

The Origin of Cardiovascular Disease

Now explained



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RESEARCH INSTITUTE

The origin of Cardiovascular Disease and the role of lipoproteins

- What is Cardiovascular Disease (CVD)
- Conventional understanding of CVD
- Inadequacy of the current concept of CVD – the need for a new rationale
- Modern new understanding of CVD developed by Dr. Rath
- Lipoproteins and their role in CVD
- Vitamin C and cardiovascular health
- Implications of this new understanding

What is Cardiovascular Disease (CVD)

Disease of the blood vessels of the heart and the body.

The underlying disease process is called **Atherosclerosis**:

- Hardening and narrowing of the arteries.
- Risk of blocking the blood flow in the arteries causing heart attack and stroke.



What causes Cardiovascular Disease

Focus 1

Old versus New Thinking

Focus 2

Conventional Thinking

- ✓ High levels of **cholesterol** circulating in the bloodstream **damage** the inside of the blood vessel walls.
- ✓ Fat transporting molecules, primarily **Low-Density-Lipoprotein (LDL)**, enter the artery wall and deposit their fat content inside the wall.
- ✓ The deposition serves **no biological purpose**



Modern Concept

- ✓ Long-term **vitamin deficiencies** initiate the structural impairment of the artery wall.
- ✓ Fat transporting molecules, primarily **Lipoprotein(a)**, enter the artery wall to be deposited there for the purpose of structural repair.
- ✓ The deposition serves a **distinct biological purpose:** mend the injuries and prevent fatal blood loss.

Heart Disease

Focus 1:

Conventional Thinking



What causes Cardiovascular Disease

CONVENTIONAL MEDICINE

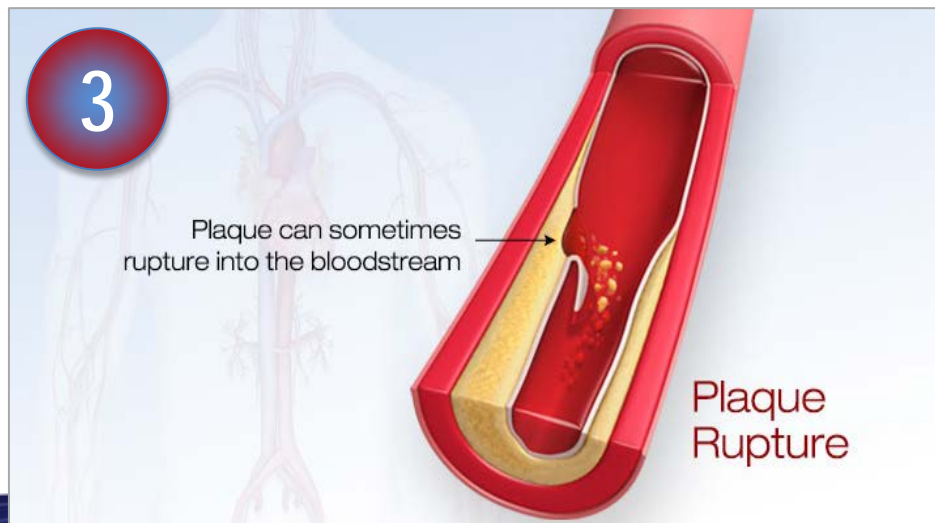
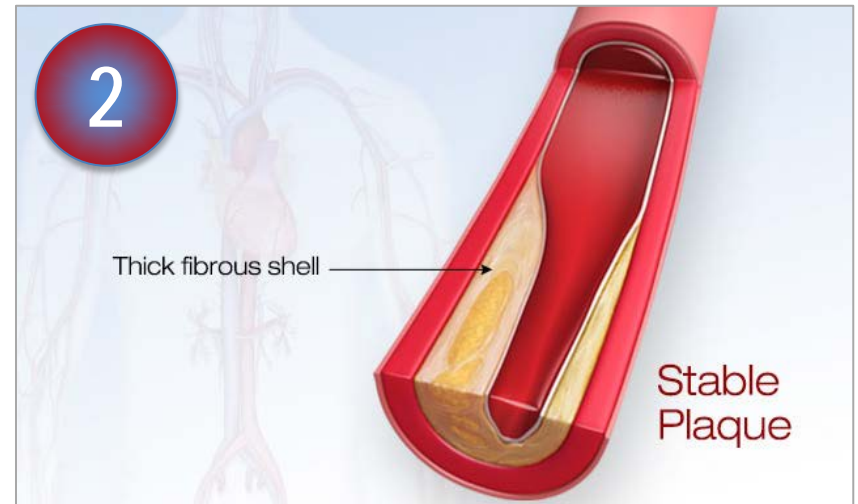
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Conventional Thinking

Development of Atherosclerosis



Conventional Thinking

Advanced Thrombosis

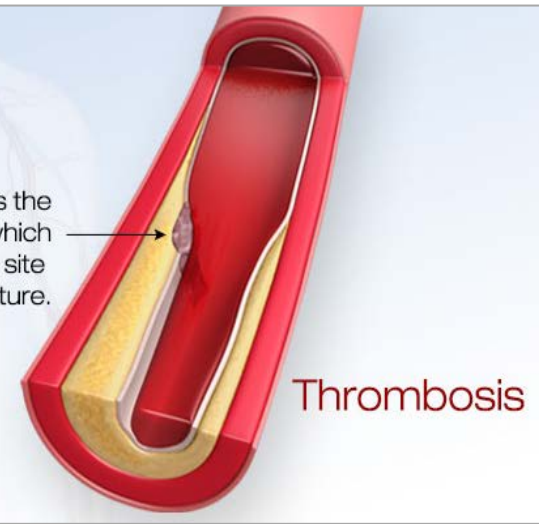
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If the blood clot enlarges to completely block the artery, all tissues supplied by that artery begin to die below the blockage.



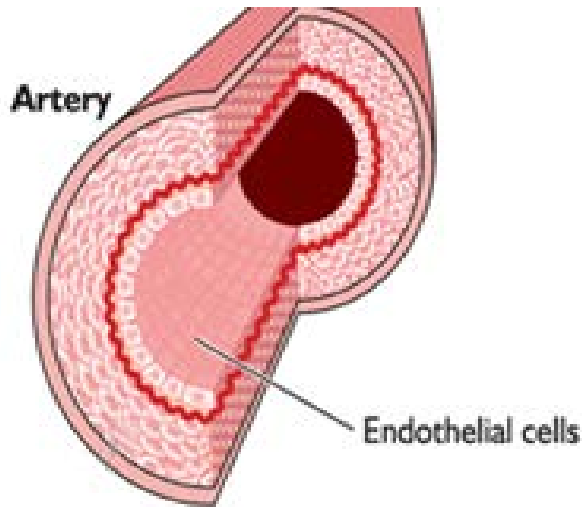
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Thrombosis is the clotting of blood which begins at the site of the plaque rupture.



Conventional Thinking

Sequence of Events



Note: The endothelium is the thin layer of cells that lines the interior surface of blood vessels, forming an interface between circulating blood and the vessel wall.

