Cell Membranes Part 2: Restoring Cell Membrane Function

Dan Carter, ND

Introduction
In part 2 we will examine approaches to improve the state of membrane function, seeing that the cell membrane can indeed by resuscitated, improving cellular function and patient health. In order to accomplish this, we need to supply membrane substrates in their most beneficial form and via appropriate routes of administration.

Phospholipids
Increasing the amount of beneficial phospholipids is accomplished through oral supplementation or intravenous (IV) administration. To maximize membrane fluidity the most beneficial phospholipid is 1,2 dioleoylphosphatidylcholine, also called Polyenyl PC (PPC). The fatty acid tails of PPC are both linoleic acid, an omega-6 doubly unsaturated fatty acid; PPC is derived from soy. In contrast, the phospholipid (lecithin) derived from egg is distearoylphosphatidylcholine, with both fatty acid tails being saturated palmitic acid. Liver disease will be used as an example of PPC benefits.

Treatment with two grams phosphatidylcholine (PC) daily for two weeks resulted in 50% decrease in ammonia levels in patients with cirrhosis and hepatic encephalopathy.1 Marked improvement of liver function following phosphatidylcholine administration in terms of an increase in metabolic and detoxifying capacity of liver was noted.2 Although the following study was not restricted to cirrhosis, 650 subjects with varying liver damage were followed for five years. Patients received 950 mg IV PC and 450-700 mg oral PC, when labs normalized they received oral PC only. All groups benefited and showed reversal of fatty degeneration and recovery from acute inflammation accelerated.3 Research has shown that phosphatidylcholine has striking hepatoprotective effects. Two animal studies using baboons fed diets high in alcohol, one group supplemented with a soy-derived polyunsaturated lecithin (60% phosphatidylcholine) and the other group unsupplemented, both fibrosis and cirrhosis were mostly prevented in the phosphatidylcholine group. Most of the unsupplemented animals in the studies, which continued for eight years, developed fibrosis or cirrhosis.4

In addition, phosphatidylcholine has demonstrated other protective effects in non-alcoholic liver disorders, including protection against various other toxic substances. Its benefits in viral hepatitis were reported some years ago by several different research groups in Europe and elsewhere. In one of these studies, individuals suffering from hepatitis type A and B were given 1.8 grams of phosphatidylcholine daily. Compared with unsupplemented controls, the phosphatidylcholine group enjoyed quicker recoveries, fewer relapses and quicker normalization of liver function tests.5, 6, 7, 8
PC is also useful for hepatitis C. In a multicenter, double-blind trial, 176 patients with chronic viral hepatitis, either B or C, were started on interferon alpha for 24 weeks and were then randomized to PC (1.8 g/day) or placebo for 24 weeks. Significantly more patients responded to PC, predominantly in the hepatitis C subgroup. Additionally, PC supplementation sustained a longer-term improvement from hepatitis C over another 24 weeks.\(^9\)

**Fatty acids**

Numerous reports have established that lipid peroxidation causes cell injury by altering the fundamental physical properties and structural organization of membrane components.\(^10\) Dietary fatty acids can renew damaged membrane lipids by fatty acid exchange.\(^11,12\) The objective is to supply essential fats in a non-damaged form, in other words alpha-linolenic acid (omega-3) and linoleic acid (omega-6) that are not oxidized or in trans-configuration. Lipid oxidation can occur in food processing and preparation,\(^13\) or as a naturally ongoing process in the body via the effect of reactive oxygen species.\(^14\) The objective then becomes to avoid oxidized fats in foods and replace the oxidized fats in cell membranes with non-oxidized fats. Avoiding damaged dietary fats is easier than dealing with the internal process. Eating a whole food diet, cooking meats at low temperature (Crock Pot, stewing), using stable fats such as olive and coconut oil, elimination of grains if sensitive (wheat is most common), and avoiding simple sugars really cuts down on the oxidative load. If a person is diabetic, then blood sugar control is extremely important as high blood sugars are very pro-oxidative. The essential fatty acids can be restored with specific supplements such as (organic cold extraction process) hemp oil (3:1 omega-6:omega-3) or properly processed organic flax meal or oil (1:4 omega-6:omega-3).

Protecting and correcting the internal environment is more challenging. “Enzymatic (catalase, superoxide dismutase) and nonenzymatic (vitamins A and E) natural antioxidant defense mechanisms exist; however, these mechanisms may be overcome, causing lipid peroxidation to take place. Since lipid peroxidation is a self-propagating chain-reaction, the initial oxidation of only a few lipid molecules can result in significant tissue damage.”[Ref 13] It would be wise to have patients taking a balanced water and fat-soluble antioxidant supplement using non-synthetic nutrient sources.

