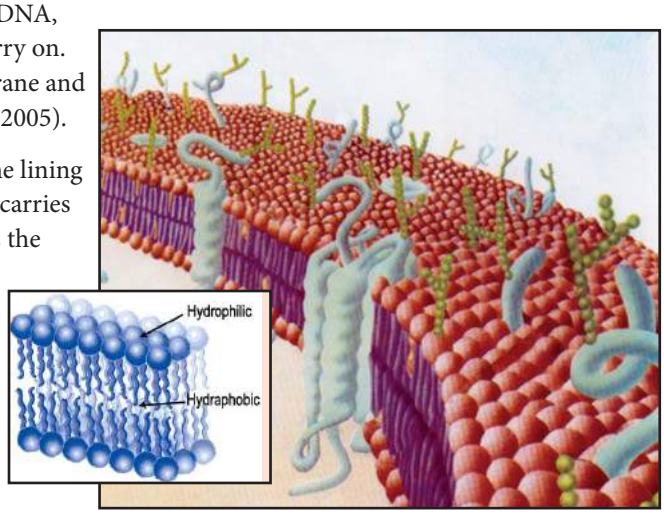
BODYBIO Bulletin

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; it is possibly the most important of all. It is one of four phospholipids that make up the membrane: Choline (PC), Ethanolamine (PE), Serine (PS), and Inositol (PI). 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 the nucleus or its DNA, and the cell will still carry on. But damage the membrane and the cell is gone (Lipton 2005).

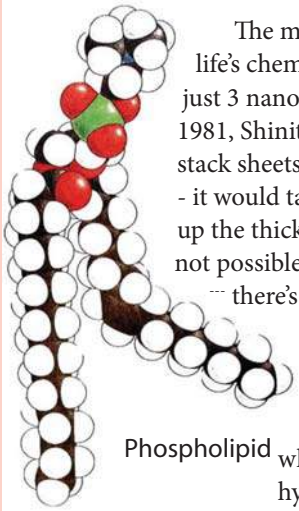
The membrane is the lining of every nerve cell that carries our signals. It manages the production of energy in the mitochondria for without its double membrane structure there is no separation of electrical charge --- no Kreb cycle, and subsequently --- no energy. The sheer volume of membrane in the 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.



Lipid Membrane

It manages all of our senses, but 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, all sitting in the membranes of 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, on the membrane, giving us the ability to see (Rodieck 1998). This, and much, much more assemble miraculously together to make up the mental and physical structure of each of us, with the lipid membrane in the center of it all.

Cellular membranes are bilipid layers of opposing phospholipids lined up soldier fashion that automatically organize themselves in a spherical shape to provide the protecting outer garment of every cell and organelle. *By spontaneously closing off to form an underwater bubble, the lipid bilayer membrane acts as Natures Test Tube, which packs the other biochemical families into a confined interior, so that biochemical evolution can proceed without being washed away in an infinite sea. In brief, lipids provide biological packaging and, in this capacity, they are the molecules which actually create the biological cell* (Rudin 1985).

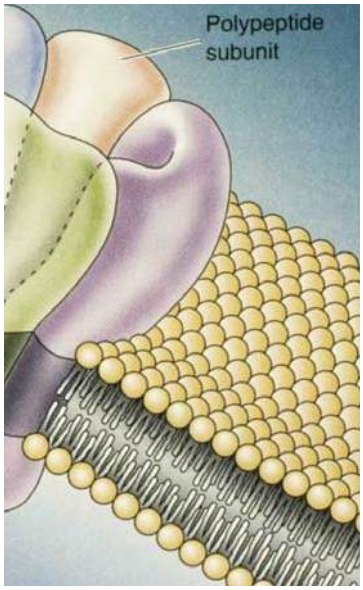


Phospholipid

The membrane is a minute spark of life's chemistry, with the lipid portion just 3 nanometers thick (Lee 1983, Owen 1981, Shinitsky 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 not possible to envision a world that tiny --- there's nothing to compare it to.

The structure of a phospholipid is a marvel. Its two lipid tails (the oil) are hydrophobic (hate water) while the head groups like PC, are hydrophilic (love water). The term is amphipathic which means that the molecule has hydrophobic and hydrophilic sections and preferences. That gives it the ability (or forces it) to self assemble with both oily tails back to back (or tail to tail) hiding from the watery environment. With the head groups looking out on either side of the cell, comfortably sticking their heads in 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 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 are embedded in the membrane as peptides, ion channels or receptors with an additional equal amount partially in or electrically attached to the membrane (Mouritsen 2005).