Stage 1:

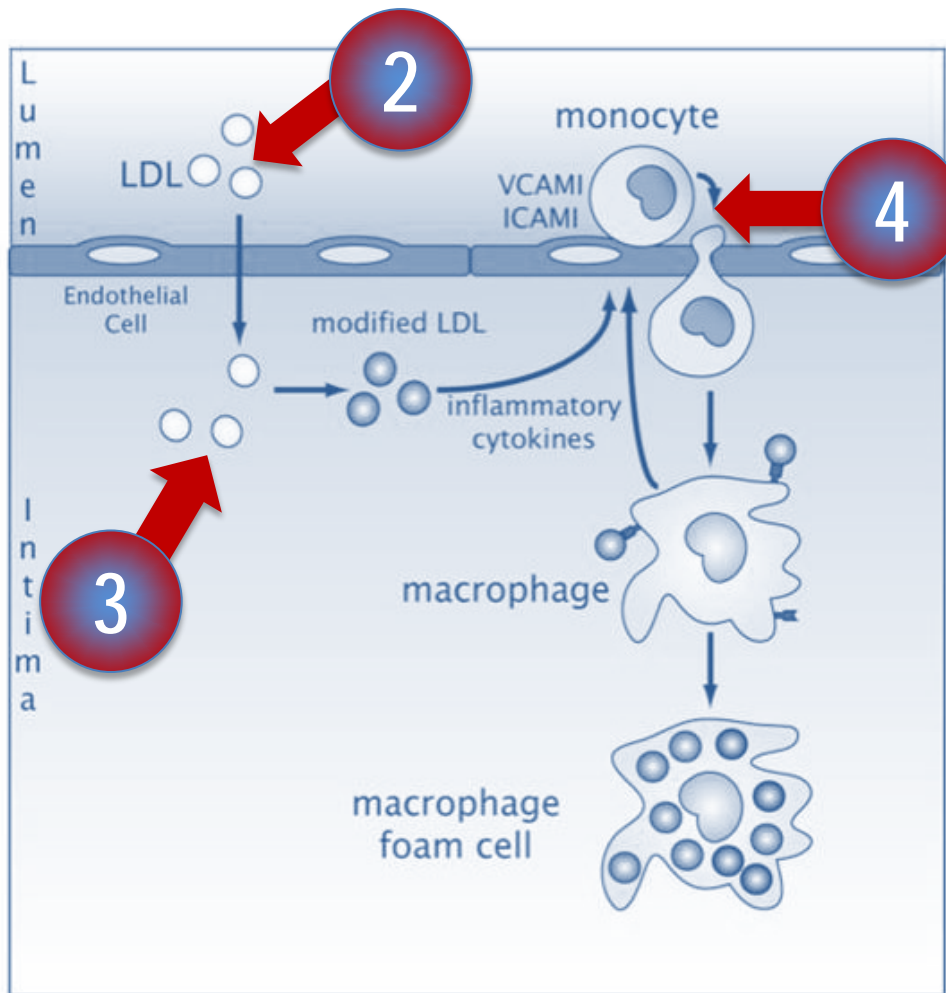
Damaged endothelium

Conventional thinking assumes that elevated blood levels of cholesterol-carrying molecules -- primarily **Low Density lipoproteins (LDL)** -- damage the endothelial cells of the blood vessel wall.

Thereby, so the conventional theory goes, the process of atherosclerosis is initiated.

Since the cholesterol blood levels are the same throughout the blood vessel system, this theory would necessarily mean that we get infarctions in all organs of our body at the same rate – not just heart attacks and strokes.

Conventional Thinking Sequence of Events



Despite the missing logic, conventional thinking assumes the following next steps:

Stage 2:

Following the alleged damage by cholesterol, the endothelium becomes more permeable to fat transporting molecules (LDL).

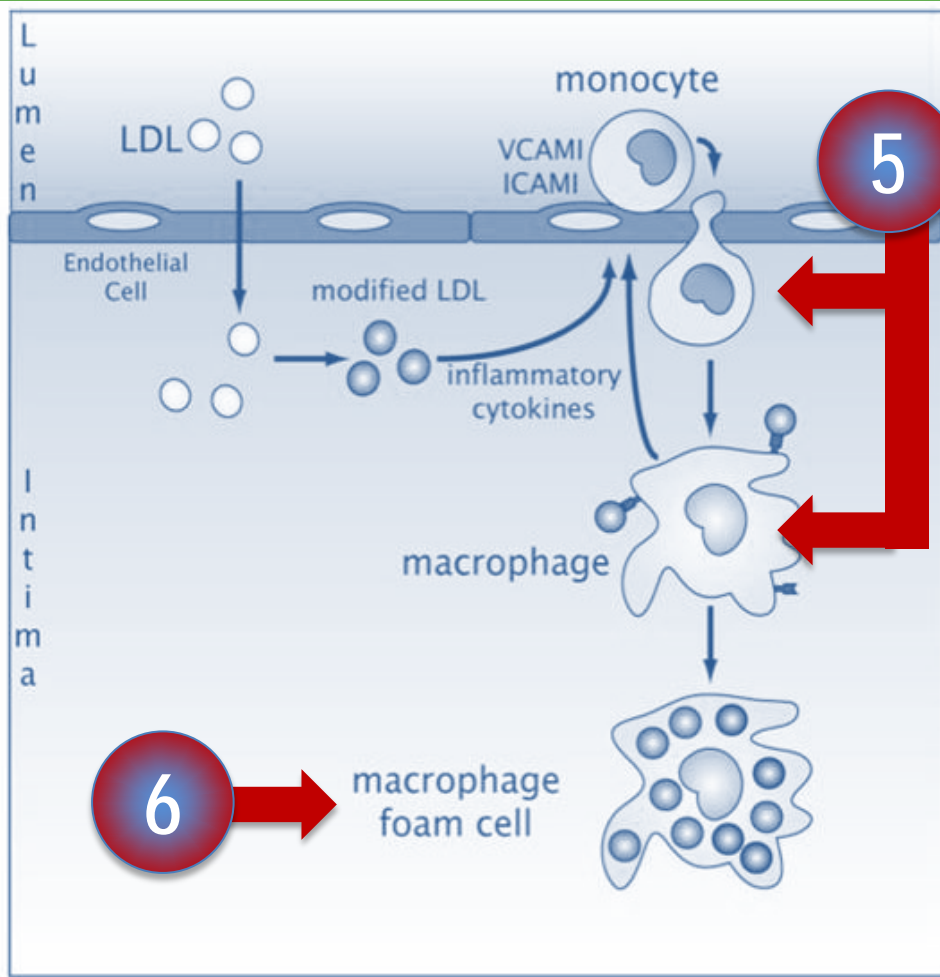
Stage 3:

LDL particles penetrate the vascular wall. They are deposited in the intima, where they may undergo oxidation.

Stage 4:

Endothelial cells respond by attracting white blood cells (monocytes) from the blood stream that allegedly enter the blood vessel wall to eat up the abundantly deposited cholesterol.

Conventional Thinking Sequence of Events



Despite the continued missing logic, conventional thinking makes further assumptions:

Stage 5:

Monocytes enter the arterial walls and transform into 'police cells' (macrophages).

Stage 6:

The macrophages absorb (oxidized) LDL molecules and transform into foam cells. Conglomerates of foam cells form fatty streaks.

Stage 7:

Eventually, so the conventional theory goes, the macrophages 'overeat' and burst, releasing free cholesterol and other molecules into the artery wall.

