Periodontal Medicine

Cardiovascular Diseases

Stroke

Pregnancy

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Learning Objectives

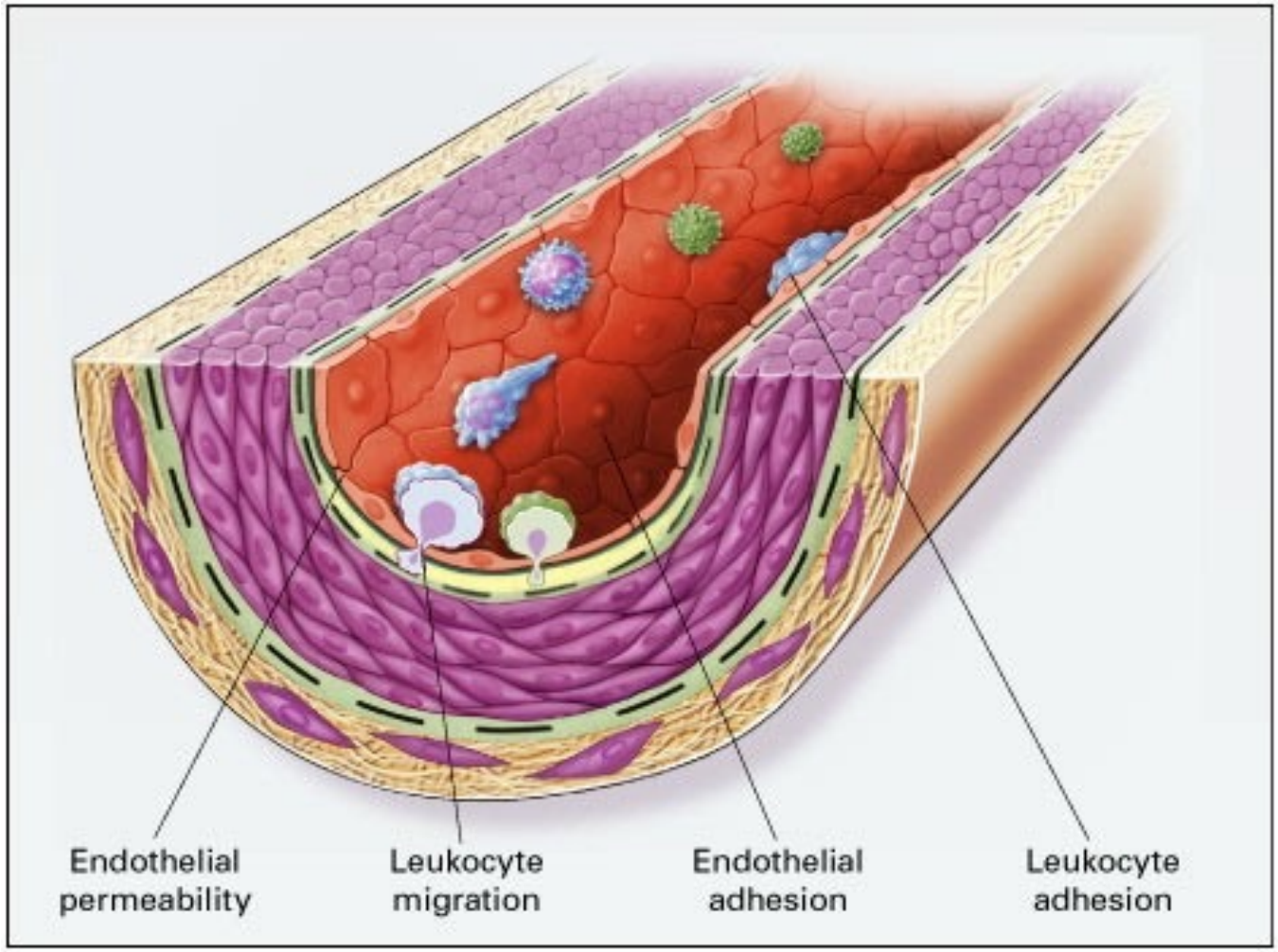
- The student should be able to provide an evidence-based discussion of the links between periodontal and systemic diseases
  - Cardiovascular Diseases
  - Stroke
  - Pregnancy


marker
clinical
hospital
medical
therapy
fibrillation
heartbeat
pulse
rhythm
body
cholesterol
pill
chest
cardiology
pain
ventricular
doctor
arrhythmia
coronary
blood
angina
lifestyle
cardiac
healthcare
prevention
diagnosis
training
Cardiovascular
treatment
pressure
stress
sick
hypertension
attack
blockage
vein
artery
medicine
arrhythmias
illness
examination
stroke
expertise
healthy
Diseases
line
ischemia
cardiovascular
surgery
heart
diabetes

CARDIOVASCULAR DISEASE
PATHOPHYSIOLOGY

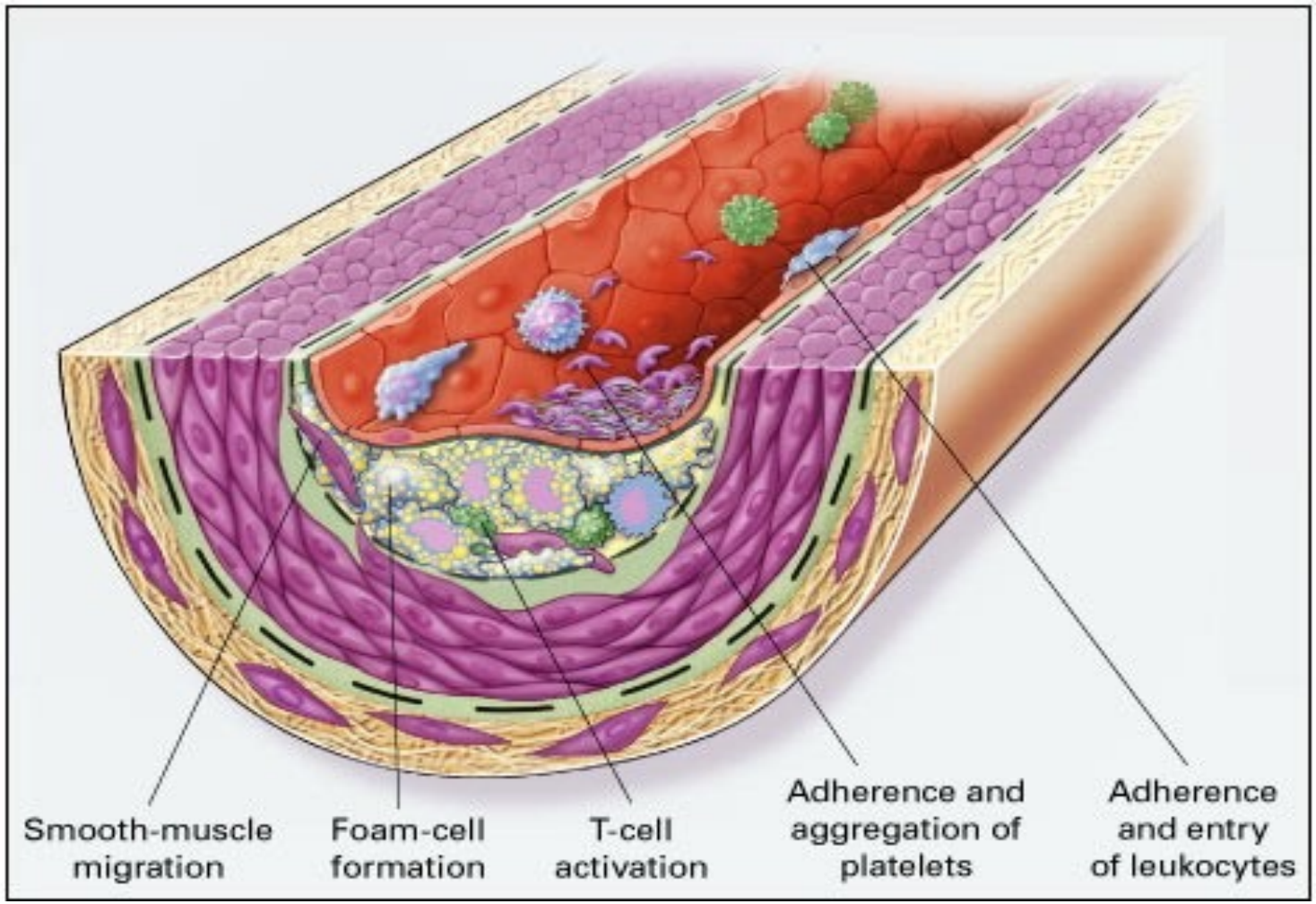
Atherosclerotic Vascular Diseases (ASVD)