Each of the four parts of the phospholipid membrane are critical but it is the makeup of those lipid tails, part saturated and part unsaturated, that give the cell the essence of life, however, as science has recently shown, the type of head group, such as PC, is also critical.

Phospholipids are made up of a head group, a glycerol backbone, and 2 fatty acid lipid tails, 16 to 24 carbons long. They're like a flexible goose neck lamp. The lipid tails comprise ~ 69 % of the total phospholipid 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. Each of our cells can produce many of the lipid tails, such as saturated (palmitic and stearic acids) and monounsaturated (oleic and nervonic acids), but not the omega 6s or the omega 3s. Those two lipid families make up the EFAs, the Essential Fatty Acids, but it is the ratio of those vital 6s and 3s that is critical.

For that we turn to the excellent research of Yehuda, Mostofsky, Rabinowitz and Carrasso (1994, 1995, 1996, 1997, 1998 a.b, 1999 a.b.c, 2000 a.b.c, 2002, 2004) from Hebrew University and Boston University, for prior to their work this field of knowledge was a desert. They have provided that important missing piece of dietary science, the balance of essential fatty acids (EFAs). EFAs provide the highly fluid character of the membrane which is the essence of life on the planet, both plants and animals. Their studies solved a long debated question --- what fats should we be eating. What is the optimum dietary ratio of omega 6 to omega 3. Yehuda et al has unequivocally shown this to be 4:1, 4 parts of ω6 : to 1 part ω3.

Joanna Budwig, a brilliant German chemist, struggled with flax oil in the 70s and 80s, as did Donald Rudin an equally brilliant MD and Harvard professor. They knew that the omega 3s were vital and used flax oil clinically since it was 50 % omega 3. Interestingly they 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, even allergies. However, the relief was brief. Rudin would then stop the flax oil and after ~ 3 months start again, and reported having a repeat of the relief of many of the symptoms each time. Neither he nor Budwig knew that the ratio of flax was wrong. It is 2 parts of omega 6 to 5 parts of omega 3 (2 : 5), which is almost the opposite of Yehuda's 4 : 1.

Substantiating a clinical basis for dietary intervention was a milestone. We could now, with reasonable confidence, adjust the diet to elevate the base ω6 fatty acids using sunflower oil for the linoleic acid (LA), and flaxseed oil for alpha linolenic (ALA)*. Raising the EFA levels in the body with the 4:1 ratio has provided positive clinical results. In addition, with the use of the red cell fatty acid test from Johns Hopkins we can view each patient's level of fatty acids and adjust their diet for precise EFA control.

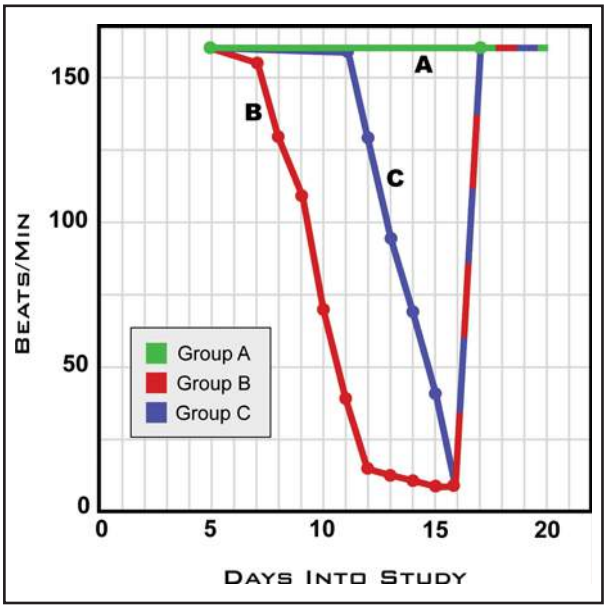
* LA and ALA are base lipids (PUFAs, polyunsaturated). For the higher order of lipids (HUFAs, highly-unsaturated FAs) we reach a metabolic impasse since humans as well as all large mammals lack sufficient FA desaturase capabilities. For the omega 6 HUFAs, GLA and Arachidonic, and the omega 3 HUFAs, EPA and DHA, we are dependent on diet, such as eggs, dairy, meat and fish. Vegetarians have fewer options since plant based AA and EPA are rare or non-existent.

Phosphatidylcholine: Of all the phospholipds, phosphatidylcholine (PC), is singularly the most important. PC is the largest ~ 50 % of the membrane with PE (phosphatidylethanolamine) at ~35 %.

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. Heart cells can be separated in a dish in vitro, but with proper feeding within a few days, they self agglomerate (gather together) and beat in unison at a rate of ~ 160 beats per minute.

To demonstrate the importance of PC, they fed one group of cultures (the A Groups) egg yolk PC and continued to do so for the life of the experiment (20 days), while two other groups (the Bs and Cs) were deprived of PC and later had it added back into their feed.

The Group A cultures are represented with a straight line (green) at the top of the chart. They had been given egg PC after day 6 and for the entire 20 days they maintained a constant beating rate of ~ 160 beats/min. Group B (Red) cultures were not as fortunate and were denied PC until day 16. The chart shows the result for after 6 days the B groups started to weaken and by day 8 began a precipitous decline in beating rate till day 12 wherein some of the B groups were only beating at ~ 20 beats/min. and others not beating at all. The Group Cs (Blue) were given PC as the A groups, but only to day 11, after which PC was removed from their feed. As you can see on the chart, almost immediately the Cs started a decline in their beating rate and 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 size and production of protein.



On day 16 all cultures, including groups B and C were given PC, and within 24 hours, the Bs and Cs recovered their beating rate to ~ 160 beats/min and continued so until the study was concluded at day 20. In addition, they also recovered most of their distorted chemistry. This was a remarkable demonstration of the power of phosphatidylcholine, or to be more precise, of the absolute necessity of it.

A Medline search on 'Phosphatidylcholine' will reward you, or inundate you, with 37,471 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 membranes 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 subsequent replacement of PC re-establishes homeostasis.

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

It is a review of 776 research papers published from 1959 to 1993 on the therapeutic value of Essential Phospholipids (EPL), which is the European reference for a high concentrated phospholipid from soy (no longer considered lecithin). It was developed by Nattermann, a German producer of lecithin products for food and cosmetics. The term EPL became recognized in medicine since Nattermann developed it both in an oral supplement and as an IV ampoule for intravenous infusions.

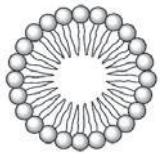
PC began to be accepted throughout Europe as a natural inexpensive medical IV treatment. However it was in Eastern Europe that it achieved a higher degree of popularity. Russia and their satellites were not as close to Big Pharma as we in the West. A natural product like PC (EPL) is a cheaper alternative to drug therapy and is 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 years, with many of these studies detailed in Guntermann's review.

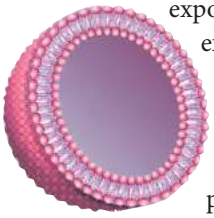
During the 70's Nattermann AG was absorbed by Aventis and Rhone Poulanc along with their PC-IV therapy. However, in spite of rave reviews in a wide range of treatments, PC received little attention. Natural products like PC are un-patentable and even with an excellent medical record have little sex appeal in the pharmaceutical world. IV-PC is not even approved in France and Rhone Poulanc is a French company. They could certainly 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. Riboflavin (B2) provided the color. Rhone Poulanc marketed their IV-PC as LipoStabil, which was clear since it had no vitamins added. Both products were produced in the same factory on the same production line. In 2005 Aventis abruptly took Essentiale off the market. It appears that the manufacturing facility is now wholly owned by Rhone Poulanc since LipoStabil is currently available worldwide and especially in Germany, Austria and Switzerland. There is ample research over the past 50 years on the efficacy of both products for similar disorders which leaves the question open for research as to the value of the added vitamins.

The Marketplace: The majority of what is currently sold on the market today as Phosphatidyl Choline is lecithin, or triple lecithin. Lecithin can not form a micelle. Even though it contains phospholipids and PC, when taken orally, it is assaulted by lipases, phospholipases, and other enzymes which remove their fatty acid chains and break down the other components. By the time fat absorption occurs, the components of the phospholipids are indistinguishable from the components of other lipids. Some head groups, like choline and inositol, are hard for the body to make, so absorption of these components from food can be important for a healthy diet. However, the job of re-assembling sought after PC from the individual components, is well nigh impossible. It might be accomplished --- if you are young and healthy; but if you're young and healthy you don't need a supplement, simply eat an egg or two.