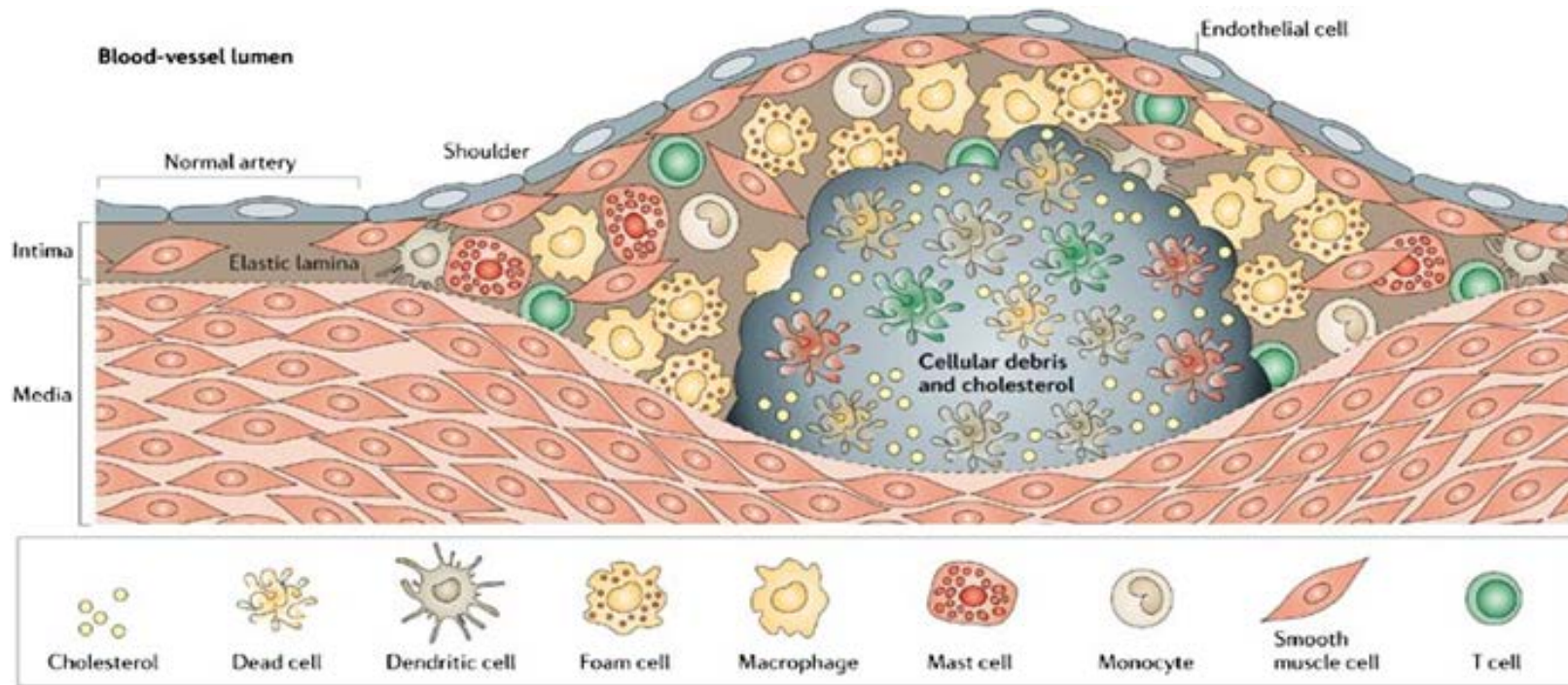
Note: Foam cell = lipid loaded macrophages, generated from massive uptake of modified LDL.

Conventional Thinking

Sequence of Events

Stage 8: Fibrous cap

Stimulated by signal molecules (cytokines), so the theory goes, smooth muscle cells (from the muscular layer of the artery wall) start to multiply and form a fibrous cap covering the lipid center (atherosclerotic plaque).



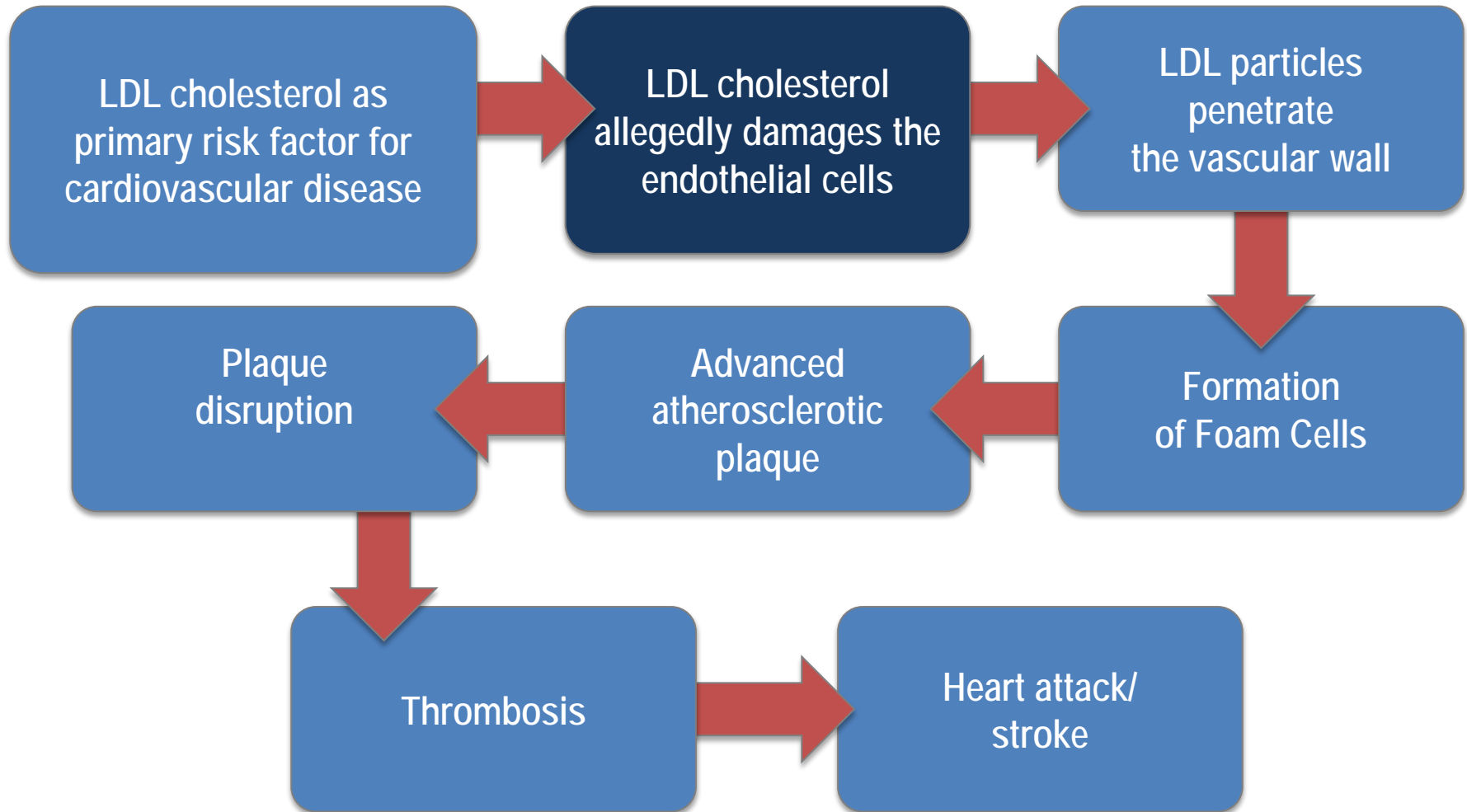
Conventional Thinking Sequence of Events

Stage 9: Plaque rupture

Eventually, the fibrous cap ruptures leading to undesirable consequences:

- ✓ thrombus formation at the site of the plaque rupture
- ✓ impaired blood flow, which can lead to **heart attacks** or **strokes**

Conventional Thinking Overview



Conventional Thinking

Problem Statements

Why the conventional thinking about high cholesterol levels as the primary origin of human cardiovascular disease
has to be urgently replaced

PROBLEM: Conventional thinking cannot solve these basic questions of cardiology (I)

High blood cholesterol is evenly distributed in the arteries and veins of the 60,000 miles (100,000 km) long vascular system of the human body. If cholesterol was damaging the blood vessels we would inevitably develop:

- a. Atherosclerotic deposits all along our blood vessel system – and not primarily in the short coronary arteries of the heart (about 30 cm long).
- b. Infarctions in ears, nose and all other organs at the same rate – not just heart attacks.
- c. Atherosclerosis not just in the arteries but also the veins.



PROBLEM: Conventional thinking cannot solve these basic questions of cardiology (II)

- c. Animals that sleep through the winter (hibernators) have extremely high blood cholesterol levels (400mg/dl and above). If high cholesterol was damaging the artery walls, thereby initiating atherosclerosis, these animals would have been extinct long ago.

“Heart disease in animals is not impossible, it simply does not generally occur.”

If the reason for this could be determined, it may cast a useful light on its occurrence in humans.”

Smith & Jones, Textbook of Veterinary Pathology



PROBLEM:
The economic consequences

Despite a missing scientific and logical rationale, the conventional thinking of CVD serves as the basis for an over \$30 billion market in cholesterol-lowering drugs.

These huge expenses are burdening the people and strangulating economies around the world.

Conventional Thinking

In summary:

There are **scientific and economic** reasons why conventional thinking about the origin of cardiovascular disease has to be urgently replaced

The modern approach



can solve this and other puzzles of cardiology.

Let's see how....

New Understanding of CVD



Focus 2:

What causes Cardiovascular Disease

Old versus new thinking

MODERN CONCEPT

- ✓ Long-term **vitamin deficiencies** initiate the structural impairment of the artery wall.
- ✓ Fat transporting molecules, primarily **Lipoprotein(a)**, enter the artery wall to be deposited there with the purpose of structural repair.
- ✓ The deposition serves a **distinct biological purpose**: mend the injuries and prevent fatal blood loss.

New Understanding Introducing a new Concept of CVD

1990

Publications by M. Rath & L. Pauling

- ✓ Atherosclerosis is an early form of scurvy.
- ✓ Lipoprotein(a) is a repair molecule that functions as a surrogate for vitamin C in the impaired vascular wall.

Proceedings of the National Academy of Sciences 1990, 87: 6204-6207
Proceedings of the National Academy of Sciences 1990, 87: 9388-9390



New Understanding Recognizing its key elements

2010

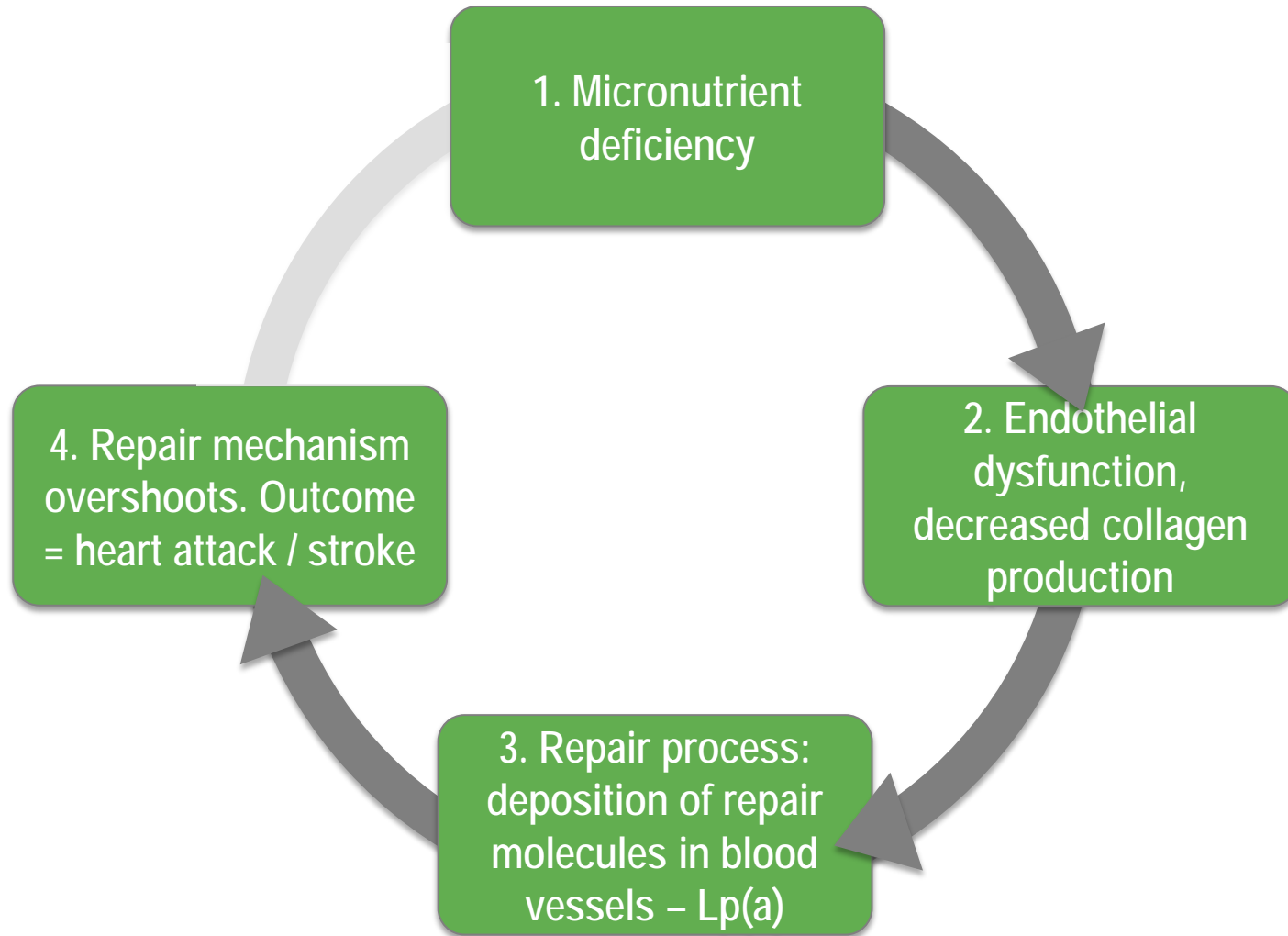
European Atherosclerosis Society (AES)

The AES stresses the significance of Lp(a)
& recommends screening for elevated Lp(a)
levels.

*... the evidence clearly supports Lp(a) as a priority
for reducing cardiovascular risk, beyond that
associated with LDL-C...*