- Ischemic heart disease
- Cerebrovascular diseases (stroke)
- Diseases of arteries, arterioles, and capillaries (peripheral vascular disease)



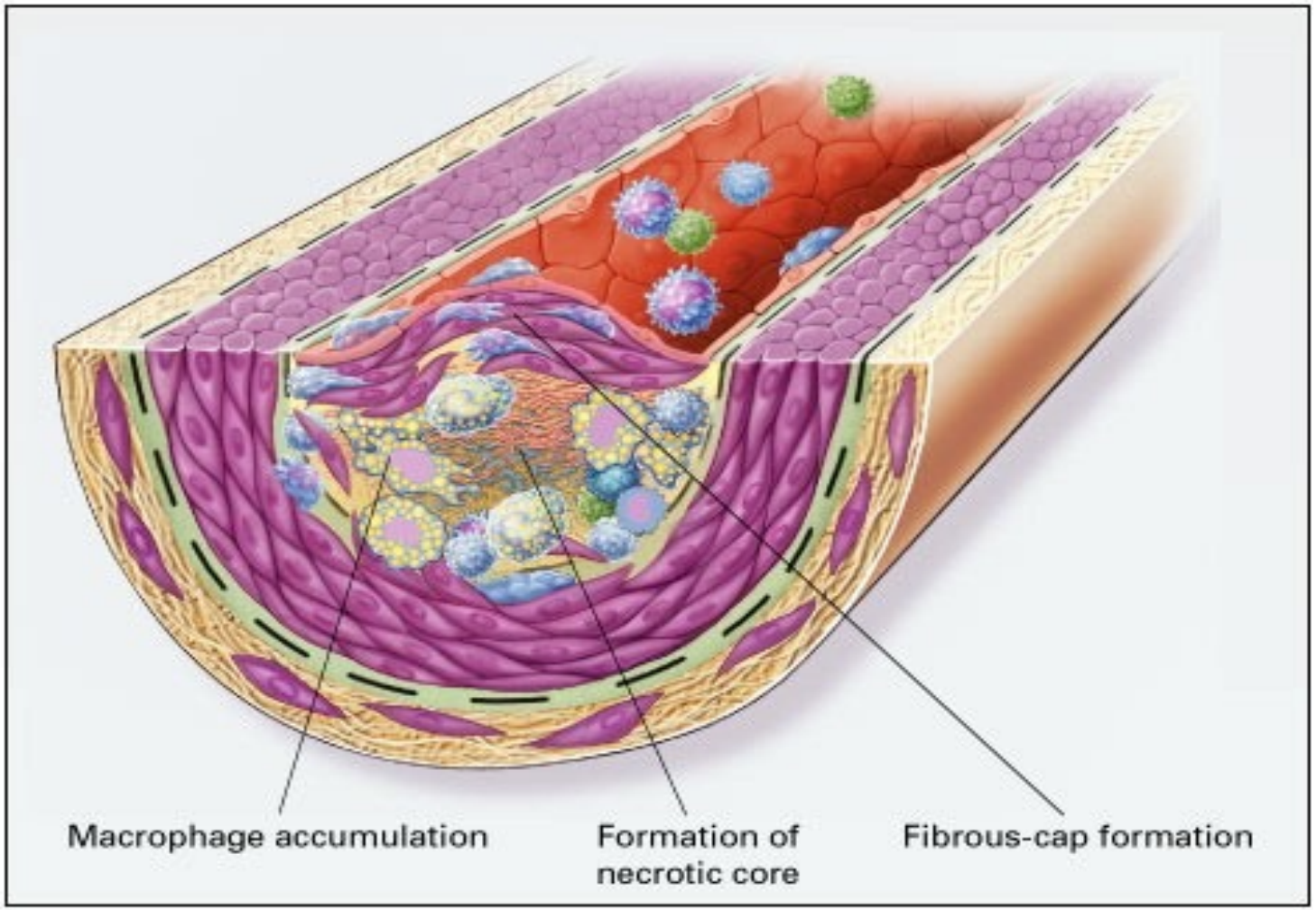
Endothelial Dysfunction in Atherosclerosis

Ross R. N Engl J Med 1999;340:115-126.



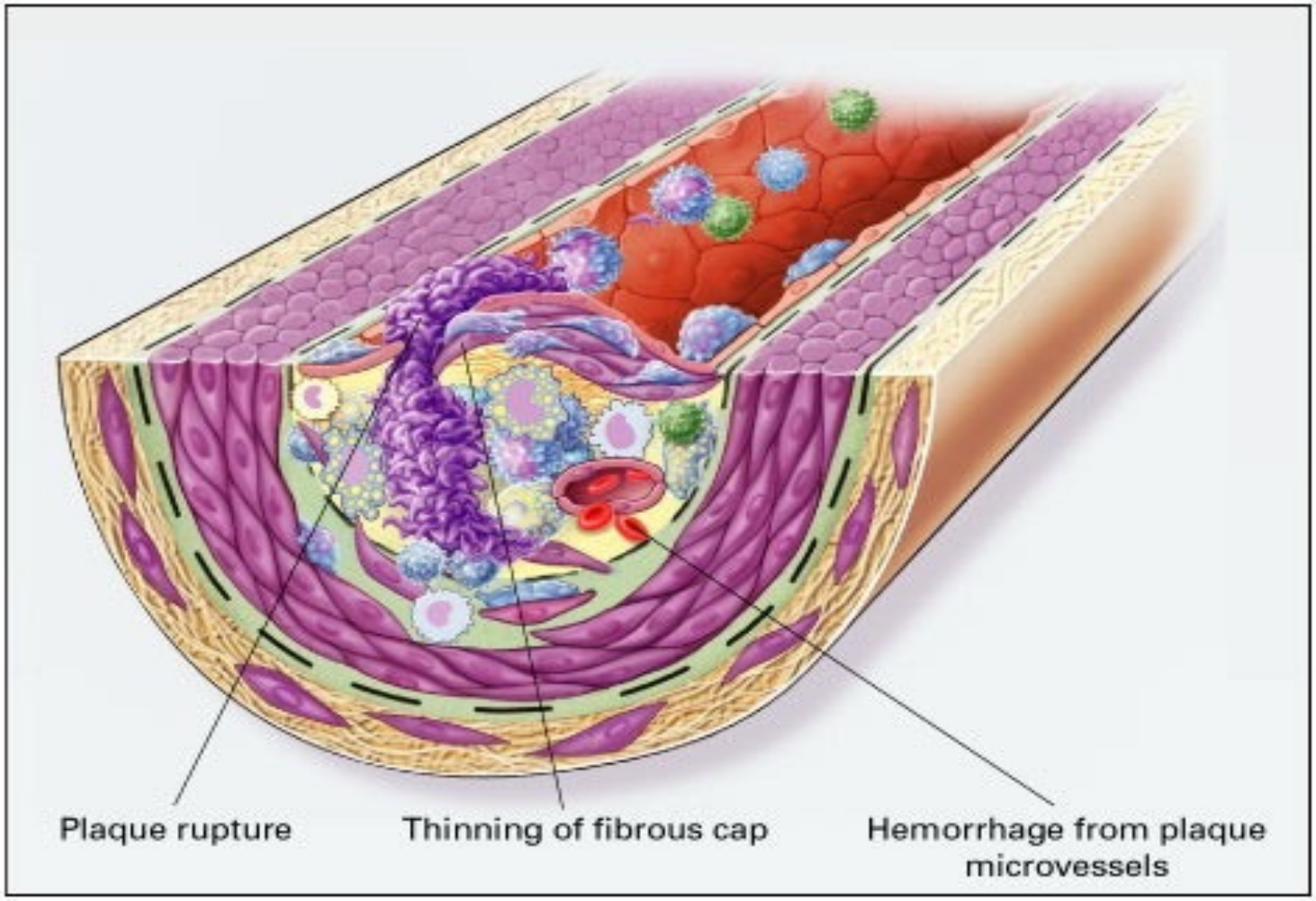
Fatty-Streak Formation in Atherosclerosis

Ross R. N Engl J Med 1999;340:115-126.