Micelle

Lecithin itself was not the answer, it needed a much higher phospholipid concentration which Nattermann developed. The 1940's German method extracted a "Pure Phospholipid" (EPL), which only recently has been duplicated by BodyBio. While the process is more expensive, discarding undesired components from lecithin and raising the phospholipid concentration encourages the formation into a micelle (Liposome). A micelle/liposome, when exposed to a watery environment forms exactly like cell, a spherical shape, only a thousand times smaller.


Liposome

The phospholipids of micelles and liposomes are identical to cellular phospholipids, however, a liposome is always a bilipid layer and more stable. That tiny sphere can then traverse the gut without being dismembered (it looks exactly like a cell), and not only deliver its-self but also deliver a tiny cargo such as a drug or even another supplement. Today, most pharmaceutical companies are engaged in liposome technology as a drug delivery agent. In the manufacturing process, the drug is trapped inside the sphere so when the liposome touches a 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 taking a drug orally.

However, the fallacy of using lecithin for any medical benefit has been difficult to see. Doesn't lecithin contain a lot of PC? It certainly does. For years there have been conflicting medical reports about the benefits of PC (Wood 1982), all of which now becomes much clearer through liposome research. In many of the research studies they would simply use lecithin in their attempt to increase PC concentration, which was logical. In those earlier studies they did not realize the digestive impact and the near impossible task of providing PC from plain lecithin.

BodyBio PC or PhosChol® will blend in plain water. They do not dissolve, rather they are miscible; mix in the watery environment. They naturally form as a liposome, or more precisely many thousands of them. Lecithin or triple lecithin, will not blend with water no matter how vigorous it is mixed. This is easily performed in a laboratory or even in your kitchen.

PC Products Currently Available: BodyBio PC and PhosChol® are the only phosphatidylcholine supplements made of pure phospholipids which form liposomes. Lipoflow™ products also form liposomes of pure phospholipids but are predominantly used for nutrient delivery. EPL from Rhone Poulanc is a high concentrated PC capsule supplement available in Europe in most pharmacies. BodyBio PC is formulated with the essential lipids at a 4:1 ratio with 16 % of the phospholipids as PE (phosphatidylethanolamine). Injectable PC is available in a 5 ml ampoule for IV therapy as LipoStabil™ from Rhone Poulanc in German speaking countries and Eastern Europe.

Wood et al, 1982, *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.*

*PhosChol is a registered trademark of Nutrasal LLC.

Phosphatidylethanolamine acts as a reservoir for PC, since, by the addition of three tiny methyl groups it is converted to PC. Thirty percent of PC cellular chemistry is normally derived from methylation (Cui 2002). To encourage this conversion of PE to PC, it is advisable to add into the diet, Folinic Acid (an advanced form of folate) and a methylated form of B-12, Methylcobalamine. Both nutrients increase methylation and as an added bonus tend to lower homosysteine levels.

Today, doctors at PK Protocol approved clinics as well as other physicians across the US and Europe are experiencing positive outcomes with PC administering it both orally and intravenously. And, they are achieving success with the very same neurological disorders that Wood and others had described negatively concerning the use of lecithin. PC is a vital component of the PK Protocol, which is currently used for difficult neurological disorders such as ALS / Motor Neuron Disease, Parkinson's, Alzheimer's, Multiple Sclerosis, Autism as well as Chronic Fatigue Syndrome, Lyme, Fibromyalgia, and Toxic Mold. Below are case studies that Dr Patricia Kane has reviewed with one of the medical doctors practicing the PK Protocol procedure.

The PK Protocol, which includes PC, also includes medical laboratory tests, especially a red blood cell fatty acid test from Johns Hopkins and a Chem 28 with CBC (with BodyBio Analysis Report) as well as specific tests pertaining to each patients presentation. While PC is a crucial piece, it should not be assumed as having the ability, on its own, to be solely responsible for the benefits discussed in the following case studies.

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure, or prevent any disease.

CASE STUDY 1 — PARKINSON'S

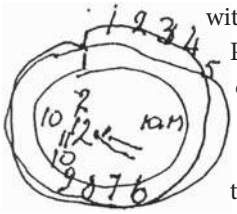
RUTH: Female patient age 77 was diagnosed with Parkinson's Disease in March 2002. Patient presented with gait disturbance, unable to dance, weakness, frequent falls, frozen facies, tremor in upper extremities left greater than right. Patient began oral nutrient supplementation with nutrient dense, low carbohydrate diet. IV therapy commenced with Glutathione Push once weekly whereby after 6 months patient felt that she was stronger and her tremor was slightly improved but no other apparent change. IV PC Lipid Exchange was added to the patient's therapy on 9 23 02 once weekly. After 8 infusions patient had a dramatic response to therapy as tremors were completely resolved, gait normalized, facial expression returned, movement was organized and fluid. Patient's red cell lipids were tested in March 2002 and re-tested in December 2002 at Johns Hopkins whereby suppression of myelination markers were significantly improved. Symptoms of Parkinson's dramatically improved. Patient continues diet, supplements and weekly IV infusions of Lipids with GSH for longevity purposes.