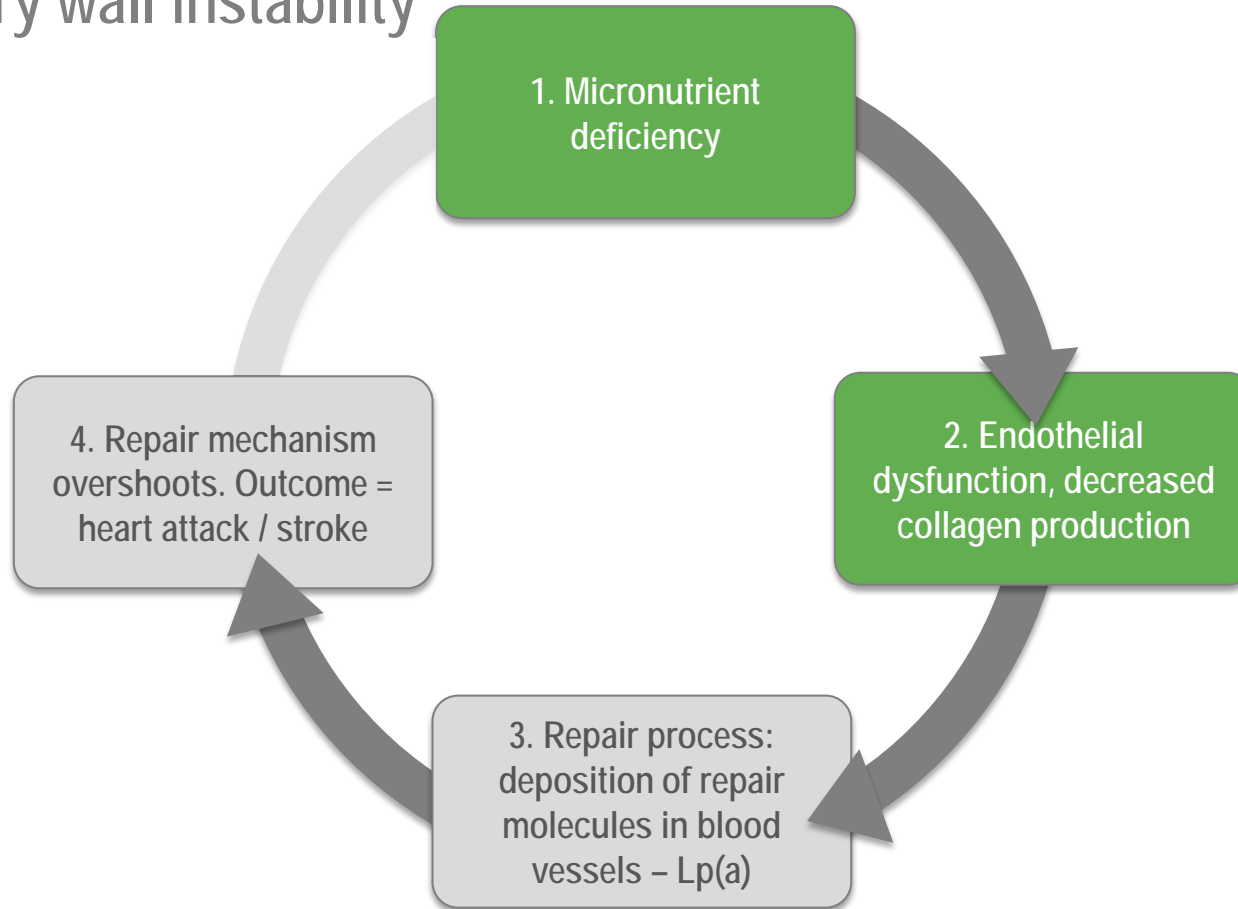


Moving from the old to the new: Key modifications



Moving from the old to the new: Key modifications

1. The underlying cause of endothelial dysfunction and artery wall instability



New Understanding

Vitamin deficiency triggers atherosclerosis

The main cause of endothelial dysfunction and vascular instability:

Long term **deficiency of micronutrients**, in particular **vitamin C**, results in a **structural weakness of the blood vessel wall** & the development of cracks.



This deficiency is **primarily manifested** at those sites of our cardiovascular system that are exposed to the **highest mechanical stress**: the coronary arteries of the heart.

New Understanding

Vitamin deficiency triggers atherosclerosis



In summary:

Cardiovascular disease does **not** start with **elevated cholesterol** levels that allegedly damage the artery walls.



Atherosclerosis starts with vitamin deficiency causing **increased gaps** between endothelial cells and the **structural impairment** of the connective tissue in the artery walls.

New Understanding

Atherosclerosis – An overshooting repair process

Our body initiates **a repair process** by depositing repair molecules inside the blood vessel walls, including

- ✓ fat carrying lipoprotein molecules
- ✓ carbohydrates (sugars)
- ✓ blood clotting (coagulation) factors



New Understanding

Atherosclerosis – An overshooting repair process

Conclusion:

Atherosclerosis is **not an arbitrary development** but the result of a biological regulatory process, which **protects** the walls against blood loss.

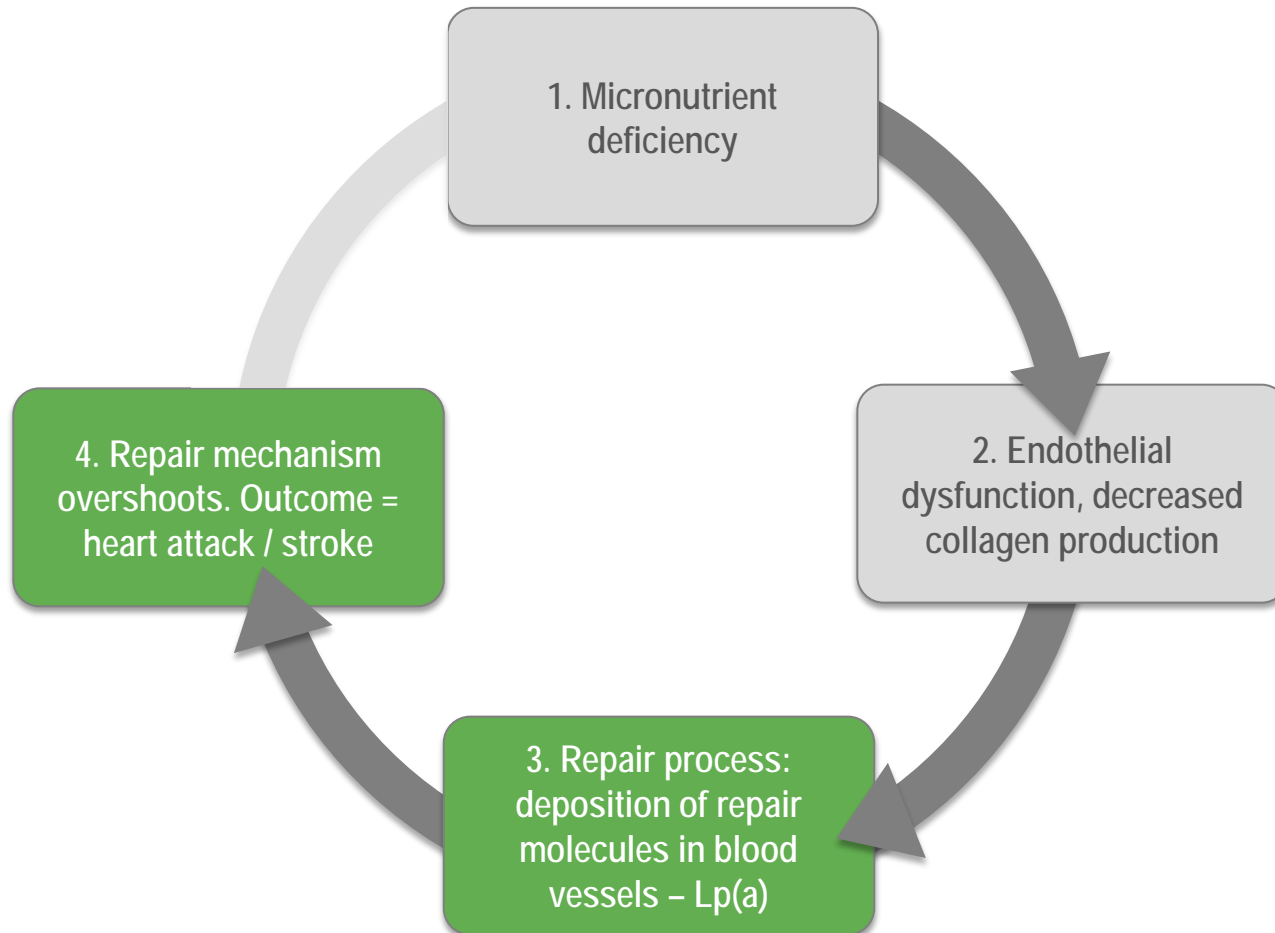
If this repair mechanism lasts for too long it overshoots, leading to the development of atherosclerotic plaques and clogging of the coronary arteries, which might result in a **heart attack**.



Moving from the old to the new:

Key modifications

2. The role of Lp(a)



Before we continue:

What are Lipoproteins?

