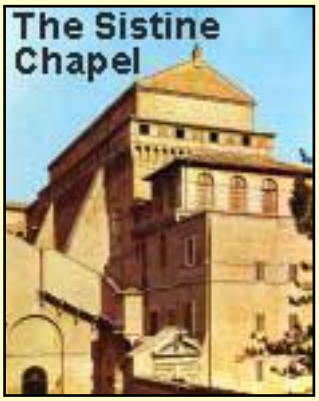
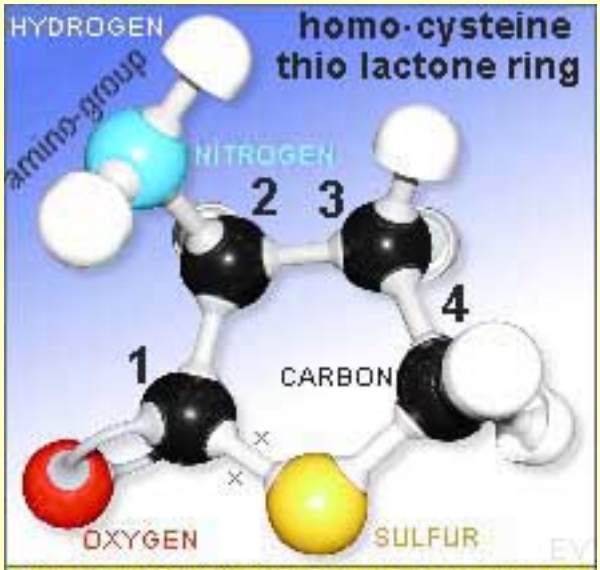
WHY ... ARTERIES FAIL



The Master Corrosive, *Homo*-Cysteine (the Evil 21st Amino Acid)

***Homo*-cysteine, a toxic *amino acid*, corrodes *cysteine* the shape and function giving 'sulfur cement' of our protein structure and machinery. Proteins are necklaces made from 20 different *amino acids*, folded into precise shapes. The sulfur in one of the 'beads', *cysteine*, does much of the folding. *Cysteine* is thus fundamental to prevent protein aging, and as goes the expression, all roads (of research) lead to Rome, ironically, *home* of the '*Cysteine*' chapel. *Homocysteine* also damgages *lysine* the centre-pin of collagen and elastin structure.**

Sulfur vulcanizes liquid latex into rubber shapes and sulfur does the same for structural and working proteins. That sulfur is part of the 3-carbon *cysteine*, made from the 4-carbon *homocysteine*, itself only made from the 5-carbon essential amino acid *methionine* [*thio* means sulfur, *meth* means a 1-carbon atom group like methane, natural gas, and *-ine* stands for protein, nitrogen or amino, like ammonia].

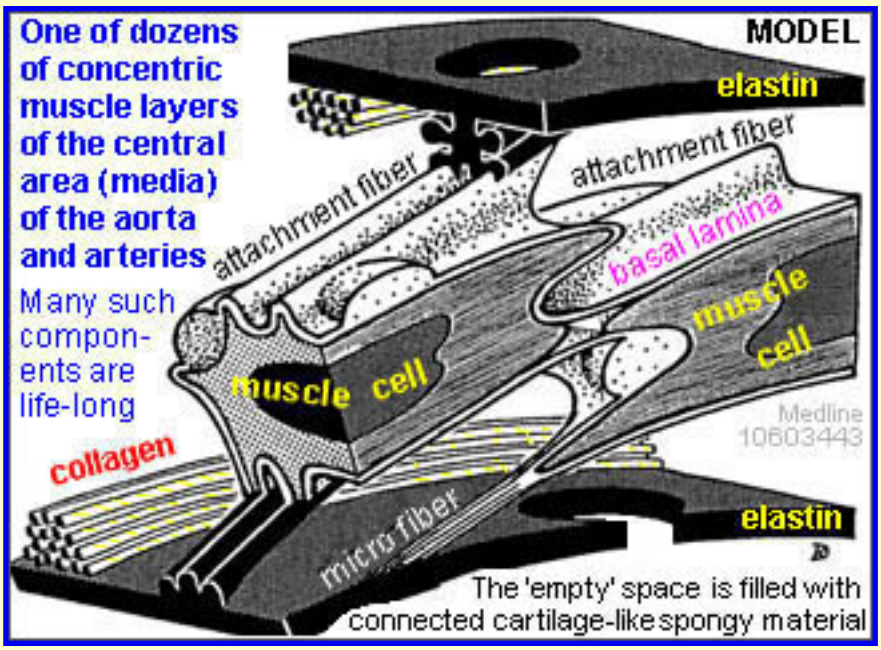


Reactive (toxic) ring able to damage any protein by long-term changing sulfur bonds and protein shape and function.