CASE STUDY 1 — ALS

MARGIE: Female patient age 40 was diagnosed with Lower Motor ALS in August 2000 and was on a rapid downhill course. Margie was a Marathon runner. She presented incapacitated, on a ventilator and tube fed, unable to move. Her only communication was the blinking of her eyes. After 3 weeks of oral and IV PC lipid exchange with the PK Protocol patient gained strength in her neck and was able to move her thumb. After 9 weeks of therapy patient was able to turn her wrist, then move her elbow, and finally lift her shoulder. Patient was also able to breath on her own without a ventilator for 5 minutes, then 10 minutes and presently 15 minutes or more. Patient was able to get out of bed and sit in a wheelchair for her daughter's birthday in March, four months after oral and IV PC therapy.

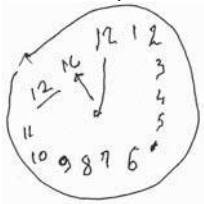
CASE STUDY 3 — ALZHEIMERS

GEORGE: Male patient, age 83, presents with short and long term memory loss, poor word retrieval, anxiety, depression, excessive sleepiness, confusion, sound sensitivity, rough dry skin and severe scoliosis. Patient was unable to perform Clock Test and drew a highly abnormal clock with the numbers outside the circle in a highly distorted pattern. Patient diagnosed with Alzheimer's in October 2003. Patient received weekly infusions of IV PC lipid exchange and GSH. He took a few supplements, diet was adequate but patient resisted taking prescribed supplements. Improvement was noted in memory, confusion, anxiety and depression. In April of 2004



We give the patient pencil and paper and ask them to draw a clock with the time at 10 minutes to 10:00.

patient was able to verbally express his concerns about his health in an organized manner. After a fall in September 2004 and resistance to taking supplements pt had severe deterioration, was disoriented and unable to express himself. George's wife felt that he needed to reside in a nursing home. He then received an infusion of Leucovorin in addition to his normal IV Therapy and for one week took 10 mg of Leucovorin daily. When he returned to the clinic one week later the transformation was profound. Patient was talking, laughing and interacting normally. He continued to take Leucovorin orally and to have weekly infusions of the IV PC lipid exchange/leucovorin/glutathione along with increased compliance of his oral supplementation. Within one month patient passed the clock test and is functioning normally.



CASE STUDY 4 — MS

JULIE: Female patient age 59 diagnosed with MS in 1987. Patient experienced mild symptoms until February 2000. Multiple plaques identified in an open brain MRI with and without contrast in 2000 as scattered foci of abnormal signal intensity in the periventricular white matter, another lesion in the right cerebellam hemisphere and the cervical spine demonstrates multiple areas of abnormal signal intensity within the cervical cord, specifically at the posterior mid sagittal cord at C2, right anterior cord at C2-3, left posterior cord at C5 and in the central cord at the T1-2 level extending inferiorly to the T2 level.. Patient presented with Relapsing-remitting MS with weakness in extremities on left side of body, spasticity, abnormal gait, muscle spasms, numbness, tingling, peripheral neuropathy, dry skin, constipation, tan stool, anxiety, depression, fatigue, headaches, heat intolerance, and poor memory. Patient initially began treatment with oral nutrient supplementation emphasizing essential fatty acids and IV Glutathione push once weekly. Patient had a positive response with increased energy, loss of numbness/tingling, mental stability but her abnormal gait and spasticity in her left leg remained. Patient was infused with the IV PC lipid exchange and GSH two times daily for three days in succession, whereby the spaciticity in her left leg resolved and her gait normalized. Patient has continued to improve in her presentation with elevated mood, memory improvement, and increased ability to exercise. Patient's red cell lipids were tested in June 2001 and re-tested in July 2002 and November 2003 at Johns Hopkins, whereby suppression of myelination markers were significantly improved. Patient presently maintains on two infusions of lipids and GSH weekly. Symptoms of MS appear to be resolved at the present time.

