PLAQUE ATTACK

ATHEROSCLEROSIS: THE VILLAIN OF THE VESSELS

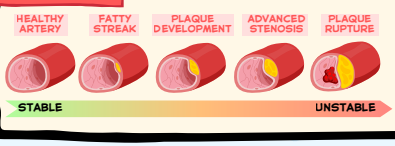
CHARACTERS

OVERVIEW

ATHEROSCLEROSIS IS THE GLOBAL LEADING CAUSE OF CARDIOVASCULAR DISEASE (CVD) WORLDWIDE.

- **19.8M** GLOBAL CVD-RELATED DEATHS ANNUALLY (WHO, 2022)
- **50%** OF WESTERN SOCIETY DEATHS HAVE ASCVD AS THE UNDERLYING CAUSE (PAHWA ET AL., 2023)
- **75%** OF HEART ATTACKS OCCUR FROM PLAQUE RUPTURE (PAHWA ET AL., 2023)
- **87%** OF INDIVIDUALS 60+ HAVE SOME DEGREE OF PLAQUE FORMATION (DILE-HANSEN ET AL., 2018)

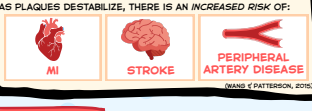
INTRODUCTION



ATHEROSCLEROSIS (ASCVD) BEGINS WITHOUT WARNING, ACCUMULATING SLOWLY.

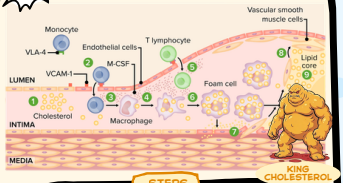
GRADUAL BUILDUP OF PLAQUES IN MEDIUM TO LARGE ARTERIES LEADING TO NARROWING AND REDUCED BLOOD FLOW OVER TIME.

AS PLAQUES DESTABILIZE, THERE IS AN *INCREASED RISK* OF:



(MANS & PATTERSON, 2015)

PATHOPHYSIOLOGY



STEPS

1. **ENDOTHELIAL DYSFUNCTION**
   INITIATING FACTORS: SHEAR STRESS, SMOKING, HYPERLIPIDEMIA

   INDUCES: ↑VASCULAR PERMEABILITY, ADHESION MOLECULE EXPRESSION → LDL INFILTRATION INTO INTIMA, OXIDATIVE MODIFICATION (OXLDL)
2. **LIPID ACCUMULATION & INFLAMMATION**
   OXLDL → MONOCYTE ADHESION/MIGRATION INTO VESSEL WALL

   MONOCYTES → **MACROPHAGES** AND ENGULF OXLDL → FOAM CELLS AGGREGATION OF FOAM CELLS → FATTY STREAKS (EARLIEST VISIBLE LESION)
3. **CHRONIC INFLAMMATORY RESPONSE**
   MACROPHAGE AND **T-CELL** RECRUITMENT SUSTAINS INFLAMMATION

   CYTOKINE AND **GF** RELEASE AMPLIFIES VASCULAR INJURY FROM FATTY STREAK → FIBROFATTY PLAQUE
4. **SMOOTH MUSCLE CELL (SMC) ACTIVATION**
   SMCS MIGRATE TO INTIMA AND **PROLIFERATE** PRODUCE **EXTRACELLULAR MATRIX** (COLLAGEN, ELASTIN) → FIBROUS CAP FORMATION

   PLAQUE GROWTH AND ARTERIAL WALL THICKENING

5. **PLAQUE PROGRESSION & INSTABILITY**
   LIPID-RICH **NECROTIC CORE** DEVELOPS BENEATH FIBROUS CAP

   MATRIX DEGRADATION (VIA PROTEASES) WEAKENS THE CAP PLAQUE RUPTURE EXPOSES THROMBOGENIC MATERIAL → THROMBOSIS AND ACUTE OCCLUSION

(SAKAKURA ET AL., 2013)

RISK FACTORS

ATHEROSCLEROSIS IS DRIVEN BY:

1. **MODIFIABLE FACTORS:** HIGH LDL, LOW HDL, HIGH BLOOD GLUCOSE/DIABETES, HYPERTENSION, SMOKING, OBESITY, AND INACTIVITY.
2. **NON-MODIFIABLE FACTORS:** AGE, SEX, AND GENETICS.
3. **OTHER PLAYERS:** HIGH LIPOPROTEIN(A) AND CHRONIC INFLAMMATION.

(FRUCHART ET AL., 2004)

CLINICAL MANIFESTATIONS

ASYMPTOMATIC IN EARLY STAGES UNTIL ARTERIAL NARROWING OR PLAQUE RUPTURE SIGNIFICANTLY IMPAIRS BLOOD FLOW.

