

## third surface

There is a third surface in each of us, as important to our life and well-being as the other two. Unseen, it is most often neglected, and usually abused.

The first surface is the one we're most careful with, since it is wired to hurt when injured ... and our brains are programmed to maintain a superficial attractiveness to others of our species. Our second surface shows only small segments of its beginning and its end. Mostly, it is hidden and mostly forgotten. Ectoderm and endoderm they're called - our skin and our gut ... but there's an even more expansive tissue surface that's completely internal and never seen. Endothelial cells of our vascular system form a third surface that covers inner walls of all arteries and capillaries and veins and the chambers of the heart, a surface of over half an acre. Only a portion of this lines arteries of large to medium size, but this is where years of neglect and abuse ultimately elicit a response that can't be ignored.

Earliest life was unicellular, the membrane surface of each living unit exposed to the outside environment, where direct transfer of electrolytes and nutrients and waste could occur. This was the world of *Archaea* and *Bacteria*, and it reigned supreme for 2 billion years. The first eukaryotes probably began to organize from endosymbiotic associations as early as 1.5 billion years ago – *Protists*. Then, 750 million years ago, the first multicellular organisms appeared. Shortly afterwards, in a burst of species diversification called the Cambrian explosion (540 million years ago), larger multicellular organisms – *Plants* and *Fungi* and *Animals* came on the scene (see \*\*\* **Survivor's Tale** \*\*\*). Some animals relied on a two-surface mode of body organization - like today's sponges - where all cells are exposed in some fashion to the external environment, though infolding causes a portion to be inside.

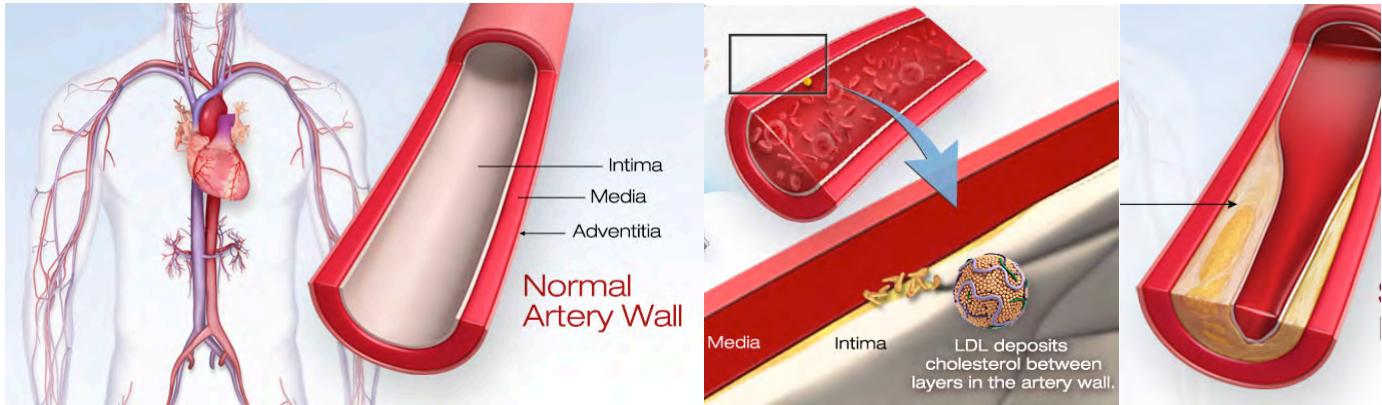
Then, an entirely new body plan came into being. Some early animals, during their development from the single-cell zygote (from which all animals must begin), developed a mesodermal space. A third surface had appeared. Fitted with a pump and valves, directional flow of interstitial fluid could occur, so as to distribute dissolved substances to cells some distance from the external surface.

Early arthropods, such as trilobites had directional flow in an open circulation, with a heart as a pump and valves and arteries, but without arterioles or capillaries or veins. Today's insects are similarly organized (see \***pump\***). Interstitial fluid (called "endolymph") was pumped forward and then percolated through the interstitial spaces surrounding all cells in its return to the heart. Gas exchange was conducted separately, via close exposure of endolymph to external water or air by way of gill-like surfaces or tracheae.

Later, vertebrates (fishes, then amphibians, then reptiles, then birds and mammals) began to use a closed circulatory system in which blood was completely contained in a vascular system of heart and arteries and capillaries and veins. Two separate circuits functioned in series, one delivering blood to gills or (later) to lungs, the other - systemic circulation - delivering blood to the rest of the body. The entire lining of this circulatory system is covered by a single layer of endothelial cells, constantly exposed to the blood and whatever materials the plasma contains.

