

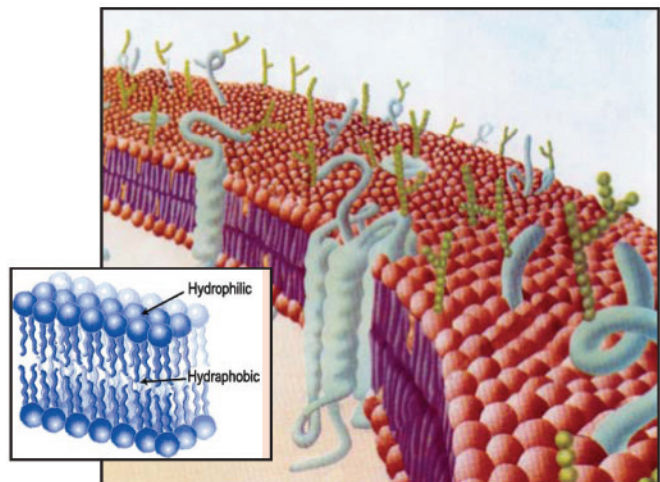
Phosphatidylcholine *Life's Designer Molecule*

By Ed Kane and Patricia Kane, PhD

Of the tens of thousands of molecules that make up the life of a cell, Phosphatidylcholine (PC) stands apart. PC is a phospholipid, one of four that link together to form the membrane. The largest is Choline (PC), 2nd, Ethanolamine (PE), 3rd, Serine (PS), and 4th, Inositol (PI), with each having the same prefix “phosphatidyl”. However, Phosphatidylcholine at ~50% is the largest concentration in the membrane and reigns supreme of all cell components. If there is the possibility of such an exalted position, PC deserves that titled role as the pinnacle of the marvelous membrane and all metabolism.

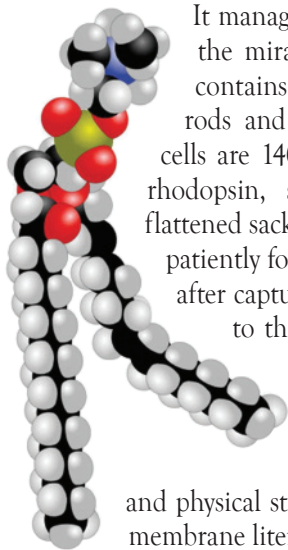
The membrane is the structural skin that surrounds the cell as well as the tiny organelles within it. But it is far more than an outside protective layer ~ it is literally the essence of life. You may damage other parts of the cell, even remove the center of the nucleus, the DNA (enucleate), and the cell will still carry on for several months. But damage the membrane and the cell is no more (Lipton 2005). “By spontaneously closing off to form an underwater bubble, the lipid bilayer membrane acts as Nature’s Test Tube, which packs the other biochemical families into a confined interior, so that biochemical evolution can proceed. In brief, lipids provide biological packaging and, in this capacity, they are the molecules which actually create the biological cell (Rudin 1985).

The membrane is a lipid envelope that encases and protects the internal working of cell. It’s the beginning



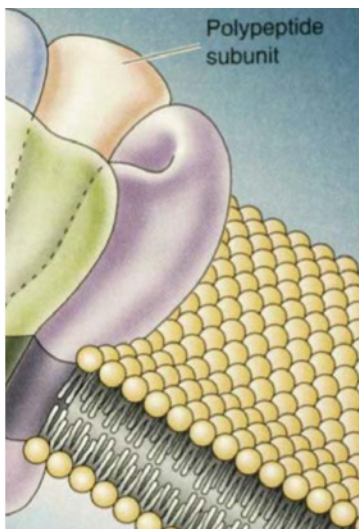
Lipid Membrane

of life itself, for without the benefits of an enclosure there is only momentary bits of chemistry that form in the primordial sea and as quickly swoosh away. There are ~100 trillion cells in the body, all with the same basic membrane structure, even for the neurons of our brain. The chemistry of neurons is only partially understood, however, the membrane is responsible for the propagation (carries) of all our messages, both sending and receiving. The dry weight of the brain is 60% fat, with the balance protein. Since the membrane manages all our thoughts and is basically fat, the term fathead should be deemed a compliment. The membrane manages the production of energy in the mitochondria, for without the double membrane structure there is no storage space for the separation of electrical charge ~ no Krebs cycle, and subsequently no energy. The sheer volume of membrane in the body is mind-bending. The liver alone has ~300,000 square feet of membrane. That’s more than 4 football fields; 4.63 to be exact.