Lipoproteins: Transport function

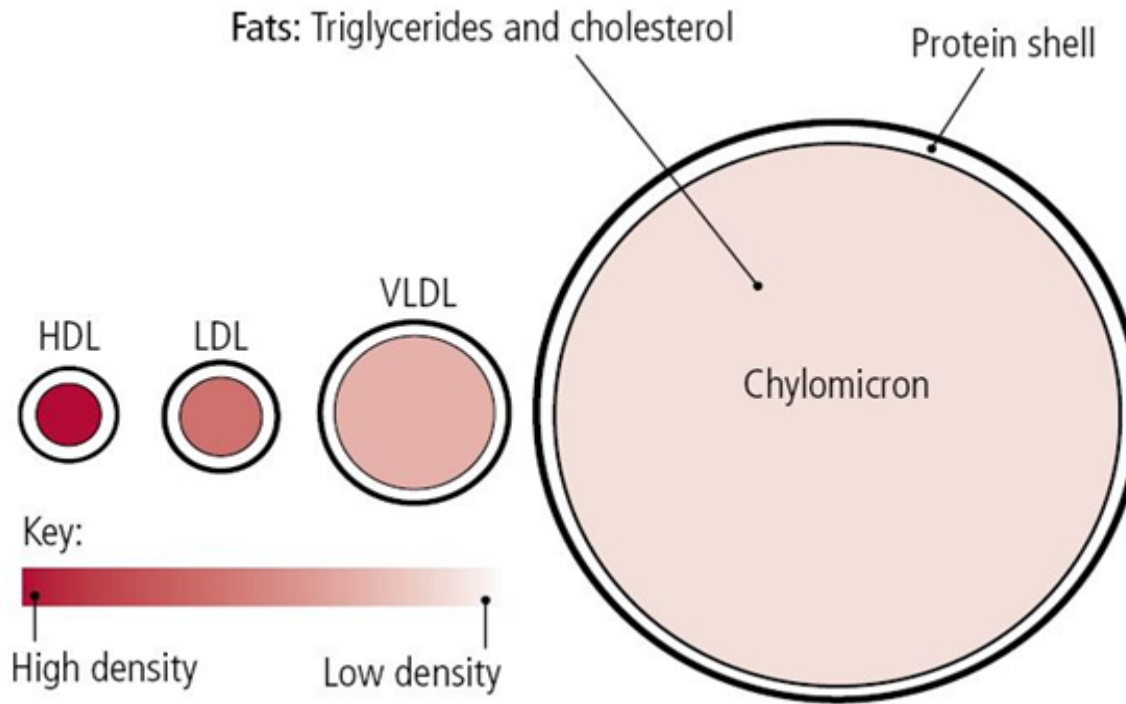


Molecules that transport lipids (cholesterol) through the body

Lipids (oil-soluble substances such as fat and cholesterol) do not travel through the body by themselves but are carried through the bloodstream in association with proteins as lipoproteins.

What are Lipoproteins?

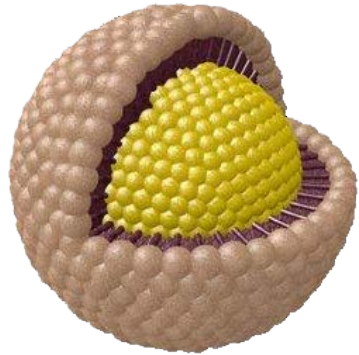
The different Subtypes



They have different densities. The higher the ratio of fat-protein, the lower the density. In other words: more fat means lower density.

What are Lipoproteins?

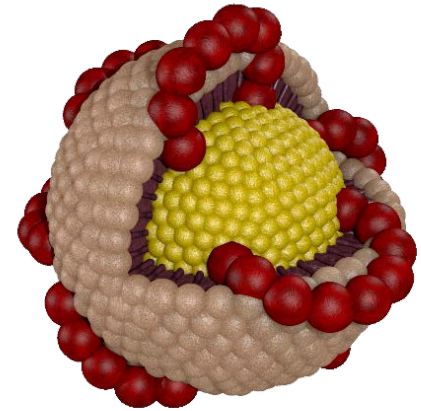
The different Subtypes



+



=



Lipid Globule

- Cholesterol
- Triglycerides
- Others

Protein

(Apolipoprotein B-100,
Apo-B-100)

Lipo-Protein

(Low Density
Lipoprotein, LDL)

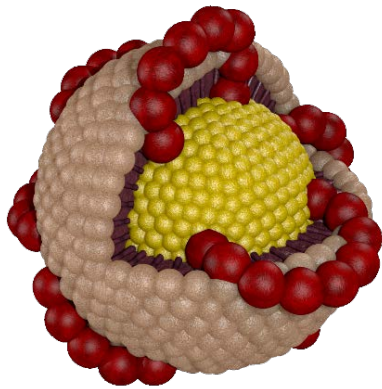
LDL

LDL – ‘Bad cholesterol’

What are Lipoproteins?

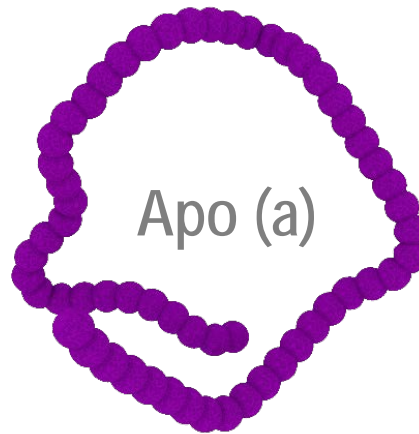
Lipoprotein(a) – the most dangerous of all

LDL



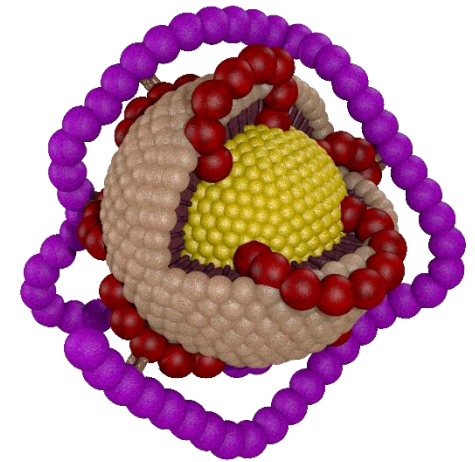
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Apo (a)



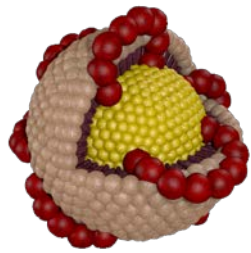
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Lp(a)



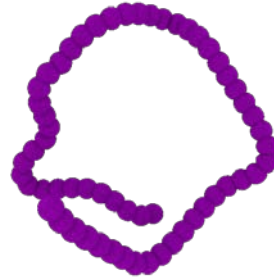
What are Lipoproteins?

Lipoprotein(a)



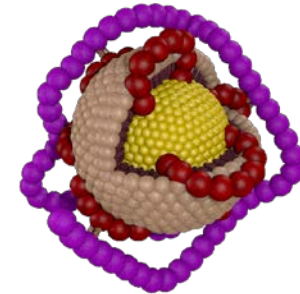
LDL

+



Apo(a)

=



Lp(a)

Lp(a) is a genetic variation of LDL (known as 'bad cholesterol')

Composed of

- A low-density lipoprotein (LDL) molecule
- An additional surface protein: apolipoprotein (a)

Apolipoproteins = protein molecules; help to stabilize the particle and serve to identify the specific lipoprotein. Allows tissues to recognize and interact with the particle.

What are Lipoproteins?

Lp(a) as a repair molecule

Key features of Lp(a):

- 1) Contains a very large biological *adhesive tape* – the **apo(a)** protein molecule.
 - ✓ One of the largest & stickiest molecules in nature
 - ✓ Structural homology to plasminogen, one of the most important molecules in the process of blood clot formation and dissolution.
- 2) Contains the LDL component: an essential substrate for the growth of new cells within the area of repair.



New Understanding

Advantages of the unique structure of Lp(a)

Because of its unique structure, Lp(a) – as opposed to LDL – easily binds to:

1. **Endothelial cells** – which form the cellular barrier between the bloodstream and the artery wall.
2. **Connective tissue** components such as collagen and elastin, as well as blood-derived molecules, for instance fibrinogen/fibrin, that are deposited inside the artery walls.



Important for repairing an artery wall that has been weakened by dietary vitamin deficiency

New Understanding

Studies confirm association between Lp(a) & atherosclerosis

- I. Lp(a) – not LDL – is the primary fat-transporting constituent of atherosclerotic plaques.
- II. Lp(a) is present in atherosclerotic lesions in amounts proportional to circulating plasma levels, but not in normal arterial walls.
(Arteriosclerosis. 1989 Sep-Oct;9(5):579-92)
- III. Both low-density lipoprotein and lipoprotein(a) have an important role in the pathogenesis of atherosclerosis.
(Virchows Archiv of Pathological Anatomy and Histopathology, 1990 417(2):105-11)

New Understanding

Studies confirm association between Lp(a) & atherosclerosis

- IV. Lp(a) is more strongly retained in the arterial wall than LDL.
- V. Lp(a) promotes clot formation and prevents their dissolution as part of the atherosclerotic process.
- VI. Lp(a) promotes the adhesion of monocytes to the endothelial surface and enhances their migration across the endothelial barrier – a function thus far attributed primarily to LDL.