Requiring *most* B-vitamins, the '4' is recycled back into *methionine* or turned into 3-carbon *cysteine*. *Homocysteine* is even more toxic when it forms a high-energy '*Evil Ring*', a '*Lethal Lactone*' looking for proteins to corrode with its sulfur and oxygen, opening at x-x in the picture. If *homocysteine* would '*thiolate*' a protein that lives about 1 hour like insulin, with 6 *cysteines* forming 3 sulfur 'bridges', we'd simply make new. When it corrodes the protein of LDL-cholesterol droplets that lives 2.5 days, things get serious. *Homocysteine* makes it a Trojan horse and affects its function. However, if corrosion is to a life-long protein with 380 *cysteines* like micro-fiber *fibrillin*, the damage can be artery fatal, as in Marfan syndrome and *homo-cysteine-uria*.

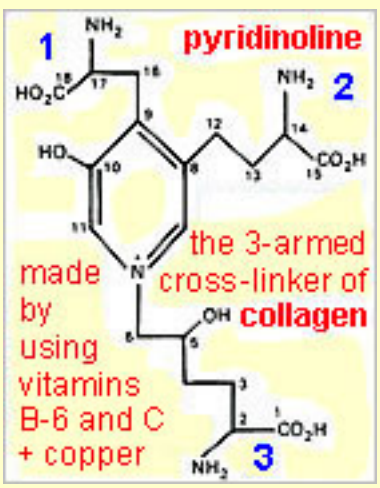
Because 'straight' *homocysteine* can fold back onto itself, if it would wind up in a protein during synthesis it could cleave the protein. Thus, it is removed .. but in that reactive ring shape --doing damage '*thiolating*' the cell and surrounding structure.

So, what's to corrode in an artery?

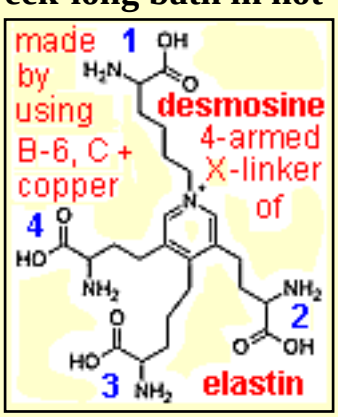


Well, I like to think of arteries as a thick multi-layer of muscle cells sandwiched between 2 structural layers. Through the outside layer come 300 capillaries per square millimeter feeding the central muscle cells. On the inside is a cell-hostile layer of just structure. There are basically 3 materials: collagen, elastin with its fibers (about 18, all proteins) and proteo-glycans (stuff also found in cartilage). Here it gets interesting. Some of these 3 structural families can be life-long and *all* are corroded, poorly made or poorly repaired in the presence of that 'Evil sulfur ring'. The 3 structural families are:

1. Collagen, bundles of 3-strand rope stronger than nylon of which the ends during assembly are kept from unraveling by *cysteine* sulfur 'bridges'. The ropes are then interconnected by 3-armed pyridinoline (see picture) that cannot be made when *homocysteine* has destroyed the machine (*lysyl*-oxidase) making this 'glue'. Copper and vitamins B6 and C are also essential. In bone, calcium builds along this rope, in artery the rope keeps it from ballooning under pressure. Collagen without shape is gelatin.



2. Elastin, an amazing 'rubber' NOT vulcanized by sulfur but by the above mentioned lysyl-oxidase but that, here, in elastin, forms 4-armed 'desmosine' cross-links. Again: high *homocysteine*, insufficient copper *or* vitamins B6 (most people) or C, no bridges. This stuff is so tough, it survives a week-long bath in hot acid or alkaline. It is secreted and then assembled into life-long 'apartments' by the fragile muscle cells, protecting them in multi layer (*laminae*) rooms with windows (*fenestrations*) and elastin frames and curtains. Without such 'happy homes' muscle cells may wander into the inside layer of the artery where they [and the artery owner] come to grief. While collagen may live for years (less than 1 year in heart), elastin's half-life is an astounding 70 years. The bad news is that the other half has to be maintained, or made anew.



3. Proteo-glycans, a family of water filled 'compressive' and 'chemical storage' molecules of arteries and joint cartilage. It has 'di-*cysteine*' sulfur bridges in a 'core-protein', and bottle brush like arms made from glucosamine and chondroitin sulfates. That is the stuff that works for joint pain and repair. *Homo*-cysteine can damage the protein and add excess sulfate to the glycan (sugar-like) arms, affecting function and making it attract LDL droplets that should not be there.