It manages all of our senses, and particularly the miracle of sight. The retina of the eye contains 100 million photo-receptor cells, rods and cones. Within each one of those cells are 140 million receivers (peptides) called rhodopsin, sitting in a stack of membrane flattened sacks in each photo-receptor cell waiting patiently for a portion of light, a photon which, after capturing one or two, sends a signal back to the brain, again on the membrane of the optic nerve, giving us the ability to see (Rodieck 1998). This and much more assemble miraculously together to make up the mental and physical structure of each of us, with the lipid membrane literally the center of it all.

The membrane is composed of phospholipids (PLs) lined up soldier fashion in a double layer of opposing PLs, with the head groups looking out into the surrounding water on either side of the membrane. The membrane is an extremely tiny spark of life's chemistry. Even "tiny" pales in being able to convey the smallness. The membrane is only 5 nanometers thick (Owen 1981, Lee 1983, Shinitzky 1984) If you were to stack sheets of them one upon the other ~ it would take 10,000 membranes to make up the thickness of a piece of paper. It's physically not possible to envision a world that small.



They automatically organize themselves into a bilipid sphere to provide the protecting outer garment of every cell and every organelle within the cell. The phospholipid structure is a marvel. Its two lipid tails (the oil) are hydrophobic, hate water, while the head groups, PC, PE etc, are hydrophilic and love water. The term is amphipathic, meaning that the molecule (the

PL) has both hydrophobic and hydrophilic ends, one end comfortable in water, and one that is not. That combination provides an automatic ability to self-assemble with both oily tails protected in the middle of the membrane. All life on the planet is water based. The cellular trick is to have a protective outer skin that shields and acts as an insulator since the chemistry inside must be able to maintain a different composition from the watery world it is now floating in.

PLs perform their self-organization with aplomb. They jump together, or flee together, for self protection since oil and water do not mix. You could say that the lipids are hiding—actually, they are. Each layer of the bilipid arrangement is completely independent of the other; there is no connection between the inner leaflet of the membrane and the outer leaflet. The two float separately but stay together because they must. The water on either side sets the rules. However, this importance of PL self-organization and the relation to our watery environment is not readily apparent.

With the head groups looking out on either side of the cell, comfortably sticking their heads into water, the cell has an ingeniously designed protective outer garment. That, however, is only the beginning, for within the membrane sits a huge selection of ion channels and receptors from our genetic library that literally run the entire cellular system, all from the comfort and protection of that oily center. It is proposed that ~30% of all the genetic output of our DNA library is embedded in the membrane as peptides, ion channels or receptors, with another ~30% attached to the membrane (60% total) (Mouritsen 2005).

Phospholipids (PL) are composed of a glycerol backbone, a head group, and 2 fatty acid lipid tails, 16 to 24 carbons long. The tails are like a flexible goose neck lamp. They comprise ~70 % of the total PL molecule ~800 Daltons (Fox 1972) and are critical to its function. A large percentage of those lipid tails are Essential Fatty Acids (EFAs), meaning that they must be part of our diet, we cannot make them. Each of the four parts of the phospholipid membrane is critical, but it is the makeup of those lipid tails, part saturated and part unsaturated, that gives the cell the essence of life

LECITHIN: Lecithin is a residue from soybean oil production and contains a relatively high concentration of PC, along with PE, PI and other phosphatides. Most vitamin manufacturers market a lecithin product and call it phosphatidylcholine. The majority of lecithin is used in the food and cosmetic industries. However, a portion is pre-encapsulated by the oil producers, ADM, Central Soya, etc., and sold to supplement packers, who market it as PC. Somehow, over the years, the terms lecithin and PC have been used interchangeably, even by medical researchers. However, they are not one and the same, nor should they be. PC, PE, PI etc, are just chemical components of lecithin.