New Understanding

Many studies confirm significant association Lp(a) & CVD

- I. Elevated lipoprotein(a) (Lp[a]) is a causal genetic risk factor for cardiovascular disease.
Source: Lipoprotein(a), cardiovascular disease, and contemporary management. *Mayo Clin Proc* (2013).
- II. Genetic variants associated with Lp(a) lipoprotein level and coronary disease.
Source: Genetic variants associated with Lp(a) lipoprotein level and coronary disease. *N Engl J Med.*(2009).
- III. Under a wide range of circumstances, there are continuous, independent, and modest associations of Lp(a) concentration with risk of CVD and stroke.
Source: Lipoprotein(a) Concentration and the Risk of Coronary Heart Disease, Stroke, and Nonvascular Mortality. *JAMA* (2009).



New Understanding

Many studies confirm preventive role micronutrients

- I. Users of vitamin C supplements appear to be at lower risk for CVD.
Source: Vitamin C and risk of coronary heart disease in women.
Journal of the American College of Cardiology (2003).

- II. In patients undergoing elective percutaneous coronary intervention, preprocedure intravenous treatment with vitamin C is associated with less myocardial injury.
Source: The effect of intravenous vitamin C infusion on periprocedural myocardial injury for patients undergoing elective percutaneous coronary intervention.
Canadian Journal of Cardiology (2013).



New Understanding

Many studies confirm preventive role micronutrients

- III. Combined treatment with vitamins C and E has beneficial effects on endothelium-dependent vasodilation and arterial stiffness in untreated, essential hypertensive patients.

Source: Supplementation with vitamins C and E improves arterial stiffness and endothelial function in essential hypertensive patients.

American Journal of Hypertension (2007).

- IV. The relation of the mortality ratio for all causes of death to increasing vitamin C intake is strongly inverse for males and weakly inverse for females.

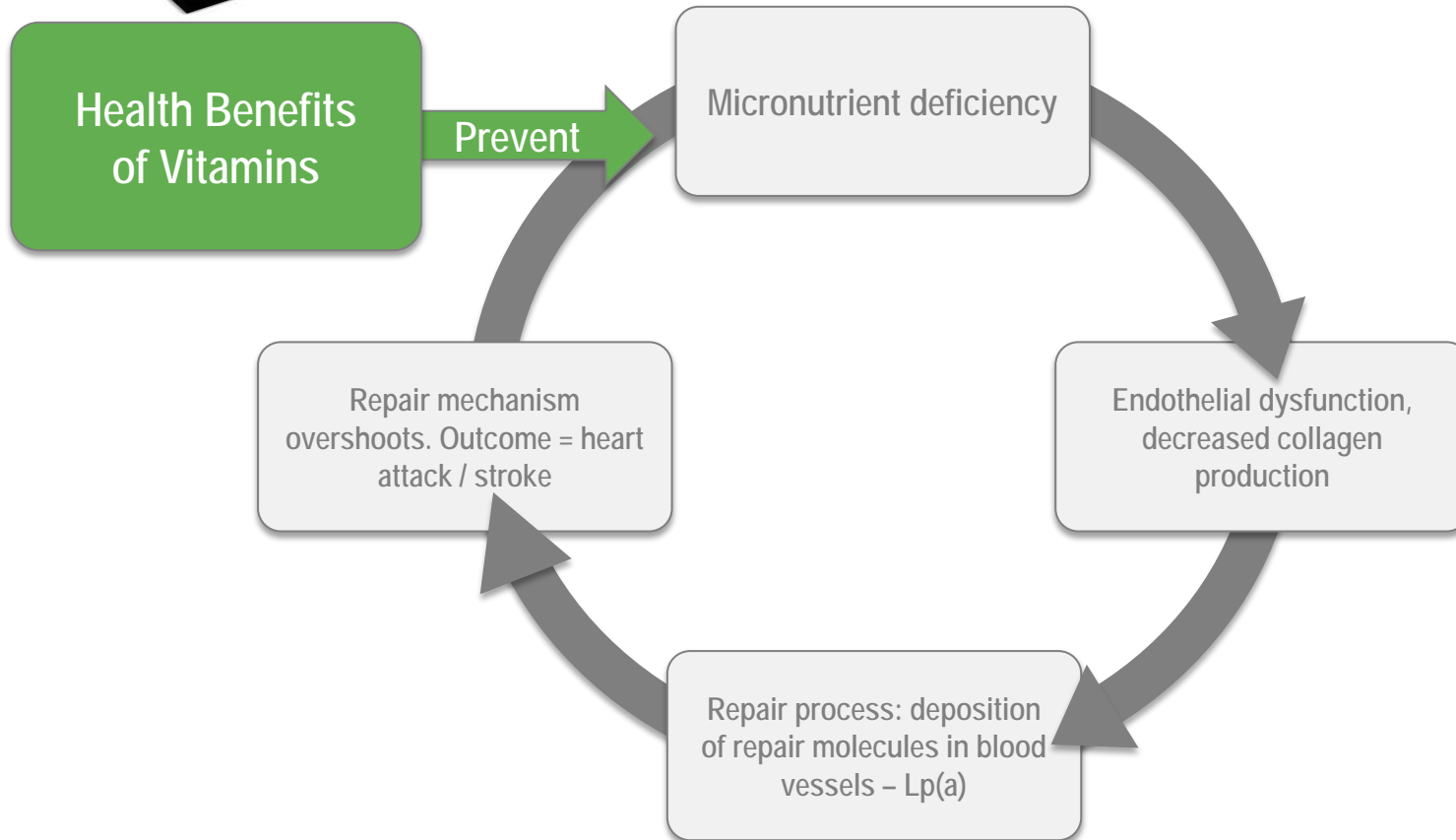
Source: Vitamin C intake and mortality among a sample of the
Epidemiology (1992).



Moving from the old to the new: Key modifications



Importance of Vitamin C



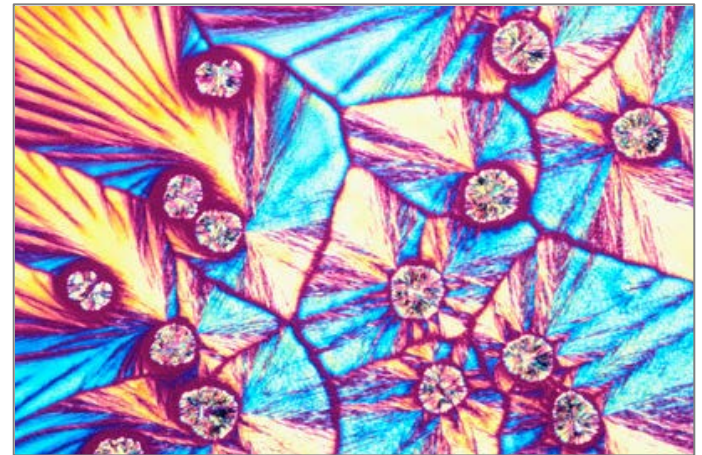
New Understanding

Vitamin C & stability of the artery walls

Vitamin C is essential for the production of **collagen** molecules, the stability structures in our blood vessels and the entire body.

Animals: produce high amounts of vitamin C and an optimum amount of collagen.
→ their artery walls are protected and stable.

Humans: have lost the ability to produce vitamin C and frequently get too few vitamins in their diet. As a consequence, impaired production of collagen leads to impaired stability of their artery walls.