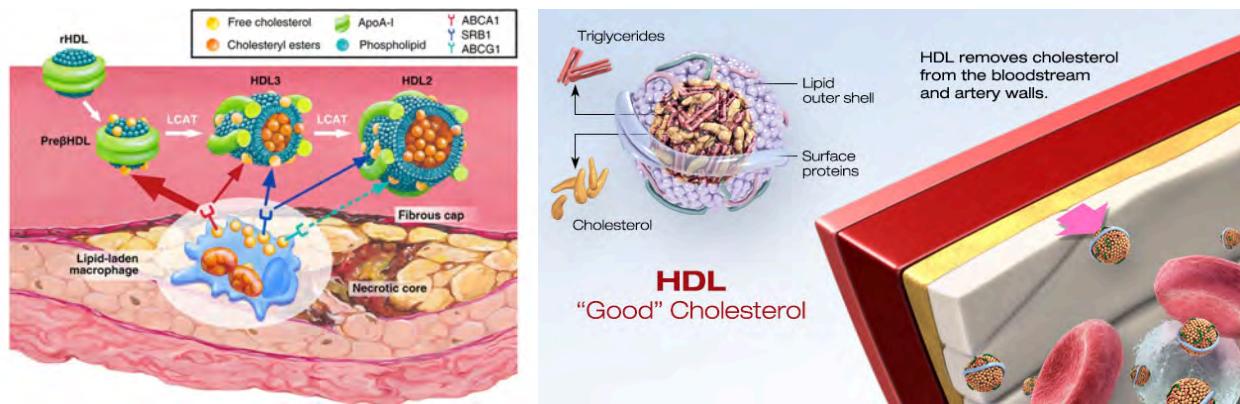
There is great resiliency in all living systems and complex mechanisms have developed to restore and maintain stability whenever a surface is injured or perturbed. We know this, for example from the remarkable ability of our skin surface to respond to a harsh abrasion or laceration or burn by healing - over time - so that in most cases, not even a scratch or scar remains. In the gut, erosions or ulcers can be treated and heal without a trace of prior injury.

The endothelial surface of large and medium sized arteries similarly respond to injury and can return toward normal, over time, once the damaging factor is removed. Constantly bathed in blood, the endothelial surface must respond to whatever chemicals or particles plasma contains. In response to chronic elevation of LDL cholesterol particles, for example, tissue macrophages, which patrol the vascular space and interstitial tissue will ingest, degrade and store esterified cholesterol in the subsurface zone just beneath the endothelial lining. Over time, this creates a distortion - a bulge in the cylindrical surface of the artery - an atheroma.



Other factors accelerate the process. Repetitive strain induced by excessive arterial pressures causes injuries which accumulate over time. Chronic plasma glucose elevation glycosylates proteins, causing damage. Various chemicals produced by burning tobacco leaves, when inhaled and thus introduced into the plasma, cause irritation to the endothelial lining, induce inflammation, and introduce macrophages to the subendothelial space.

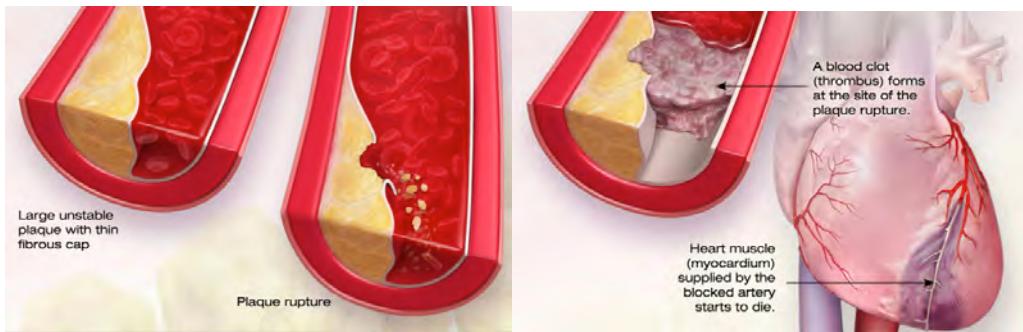
Of course, physiology teaches us that homeostatic mechanisms are always present in living systems, and processes encouraging return toward the normal state are always in play. Discoidal HDL - particles of apolipoprotein A1 associated with surface cholesterol and phospholipid - bump against endothelium and associate with available free cholesterol, esterify it and internalize it, growing the HDL disc into a sphere filled with esterified cholesterol - "reverse cholesterol transport".