The PC in Lecithin is oil based. The PC molecule is a phospholipid, which is ~70% oil because of its two lipid tails. It is partially hydrophobic (the oily tails), amphipathic, while its head group is hydrophilic. In brief, it's two-faced. To become a structural PL, It must be exposed or introduced along with many other PLs into a watery environment to form a membrane. Oil does not run away from oil, there's no need. The oily tails automatically run away from water (hydrophobic), which becomes the driving force for the formation of the membrane. Take that hydrophobic force away, which oily lecithin does, and the molecule cannot perform as intended. It will not become an important cellular structural component. Once lecithin is ingested, the lipases of the digestive tract cleave apart the PLs, removing the lipid tails and the head groups such as choline, and are recycled as cellular raw material. That's basic fatty acid digestion. Taking lecithin as a food or supplement can raise choline levels. Adding additional choline has recently been shown to be potentially harmful. (see below.)

YEHUDA: Each of our cells can produce non-essential FAs, such as the saturated palmitic and stearic acids and the monounsaturated oleic and nervonic acids, but not the essential FAs (EFAs), the omega 6 or the omega 3s. Those two lipid families are the EFAs. However, it is the ratio of those vital n6s and n3s that is critical. For that we are indebted to the research of Yehuda, Mostofsky, Rabinowitz and Carrasso from Bar Ilan University, Haifa, Israel. They have unlocked the most important missing piece of dietary science – the balance of the essential fatty acids. It is difficult to describe the value this discovery represents. We are only in the infancy of understanding fatty acid biochemistry. EFAs provide the highly fluid character of the membrane, which is the essence of life in both plants and animals. The studies of Yehuda et al solved a long debated question ~ what fats should we be eating? What is the optimum dietary ratio of n6 to n3. Yehuda et al have unequivocally shown this to be 4:1, 80% n6 to 20% n3*, and from our brief dozen years of employing the 4:1 ratio, our clinical success has been extremely positive.

Finding a research basis for dietary EFAs was a milestone. We could now, with reasonable confidence, adjust the diet to elevate the base EFAs* using sunflower oil for linoleic (LA), and flaxseed oil for linolenic (ALA). Raising the EFA levels in the body using the 4:1 ratio has not only provided positive clinical results but has unlocked a hidden secret for nutritional health. As FA researchers, we had strongly felt that raising fluidity alone was the underlying need, but without Yehuda we were just guessing. Adding in excessive amounts of fish oil was rapidly proving unhealthy, as was the excess of omega 6 oils that were part of our newly-processed food world. Balancing the EFAs was the answer, and not

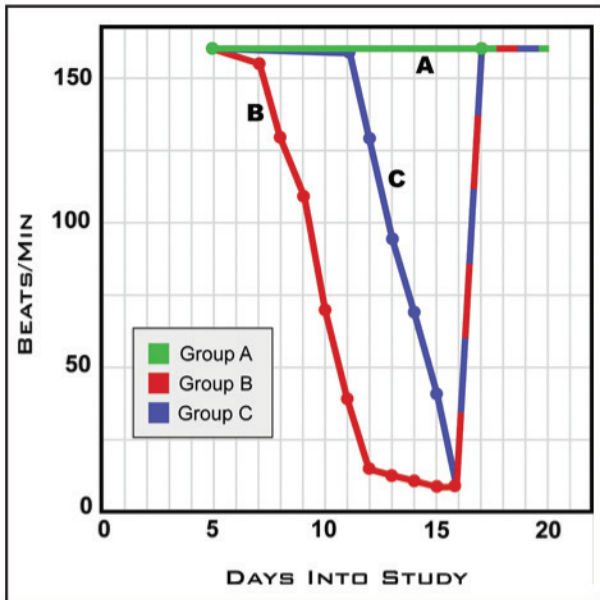
only was it a relief clinically for our patients, but also it's inexpensive as well – a clearly elegant solution. The value of Yehuda's research to the future health of society is so significant it warrants a Nobel Award.