Lowering *homo*-cysteine

When *methionine* donates its 1-carbon *methyl* group [-CH3] to one of about 100 enzymes (protein machines), it turns into that temporary toxin. Strategies :

First, eat foods with *methyls*, like eggs, liver, soybean lecithin and foods with betaine (tri-*methyl*-glycine, TMG) such as wheat bran, germ and spinach. Eating such 'high choline' foods (including beans, rice, peas, lentils) we don't spend *methyl* from methionine needed for more vital roles. Insufficient (B-vitamin regenerated) *methionine* and your DNA looks like if radiated by X-rays, says Bruce Ames. Think: cancer, birth and pregnancy problems (spine, harelip, clubfoot, preeclampsia, severe heart defects, other).

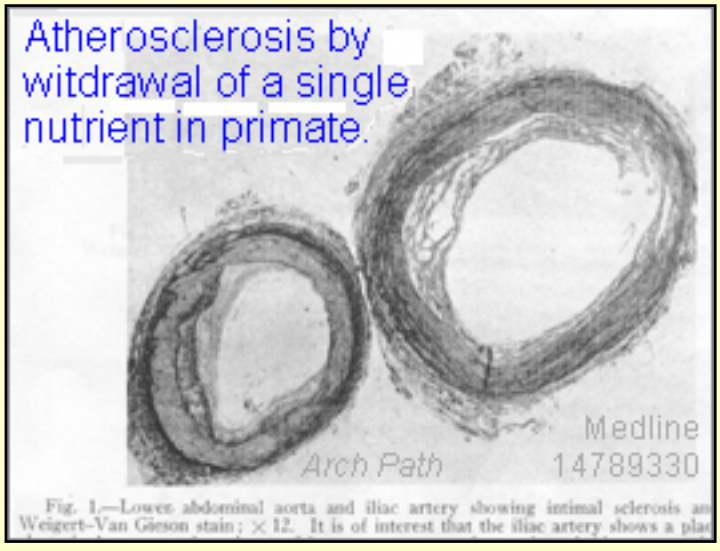


Fig. 1.—Lower abdominal aorta and iliac artery showing intimal sclerosis as Weigert-Van Gieson stain; ×12. It is of interest that the iliac artery shows a plac

Second, subtract one carbon to make *cysteine* for which many of us need 3 to 15x more vitamin B-6 than average intakes, or about 5 - 25 mg/d. No B-6 and atherosclerosis is quick and massive (picture). Alternatively, add one carbon to re-generate methionine with *betaine* (see above; 2-5 g/day) or with vitamin B12 plus *folic acid* and here, without *both*, nothing happens and homocysteine sky rockets. Magnesium, copper, zinc and vitamin B2 also help reduce corrosive homocysteine. Sadly, the best 'well balanced' diet has insufficient amounts of most actors.

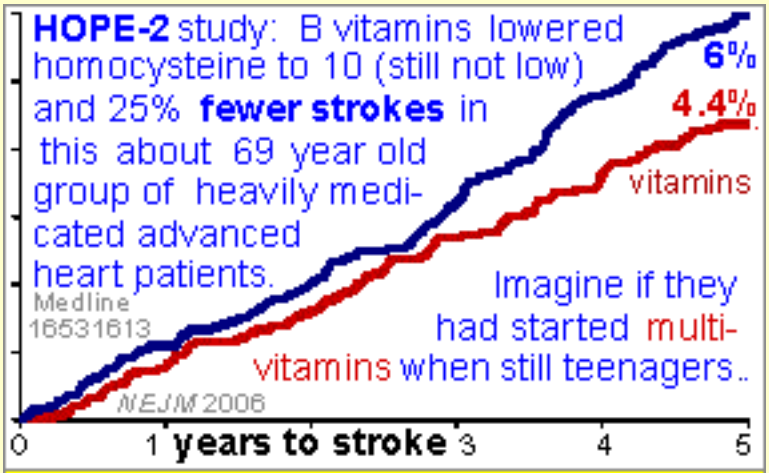
Third, coffee (sorry), smoking, mental stress, high-dose niacin (to raise the 'happy' HDL-cholesterol) and drugs like fibrate and methotrexate raise *homocysteine*. In each case a multi-vitamin as described here reverses that corrosive increase.