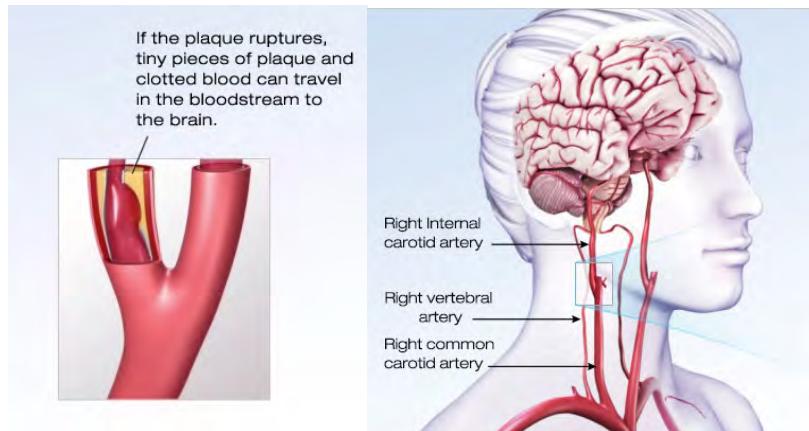
It is the constant, chronic balance or imbalance of these two-way processes that finally lets the owner of a particular third surface know that all is not well. These are all months-long, years-long interactions and occur unseen and unfelt. When an atherosclerotic lesion begins to crowd the vessel lumen, exceeding 70-80% in cross-sectional stenosis, restriction to flow causes angina, claudication, or neurologic symptoms. In the aorta, large areas of atherosclerotic lesions may weaken the wall, which can stretch over time to form an aneurysm.

More dramatically, however, there are sudden events which become moments in time that are easier to remember and can be devastating. When significant areas of the endothelial surface are covered with atherosclerotic lesions, probabilities increase that certain particular areas of the endothelial surface will break, exposing subendothelial contents directly to the bloodstream.

Break in any vessel elicits an immediate repair response, and platelets conglomerate to form a clot. In smaller arteries, such as the coronary vessels that deliver flow to myocardium, this may result in sudden worsening or complete obstruction of arteries which are, after all, less than 3 mm in diameter, even when normal. Most of the time, the lesion resulting in an episode of unstable angina or myocardial infarction is less than 60% stenotic, not critically narrowed, and, thus the individual is asymptomatic prior to the event. It's the break in the surface, the exposure of blood elements to what's just outside the vascular space that triggers the ensuing drama.