*LA and ALA are base polyunsaturated FAs (PUFAs). For the higher order of lipids (HUFAs, highly-unsaturated FAs) we reach a metabolic impasse because humans and all large mammals lack sufficient FA desaturase enzyme capacity to metabolize the HUFAs. For the n6 HUFAs, GLA and AA, and the n3 HUFAs, EPA and DHA, we are dependent on diet, such as eggs, dairy, meat and fish. Vegetarians have fewer options since plant based AA and EPA/DHA are rare or non-existent, however, algae is a becoming a possible solution.

BUDWIG AND RUDIN: Joanna Budwig, a brilliant German scientist with PhDs in both chemistry and physics, and Donald Rudin, an equally brilliant MD and Harvard professor, both recognized that the n3s, linolenic (ALA), were missing from our diet, due in no small part from the meteoric rise of the large food producers in the last century. Both Budwig and Rudin struggled with flax oil for their patients, since flax contained 55% ALA. They each had success with patients in relieving various symptoms, such as cold sensitivities, dry skin, tanning, eye pressure, diabetes, headache, tinnitus, palpitations, hand eczema, rheumatoid pain, racing thoughts, and even allergies. However, the relief was a brief 3-6 months duration, after which Rudin would stop the flax oil. After ~3-4 months he would try it again, reporting that there was a relief of symptoms each time he repeated the flax oil treatment if he spaced it a few months between. Neither he nor Budwig knew the problem was the ratio. Flax is 2 parts of n6 to 5.5 parts of n3 (2:5.5), which is almost the exact opposite of Yehuda's 4:1. Imagine how much further we could have progressed if they had known of the correct ratio then.

YECHIEL AND BARENHOLTZ: In 1985 Yechiel and Barenholtz, from Hebrew University, authored a significant paper highlighting phosphatidylcholine and its relationship to aging and disease (Yechiel 1985a,b, 1986, Muscona-Amir 1986). Using rat myocytes (heart cells) in a 20 day in-vitro study, they demonstrated the ability of PC to completely rejuvenate cells that were all but expired. Myocytes can be separated in a petri dish, and with proper feeding, survive. After ~two days, they congregate together in each dish and begin to beat in unison at a rate of ~160 beats per minute.

To demonstrate the power of PC, the researchers fed group (A) egg yolk PC for the life of the experiment (20 days), but not so to groups B and C. However, they received it in their feed later. Group A is represented with a straight line (Green) at the top of the chart. They were given egg PC after day 6 and for the entire 20 days



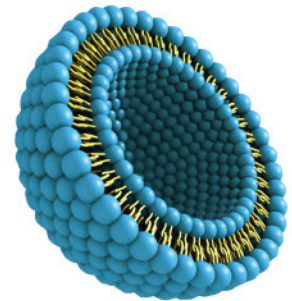
they maintained a constant beating rate of ~160 beats/min. Group B cultures (Red) were not as fortunate and were denied PC. After 6 days the Group B cells started to weaken; after day 8 began a precipitous decline in the beating rate, reaching a low point by day 12 with some of Group Bs beating at ~20 beats/min, and some not beating at all. Group C (Blue) was given PC like Group A, after day 6, but only up to day 11, after which PC was removed from their feed. As you can see on the chart, almost immediately the Group C started a similar decline in their beating rate, which mirrored the decline of group B with a 5 day drop to ~20 beats/min. In addition, both B and C groups suffered a variety of cellular distortions in cell size and in production of protein, specifically an elevated Creatinine PhosphoKinase.

On day 16 all cultures were given PC, and within 24 hours, the Bs and Cs recovered their beating rate to ~160 beats/min and continued until the study was concluded at day 20. In addition, they also recovered most of their distorted chemistry, even lowering CPK. This was one of the most remarkable demonstration of the cellular power of phosphatidylcholine, or to put it in more precisely, the absolute necessity of PC and life.