CASE STUDIES 5 AND 6 — AUTISM

BRANDON AND MARK: Male twins, age 3, were diagnosed with Autism at age 2.4 years. Brandon presented with poor coordination, learning problems, dark circles under eyes, tantrums, poor eye contact, not toilet trained, no speech, poor motor planning, short attention span, refusal to eat other than a few bites of waffle at breakfast. Mark presented with ecolalia, speech delay, garbled speech, severe hyperactivity, earaches, not toilet trained, bags under eyes, poor eye contact. Twins had an uncomplicated gestation, full term delivery, breast fed 4 months. Patients began limited changes in diet due to resistance of change, however, Brandon began eating more food after the addition of more salt in his food (low sodium) per serum electrolytes. After the fourth infusion of IV PC lipid exchange, Leucovorin and Glutathione, on December 21, 2004, Brandon began speaking in full expressive sentences and playing in an appropriate manner. The twins began to dramatically improve in motor planning, toilet training, speech, stable mood, learning and speech. By April 2005 Mark no longer exhibited signs of developmental delay or ASD and was placed in a normal preschool. By July 2005 Brandon had lost all signs of autism, had full speech and expression, and normal social play. By September of 2005 Brandon was placed in a normal preschool along with his twin.

CASE STUDY 7 — AUTISM

SEAN: Male patient, Sean age 5, diagnosed with Autism at age 2 with moderate progression of autistic features. Patient presents with poor memory, speech delay, self-stim, insomnia, hyperactivity, dilated pupils, disorientation, anxiety, apathy, sound sensitivity, incontinence, tan stool, loss of appetite, fatigue, light sensitivity, sleep disturbance, dry skin, hypotonia, abnormal gait, and failure to gain weight and grow. Patient began with oral supplementation of balanced oil, electrolytes and liquid minerals over a 2 month period whereby he experienced improved eye contact, increased awareness, better motor planning and more interaction with family and teachers. IV PC lipid exchange and GSH therapy was then introduced whereby after the fourth infusion patient spoke to a stranger in a store saying 'hello' and 'goodbye' appropriately. In addition, he spoke on the phone to a relative at great length using descriptive language. His artwork changed in that it had much more detail. He began using complex words and sentence structure and appeared to be thinking in a more organized matter. After the seventh infusion patient has been able to eat full meals, gained one pound, read out numbers on road signs, have complete conversations, appropriately interact socially with other children, pupils are no longer dilated, able to sleep through the night, accomplish urinary control, established eye contact. Patient told his mother, 'Mama, I just get smarter everyday, don't I?'

For further information on the PK protocol, please call: BodyBio at 888 320 8338.

References

Baumann A., Biochem Z, 1913, 54, 30 and Renall M.H., Biochem Z 1913, 55, 296. **Ethanolamine**

Cui Z, Houweling M, (Review), **Phosphatidylcholine and Cell Death**, Biochemica et Biophysica Acta 2002, (1585) 87-96.

Feulgen R.Z., Physiol Chem 1939, 260, 217. **Folch made an important scientific contribution in isolating from brain phosphatidylethanolamine, phosphatidylserine and an inositol phospholipid as components of "cephalin" in 1942 and a "diphosphoinositide" in 1949** (Folch J., J Biol Chem 1949, 177, 497). **Cardiolipin was also isolated from brain in 1944** (Pangborn M.C., J Biol Chem 1944, 153, 343) .

Fox JM, **A glossary of essential phospholipids, lipids, and lipoproteins in: Phosphatidylcholine, Biochemical and Clinical Aspects of Essential Phospholipids.** (H. Peters, Ed.), Springer Press, Berlin-Heidelberg-New York (1976), 2-7

Gobley (J Pharm Chim 1850, 17, 401 and J Pharm Chim 1874, 19, 346)

Gundermann KJ, PhD, MD, Associate Professor at the Institute of Pharmacology and Toxicology, Medical Academy, Szczecin, Poland. **"The Essential Phospholipids as a Membrane Therapeutic" 1993.**

Lee G, **Lipid phase transition and mixtures. In: Membrane Fluidity in Biology.** (Aloia, RC, Ed.) Academic Press, New york, 2 (1983) 43-88

Lipton RH 2005

Moscona-Amir E, Henis YI, Yechiel E, Barenholz Y, Sokolovsky M., Biochemistry 1986 Dec 2;25(24):8118-24. **Role of lipids in age-related changes in the properties of muscarinic receptors in cultured rat heart myocytes.**