Formation of an Advanced, Complicated Lesion of Atherosclerosis

Ross R. N Engl J Med 1999;340:115-126.



Unstable Fibrous Plaques in Atherosclerosis

Ross R. N Engl J Med 1999;340:115-126.

Risk factors

- Increasing age
- Male sex
- Hypertension
- Diabetes mellitus
- Smoking
- Low serum levels of high-density lipoprotein (HDL) cholesterol

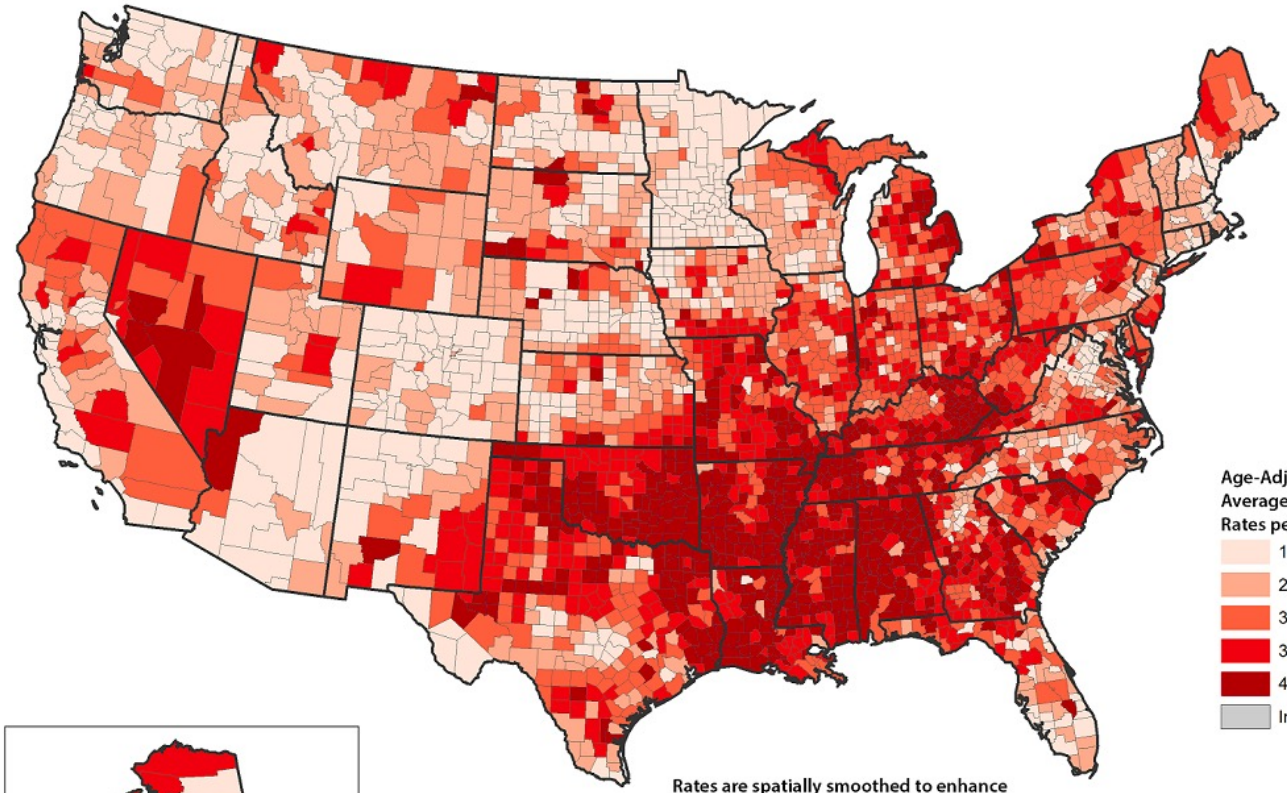
Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003

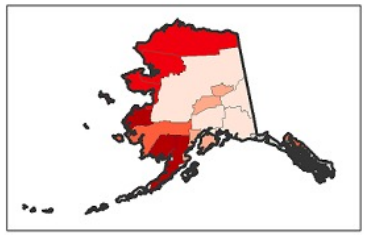
Ockene IS, Miller NH. Cigarette smoking, cardiovascular disease, and stroke: A statement for healthcare professionals from the American Heart Association Task Force on Risk Reduction. *Circulation* 1997

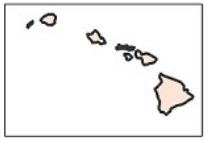
ASVD - Prevalence

- ASCVD is the number #1 cause of death globally, accounting for approximately 31% of deaths worldwide
- In the United States accounts for 1 in 4 deaths
- Number of adults with diagnosed heart disease: 27.6 million (11.5%)
- 659,000 deaths annually in the US, 1 death every 36s

Heart Disease Death Rates, 2014-2016
Adults, Ages 35 +, by County







Age-Adjusted
Average Annual
Rates per 100,000

- 103.4 - 284.2
- 284.3 - 324.9
- 325.0 - 365.9
- 366.0 - 426.5
- 426.6 - 1170.5
- Insufficient Data

Rates are spatially smoothed to enhance the stability of rates in counties with small populations.

Data Source:
National Vital Statistics System
National Center for Health Statistics

www.cdc.gov/dhdsp/maps

Epidemiology
Periodontitis & Atherosclerotic Cardiovascular disease

- The association has varied greatly in a number of studies
- Reasons for variation
  - Variations in study populations
  - Differing measures and definitions of periodontitis

Mattila KJ, Valtonen VV, Nieminen M, Huttunen JK. Dental infection and the risk of new coronary events: Prospective study of patients with documented coronary artery disease. *Clin Infect Dis* 1995

Epidemiology – Periodontitis & ASVD

- **Meta-analysis studies:**
- Periodontal disease is a risk factor or marker independent of traditional CAD risk factors (relative risk estimates from 1.24 – 1.35)
- The association may be greater in a population under the age of 60 with more severe periodontitis and in males as compared to females

Humphrey LL, Fu R, Buckley DI, Freeman M, Helfand MJ. Periodontal disease and coronary heart disease incidence: A systematic review and meta-analysis. *J Gen Intern Med* 2008
Bahekar AA, Singh S, Saha S, Molnar J, Arora R. The prevalence and incidence of coronary heart disease is significantly increased in periodontitis: A meta- analysis. *Am Heart J* 2007
Dietricj et. Al. (2013), Blaizot, A. et al, 2009; Mustapha, I.Z. et al, 2007; Zeng, XT et al, 2016

Epidemiology – Periodontitis & ASVD

Summary:

- Epidemiology: modest but significant association
  - RR1.2-1.5 for CHD and 1.2 –2.8 for Stroke
- Variation among populations
  - Variation in assessment of periodontal disease and CVD definitions
- The AHA Scientific Statement (Lockhart 2012) outlines epidemiology:
  - Current evidence (interventional studies) is lacking to show causality

Shared risk factors

- Increasing age
- Smoking
- Alcohol abuse
- Race/ethnicity
- Education and SES
- Male sex
- Diabetes mellitus
- Overweight or obesity

The Link : Inflammation

Inflammation & ASVD

Atherosclerotic CVD events increase in patients with chronic inflammatory diseases:

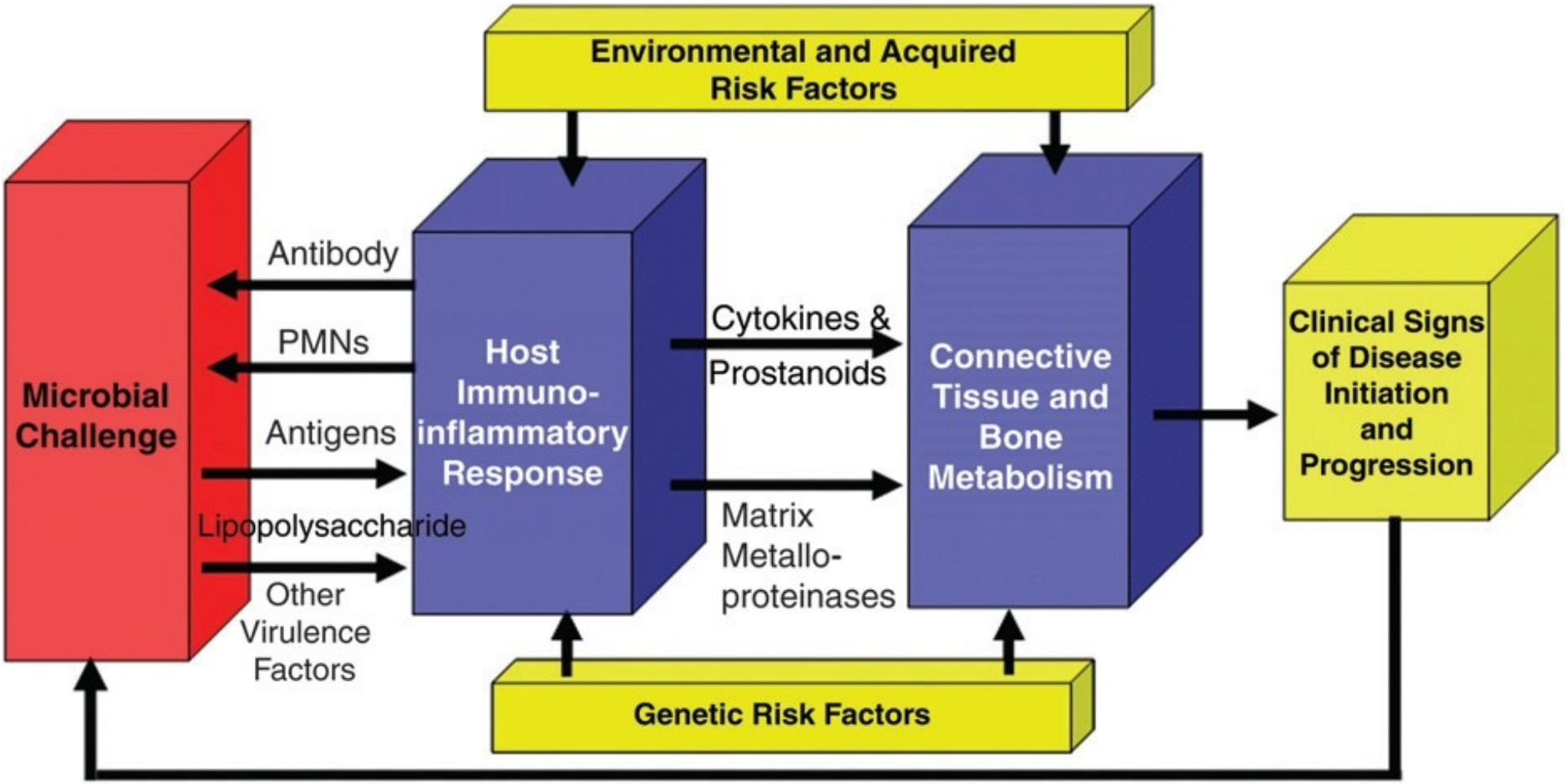
- Rheumatoid arthritis
- Psoriasis
- Systemic lupus erythematous
- Respiratory and urinary tract infections
- Periodontitis

Periodontitis & ASVD –
Biologic Plausibility

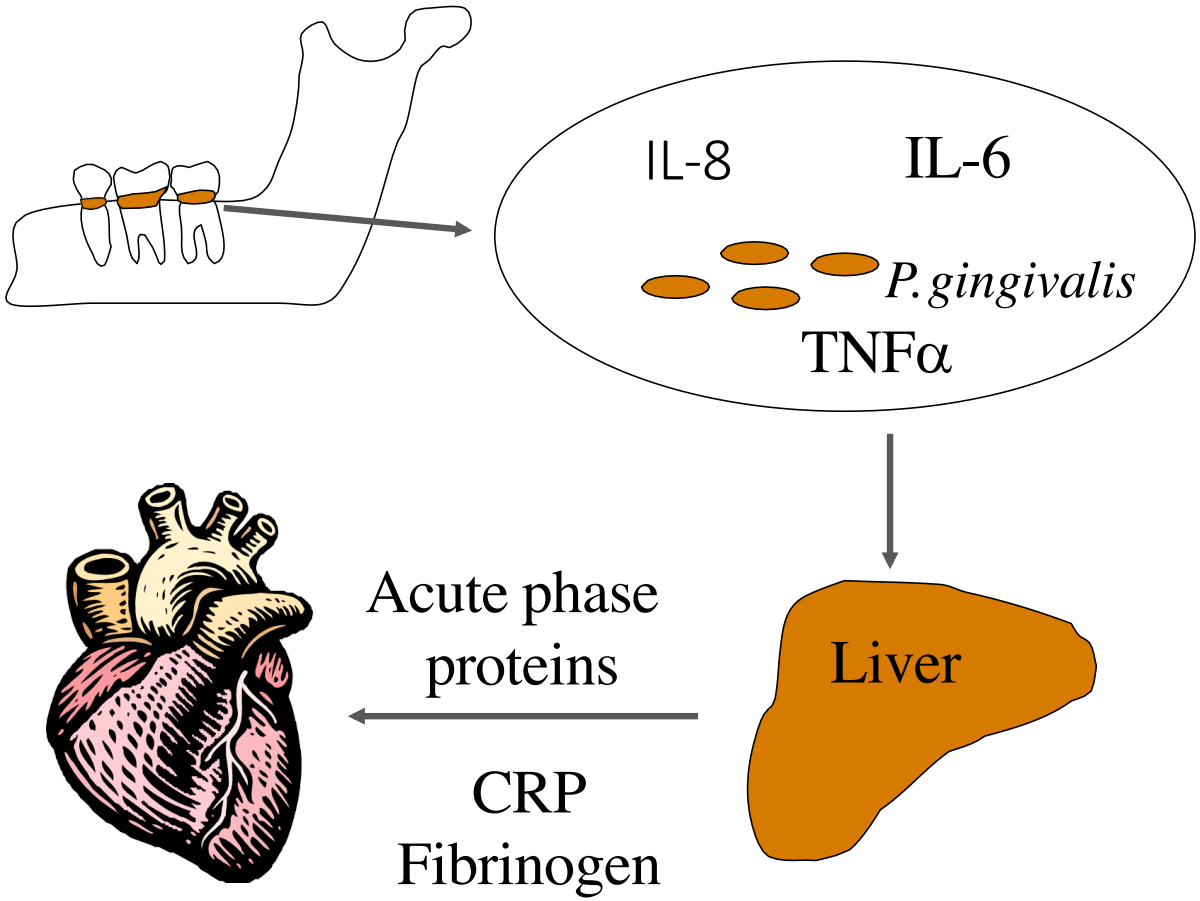
- Systemic exposure to periodontal pathogens: loss of epithelial integrity within pocket — transient bacteremia

- *Direct effects* of bacterial products on platelets and invasion of vascular endothelia
  - Direct endothelial invasion (Gibson et al. 2006)
  - Autoimmunity or molecular mimicry (Gibson et al. 2006)
  - Immunologic sounding and systemic inflammation (Gibson et al. 2006)
  - PD and CRP in subjects with periodontitis (Slade 1998)

Periodontitis & ASVD –
Indirect mechanisms relating periodontitis to systemic inflammation



Page RC, Kornman KS. The pathogenesis of human periodontitis: An introduction. *Periodontology 2000* 1997;14:9-11.


IL-8
IL-6
P. gingivalis
TNFα
Liver
Acute phase proteins
CRP
Fibrinogen

C-Reactive protein (CRP)

Higher quantiles by a high-sensitivity assay (hsCRP) predict future:

- Acute MI
- Unstable angina pectoris
- Systemic arterial hypertension
- Diabetes mellitus
- Stroke

Berk BC, Weintraub WS, Alexander RW. Elevation of C-reactive protein in "active" coronary artery disease. *Am J Cardiol* 1990

Pai JK, Pischon T, Ma J, et al. Inflammatory markers and the risk of coronary heart disease in men and women. *N Engl J Med* 2004

CRP & Periodontitis

Elevated CRP Levels in Periodontitis

- Loos et al (2000)
- Noack et al (2001)

Treatment decreases CRP levels:

- Iwamoto (2003)
- D'Aiuto F. Ready D. Tonetti MS (2004)

OTHER INFLAMMATORY MARKERS

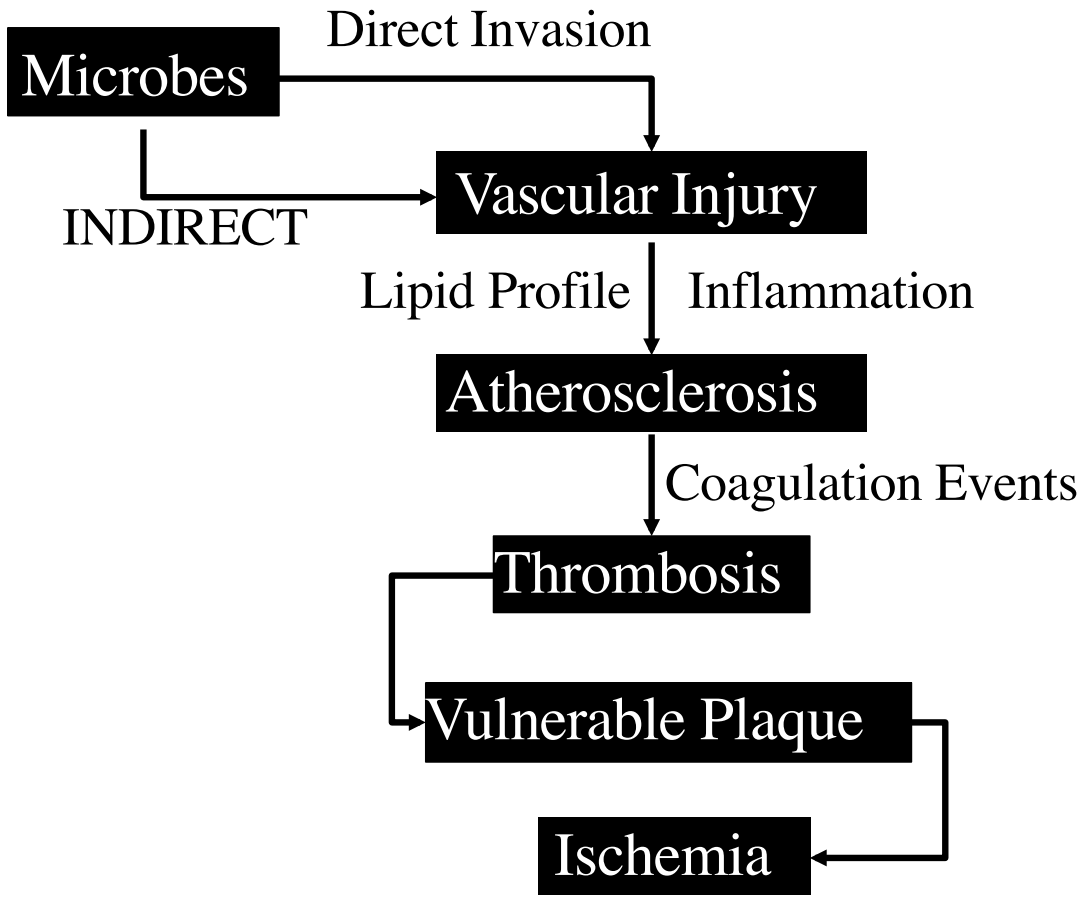
- Erythrocyte sedimentation rate (ESR)
- Chemokine and cytokine levels
  - IL-6
  - IL-8
  - IL-10
  - IL-18
  - TNF- α
  - Monocyte chemoattractant protein-1 (MCP-1)

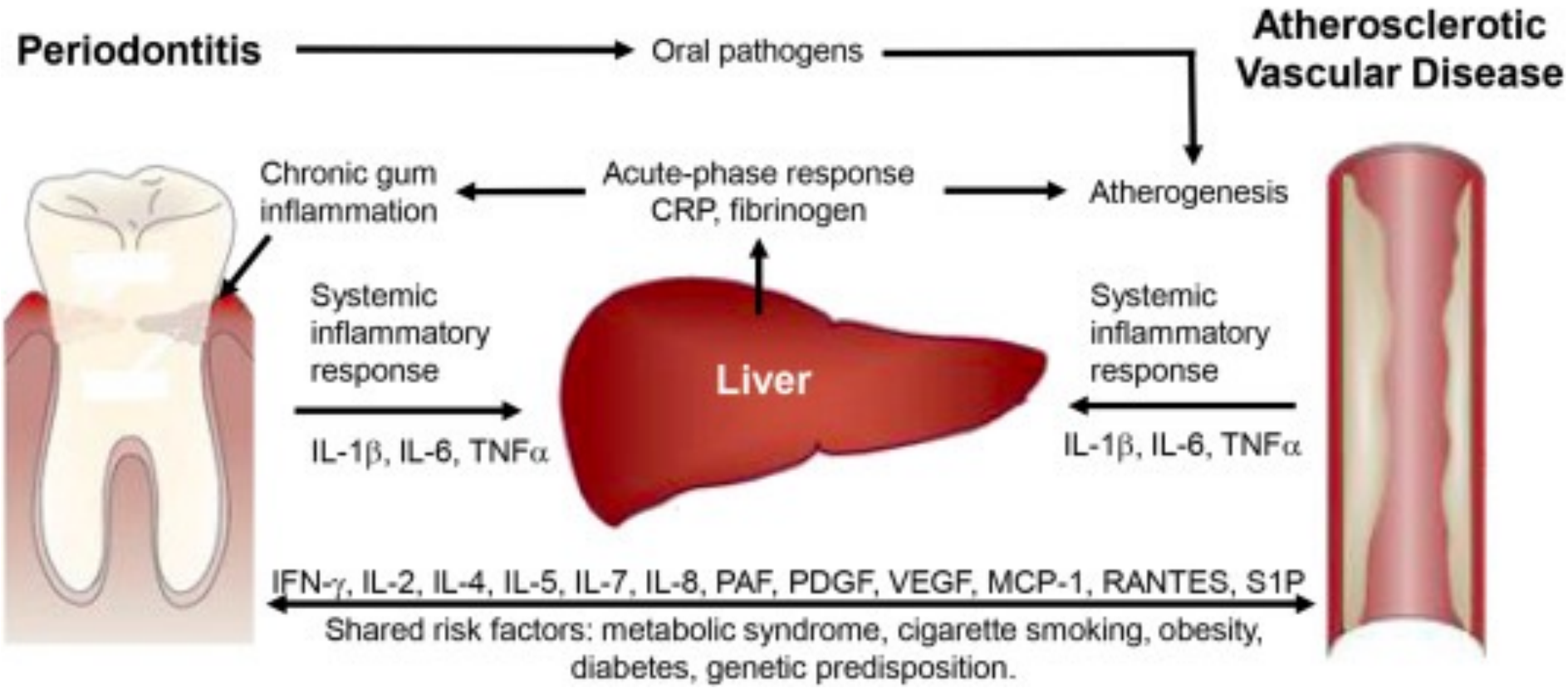
Armstrong EJ,Morrow DA, Sabatine MS. Inflammatory biomarkers in acute coronary syndromes: Part I: Introduction and cytokines. *Circulation* 2006

Periodontitis & ASVD –

DIRECT ROLE OF PERIODONTAL PATHOGENS IN ATHEROMA FORMATION

- *P. gingivalis* in atheromas
- *P. gingivalis* invades endothelial cells
- *P. gingivalis* aggregates platelets (Herzberg and Meyer (1996)
- Atheromas from 50 endarterectomy procedures
  - 44% were positive for at least one periodontal pathogen: *B. forsythus*, *P. gingivalis*, A. *actinomycetemcomitans*, and *P. intermedia*


Microbes
Direct Invasion
INDIRECT
Vascular Injury
Lipid Profile
Inflammation
Atherosclerosis
Coagulation Events
Thrombosis
Vulnerable Plaque
Ischemia



Aarabi, G. et al. 2015

Periodontal Treatment and CVD

- Periodontal treatment effects:
  - Decrease in CRP levels (D'Aiuto, F el al, 2013; Paraskevas, S. et al, 2008; Teeuw, W et al, 2014; Freitas, C.O. et al, 2012)
  - Improvement in endothelial function (Lockhart, P.BN. et al, 2012, D'Aiuto, F el al, 2013)
  - Reduction in carotid intima-medial thickness (c-IMT) (Zeng, X.T. et al, 2016)

- No evidence of changes in atherogenesis or disease outcomes (Lockhart, P.B. et al, 2012, Li, C. et al, 2016)

CLINICAL GUIDELINES

European Federation of Periodontology and American Academy of Periodontology (EFP/AAP) Joint Workshop Proceedings, 2012

Consensus report of the joint workshop on periodontitis and cardiovascular diseases by the European Federation of Periodontology and the World Health Federation (EFP/WHF), 2019

SO WHAT DO I TELL MY PATIENTS?

- Patients with CVD should be advised that periodontitis may have a negative impact on CVD and may also increase the risk of CVD events.

- Patients should be advised that effective periodontal therapy may have a positive impact upon CV health.

Clinical Guidelines

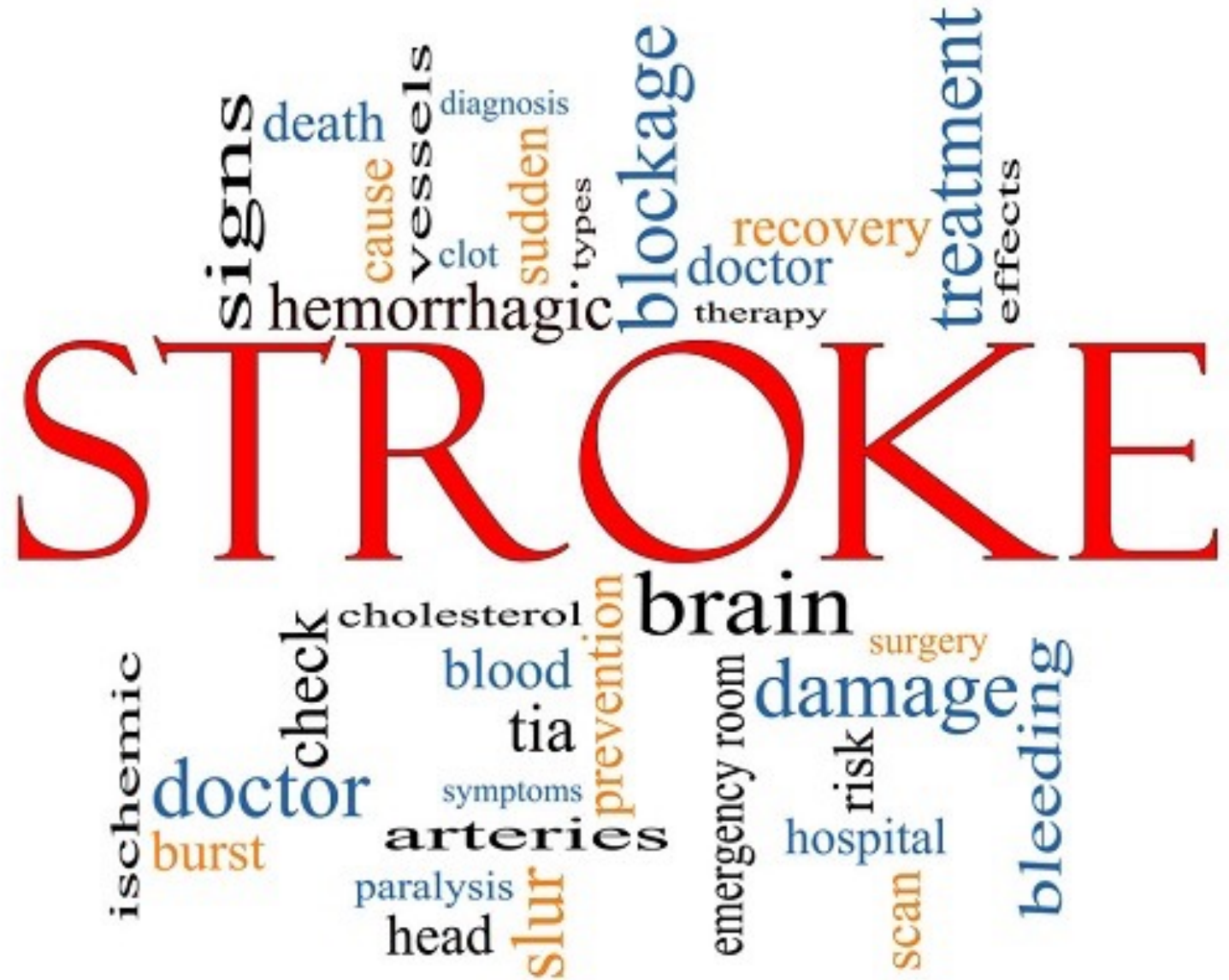
CVD <u>with</u> a Previous Diagnosis of Periodontitis:

Oral health care providers and physicians closely collaborate to optimize CVD risk reduction

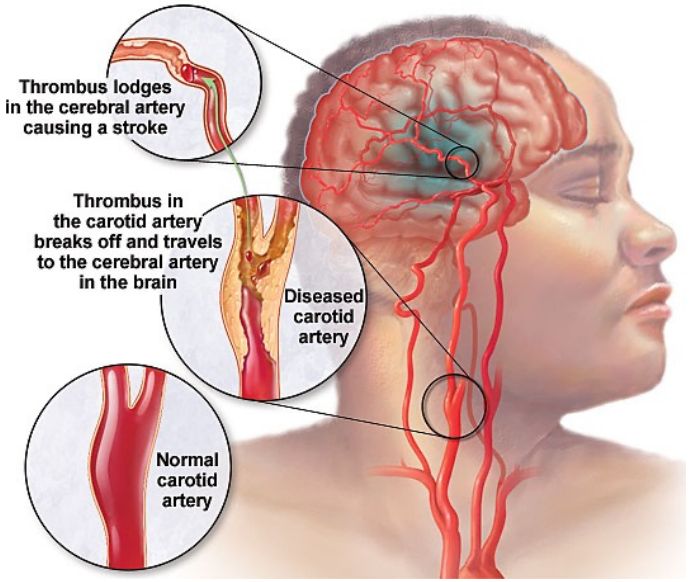
Clinical guidelines

CVD <u>without</u> a Previous Diagnosis of Periodontitis:

- Periodontal evaluation – especially in patients with signs or symptoms of periodontal disease (bleeding, missing teeth) or unexplained elevations of hsCRP
- If Periodontitis is detected – treatment focused on reduction of infection/inflammation