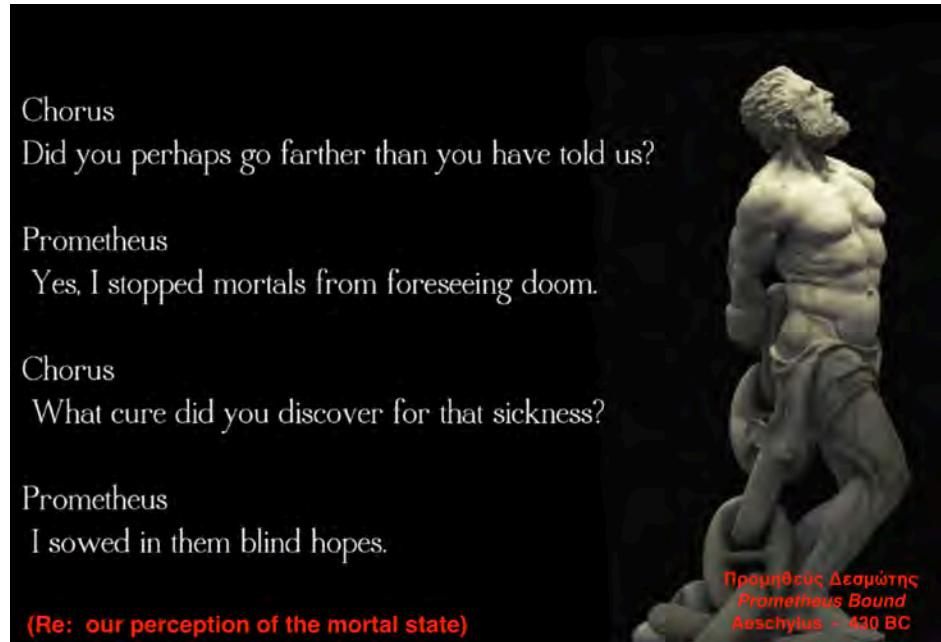
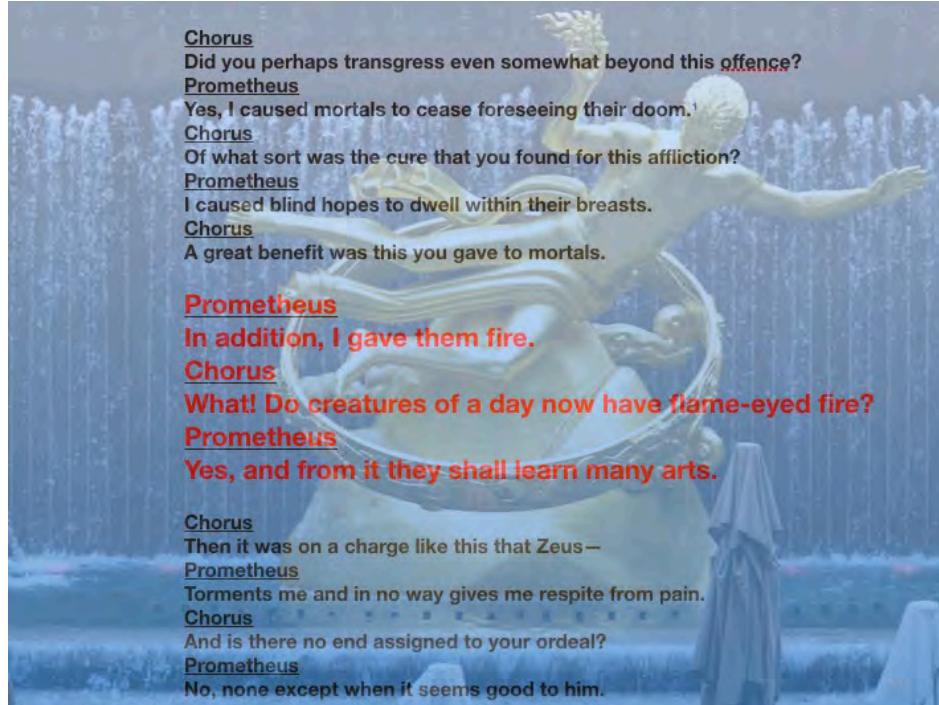


In larger arteries, such as the carotids, disruption of endothelial surface also exposes atherosclerotic material eliciting platelet clotting. These clots, however, rather than occluding the entire (larger) vessel, tend to dislodge and move downstream into the cerebral circulation, where they become trapped in smaller arteries in the brain. Transient ischemic attacks or a stroke result.



Human consciousness is bound closely to our highly developed visual cortex. Many word roots and metaphors used in our language acknowledge this linkage of sight and mind. We *see it now*, have *insight*, *get the picture*, *see it clearly*. Out of sight, out of mind ... and a chronic process, one that is unseen on the third surface, does not often rise into our consciousness. This affects our behavior, of course, what we do and what we avoid doing in our daily lives.

Our minds also have difficulty with awareness of time, the fourth dimension of reality. Because of this, our future seems to stretch out before us without a clear end, though we know that we are mortal. Aeschylus captured this psychological reality in his play, *Prometheus Bound*. In Greek mythology, Prometheus was the Titan who created man and later sided with the gods in their successful overthrow of the Titans. Against the will of Zeus, he stole fire and gave it to man, enabling humans to develop artistic and technological advances. For this, he was punished.



**Chorus:** Iron-hearted and made of stone, Prometheus, is he who feels no compassion at your miseries. For myself, I would not have desired to see them; and now that I see them, I am pained in my heart.

**Prometheus:** Yes, to my friends indeed I am a spectacle of pity.

**Chorus:** Did you perhaps transgress even somewhat beyond this offence?

**Prometheus:** Yes, I caused mortals to cease foreseeing their doom.

**Chorus:** Of what sort was the cure that you found for this affliction?

**Prometheus:** I caused blind hopes to dwell within their breasts.

**Chorus:** A great benefit was this you gave to mortals.

**Prometheus:** In addition, I gave them fire.

**Chorus:** What! Do creatures of a day now have flame-eyed fire?

**Prometheus:** Yes, and from it they shall learn many arts.

**Chorus:** Then it was on a charge like this that Zeus—

**Prometheus:** Torments me and in no way gives me respite from pain.

**Chorus:** And is there no end assigned to your ordeal?

**Prometheus:** No, none except when it seems good to him.