INTRODUCTION TO CALCIUM-EAP (COLAMINE PHOSPHATE)

(This information is derived from a speech presented by Dr. George N. Morrissette,M.D. of Lewiston, Maine-November 1990.)

Calcium-EAP (Colamine Phosphate)

"The basic component of Calcium-EAP, phosphoric acid mono-(2-aminoethyl)-ester, is a naturally occuring metabolite of the organism. As far as its effects are concerned Calcium - EAP belongs to the electrolytic transporter category. Calcium-EAP's anti-inflammatory facility is a result of complex calcium being introduced into the cell and its being fixed long-term in the intracellular space." Excerpt from brochure about Calcium-EAP from Dr. F. Kohler Chemie GmbH.

For many years the MS treatment with Calcium-EAP was known as the so called "Nieper-Treatment" of MS-Therapy. This therapy includes several medications which vary from case to case. It is evident that many patients have improved under this therapy.

The results of the Calcium-EAP Survey of George N. Morrissette, M.D. with 151 (initial) cases are surprising (see page 7). Although the response to Calcium-EAP appears to be promising, further prospective comparative clinical trials are needed to assess the efficacy of the Calcium-EAP treatment.

To give an idea of the proposed mechanism of action, one has to consider the pathogenenis of MS.

The etiology is not known today in detail but findings suggest at least four dominant factors involved.

* Virus infections
* Immunopathological reactions
* Metabolic disorders
* Underlying genetic predisposition

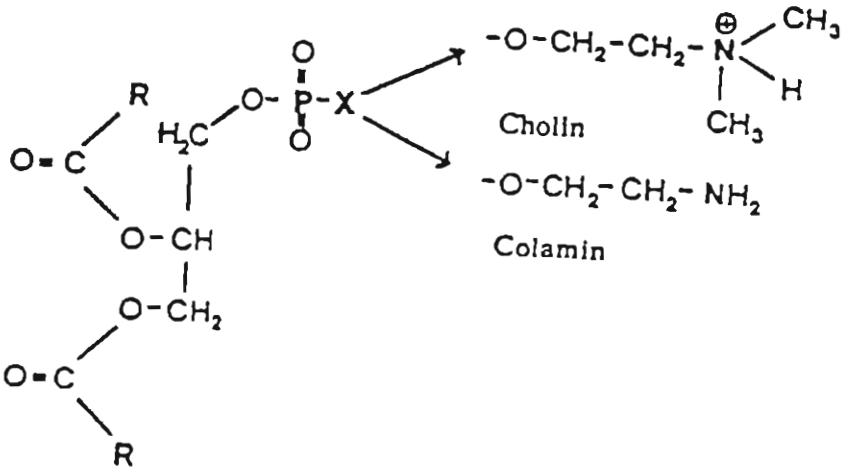
All these factors lead to demyelinization of the neuron sheath. The clinical manifestation with its variety of symptoms can be correlated to the locus of pathological action. The lack of neurotransmission results from the destruction of the membranes of the neuron, especially the axon, and causes ineffective triggering of chemoelectrical signal transmission. The diagnosis is focused mainly on clinical symptoms in addition to the examination of gamma-Globulin in CSF, CT--scan, evoked potentials (SSEP, VEP) (1-8) and MRI.

Calcium plays a vital role in cellular signal transmission. Precise control and regulation of cytoplasmic free ionic calcium concentration is required for intracellular calcium-mediated physiology. Calmodulin is the calcium receptor-protein which serves to regulate various calcium-dependent enzymes. Calcium as "universal messenger" was first introduced by E. Sutherland (9) in 1962.

The role of calcium in stimulating secretion-coupling in endocrine cells also is described in various papers (10-25).

Calcium is essential to neuronal functions, and the understanding of calcium metabolism in the nervous system is increasing but not yet completely understood.

Phospholipid molecules exist in biological membranes of every type of organism throughout nature. The best known and most important phospholipid, based on choline, is phosphatidylcholine.



Glycerophosphatides

The molecular composition (%) of phospholipids in the myelin membrane show high concentration of two very close chemical structures, phosphatidyl-ethanolamine (phosphatidyl-EAP), and phosphatidyl-choline.

lipid	40%
sphingomyelin	5%
phosphatidyl-ethanolamine	15%
phosphatidylserine	5%
phosphatidylcholine	13%
phosphatidylinositol	2%

In other cell membranes the phospholipid content is even higher (Nucleus 84%, Microsome 87%, Mitochondria 78%, Golgi's complex 62%) (40-41).

In the past few years numerous studies have shown the interaction of phospholipid-methylation in the transmission of biological signals in many types of cells (42).

One could assume the effectiveness of Ca-EAP and Phosetamin is secondary to an increase in conductivity of the nerve tissue. The lesion of the membrane after any cytotoxic reactions causes pathophysiological increase of permeability and destruction of the lipid layer. It is known, that Mg++ and Ca++ can avoid further increases of permeability.

In combination with a natural phospholipid structure a complex compound like Ca-EAP and Mg-EAP (Phosetamin), can be linked to a membrane receptor to stimulate Ca ++, Mg ++ dependent ATPase activity and to increase the conductivity (43).

Ca-EAP is manufactured in two application forms, for i.v. injection and oral application (sugarcoated pills). Both preparations are registered and marketed in Germany since 1966.

Composition of Ca-EAP:
One ampule (10 ml) contains 400 mg of the complex salt calcium phosphoric-acid-mono-(2-aminoethyl)-ester. One pill contains 380 mg of the complex salt calcium phosphoric acid-mono-(2-aminoethyl)-ester.

Indications:

Autonomic and peripheral diabetic neuropathies, cerebellar ataxia of multiple sclerosis, allergic and inflammatory dermatitis, urticaria, rhinitis, osteoporosis, parodontopathy, exudative and hemmorhagic disorders, gastric ulcera, calcium deficiency, also ALS and Friedreich's ataxia.

Dosage:

At the start of parenteral treatment, 1 ampule i.v. daily over one week. Continuation of treatment with 3-5 ampules per week. For all treatment 3 x 1 to 3 x 3 pills daily.

The enteric coated pills may not be sucked or chewed up. Intramuscular and subcutaneous injections are prohibited.

Side effects and concomitant phenomena:

Calcium-EAP is usually well tolerated. In the case of latent or manifest hepatitis, headache and chills will sometimes occur after intravenous injection. In such cases the drug should be injected very slowly. In rare instances it may happen that sensitive patients undergoing intensive treatment show pancreatic and biliary dyskinesia. These complications can be removed or avoided with 3-4 pills of Phosetamin. It is not necessary to interrupt the treatment with Calcium-EAP. Patients on digitalis must be followed carefully in the early stage of treatment.

History and clinical relevancy of Calcium-EAP:

Chargaff(52) and later in 1944 Keston found that ethanolamine phosphoric acid acts as intermediate of the metabolism of phosphatidyl ethanolamine in many tissue, especially in the brain. In the early 50's several papers were published about the metabolic pathways and physiological mechanism of different phospholipids.

The biochemist Dr. Franz J. Kohler found during his research on metabolic pathways of energy turnover and kinetics of enzyme activity, that aspartic acid is the major amino acid in this respect. Later in 1954 to 1956, he and Laborit introduced a new concept of electrolyte substitution, which led to the first clinically tested potassium-magnesium-aspartate.

Dr. H.A. Nieper was one of the first physicians, who performed the clinical trials and discussed the scientific background of this new concept with Dr. Franz J. Kohler. Looking for other ligands with biological relevancy of specific tissues, Dr. Franz Kohler proposed EAP because of its high content in brain tissue, known several years ago.

Dr. H.A. Nieper was excited about this hypothesis and started testing this new class of substances and a few papers about this subject were published (45-51),(1965-1970).

For economic reasons, the Dr. F. Kohler Chemie GmbH, established in 1959, has focused their activities on the therapeutic relevancy of the aspartate-minerals. About 400

scientific and medical papers were initiated in the last 25 years.

Nevertheless Dr. H.A. Nieper went on with the treatment of the EAP-compounds for several indications showing in many cases good results, but was never able to carry out acceptable prospective randomized trials to give evidence for his treatment.

In the early 80's Dr. F. Gernot Kohler realized the efficacy and safety of the EAP's and has initiated a number of trials in animals in the treatment of diabetic neuropathy.

The treatment of MS with Ca-EAP and Phosetamin is not a cure but we hope it will serve a therapeutic role for management until a complete cure is found.

The following protocol of MS-Therapy represents the "Nieper treatment" which varies from case to case.

An Example:

Calcium EAP* (i.v. 30-60 sec.) first 2 weeks 5 x 1 ampule (pulse rate should not increase more than 10% of normal frequency)
Calcium-EAP* i.v. follow up treatment 3 times per weeks 1 ampule (use only arms, wrist and dorsum of hands)
Phosetamin* 3 x 2 to 3 x 3 pills daily
Calcium EAP* 3 x 1 pill daily
Inzelloval* 3 x 1 pill daily
Mandelonitril 2 x 10 drops
Ixoten for 3-6 months 1 tablet daily

* Kohler products

RESULTS OF THE CA-EAP SURVEY*
TABLE 2: GENERAL RESPONSE TO CA-EAP

	Code	No. of Patients
1. Much worse (Significant deterioration in many areas)	(---)	0
2. Moderately worse (Deterioration in several areas)	(--)	5
3. Mild deterioration	(-)	22
4. Stabilization	(+)	29
5. Mild improvement	(±)	32
6. Moderate improvement (several areas)	(++)	36
7. Marked improvement (Significant in many areas)	(+++)	27
TOTAL		151

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