A Medline search on 'Phosphatidylcholine' will reward you, or inundate you, with ~50,000 citations. To review them would easily take a year or two, but it speaks volumes of the importance of PC. In all of our studies, we have yet to uncover a report as powerful as that of Yechiel and Barenholtz. However, there are two that are noteworthy. The review by Cui and Howeling, *PC and Cell Death*, 2002, that focuses on the ability of PC to reverse a number of biochemical distortions and prevent cellular necrosis and/ or apoptosis. Apoptosis is a controlled, regulated death, while necrosis is a rupture of the

membrane with the release of vital components into the surrounding blood stream. Cui et al presented their prior biochemical studies and many others, demonstrating that perturbation of PC leads to cell death, and the replacement of PC re-establishes homeostasis.

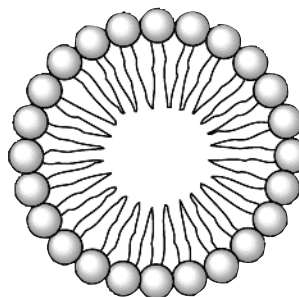
The work of K.J. Gundermann, PhD, MD, is also highly noteworthy. In his book ("The Essential Phospholipids as a Membrane Therapeutic" 1993), he thoroughly covers the use of PC in the studies of toxicology and hemorrhology, and in the treatment of lipid peroxidation, alcoholic & diabetic fatty liver, malnutrition, kidney, cirrhosis, gastrointestinal, neurological, lung, psoriasis, MS, cerebral circulation, elevated lipids, atherosclerosis and even drug enhancement.



Liposome

The book is a review of 776 research papers published from 1959 to 1993 on the therapeutic value of Essential Phospholipids (EPL), and is the European reference for a concentrated phosphatidylcholine (also made from soy, but water based). This product was developed by Nattermann, a German producer of lecithin products for food and cosmetics. EPL became recognized in general medicine under the names of Essentiale and Lipostabil. Nattermann developed them in both an oral supplement called Forte (not in oil), and an ampoule for intravenous infusions, a PC water/bile mixture similar to the body's natural bile-oil carrying system.

EPL was accepted throughout Europe as a natural medical i.v. treatment. However it was in Eastern Europe that it achieved a higher degree of popularity. Russia and her satellites were not as close to Big Pharma as we in the West. A natural product like PC (EPL) was a less expensive alternative to Western drug therapy, and is considered efficacious for a wide variety of disorders. The result was an almost total acceptance of PC by doctors throughout the Communist World. Their experience with PC provided a rich history of therapeutic use, both orally and as an IV for ~50-60 years, with many of these studies detailed in Gundermann's review.



Micelle

During the 70's Nattermann AG was absorbed by Aventis and

Rhone Poulanc (later sold off). However, in spite of rave reviews in a wide range of treatments, PC received little attention in the West. Natural products like PC are unpatentable and, even with an excellent medical record, have little sex appeal in the pharmaceutical world. IV-PC is not approved in France—and Rhone Poulanc is a French company. They certainly could have organized its approval if healing had a higher priority.

Aventis marketed their IV-PC under the brand name of Essentiale, which was yellow in color. B-Vitamins were included, with riboflavin (B2) providing the color. Rhone Poulanc marketed their IV-PC as Lipostabil, which was clear, no vitamins added. Both products were produced in the same factory on the same production line. In 2005 Aventis abruptly took Essentiale off the European market and in 2011 Lipostabil ceased production. However, Essentiale is still available in the US, coming from Switzerland.

Lecithin and The Marketplace: The majority of PC currently sold today is lecithin, or triple lecithin. The membrane of a cell is a liposome, and oil based lecithin cannot form a liposome. As noted earlier, even though lecithin or triple lecithin contains PC and PE, when taken orally they are assaulted by lipases, phospho-lipases etc, which remove the fatty acid chains and the head groups. By the time fat absorption occurs in the gut, the components of the phospholipids are indistinguishable from the components of other lipids, such as triglycerides. However, while the job of re-assembling PC from the individual components is questionable, it is possible, but only if you're young and healthy. But if you're young and healthy you don't need a supplement. Simply eat an egg or two.