Mostofsky DI, Yehuda S, Rabinovitz S, Carasso R., Neuropsychobiology. 2000;41(3):154-7. **The control of blepharospasm by essential fatty acids.**

Mouritsen OG, Springer-Verlag Berlin Heidelberg 2005. ch1:pg 16. **Life - as a Matter of Fat.**

Owen JS, Hutton RA, Day RC, Bruckdorfer KR, McIntyre N, J lipid Res. 23 (1983) 124-132. **Decreased erythrocyte membrane fluidity and altered lipid composition in human liver disease.**

Rabinovitz S, Mostofsky DI, Yehuda S., Psychoneuroendocrinology. 2004 Feb;29(2):113-24. **Anticonvulsant efficiency, behavioral performance and cortisol levels: a comparison of carbamazepine (CBZ) and a fatty acid compound (SR-3).**

Rodieck RW, **The First Steps in Seeing,** 1998, Ch 10, **Photoreceptor** Attributes, pg 214, Sinauer Associates, Sunderland MA 01375,

Rudin Do, unpublished manuscript, "The Omega Factor: Our Nutritional Missing Link" 1985. Chapter 7:pg 18.

Shinitsky M., **Membrane fluidity and cellular functions.**, Physiology of Membrane Fluidity, CRC Press, Boca Raton FL (1984) 1045-1049

Thudichum JLW 1829-1901, A Treatise on the Chemical Constitution of the Brain., London, Bailliere, Tindall, and Cox, 1884. **Concluded that phospholipids are "the center, life, and chemical soul of all bioplasm".**

Yechiel E, Barenholz Y., J Biol Chem 1985 Aug 5;260(16):9123-31. **Relationships between membrane lipid composition and biological properties of rat myocytes. Effects of aging and manipulation of lipid composition.**

Yechiel E, Barenholz Y, Henis Y. (1985) **Lateral Mobility and Organization of Phospholipids and Protein in Rat Myocyte membranes.** J. Biol. Chem., **260**, 9132-9136

Yechiel E, Barenholz Y., Biochim Biophys Acta 1986 Jul 10;859(1):105-9. **Cultured heart cell reaggregates:**

a model for studying relationships between aging and lipid composition.

Wood JL, Allison RG, Fed Proc. 1982 Dec;41(14):3015-21. **Effects of consumption of choline and lecithin on neurological and cardiovascular system**

Yehuda S, Rabinovitz S, Carasso RL, Mostofsky DI., Neurobiol Aging. 2002 Sep-Oct;23(5):843-53. **The role of polyunsaturated fatty acids in restoring the aging neuronal membrane.**

Yehuda S; Rabinovitz S; Carasso RL; Mostofsky DI., Int J Neurosci - 01-Jan-2000; 101(1-4): 73-87. **Fatty acid mixture counters stress changes in cortisol, cholesterol, and impair learning.**

Yehuda S, Rabinovitz S, Mostofsky DI., J Neurosci Res. 1999 Jun 15;56(6):565-70. **Essential fatty acids are mediators of brain biochemistry and cognitive functions.**

Yehuda S, Rabinovitz S, Mostofsky DI., Eur J Pharmacol. 1999 Jan 15;365(1):27-34. **Treatment with a polyunsaturated fatty acid prevents deleterious effects of Ro4-1284.**

Yehuda S, Rabinovitz S, Mostofsky DI., Med Hypotheses. 1998 Feb;50(2):139-45 **Essential fatty acids and sleep: mini-review and hypothesis.**

Yehuda S, Rabinovitz S, Mostofsky DI., Neurochem Res. 1998 May;23(5):627-34.

Modulation of learning and neuronal membrane composition in the rat by essential fatty acid preparation: time-course analysis.

Yehuda S, Rabinovitz S, Carasso RL, Mostofsky DI., Peptides. 1998;19(2):407-19. **Fatty acids and brain peptides.**

Yehuda S, Rabinovitz S, Mostofsky DI, Huberman M, Sredni B., Eur J Pharmacol. 1997 Jun 5;328(1):23-9. **Essential fatty acid preparation improves biochemical and cognitive functions in experimental allergic encephalomyelitis rats.**

Yehuda S, Rabinovtz S, Carasso RL, Mostofsky DI., Int J Neurosci. 1996 Nov;87(3-4):141-9. **Essential fatty acids preparation (SR-3) improves Alzheimer's patients quality of life.**