STROKE
signs
death
diagnosis
vessels
cause
clot
sudden
types
blockage
hemorrhagic
recovery
doctor
therapy
treatment
effects
brain
cholesterol
blood
tia
prevention
surgery
damage
bleeding
ischemic
check
doctor
burst
symptoms
arteries
paralysis
head
slur
emergency room
risk
hospital
scan


STROKE AWARENESS
Know the Facts:
Someone in the United States suffers a stroke
(4th leading cause of death in the nation).*
every 40 seconds
30,000
Brain cells die every second during a stroke.**


Thrombus lodges in the cerebral artery causing a stroke
Thrombus in the carotid artery breaks off and travels to the cerebral artery in the brain
Diseased carotid artery
Normal carotid artery


F
FACE DROOPING
A
ARM WEAKNESS
S
SPEECH DIFFICULTY
T
TIME TO CALL 911

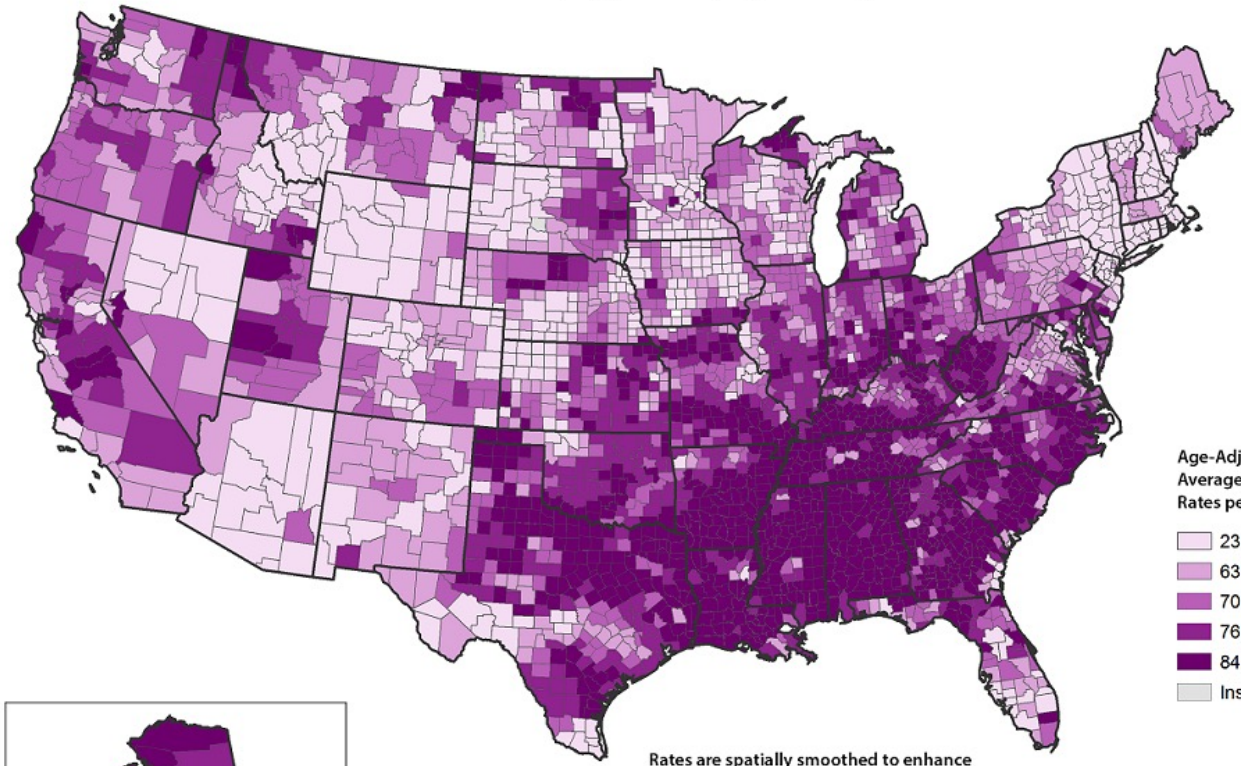
STROKE - EPIDEMIOLOGY

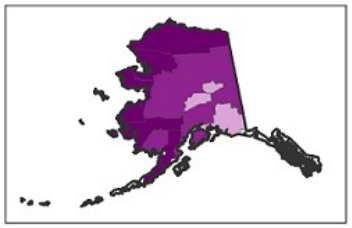
- The 5th leading cause of death in the United States, killing about **140,000 Americans** each year—that's **1 of every 20 deaths**.

- Someone in the United States has a stroke every **40 seconds**. Every **four minutes**, someone dies of stroke.

- Every year, about **795,000 people** in the United States have a stroke. About 610,000 of these are first or new strokes; 185,000 are recurrent strokes.

Stroke Death Rates, 2014 - 2016
Adults, Ages 35+, by County





Age-Adjusted
Average Annual
Rates per 100,000

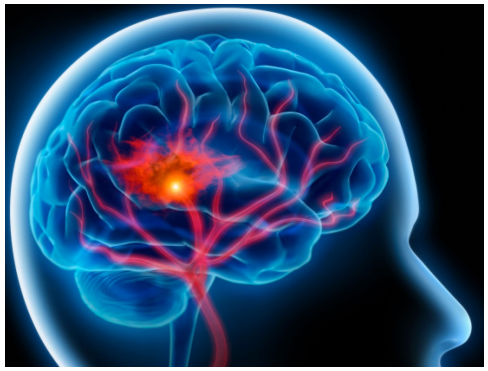
- 23.1 - 62.9
- 63.0 - 70.0
- 70.1 - 76.4
- 76.5 - 84.1
- 84.2 - 194.9
- Insufficient Data

Rates are spatially smoothed to enhance the stability of rates in counties with small populations.

Data Source:
National Vital Statistics System
National Center for Health Statistics

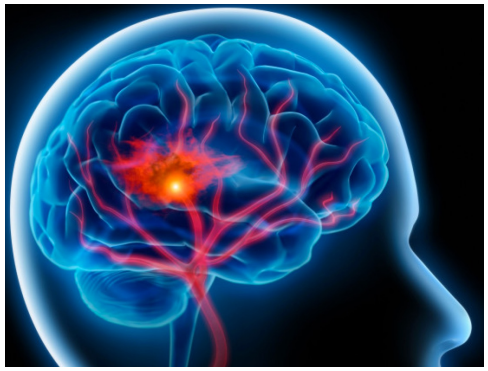
CDC

Stroke



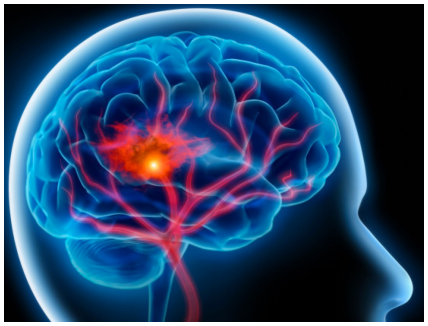
- Hemorrhagic - from a vascular bleed such as an aneurysm
- Non-hemorrhagic - usually caused by thromboembolic events and cerebrovascular atherosclerosis

Stroke



- Risk Factors
  - hypertension,
  - history of a previous stroke,
  - diabetes,
  - smoking, and
  - CHD (Coronary Heart Disease)
  - Recent systemic bacterial or viral infection (5x risk)
    - significantly greater ischemia
    - more severe post-ischemic neurologic defect
    - slightly higher levels of plasma fibrinogen
    - significantly higher levels of CRP

Periodontal Disease and Stroke

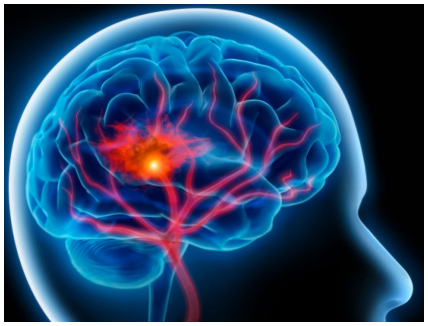


- Case-control studies:
  - Poor oral health was a significant risk factor for cerebrovascular ischemia
  - BOP, suppuration, SubG calculus, and the number of periodontal or periapical lesions were significantly greater in male stroke patients

- Men under age 50: Association between significant dental infection (poor oral health) and stroke, 25% vs. 2.5%

- Patients 50 and older:
  - Significantly more severe periodontitis and more periapical lesions than controls
  - Poor dental health an independent risk factor

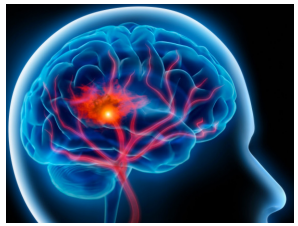
Periodontal Disease and Stroke



- <u>18 year longitudinal study:</u>
  - > 20% mean radiographic bone loss at baseline = 3x risk for Stroke
  - Periodontitis was a greater risk factor for stroke than was smoking and was independent of other known risk factors.