Some head groups, like choline and inositol, are hard for the body to make, so absorption of these components from food can be important to a healthy diet (Onken 1996). However, as the recent 2011 *Nature* study showed, the value of raising choline levels is now questionable (Wang Z et al, *Nature*, 2011, Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease). The details of the danger of raising choline are important to learn since there are many people taking supplements under the guise of Phosphatidylcholine (Triple Lecithin). That may very possibly be putting themselves at risk.

Lecithin itself was not the answer; it needed a much higher phospholipid concentration, which Nattermann was developing. The 1940's German method extracted a "Pure Phospholipid" (EPL), which only recently has been duplicated by BodyBio. While the process is more expensive, the exercise of discarding undesired components from lecithin (basically the oil) leaves a water

based product (BodyBio PC) that encourages formation into a Liposome. A micelle/liposome, when exposed to a watery environment, forms exactly like a cell, with a spherical shape, only a thousand times smaller.

The PLs of micelles and liposomes are identical to cellular PLs, however, a liposome is a bilipid layer and appears (looks like) a cell membrane. That tiny sphere can then traverse the gut without being dismembered, and not only deliver itself but also deliver a tiny cargo, such as a drug (Big Pharma employs Liposome technology for a wide range of drugs) or even another supplement. Today, most pharmaceutical companies are engaged in liposome technology. In the manufacturing process, the drug is trapped inside the sphere and, as the cell-like liposome reaches a normal cell, it is absorbed by endocytosis; the tiny sphere becomes one with the cell membrane and delivers the drug or nutrient inside the cell, an efficient method of absorption for either a drug or a vitamin.

The fallacy of using lecithin has been difficult to see. For years there have been conflicting medical reports about the benefits of Lecithin-PC (Wood 1982), which now becomes understandable through liposome research and the *Nature* study.

BodyBio PC will blend in plain water. It does not dissolve. Rather, it is miscible; it mixes in the watery environment, and naturally forms a liposome, or more precisely, tens of thousands of PLs will. Lecithin or triple lecithin will not blend with water no matter how vigorously it is mixed. We are well aware that oil and water do not mix. This is easily seen in a laboratory or in the kitchen with lecithin or BodyBio PC.

PC Products That Work: BodyBio PC, PhosphaLine®, PhosChol®, Essentiale Forte N (Europe), PC Injectable by prescription only in 5 ml ampoule for IV therapy as Essentiale® N from Paracelsus Apotheke.

Wood et al, 1982 comments, because high intakes of lecithin or choline produce acute gastrointestinal distress, sweating, salivation, and anorexia, it is improbable that individuals will incur lasting health benefits from self-administration.

PE acts as a reservoir for PC, since, by the addition of three methyl groups it is converted to PC. Thirty percent of PC is endogenously derived from methylation (Cui 2002). To encourage this conversion of PE to PC, it is advisable to add into the diet folic acid (an advanced form of folate) and a methylated form of B-12, methylcobalamin. Both nutrients increase methylation and tend to lower homocysteine levels.

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This report concerns possible adverse health effects and benefits that might result from consumption of large amounts of choline, lecithin, or phosphatidylcholine. Indications from preliminary investigations that administration of choline or lecithin might alleviate some neurological disturbances, prevent hypercholesterolemia and atherosclerosis, and restore memory and cognition have resulted in much research and public interest. Symptoms of tardive dyskinesia and Alzheimer's disease have been ameliorated in some patients and varied responses have been observed in the treatment of Gilles de la Tourette's disease, Friedreich's ataxia, levodopa-induced dyskinesia, mania, Huntington's disease, and myasthenic syndrome. Further clinical trials, especially in conjunction with cholinergic drugs, are considered worthwhile but will require sufficient amounts of pure phosphatidylcholine. The public has access to large amounts of commercial lecithin. Because high intakes of lecithin or choline produce acute gastrointestinal distress, sweating, salivation, and anorexia, it is improbable that individuals will incur lasting health benefits from self-administration of either compound. Development of depression or supersensitivity of dopamine receptors and disturbance of the cholinergic-dopaminergic-serotonergic balance is a concern with prolonged, repeated intakes of large amounts of lecithin.

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