I. INTRODUCTION TO VASCULAR DISEASE

A. Magnitude of Problem

1. 400,000 strokes with 170,000 deaths
2. 550,000 CHD deaths
3. More than all cancers combined

B. Associated With Smoking

1. 1983 SGR
   a. Raised lesions ↑ 50% in coronaries
   b. Raised lesions ↑ 100% in abdominal aorta

C. Importance

1. Public relations
2. Health care - No CABG in England?
3. Regulatory - OSHA, NIOSH
4. Legislative
   a. Taxes
   b. Bans
5. Lawsuits
   a. Plaintiff has causation problems
   b. Risk/utility
   c. Contributing factor

II. **ATHEROSCLEROSIS IS UNDERLYING INJURY**

A. Seen at Autopsy

1. Fatty streaks in infants
2. Disease in Korea - some moderate
3. Virtually all MI's
   a. Thrombosis
   b. Spasm (cocaine?)
   c. Arrhythmia
4. Many target organs

B. Theories of Progression

1. Endothelial injury
2. Thrombosis
3. Smooth muscle proliferation
4. Cholesterol deposits
   a. Connective tissue
   b. Vascularization
   c. Calcium
      - Irreversible?

III. HEART DISEASE

A. Narrowed Coronary Arteries

1. Angina

2. MI

a. Scarring ± CHF

b. Death

B. Many Factors Have Been Associated

1. "Major Risk Factors"

a. Smoking

b. Hypertension

c. Diabetes (eye and kidney)

2. Confounders

a. Sex (only coronaries, Caucasians partic.)

b. Age (smoking association decreases)

c. Genetics

(1) Dyslipoproteinemias (Lp(a) varies 1000x)

(2) ATHS gene?

d. Stress

(1) Type A

(2) Hostility

e. Exercise

f. Diet

(1) Fat

(2) Cholesterol

(3) Fish

(4) Coffee

(5) Alcohol

(6) Iron

g. Periodontitis, etc. (>200)

C. Association Based on Epidemiology

1. Low RR
    a. 1.7 overall, 3.0 heavy (1990 SGR)
    b. ↓ with age
    c. ↑ with BCP
2. Incidence ↓ 40%
    a. Started 1940
        - Not just ↓ smoking
    b. Lifestyle or diet?
3. Anomalous results
    a. ↓ angina in ♀ ex-smokers - Framingham
    b. Indians in London
    c. Japanese
        (1) Low CHD despite heavy smoking
        (2) ↑ in Hawaii
4. Effects of cessation unclear
    a. Biphasic ↓ risk
    b. Quitters are different

D. Intervention Trials Unsuccessful

1. WHO (5 countries)
2. MRFIT

E. Animal Studies

1. Rabbits
2. Pigeons
3. Monkeys
4. Baboons

F. Possible Mechanisms for Tobacco Smoke

1. Endothelial injury
    a. CO
    b. WBC's
    c. Spasm
    d. Nicotine
        (1) 2° catecholamine release?
        (2) Umbilical artery
        (3) IV to dogs
2. ↓ HDL (mostly $HDL_{2 \text{ or } 3}$)
3. ↑ LDL
    a. Necessary?
    b. ↑↑ with oxidation
        (1) Free radicals
        (2) Vitamin E
4. Thrombosis
    a. ↑ platelet cohesiveness, ↑ fibrin, ↑ PDGF
    b. Block with 20 mg ASA bid
5. Arrhythmia
6. Monoclonal theory
    a. Altered DNA (Benditt)
    b. ↑ adducts in heart (Randerath)
7. Combination (most likely?)
    a. Smoking + ↑ cholesterol
    b. Lp(a) + ↑BP
    c. Additive or synergistic

IV. **STROKE**

A. Infarct or Hemorrhage

B. Hypertension Very Important

- ↓ incidence 2° treatment

C. Associated With Smoking

1. Duration > intensity
2. ↑ shortly after smoking
3. Thickened carotids on Doppler

D. Smoking + ↑ BP - RR12 (BMJ)

V. **PERIPHERAL VASCULAR DISEASE**

A. Progressive Atherosclerosis

1. Claudication
2. Gangrene
3. RR 1.8 - 5.6

B. Aortic Aneurysm

C. Buerger's Disease (Thromboangiitis Obliterans)

1. Rare but specific for smoking
2. Inflammatory (allergic?)
3. Arteries and veins
4. Lose limbs gradually

VI. **IMPORTANCE**

- **A. PR**
- **B. Health Care**
- **C. Regulation**
- **D. Legislation**
- **E. Lawsuits**
  - 1. Traditional cases
    - a. General causation - unproven
    - b. Specific causation - other factors
    - c. Proximate cause - diet has - RR
    - d. Awareness (personal choice)
  - 2. Buerger's Disease
    - a. Assumption of risk
    - b. SOL
  - 3. Risk/utility