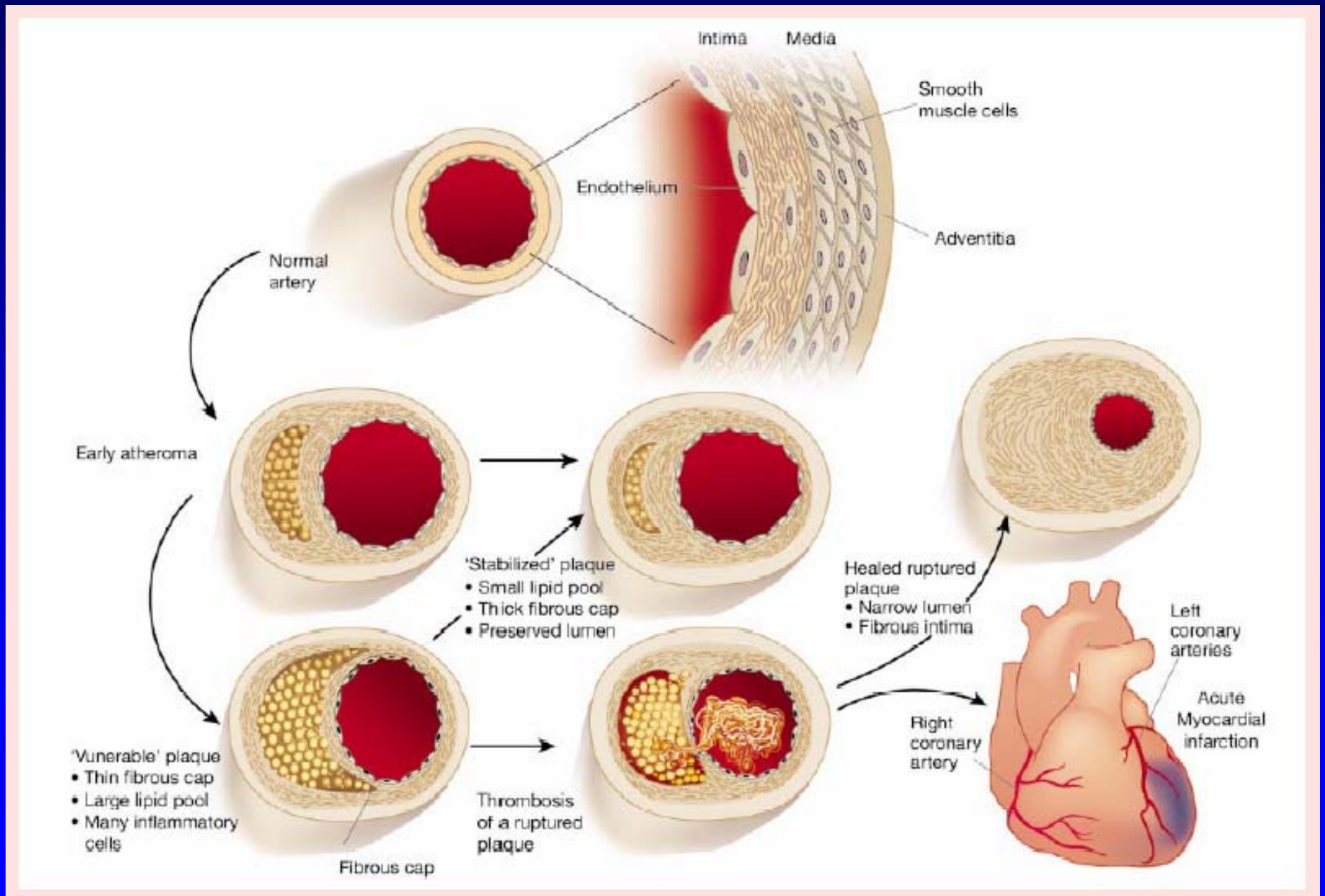


AMI


Blood monocyte
Monocyte adhered to epithelium
Arterial lumen
Monocyte migrating into intima
Monocyte becoming intimal macrophage
Dying macrophage
Apoptotic bodies
Macrophage foam cell
Adhesion molecule VCAM-1
CCR2
Tissue factor
ROS
Cytokines
MMPs
Arterial intima
MCP-1
Scavenger receptor
M-CSF
Lipid droplets
Modified lipoprotein particle


Endothelium
Arterial lumen
Degranulating mast cell
Heparin
TNF-α
CCR3
Arterial intima
Angiotensin I
Tryptase
Chymase
Active form (Angiotensin II)
Pro MMP
Active MMP
Eotaxin
Intimal mast cell


T lymphocyte
Endothelium
Arterial lumen
Tissue factor
MMPs
Macrophage or other antigen-presenting cell
Cytokines
CD154
CD40
Arterial intima
CXCR3
IP-10
Mig
I-TAC
Antigen receptor
Antigens (Ox–LDL, HSPs, etc)
T_H1
T_H2
IL-1
IFN-γ
TNF
IL-10
IL-4


Intima
Media
Smooth muscle cells
Endothelium
Adventitia
Normal artery
Early atheroma
'Stabilized' plaque
• Small lipid pool
• Thick fibrous cap
• Preserved lumen
Healed ruptured plaque
• Narrow lumen
• Fibrous intima
'Vunerable' plaque
• Thin fibrous cap
• Large lipid pool
• Many inflammatory cells
Fibrous cap
Thrombosis of a ruptured plaque
Left coronary arteries
Acute Myocardial infarction
Right coronary artery