Yehuda S, Brandys Y, Blumenfeld A, Mostofsky DI., Int J Neurosci. 1996 Sep;86(3-4):249-56. **Essential fatty acid preparation reduces cholesterol and fatty acids in rat cortex.**

Yehuda S, Carraso RL, Mostofsky DI., Neuroreport. 1995 Feb 15;6(3):511-5. **Essential fatty acid preparation (SR-3) rehabilitates learning deficits induced by AF64A and 5,7-DHT.**

Yehuda S, Carasso RL, Mostofsky DI., Eur J Pharmacol. 1994 Mar 11;254(1-2):193-8. **Essential fatty acid preparation (SR-3) raises the seizure threshold in rats.**

BODYBIO

FAT DIGESTION: Triglycerides (TAG) are the major fats in human diet, contributing 90 to 95% of dietary fat energy. The majority of phospholipids (PL) is phosphatidylcholine (PC), which originates mostly from hepatic and biliary origin at ~10-20 g daily. Dietary PLs contribute to ~ 1-2 g per day (Carey 1992, Tso 1994).

The first step in dietary fat digestion starts with the separation of the lipid tails and the head groups and occurs in the stomach by gastric lipase with partial hydrolysis of TAG (triglycerides), resulting in DAG (diglycerides) and free fatty acids (Carey 1992,83, Borgstrom 1977, Liao 1984). The remaining digestion of TAG occurs in the duodenal by pancreatic lipase, with hydrolysis (cleaving) at the sn-1 and sn-3 position, releasing a mono-glyceride and two free fatty acids. (Borgstrom 1977, Mattson 1966). Pancreatic lipase is abundantly present in pancreatic juice. Only severe pancreatic insufficiency results in lipid malabsorption.

Dietary cholesterol is mainly present as free cholesterol and only 10-15% as cholesterol ester. Cholesterol esters must be hydrolyzed in the duodenum by pancreatic cholesterol esterase (CE) before absorption can take place. Human cholesterol esterase does not only hydrolyze cholesterol esters but also acts on TAG (sn-1, sn-2, sn-3) and PL (sn-1, sn-2) (Lombardo 1980) and its activity is greatly enhanced by the presence of bile salts.

Digestion of free phospholipids (PLs including PC but excluding micelle and liposome formations) occurs entirely in the duodenal lumen by pancreatic phospholipase A2. PLA2 hydrolyzes (cleaves) the fatty acid at the sn-2 position, resulting in free fatty acids and lyso-phosphatidylcholine (lyso-PC). Further hydrolysis of the head group and the fatty acid at the sn1 position are acted on by phospholipases PLA1, PLB, PLC and PLD.

The individual components of PLs and TAGs including their hydrophilic polar head-groups as well as cholesterol, mono glycerides, FFAs, etc. secure themselves with bile acids inside of mixed micelles for protection against the aqueous world and are about 4 nm in diameter (Carey 1970, 83, 92, Tso 1994, Verkade 2000). Re-organization of those substrates into PLs occurs on the cellular endoplasmic reticulum. The act of gaining the preferred phosphatidylcholine by reassembling the desired components is highly suspect.

MC. Carey and O. Hernell. Digestion and absorption of fat. *Semin Gastrointest Dis* 1992. 3: 189-208.

MC. Carey, DM. Small, and CM. Bliss. Lipid digestion and absorption. *Annu Rev Physiol* 1983. 45: 651-77.

P. Tso. Intestinal lipid absorption. In: Tso P, ed. *Physiology of the gastrointestinal tract*. 3 ed. New York: Raven Press, 1994. 1867-907.

HJ. Verkade and P. Tso. Biophysics of intestinal luminal lipids. In: Mansbach CM, Tso P, Kuksis A, eds. *Intestinal Lipid Metabolism*, 2000. 1-18.

B. Borgstrom. Digestion and absorption of lipids. Int Rev Physiol 1977. 12: 305-23.

TH. Liao, P. Hamosh, and M. Hamosh. Fat digestion by lingual lipase: mechanism of lipolysis in the stomach and upper small intestine. *Pediatr Res* 1984. 18: 402-9.

FH. Mattson and RA. Volpenhein. Carboxylic ester hydrolases of rat pancreatic juice. *J Lipid Res* 1966. 7: 536-43.

D. Lombardo and O. Guy. Studies on the substrate specificity of a carboxyl ester hydrolase from human pancreatic juice. II. Action on cholesterol esters and lipid-soluble vitamin esters. *Biochim Biophys Acta* 1980. 611: 147-55.

Printed in USA
Part No. 902.2