When lipid peroxidation overcomes natural defenses it is more efficacious to go with a fat-soluble antioxidant such as alpha lipoic acid (ALA) administered IV. Many viral infections, including hepatitis C, induce increased oxidative stress on target tissues.\(^15\) Toxins may also result in oxidative stress that is life threatening due to depletion of liver glutathione, e.g acetaminophen\(^16\) and amanita mushroom (Amanita phalloides).\(^17\) Acetaminophen toxicity is treated with N-acetyl-cysteine (NAC), whereas mushroom...
toxicity has been treated with NAC and silibinin (water-soluble milk thistle extract), as well as ALA.\textsuperscript{18} Another recent study used a combination of ALA and alpha-tocopherol to treat acetaminophen generated oxidative stress.\textsuperscript{19}

Toxic metals are known to cause oxidative damage to bio-molecules by initiating free radical mediated chain reactions resulting in lipid peroxidation, protein oxidation and oxidation of the nucleic acids DNA and RNA. ALA is a useful treatment consideration due to its dual actions as an antioxidant and toxic metal chelator.\textsuperscript{20}

Oxidized LDL (Low density lipoprotein) cholesterol
All of the lipoprotein particles associated with cholesterol transport through systemic circulation are microscopic spherical micelles composed of a mono-layer of phospholipid, associated protein, and in the case of LDL this is apoprotein B-100; the core is composed of cholesterol esters and triglycerides. The American diet contains large quantities of oxidized fatty acids and oxidized cholesterol because a large portion of the fat and cholesterol in the diet is often prepared in a fried, heated, or processed form.\textsuperscript{21}

Linoleic acid (the omega-6 fatty acid found abundantly in industrial seed oils) is the main polyunsaturated fatty acid in LDL, due to its common presence in processed foods. It has been found that diets high in (damaged, oxidized) linoleic acid results in faster LDL oxidation in comparison with and oleate (olive oil) diet.\textsuperscript{22} A 2008 study noted that dietary consumption of olive oil improved the fatty acid profile in LDL, the changes being associated with a reduction of the oxidative damage to lipids.\textsuperscript{23} Oxidized LDL damages the endothelial cell monolayer and appears to play a pivotal role in initiating and deteriorating thromboembolic complications.\textsuperscript{24}

Antioxidant vitamins
Supplementation with vitamin C or vitamin E alone diminished lipid peroxidation to a similar amount. Supplementation with a combination of vitamins C and E resulted in no benefit beyond that of either vitamin alone.\textsuperscript{25} A 2001 study in JAMA revealed that healthy individuals did not appear to benefit from supplementation with alpha-tocopherol when lipid peroxidation was measured.\textsuperscript{26} More recent research supports supplementation with a full spectrum vitamin E (mixed tocopherols) to attenuate oxidative/inflammatory damage to endothelium.\textsuperscript{27}

Summary
- Evaluate the patient and determine the principle pathology and order of treatment.
• Sicker patients require IV treatment. A toxic metal pre and post provocative challenge test is appropriate (urine). If significant toxic metal loads are present, IV chelation using Ca-EDTA or DMPS (as appropriate) should be administered. Nutrient IVs should be administered 2 days post chelation at a ratio of 1:1 to 1:5 (nutrient/chelation), with more ill patients at a higher ratio.
• A series of 30-60 IV treatments with polyenyl phosphatidylcholine (PPC). This not only helps restore cell membranes, and thus cell functionality, but also decreases atherosclerotic plaque load. Due to compounding issues surrounding the manufacture of quality PPC the author recommends Plaquex (no financial conflict of interest).
• Patients with liver involvement, viral diseases, or mitochondrial collapse will benefit from IV lipoic acid infusions.

| IV Therapy Reminder: All of the above IV protocols need to be infused separately; the drugs are not compatible with each other in IV bags. They can be infused sequentially; IV lines should be flushed between treatments. Appropriate IV training using these drugs is assumed. |

• Avoid food sources of oxidized fatty acids and oxidized LDL, as well as trans-fats. Low sugar diet and control of diabetic blood glucose levels are imperative. High blood sugars are significantly oxidative.
• Replace essential fatty acids with cold processed organic hemp or flax oil. Marine omega-3 oils are helpful when the inflammatory pathways are over reactive.
• Give a spectrum of naturally derived (non-synthetic) fat and water soluble antioxidants.

References

1 Vnitr Lek 2000 Apr;46(4):199-204.
Dan Carter, ND, graduated from National College of Naturopathic Medicine (NCNM) and completed a 2-year family practice residency. He was appointed to a full-time faculty position in 1997 and served as a core faculty member through 2003. He has been in private practice in Bozeman, Montana since 2004 and is currently offering expert consulting services focusing on cardiovascular disease, metabolic syndrome, hormone restoration and IV nutrient therapies.

Dan has been an ACAM member since 2007 and has been a speaker at past ACAM conferences.

References: