

Mesotherapy Materia Medica

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Mesotherapy involves the injection of natural substances and allopathic medications. This first of two sections is meant to be an overview of the most commonly used medications in by mesotherapists in the US. The second section will be included in the next issue of the American Journal of Mesotherapy. I have included phosphatidylcholine even though many do not consider its use to be classified as mesotherapy. Additionally, I have included substances that I personally do not use (i.e. aminophylline, L-Carnatine). However, because of their widespread use, they merit discussion.

1. Phosphatidylcholine (PTC)

a) Mesotherapy Indication(s)

Treatment of localized fatty deposits, cellulite, and lipomas.

b) FDA Approved Use/Drug Class

Because PTC is considered a nutritional supplement it does not fall under the jurisdiction of the FDA. PTC has been proven helpful in the restoration of liver function in a number of disorders, including alcoholic fibrosis, and possibly viral hepatitis. There is some literature which suggests it may be of value for the treatment of bipolar disorder. There is some evidence that PTC may be useful in the management of Alzheimer's disease and some other cognitive disorders. A possible future role in cancer therapy is also suggested by recent research. Clinicians have experimented with PTC for the treatment of tardive dyskinesia.

c) Clinical Pharmacology/Pharmacokinetics

PTC is a phospholipid that is a major constituent of cell membranes. PTC is 1, 2-diacyl-:ussn:ue-glycero-3-phosphocholine, PtdCho and lecithin.. PC is metabolized to choline, fatty acids and glycerol.

d) Contraindications/Warnings/Precautions/Drug interactions

There are no known contraindications to PTC. Those with malabsorption problems may develop diarrhea or steatorrhea when using PTC supplements orally. Those with the antiphospholipid-antibody syndrome should exercise caution in the use of oral PTC supplements.

e) Adverse Reactions/Side Effects

No major side effects have been reported from oral administration of PTC apart from occasional nausea, diarrhea and increased salivation. When injected, it is normal for the patient to experience welting, soreness and swelling at the site of treatment. The welting generally goes down within a few hours, the swelling and soreness however can be moderate to severe for 1-2 weeks following the treatment. It is paramount to thoroughly explain/warn patients that this is to be expected and planned for. Patients will often describe this sensation to be akin to muscle soreness after strenuous exercise. Patients often report other reactions such as swelling, welting and itching at the injection site. Occasionally, patients will report skin numbness which may last for months. Again, it is very important to stress this to patients, they are generally so excited about receiving treatment they do not completely listen and then they become fearful one to two hours after the treatment when they are covered in red welts and in pain. They need to know that this is not an allergic reaction, it is a normal reaction. Instruct patients that if they have a skin reaction on areas that were not treated or if they experience difficulty breathing, this is in fact an allergic reaction and requires attention. Also patients will often report a feeling of "lumpiness" several days after the treatment. Assure them that this means the treatment is working and the "lumpiness" will eventually resolve with further treatments. Occasionally, patients will report cholinergic reactions such as nausea, vomiting, and diarrhea.

f) Management Guidelines for Overdose/Adverse Reactions/Side Effects

The most important aspect of post treatment management is doctor/patient communication. If you make it very clear to people what to expect, they will not become fearful when the normal side effects take place. There has never been a reported case of overdose of PTC. For the soreness and swelling, ice packs (never longer than 15 minutes at a time) and OTC analgesics are recommended.

2. Aminophylline

a) Mesotherapy Indication(s)

Cellulite, localized fatty deposits.

b) FDA Approved Use/Drug Class

Bronchodilators; Xanthine derivatives; antiasthmatic; bronchodilator; COPD agent; ethylenediamine derivative

c) Clinical Pharmacology/Pharmacokinetics

Aminophylline, a xanthine bronchodilator, is a 2:1 complex of theophylline and ethylenediamine. Aminophylline injection solution of theophylline in water for injection. Aminophylline (dihydrate) is approximately 79% of anhydrous theophylline by weight. The solution contains no bacteriostat or antimicrobial agent and is intended for use only as a single-dose injection.

Aminophylline competitively inhibits phosphodiesterase, the enzyme that degrades cyclic 3',5'-adenosine monophosphate (cAMP). Increased concentrations of intracellular cAMP may mediate most of the pharmacologic effects of the drug. Aminophylline exhibits many of the beta-adrenergic effects of epinephrine and thereby increasing cellular metabolic activity and lipolysis.

d) Contraindications/Warnings/Precautions/Drug interactions

Aminophylline is contraindicated in individuals who have shown hypersensitivity to its components, including ethylenediamine. It is also contraindicated in patients with active peptic ulcer disease, and in individuals with underlying seizure disorders (unless receiving appropriate anticonvulsant medications). In IV dosages used for bronchodilation, toxic synergism with ephedrine has been documented and may occur with other sympathomimetic bronchodilators. In addition, the following drug interactions have been demonstrated at IV doses: allopurinol (high-dose), cimetidine, ciprofloxacin, erythromycin, troleandomycin, lithium carbonate, oral contraceptives, phenytoin, propranolol, rifampin. In the doses used in mesotherapy, these interactions may not be problematic, however should be considered.

e) Adverse Reactions/Side Effects

The following adverse reactions have been observed, but there has not been enough systematic collection of data to support an estimate of their frequency. The most consistent adverse reactions are usually due to overdose and are therefore rare and mild in mesotherapy treatments because of the low doses used.

Gastrointestinal: Nausea, vomiting, epigastric pain, hematemesis, diarrhea.

Central Nervous System: Headaches, irritability, restlessness, insomnia, reflex hyperexcitability, muscle twitching, clonic and tonic generalized convulsions.

Cardiovascular: Palpitation, tachycardia, extrasystoles, flushing, hypotension, circulatory failure, ventricular arrhythmias.

Respiratory: Tachypnea.

Renal: Potentiation of diuresis.

Others: Alopecia, hyperglycemia, rash.

f) Management Guidelines for Overdose/Adverse Reactions/Side Effects

Discontinue drug immediately. Treatment is supportive and symptomatic. Avoid administration of sympathomimetic drugs. Administer intravenous fluids, oxygen and other supportive measures to prevent hypotension. For hyperthermia, use a cooling blanket or give sponge baths as necessary. Maintain patent airway and transport in case of respiratory depression.

3. L-Carnitine

a) Mesotherapy Indication(s)

Cellulite, localized obesity, fatty deposits.

b) FDA Approved Use/Drug Class

L-Carnitine is a nutritional supplement and therefore does not fall under the jurisdiction of the FDA. The strongest evidence for the use of oral supplemental with L-carnitine may be in the management of cardiac ischemia and peripheral arterial disease. It has been shown to lower triglyceride levels and increases levels of HDL-cholesterol in some cases. It is used with some benefit in those with primary and secondary carnitine deficiency syndromes. There is less evidence to support arguments that carnitine is indicated in liver, kidney and immune disorders or in diabetes and Alzheimer's disease. There currently exists little meaningful evidence that oral supplementation with L-carnitine boosts energy, increases athletic performance or inhibits obesity.

c) Clinical Pharmacology/Pharmacokinetics

L-carnitine (levocarnitine) was formerly called vitamin BT. L-carnitine is a quaternary amine and belongs to the same chemical family as choline. L-carnitine, an amino acid derivative, is found in nearly all cells of the body. L-carnitine transports long-chain fatty acids across the inner mitochondrial membranes in the mitochondria, where they are processed by beta-oxidation to produce biological energy in the form of adenosine triphosphate or ATP. In cardiac and skeletal muscle,

a major contribution of bioenergy comes from the beta-oxidation of long-chain fatty acids. Long-chain fatty acids require L-carnitine to transport them across the inner membranes of the mitochondria, wherein their metabolism produces bioenergy. Following the delivery of long-chain fatty acids into other mitochondria, L-carnitine, either by itself or esterified to an acyl group, recrosses the mitochondrial membrane to allow for continual use in this shuttle process. Another function of L-carnitine is to remove short-chain and medium-chain fatty acids from the mitochondria in order to maintain coenzyme A levels in these organelles.

d) Contraindications/Warnings/Precautions/Drug interactions

There are no known contraindications or drug interactions for L-Carnitine. Caution with patients with seizure disorders.

e) Adverse Reactions/Side Effects

Mild gastrointestinal symptoms have been reported in with oral L-carnitine, including transient nausea and vomiting, abdominal cramps and diarrhea. Although rare, seizures have been reported to occur in those with or without pre-existing seizure disorders receiving either PO or IV L-carnitine. In those with pre-existing seizure activity, an increase in seizure frequency and/or severity has been reported.

f) Management Guidelines for Overdose/Adverse Reactions/Side Effects

There have been no reports of toxicity from L-carnitine overdose. In the case of seizures, the first consideration is prevention, best accomplished by careful and constant monitoring of the patient's state of consciousness during the treatment. At the first sign of change, oxygen should be administered. The first step in the management of convulsions consists of immediate attention to the maintenance of a patient airway and assisted or controlled ventilation with oxygen and delivery system capable of permitting immediate positive airway pressure by mask.

4. Hyaluronidase

a) Mesotherapy Indication(s)

Cellulite, scars, adhesive capsulitis.

b) FDA Approved Use/Drug Class

Hyaluronidase's on label uses are as an adjuvant to increase the absorption and dispersion of other injected drugs, for hypodermoclysis; and as an adjunct in subcutaneous urography for improving resorption of radiopaque agents.

c) Clinical Pharmacology/Pharmacokinetics

Hyaluronidase is a spreading or diffusing substance which modifies the permeability of connective tissue through the

hydrolysis of hyaluronic acid, a polysaccharide found in the intercellular ground substance of connective tissue. This temporarily decreases the viscosity of the cellular cement and promotes diffusion of injected fluids or of localized transudates or exudates, thus facilitating their absorption. Normally, solutions injected subcutaneously spreads very slowly, but hyaluronidase causes rapid spreading thus proving helpful in better penetrating mesotherapy solutions into fibrotic cellulite deposits.

d) Contraindications/Warnings/Precautions/Drug interactions

Hypersensitivity to hyaluronidase has been reported in rare cases. Although often falsely negative, preliminary test for sensitivity is considered "best practice" and should be conducted though an intradermal injection of approximately 0.02 ml of the solution. A positive reaction consists of a wheal with pseudopods appearing within five minutes and persisting for 20 to 30 minutes and accompanied by localized pruritis. Transient vasodilation at the site of the test (erythema) will frequently occur and is **not** a positive reaction; is a normal reaction and to be expected. Do not mix hyaluronidase and hyaluronic acid in the same syringe.

e) Adverse Reactions/Side Effects

The subcutaneous administration of hyaluronidase has been associated with very few adverse reactions. Urticaria rarely will occur. Anaphylactic-like reactions following retrobulbar block or intravenous injections have occurred in isolated cases. Cardiac fibrillation has been encountered once. This author has encountered one incidence of mild allergic reaction caused by injection with hyaluronadase which was mild and tolerable to the patient.

f) Management Guidelines for Overdose/Adverse Reactions/Side Effects

Symptoms of a toxicity reaction consist of local edema or urticaria, erythema, chills, nausea, vomiting, dizziness, tachycardia, and hypotension. Treatment should be discontinued and supportive measures initiated immediately. Agents such as epinephrine, corticosteroids, and antihistamines should always be available for emergency treatment.

5. Hyaluronic Acid (Sodium Hyaluronate)

a) Mesotherapy Indication(s)

"Meso-Glow", treatment of fine lines, arthritis

b) FDA Approved Use/Drug Class

Osteoarthritis, cosmetic treatment of fine lines on the face.

c) Clinical Pharmacology/Pharmacokinetics

Sodium hyaluronate is a viscous solution consisting of a high molecular weight (500,000-730,000 daltons) fraction of purified natural sodium hyaluronate in buffered physiological sodium chloride. Hyaluronic acid is a natural complex sugar of the glycosaminoglycan family and is a long-chain polymer containing repeating disaccharide units of Na-glucuronate-N-acetylglucosamine.

d) Contraindications/Warnings/Precautions/Drug interactions

Contraindicated in patients with known hypersensitivity to hyaluronate preparations. Avoid the use of disinfectants containing quaternary ammonium salts for skin preparation because hyaluronic acid can precipitate in their presence.

e) Adverse Reactions/Side Effects

Anaphylactoid and allergic reactions have been reported with this product.

f) Management Guidelines for Overdose/Adverse Reactions/Side Effects

Should anaphylactoid or allergic reaction occur, treatment should be discontinued and supportive measures initiated immediately. Agents such as epinephrine, corticosteroids, and antihistamines should always be available for emergency treatment.

6. Pentoxifylline

a) Mesotherapy Indication(s)

Can be used with any mesotherapy solution and in France is frequently used for treatment of pain disorders. This author has had appreciable clinical success treating spinal stenosis with the injection of pentoxifylline. Pentoxifylline (Trental) bears some semblance to the French drug buflomedil (Fonzylane) which is used extensively by European mesotherapists however is not available in the US.

b) FDA (or international equivalent) Approved Use/Drug Class
Intermittent Claudication; Hemorrhologic agents; Xanthine derivatives; dimethylxanthine derivative.

c) Clinical Pharmacology/Pharmacokinetics

Pentoxifylline improves the flow properties of blood by decreasing its viscosity, but is not an anti-platelet aggregator. In patients with chronic peripheral arterial disease, this increases blood flow to the affected microcirculation and enhances tissue oxygenation. The precise mode of action of pentoxifylline is unknown. Pentoxifylline administration has been shown to increase erythrocyte flexibility. Pentoxifylline has been shown to increase leukocyte deformability and to inhibit neutrophil adhesion and activation. Tissue oxygen levels have been shown to be significantly increased by therapeutic doses of pentoxifylline in patients with peripheral arterial disease.

d) Contraindications/Warnings/Precautions/Drug interactions

Pentoxifylline should not be used in patients with recent cerebral and/or retinal hemorrhage or in patients who have previously exhibited intolerance to this product or methylxanthines such as caffeine, theophylline, and theobromine. This is to be taken into consideration when using aminophylline; they are considered to negatively interact at on-label-use doses. Concomitant administration of pentoxifylline and theophylline can lead to increased theophylline levels and theophylline toxicity in some individuals. In mesotherapy practice, drug interaction has not been reported to be a problem and the decision to mix these medicines should be left to the judgment of the treating physician.

e) Adverse Reactions/Side Effects

At on-label oral doses (400mg po qd) the following effects have been reported:

Cardiovascular: Dyspnea, edema, hypotension.

Digestive: Anorexia, cholecystitis, constipation, dry mouth/thirst.

Nervous: Anxiety, confusion, depression, seizures.

Respiratory: Epistaxis, flu-like symptoms, laryngitis, nasal congestion.

Skin and Appendages: Brittle fingernails, pruritus, rash, urticaria, angioedema.

Special Senses: Blurred vision, conjunctivitis, earache, scotoma.

Miscellaneous: Bad taste, excessive salivation, leukopenia, malaise, sore throat/swollen neck glands, weight change

f) Management Guidelines for Overdose/Adverse Reactions/Side Effects

Overdosage with pentoxifylline has been reported. Symptoms appear to be dose related and one would think it to be highly unlikely that one could cause an overdose with mesotherapy. A report from a poison control center on 44 patients taking overdoses of enteric-coated pentoxifylline tablets noted that symptoms usually occurred 4-5 hours after ingestion and lasted about 12 hours. The highest amount ingested was 80 mg/kg; flushing, hypotension, convulsions, somnolence, loss of consciousness, fever, and agitation occurred. All patients recovered. Treatment consists of maintaining systemic blood pressure, and controlling convulsions.

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7. Mannitol

a) Mesotherapy Indication(s)

Cellulite, localized obesity, fatty deposits.

b) FDA Approved Use/Drug Class

Ocular hypertension; cerebral edema, poisoning, renal failure, osmotic diuretic, antiendometriosis agent; disease-modifying antirheumatic drug, gastrointestinal antisecretory agent; hexahydric alcohol

c) Brand names (where applicable)

Mannitol, Osmitol, Resectisol.

d) Clinical Pharmacology/Pharmacokinetics

Mannitol is an osmotic diuretic. Mannitol is a 6-carbon sugar alcohol prepared commercially by the reduction of dextrose. Although inert metabolically in humans, it occurs naturally in fruits and vegetables. It induces diuresis by elevating the osmolarity of the glomerular filtrate and thereby hindering tubular reabsorption of water. Excretion of sodium and chloride is also enhanced.

e) Contraindications/Warnings/Precautions/Drug interactions

Contraindications include: renal disease, pulmonary edema, intracranial bleeding, severe dehydration, CHF.

f) Adverse Reactions/Side Effects

Isolated cases of adverse reactions, such as pulmonary congestion, fluid and electrolyte imbalance, acidosis, electrolyte loss, dryness of mouth, thirst, marked diuresis, urinary retention, edema, headache, blurred vision, convulsions, nausea, vomiting, rhinitis, arm pain, skin necrosis, thrombophlebitis, chills, dizziness, urticaria, dehydration, hypotension, tachycardia, fever and angina-like chest pains have been reported during or following IV mannitol infusion and are unlikely to occur at mesotherapeutic doses.

g) Management Guidelines for Overdose/Adverse Reactions/Side Effects

If an adverse reaction does occur, discontinue treatment, evaluate the patient, institute appropriate therapeutic countermeasures and save the remainder of the fluid for examination if deemed necessary.

8. Lidocaine (without epinephrine).

a) Mesotherapy Indication(s)

Used as an anesthetic in mesotherapeutic solutions.

b) FDA Approved Use/Drug Class

Ventricular arrhythmia, topical anesthesia, local anesthesia, regional anesthesia, infiltration anesthesia, spinal anesthesia

c) Clinical Pharmacology/Pharmacokinetics

The molecular formula for lidocaine HCl is $C_{14}H_{22}N_2O \cdot HCl$. Lidocaine stabilizes the neuronal membrane by inhibiting the

ionic fluxes required for the initiation and conduction of impulses thereby effecting local anesthetic action.

d) Contraindications/Warnings/Precautions/Drug interactions

Lidocaine is contraindicated in patients with a known history of hypersensitivity to local anesthetics of the amide type or to other components of any of the forms of this drug. Lidocaine should be used with caution in persons with known drug sensitivities. Patients allergic to para-aminobenzoic acid derivatives (procaine, tetracaine, benzocaine, etc.) have not shown cross sensitivity to lidocaine.

e) Adverse Reactions/Side Effects

Adverse experiences following the administration of lidocaine are, in general, dose-related and may result from high plasma levels caused by excessive dosage, rapid absorption of inadvertent intravascular injection, or may result from a hypersensitivity, idiosyncrasy or diminished to tolerance of the patient. Serious adverse experiences are generally systemic in nature and primarily affect the Central Nervous System and Cardiovascular System. Allergic reactions may occur as a result of sensitivity either to local anesthetic agents or to the methylparaben used as a preservative in the multiple-dose vials. Allergic reactions as a result of sensitivity to lidocaine are extremely rare and, if they occur, should be managed by conventional means. The detection of sensitivity by skin testing is of doubtful value.

f) Management Guidelines for Overdose/Adverse Reactions/Side Effects

The first consideration is prevention, best accomplished by careful and constant monitoring of the patient's state of consciousness during the treatment. At the first sign of change, oxygen should be administered. The first step in the management of convulsions consists of immediate attention to the maintenance of a patient airway and assisted or controlled ventilation with oxygen and delivery system capable of permitting immediate positive airway pressure by mask. If not treated immediately, both convulsions and cardiovascular depression can result in hypoxia, acidosis, bradycardia, arrhythmias and cardiac arrest. If cardiac arrest should occur, standard cardiopulmonary resuscitative measures should be instituted and immediate transport to the nearest ER.

9. Procaine (without epinephrine).

a) Mesotherapy Indication(s)

Local anesthetic, vasodilator

b) FDA Approved Use/Drug Class

Local anesthetic, local anesthetic for major infiltration and peripheral nerve block.

c) Clinical Pharmacology/Pharmacokinetics

Procaine HCl is a benzoic acid, 4-amino-, 2-(diethylamino) ethyl ester, monohydrochloride, the ester of diethylaminoethanol and para-aminobenzoic acid. Procaine, like other local anesthetics, block the generation and the conduction of nerve impulses, presumably by increasing the threshold for electrical excitation in the nerve, by slowing the propagation of the nerve impulse, and by reducing the rate of rise of the action potential. In general, the progression of anesthesia is related to the diameter, myelination, and conduction velocity of affected nerve fibers. Clinically, the order of loss of nerve function is as follows: pain, temperature, touch, proprioception, and skeletal muscle tone.

d) Contraindications/Warnings/Precautions/Drug interactions

Procaine HCl is contraindicated in patients with a known hypersensitivity to procaine, drugs of a similar chemical configuration, or a para-aminobenzoic acid or its derivatives. Systemic absorption of local anesthetics produces effects on the cardiovascular and the central nervous systems. At blood concentrations achieved during mesotherapy, changes in cardiac conduction, excitability, refractoriness, contractility, and peripheral vascular resistance are unlikely. Procaine contains acetone sodium bisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low.

e) Adverse Reactions/Side Effects

Same as for Lidocaine.

f) Management Guidelines for Overdose/Adverse Reactions/Side Effects

Same as for Lidocaine

1. Melilotus Officinalis:

Common names: Yellow Clover, King's Clover, Melilot, Sweet Lucerne, Wild Laburnum. Melilotus has been traditionally used to relieve the symptoms of chronic decreased venous return, including pain, heaviness, night cramps, itching, and swelling in the legs. It has also used in the treatment venous inflammation, blood clots, hemorrhoids, and congestion of the lymph system. Applied externally, it has been used to speed the healing of bruises.

In the eclectic botanical tradition, Melilotus has been used as a diuretic and homeopathic practitioners recommend it for hemorrhaging and headache. The flowering above-ground part of the plant contains flavones and trace amounts of

coumarin. Melilotus is believed to reduce inflammation and swelling by increasing venous return and its wound-healing properties have been confirmed in animal experiments. Melilotus is used in mesotherapy to promote venous return and lymphatic flow of lower extremities. Melilotus is available in injectable form in homeopathic preparations. There have been human case reports of drug interactions from Melilotus herbal extract (not the injectable, homeopathic form) with salicylates, acetaminophen and bromelain due to potentiating hemorrhagic diathesis. When used in consistently high doses (unachievable with mesotherapy) Melilotus can cause headache and stupor. Cases of transitory liver damage resulting from high doses of Melilotus have been reported; therefore caution should be exercised with those patients with documented or suspected liver disease.

2. Vitamin A

Vitamin A refers to the group of fat-soluble substances that are structurally related to and possess the biological activity of the parent substance of the group called all-*trans* retinol or retinol. Vitamin A plays vital roles in vision, epithelial differentiation, growth, reproduction, pattern formation during embryogenesis, bone development, hematopoiesis and brain development. It is also important for the maintenance of the proper functioning of the immune system. It is used in mesotherapy to assist in epithelial growth and keratinisation.

3. Vitamin C

Ascorbic acid is the major dietary form of vitamin C. The terms vitamin C, ascorbic acid and ascorbate are commonly used interchangeably. Many of the symptoms of scurvy, particularly those having to do with connective tissue, can be explained by the known biochemical roles of vitamin C, particularly its role as a cofactor for prolyl and lysyl hydroxylase, enzymes important in the formation of collagen. Collagen synthesized in the absence of ascorbic acid—as occurs in scurvy—cannot properly form fibers, resulting in blood-vessel fragility, among other defects. In the prolyl and lysyl hydroxylase reactions, as well as in most of the biochemical reactions ascorbic acid participates in, it acts as a reducing agent. In these reactions, the vitamin reduces ferric and cupric ions to their ferrous and cuprous states, forms which are required for the reactions to proceed. Ascorbic acid is also involved in the biosynthesis of other connective-tissue components, including elastin, fibronectin, proteoglycans, bone matrix and elastin-associated fibrillin. It also appears to play a role in collagen gene expression and cellular procollagen secretion.

4. Vitamin E

Vitamin E is the collective term for a family of chemical substances that are structurally and, in some cases, biologically related to the best known member of this family, alpha-tocopherol. Vitamin E is a fat-soluble vitamin and an essential nutrient for humans. However, in contrast with the other vitamins present in human nutrition, its exact biochemical role remains unknown. Vitamin E has antioxidant activity. It may also have anti-atherogenic, antithrombotic, anticoagulant, neuroprotective, antiproliferative, immunomodulatory, cell membrane-stabilizing and antiviral actions.

5. Thiamin (Vitamin B1)

Thiamin may have antioxidant, erythropoietic, cognition-and mood-modulatory, antiatherosclerotic and detoxification activities. It has putative ergogenic activity.