CORONARY ARTERIES

- **STABLE ANGINA:** EXERTIONAL CHEST PAIN
- **ACUTE CORONARY SYNDROME:** UNSTABLE ANGINA, MYOCARDIAL INFARCTION
- DYSPNEA
- FATIGUE

CAROTID & CEREBRAL ARTERIES

- TRANSIENT ISCHEMIC ATTACKS (TIAS)
- ISCHEMIC STROKE
- DIZZINESS
- WEAKNESS
- VISION OR SPEECH DISTURBANCES

PERIPHERAL ARTERIES

- INTERMITTENT CLAUDICATION
  - PAIN WITH WALKING, RELIEVED BY REST
- REDUCED PULSES, COOL EXTREMITIES
- CRITICAL LIMB ISCHEMIA (REST PAIN, ULCERS, GANGRENE)

RENAL ARTERIES

- SECONDARY HYPERTENSION
- PROGRESSIVE RENAL INSUFFICIENCY
  - GENERAL FEATURES OF ADVANCED DISEASE
- SYMPTOMS TRIGGERED BY REDUCED PERFUSION OR ACUTE PLAQUE RUPTURE WITH THROMBOSIS

OTHER MANIFESTATIONS
- PANCREATIC AND HEPATOBILIARY DISEASE
- OCULAR/RETINAL DISEASES

CAN LEAD TO LIFE-THREATENING ISCHEMIC EVENTS

(SAKAKURA ET AL., 2013)

DIAGNOSTIC APPROACHES

BLOOD TESTS

MEASURE BLOOD SUGAR AND CHOLESTEROL, BOTH OF WHICH ARE RISK FACTORS FOR ASCVD.

MAY INCLUDE A C-REACTIVE PROTEIN (CRP) TEST TO DETECT INFLAMMATION IN THE ARTERIES.

ECG

NON-INVASIVE TEST THAT MEASURES THE ELECTRICAL ACTIVITY OF THE HEART.

IT IS USED TO DETECT:
- REDUCED BLOOD FLOW
- ABNORMAL RHYTHMS
- SIGNS OF DAMAGE

EXERCISE STRESS TEST

MONITORS HEART ACTIVITY DURING PHYSICAL EXERTION OR MEDICATION-INDUCED STRESS.

IT IS USED TO DETECT:
- ABNORMALITIES IN BLOOD FLOW
- CHANGES IN HEART FUNCTION NOT SEEN AT REST

ANGIOGRAM (CORONARY ANGIOGRAPHY)

AN IMAGING PROCEDURE THAT USES A CATHETER AND CONTRAST DYE TO VISUALIZE THE CORONARY ARTERIES.

IT IS USED TO DETECT:
- NARROWED/BLOCKED ARTERIES
- REDUCED BLOOD FLOW
- LOCATION AND SEVERITY OF PLAQUE BUILDUP

ECHOCARDIOGRAM

AN IMAGING TEST THAT USES SOUND WAVES TO VISUALIZE HEART STRUCTURE AND BLOOD FLOW (SOMETIMES USED DURING STRESS TESTING).

IT IS USED TO DETECT:
- ABNORMALITIES IN HEART SIZE AND SHAPE
- IMPAIRED BLOOD FLOW
- FUNCTIONAL ISSUES

(POZNIAK ET AL., 2023) (MENG ET AL., 2022)

TREATMENT & MANAGEMENT

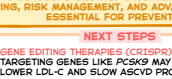
1. **LIFESTYLE**

2. **MEDICATION**

3. **INTERVENTIONS**

(LEWIS, 2009) (JAMKHANDE ET AL., 2014) (LIU ET AL., 2022)

CONCLUSION



ASCVD DEVELOPS SILENTLY OVER TIME, MAKING EARLY SCREENING, RISK MANAGEMENT, AND ADVANCES IN TREATMENT ESSENTIAL FOR PREVENTION.

NEXT STEPS

1. GENE EDITING THERAPIES (CRISPR): TREATMENTS TARGETING GENES LIKE *PCSK9* MAY PERMANENTLY LOWER LDL-C AND SLOW ASCVD PROGRESSION.
2. ADVANCED MOLECULAR IMAGING: NEW TECHNIQUES USING NANOPARTICLES AND TARGETED TRACERS CAN DETECT HIGH-RISK PLAQUES EARLIER AND MORE PRECISELY.
3. AI-ASSISTED ECG: USES AI TO DETECT SUBTLE CHANGES IN ECG TO IMPROVE ASCVD RISK PREDICTION.

(MARTÍNEZ-SELLÉS & MARINA-BREYSSE, 2023) (WALKER ET AL., 2021) (LIBBY ET AL., 2019)