Vitamin C crystals under microscope

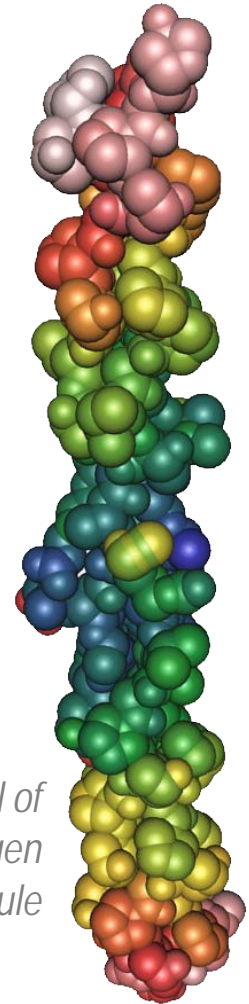
New Understanding

Vitamin C & stability of the artery walls

Collagen

The substance that holds the entire body together

- ✓ A large fibrous protein, made up of three chains of amino acids, the majority of which are Lysine and Proline
- ✓ The main component of **connective tissue**
As such, collagens have an important role in
 - Tissue architecture/integrity
 - Tissue strength



*A model of
a collagen
molecule*

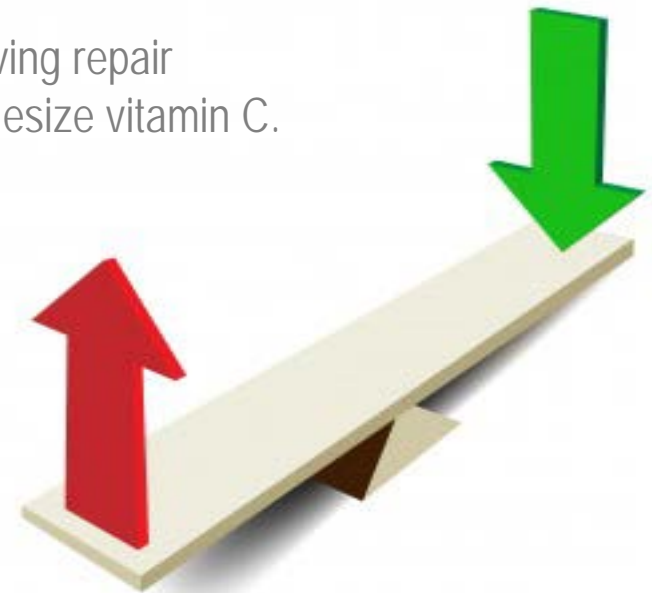
New Understanding

Relation of Lp(a) and vitamin C

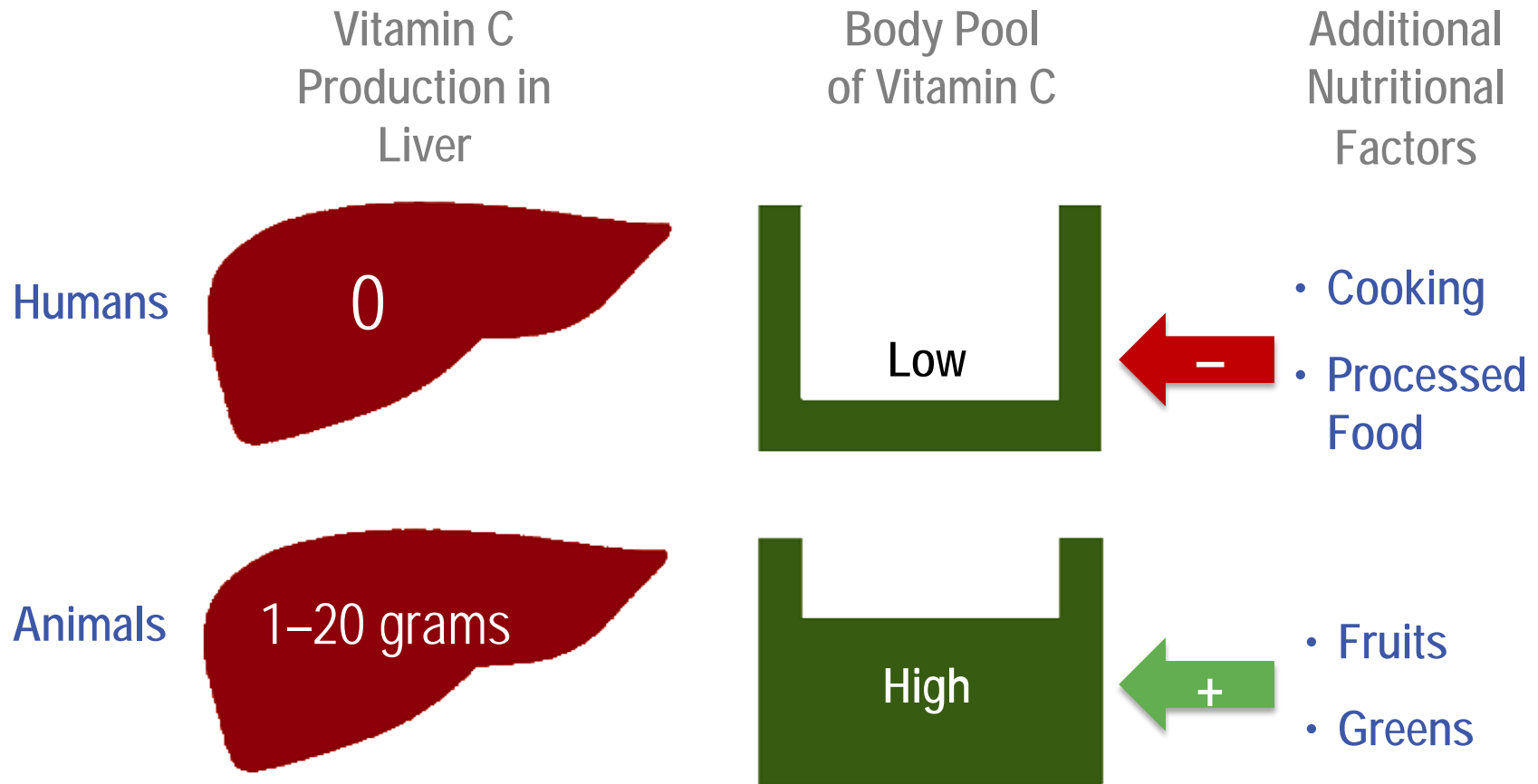
There seems to exist an inverse relationship between the internal production of Lp(a) and vitamin C (ascorbate).

- Animals: produce high amounts of Vitamin C, but they don't produce Lp(a)
- Humans: produce Lp(a), but don't produce Vitamin C

During the evolution of man, Lp(a) surfaced as a life-saving repair molecule after our ancestors had lost the ability to synthesize vitamin C.



New Understanding Vitamin Body Pool



New Understanding

Now, we can solve these medical puzzles

Medical Puzzles:

1. Why do atherosclerotic deposits develop primarily in the arteries of the heart – but rarely in other organs?
2. Why do these deposits develop in our arteries – but not in our veins?

Answers:

- ✓ The arteries of the heart – exposed to the high mechanical stress of a constant heart beat – have the highest demand for micronutrients.
- ✓ Here the deficiency of vitamin C and other nutrients are unmasked the earliest, causing weakening of the artery wall structure and starting a 'repair' process.



New Understanding

Now, we can solve these medical puzzles

Medical Puzzles:

3. Why are cardiovascular diseases essentially unknown in animals but a predominant cause of death in humans?

Answers:

- ✓ Most animals, with a few exceptions, produce vitamin C in their bodies. This assures optimum collagen production and strong, elastic arteries.
- ✓ Humans cannot produce vitamin C and with an inadequate dietary intake the collagen production becomes compromised, leading to a loss of vascular wall integrity. This triggers biological 'repair' mechanisms, resulting in increased deposition of lipoproteins (Lp(a) and LDL) and atherosclerosis.





Now that we can correctly identify
the underlying cause of heart disease,
the road to its natural control
is wide open.