6. Pantothenic Acid (Vitamin B5)

Pantothenic acid (vitamin B5), is an essential nutrient in human nutrition. Pantothenic acid is involved in a number of biological reactions, including the production of energy, the catabolism of fatty acids and amino acids, the synthesis of fatty acids, phospholipids, sphingolipids, cholesterol and steroid hormones, and the synthesis of heme and the neurotransmitter acetylcholine.

7. Vitamin B6

Although Vitamin B₆ includes six different vitamers, the term vitamin B₆ is commonly used interchangeably with just one of the vitamers, pyridoxine. Vitamin B₆, principally in the form of the coenzyme pyridoxal 5'-phosphate, is involved in a wide range of biochemical reactions, including the metabolism of amino acids and glycogen, the synthesis of nucleic acids, hemoglobin, sphingomyelin and other sphingolipids, and the synthesis of the neurotransmitters serotonin, dopamine, norepinephrine and gamma-aminobutyric acid (GABA). Vitamin B₆ has demonstrable antineurotoxic activity as well as putative antiatherogenic, immunomodulatory, anticarcinogenic and mood-modulatory activities. High serum concentrations of theophylline has been known to cause seizures. It is thought that this is due to reaction of theophylline with pyridoxal 5'-phosphate, leading to lowered plasma levels of the vitamin. Pyridoxal 5'-phosphate is involved in the metabolism of gamma-aminobutyric acid (GABA). GABA is a major inhibitory neurotransmitter in the central nervous system. When cerebral concentration of GABA decreases below a threshold level, seizures and other neurological disorders, may occur. The concentration of GABA in the brain is controlled

by two pyridoxal 5'-phosphate-dependent enzymes, glutamate decarboxylase (GAD) and GABA transaminase (GABA-T). A decrease in the levels of GABA in the brain secondary to decreased levels of pyridoxal 5'-phosphate can lead to seizures. It has been found that the administration of vitamin B₆ to mice treated with theophylline reduced the number of seizures, and the vitamin administered to rabbits reversed electroencephalogram changes caused by high doses of theophylline. Therefore, although seizures are unlikely to be caused by mesotherapeutic doses of aminophylline and theophylline, those with preexisting seizure disorders may benefit, or at least take comfort from the addition of B6 to their mesotherapy solutions.

8. Vitamin B12

Vitamin B₁₂ is the most chemically complex and one of the most biologically interesting of all the vitamins. Because of the striking dark red color of its crystals, vitamin B₁₂ has been called "nature's most beautiful cofactor." Its close relatives hemoglobin, chlorophyll and the cytochromes are also brightly colored complex organometallic substances, which, along with vitamin B₁₂ and some others derived from the parent molecule called uroporphyrinogen III, have led to their being known as the pigments of life. Vitamin B₁₂ works in close partnership with folate in the synthesis of the building blocks for DNA and RNA synthesis as well as the synthesis of molecules important for the maintenance of the integrity of the genome. It is also essential for the maintenance of the integrity of the nervous system and for the synthesis of molecules which are involved in fatty acid biosynthesis and the production of energy.

9. Copper

Copper is an essential trace mineral in animal and human nutrition. Copper may have antioxidant activity. There is some experimental indication that supplemental copper may have some anticancer effects and may be of benefit in some with arthritis. Claims that it is protective against cardiovascular disease apply primarily to those with copper deficiency.

10. Selenium

Selenium is an essential trace element involved in the defense against the toxicity of reactive oxygen species, in the regulation of thyroid hormone metabolism and the regulation of the redox state of cells. Selenium may also have immunomodulatory, anticarcinogenic and anti-atherogenic activities. It may have activity in detoxification of some metals and other xenobiotics and activity in fertility enhancement in males.

11. Zinc

Zinc is an essential element with a wide range of biological roles such as catalytic, structural or regulatory roles in the more than 200 zinc metalloenzymes that have been identified in biological systems. These enzymes are involved in nucleic acid and protein metabolism and the production of energy, among other things. Zinc plays a structural role in the formation of the so-called zinc fingers. Zinc fingers are exploited by transcription factors for interacting with DNA and regulating the activity of genes. Another structural role of zinc is in the maintenance of the integrity of biological membranes resulting in their protection against oxidative injury, among other things. Zinc may have immunomodulatory activity as well as antioxidant activity. Zinc has putative antiviral, fertility-enhancing and retinoprotective activities.

Bibliography:

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