- <u>Meta-analysis:</u>
  - The risk of stroke was significantly increased by the presence of periodontitis [relative risk 1.63 (1.25, 2.00)].
  - Tooth loss was also a risk factor for stroke [relative risk 1.39 (1.13, 1.65)]. (Lafon, A. et al. 2014)

Periodontal Disease and Stroke

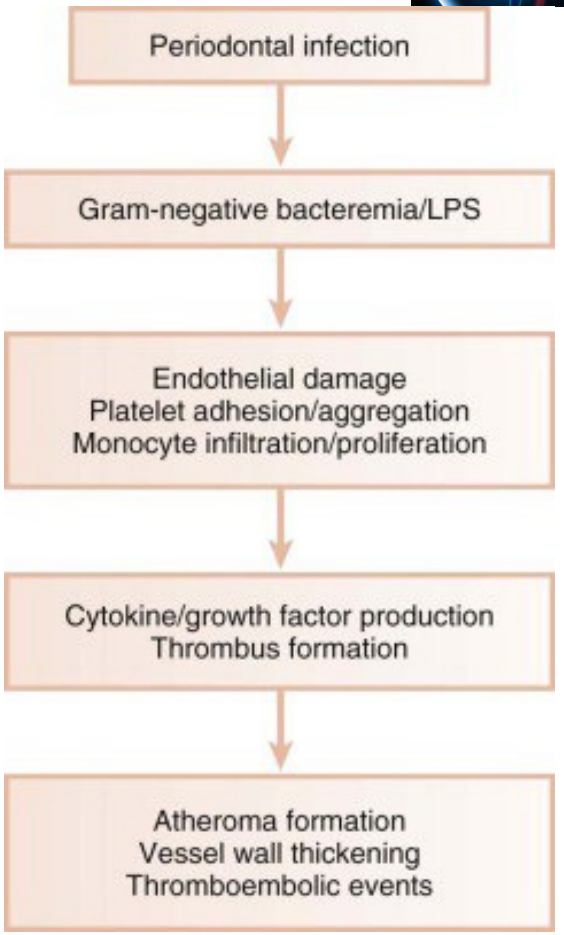


- Periodontal disease primarily associated with increased risk of non-hemorrhagic stroke

- Recent evidence suggests an association between periodontitis and haemorrhagic stroke as well, greater in males, obese patients and non-diabetics. (Sfyroeras *et al.,* 2012)

Periodontal Disease and Stroke

- Direct Effect
- Indirect Effect:
  - Elevated production of fibrinogen and CRP increase the risk of stroke
  - Bacteremia with PAAP-positive bacterial strains (*S. Sanguis, P. gingivalis*) increase platelet aggregation, contributing to thrombus formation and subsequent thromboembolism, the leading cause of stroke.

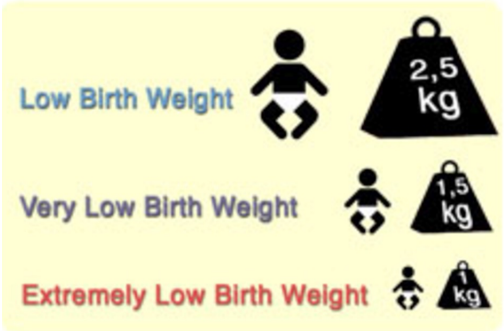


PAAP-Platelet aggregation-associated protein

Pregnancy and Periodontal disease

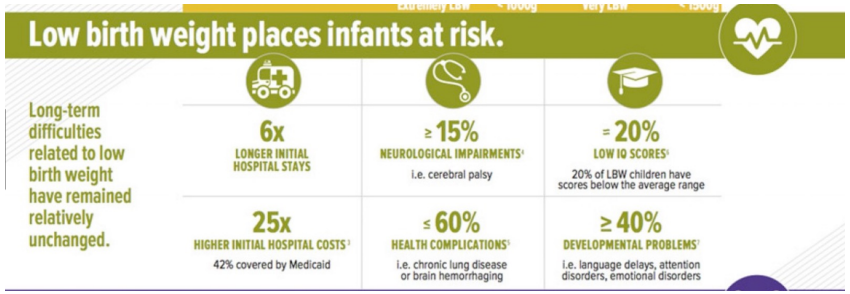
Adverse pregnancy outcomes

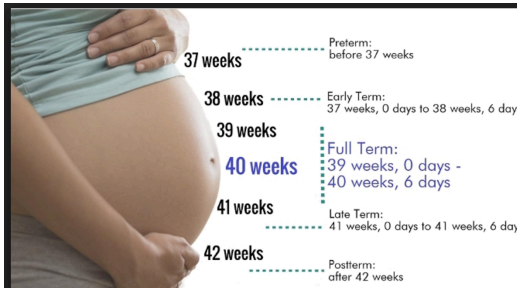
- Low birthweight (<2500 g) or
- Very low birthweight (<1500 g),



- Pre-term birth (<37 weeks) or
- Very pre-term (< 32 weeks),

- Growth restriction (weight for gestational age),
- Pre-eclampsia (commonly defined as maternal hyper-tension and proteinuria after the 20th gestational week)
- Miscarriage and/or
- Still birth.





Periodontitis and adverse pregnancy outcomes: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases 2013

- Low birthweight, pre-term birth and pre-eclampsia have been associated with maternal periodontitis exposure.

- However, the strength of the observed associations is modest and seems to vary according to the population studied, the means of periodontal assessment and the periodontal disease classification employed.

PERIODONTITIS AND ADVERSE PREGNANCY OUTCOMES:
CONSENSUS REPORT OF THE JOINT EFP/AAP WORKSHOP ON PERIODONTITIS AND SYSTEMIC DISEASES 2013

- Biological mechanisms: Two major pathways have been identified-
  - Direct: Oral microorganisms and/or their components reach the foetal placental unit and
  - Indirect: Inflammatory mediators circulate and impact the foetal-placental unit.

PERIODONTITIS AND ADVERSE PREGNANCY OUTCOMES:
CONSENSUS REPORT OF THE JOINT EFP/AAP WORKSHOP ON PERIODONTITIS AND SYSTEMIC DISEASES 2013

- Goal of professional intervention should be to reduce the bacterial load and signs of inflammation.
- Frequent monitoring should be maintained throughout pregnancy
- Periodontal treatment should be the standard non-surgical periodontal therapy with the goal of reducing the subgingival biofilm and the signs of periodontal inflammation. If possible, extensive traumatic interventions should be avoided.
- In presence of localized gingival enlargements, surgical excision should be delayed if possible until the inflammation has been controlled.
- Recommend supportive measures (oral hygiene instruction) and re-evaluation after delivery.

Periodontitis and adverse pregnancy outcomes: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases 2013

- Although periodontal therapy has been shown to be safe and leads to improved periodontal conditions in pregnant women, case-related periodontal therapy with or without systemic antibiotics does not reduce overall rates of pre-term birth and low birthweight.

Acknowledgements

- CVD and Periodontitis – Adapted from Dr. Katancik's lecture

- Questions?

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