Know your *homo*-cysteine

Most heart disease, stroke, macular degeneration, cancer, Alzheimer's, joint and bone disease (fracture) does not happen when keeping your life-long homocysteine near SIX [6 µmol/L]. This theory of *healthy aging* unites all roads of research. When all road signs read *Rome*, it may be wise to heed their advice. When your car or proteins are damaged by corrosion, can a 'car'diologist, blood pressure or cholesterol drug really restore youth?

That magic number of SIX is found in 15 year old U.S. males and 22 year old females since folic acid was added to the flour supply. *homocysteine* was '22' in over 90 year olds near Boston and in 24 year olds in New Delhi where the common foods have essentially no folic acid and vitamin B12. Seven cents per year would add folic acid, B12 and vitamin B6 to the flour supply. This would drop homocysteine by half. Instead, a monumental heart disease epidemic in India and other countries where micro-nutrients are under supplied is under way. Massive and early in life! Highest rate heart disease Pakistan is a prime example. Less than $0.50 per year is the world-price to replenish required amounts of most micro-nutrients. Scientists argue and politicians don't act while Rome burns!

It's 'genetic' is a way for experts to tell you they don't know, and genes can't explain epidemics anyhow, but in homocysteine genes do play roles in about 10% of us. Women have life-long exposure to *homocysteine* 10-15% below men and get heart attacks 10 years later in life. You can't change your genes or gender and may never know your homocysteine level so taking a high 'potency' multi-vitamin + mineral supplement is brilliant prevention, even helping 'bad genes' and leveling the gender gap for men. Such 'anti-rust' vitamins slowly repair existing damage resulting in 25% fewer strokes; also, fewer bone fractures (likely by better collagen) and just possibly less macular degeneration. The latest: Stopping brain shrinkage with age. Nutrients nourish reactions, drugs block them. When homocysteine is over 'six' (maybe seven), you're under nourished for your genes and long-term health.

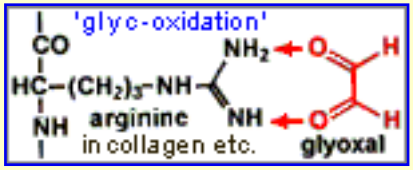


Multivitamins make stronger artery AND bone structure (collagen) by lowering homocysteine.

Our defenses against *homo*-cysteine

Our defenses: first, we sacrifice about 20 grams per day of blood proteins that bind homocysteine, *albumin* and *hemoglobin*. Next, our blood has about 1/2 a gram of "PON". Like its sister protein BLH, but that works *within* the cell, *PON* detoxifies the 'lethal lactone' formed whenever cells make proteins in the presence of homocysteine. PON travels outside the cell attached to the happy HDL-(good)cholesterol protein, and when PON works well, about half the mortality!

Homo-cysteine is not alone



Homo*-cysteine corrosion** starts early and targets sulfur in proteins as well as the 'free' *amino* of their *lysine*. Excess blood sugar in diabetes also generates toxins attacking *lysine* as well as *arginine*, another component vital for protein structure and function. One such toxin is ***glyoxal ($C_2H_2O_2$), also made by **frying temperatures**. Now we have two types of corrosives teaming up to destroy proteins in arteries, capillaries and finally organs and bone. While *homocysteine* is controllable by B-vitamins, blood sugar is made from sugars and starch and the more rapidly they are released from refined or cooked foods, the worse diabetic control becomes. In diabetes, a measure of sugar protein damage is '*glycated*' hemoglobin called **HbA1c**. When proteins are degraded by ***thiolation*** and ***glycation*, so is their owner**. Damage prevention is key since repair is never easy. The story is more complex but these are the basics!

Homo sapiens is alone

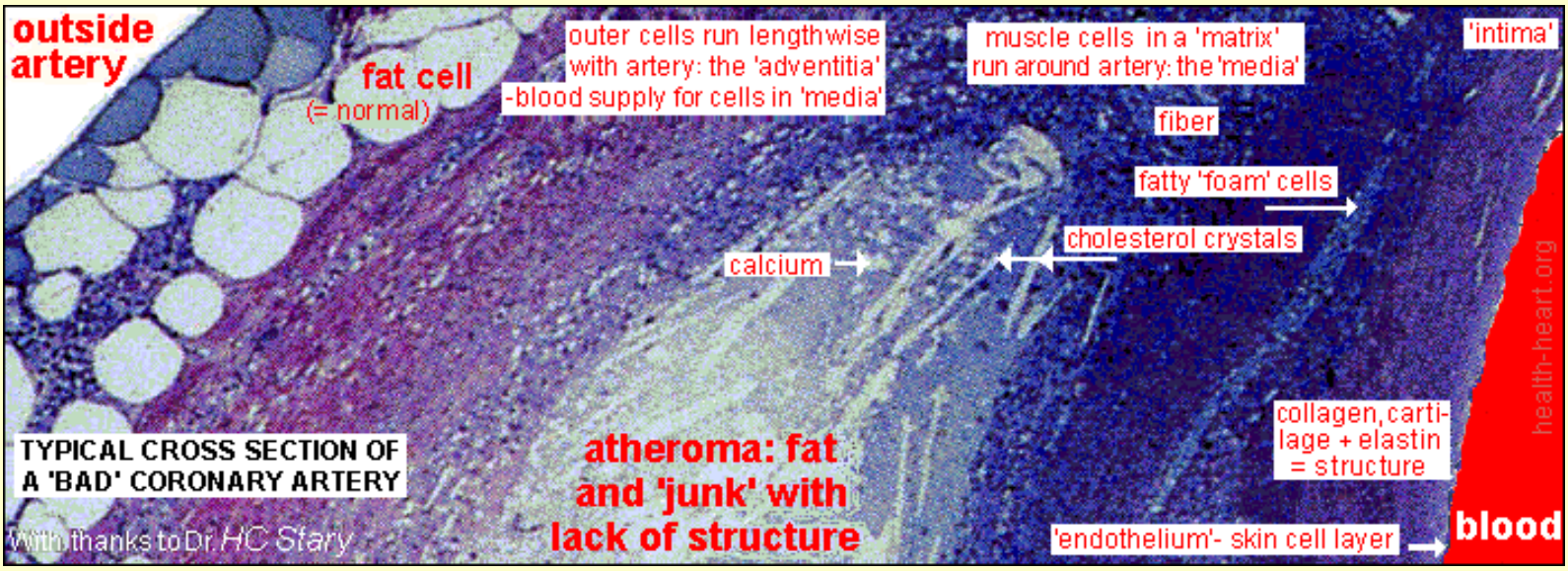
We're alone in the animal kingdom using fire and electricity--and naturally getting *athero*-sclerosis. We poison rabbits with cholesterol or remove genes from mice to study what anyone near a food store does 'naturally'. Big fish eat little fish raw and whole; we deep fry fish fillets. Comparable animals get 3x the B vitamins we do from even 'good' diets. For starters, *anything* we do to food destroys folic acid and B6, anything. U.S. heart deaths started dropping when vitamins were added to breakfast cereals in the 1960's and the decline **trippled** after 1998 when folic acid fortification became mandatory; **more so in stroke deaths.** A high dose multi-vitamin/mineral brings us back to the micro-nutrient levels of our animal cousins, the levels our genome evidently developed on. Add omega-3 oils (canola-rapeseed, fish oil pills) and some magnesium and (often) vitamin D, and long-term heart health may become a reality.

More about benefits -- and with thanks for critique to Drs. Genest, Kauffman, McCully and Rose.

BELOW, some related pictures and text from the home page. Eddie Vos Jan. 1, 2020.

- ARTERY DECLINE: CHEMICAL CORROSION, *NOT* THE CLOGGING OF A DRAIN PIPE -

Over simplified best theory. Artery walls are a muscle layer sandwiched between 2 structural layers. Lack of B-vitamins causes excess *homo*-cysteine that dumps its sulfur onto the 'cartilage' of the inside layer (the *proteo-glycans* of the *intima*), unravels *collagen* 'cables' and 'crumbles' rubbery *elastin*. This 'excess sulfation' helps trap LDL's cholesterol, and then *calcium*, as in *stage 4* lesions shown below and where finally the muscle layer, the *media*, is infiltrated. *Elastin*-network 'crumbling' in the *media* frees muscle cells that move and destroy artery architecture. Crumbled elastin 'loves to' accumulate cholesterol and calcium. *Homo*-cysteine degrades the shape and thus function giving *cysteine* sulfur bonds in your life-long proteins*. It also promotes clotting and inflammation (Il-8). B-vitamins with vitamin C, copper and zinc *prevent* such damage and repair some of it. Incidentally, excess sugar (*glyoxal*) in diabetes damages elastin and collagen in a very similar manner. [homo-cysteine + response-to-LDL-retention theories: CVD as a 'sulfur disease'. *) Analogy: liquid latex is vulcanized into the shape of a tire by sulfur bonds; homo-cysteine degrades such sulfur bonds in our permanent structural proteins.]



'Marinate' an artery for 5 days in hot acid and only elastic tissue is left! Homo-cysteine has special ways of slowly degrading and 'unraveling' this *fiber reinforced elastomer* architecture. Not good.