

Practical Aspects of Parenteral Orthomolecular Therapy

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The first line of treatment in orthomolecular therapy is manipulation of the diet, oral supplementation of deficient nutritional factors, and the use of vitamins for their pharmacological effect. Parenteral therapy is sometimes used to bypass GI absorption or to hasten therapeutic response.

Parenteral administration of indicated nutrients can have a dramatic effect when the same substances given orally have failed to produce a response.

All injectable vitamins and minerals have an additional advantage for allergic and hypersensitive patients in that they are synthetic and do not come mixed with food related excipients. This does not eliminate, but certainly decreases the incidence of adverse reactions.

In the past five years I have given thousands of injections, and will report here my personal experience. The purpose of this paper is to familiarize a physician new to this therapy with its practical aspects.

Technique

General reactions to injections such as apprehension towards needles and pain are not uncommon; sometimes they are very marked. The adverse reactions after an injection can be

psychosomatic and not physiological. The apprehensive patient must be handled gently and anxiety alleviated. Sometimes the supine position is chosen to prevent falls due to vasovagal response. Otherwise, the sitting position is adequate.

For intravenous injection by syringe, I find the G25 needle best, but for many patients G21-23 are also acceptable. A smaller needle is less traumatic. For a gravity drip G21 is best as G25 is often too small and takes too long a time to run through.

Smaller volumes of up to 10 ml can be given with a needle attached to the syringe. For volumes upwards of 5 or 10 ml a butterfly needle with short plastic tubing is most comfortable.

Finding a suitable vein requires a degree of skill which some of us may have to learn. I have yet to find a person who under normal circumstances has no available veins in the arm and I have seen some dreadful cases. Two most important rules are: insert the needle into a steady vein with a reasonably shallow angle and then pass the needle in the direction of the venous lumen. Make sure that your venipuncture is not the last one

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possible at that site. When the needle does not stay in its proper place, punctures the vein through both sides, if the tip remains in the vein wall or if the solution goes interstitial withdraw the needle and apply firm pressure with a thumb for at least 1 full minute. Next go on to locate another site. Applying a tourniquet proximally on the same arm as an unsuccessful venipuncture can cause an interstitial hemorrhage of that puncture. It is best to proceed to the other arm or locate a more distal site. Correctly performed venipuncture will not bruise and the vein will be available again and again without being obliterated.

Intramuscular injections of one to two ml can be given in the deltoid muscle. For larger volumes of up to 5 ml per injection the site to choose is the upper outer quadrant of the gluteal region. The needle should be inserted in one continuous motion, quite fast and forcefully like a dart. Very little discomfort will be felt. Injecting the fluid too fast, especially with large volumes will suddenly stretch the muscle and cause more pain. Too slow insertion of the needle and slow injection will unnecessarily prolong this minor trauma. Verbal distraction works best; it is the art of medicine. Nurses are sometimes said to give better needles than doctors. They often have more experience. Talk to patients who get frequent injections and find out from them which nurse gives needles best. Learn from her and your technique will be appreciated for years to come.

For intramuscular injection, I use G25 but a long needle will sometimes bend on tough skin. Viscose solutions will require a larger bore needle. Too short a needle will only result in a deep subcutaneous administration. Therefore a 2.5 cm length will be the average requirement. It is my experience that changing to a new needle after filling the syringe will decrease discomfort (however I seldom do it).

I also make a point of using a bandage to cover the injection site. Even a small amount of blood can stain and damage clothes.

The following general problems are associated with parenteral administration regardless of whether the substances are vitamins or other medications: phlebitis, thrombosis, abscess, bacterial or fungal contamination, particulate

matter contamination, chemical contamination, incompatibility and product degradation (Dukes, 1980). In addition any substance can potentially cause an adverse or an allergic reaction either alone or in combination. Using standard medical techniques and common sense will minimize many potential problems.

Adverse effects of prolonged parenteral therapy are largely unknown; however, all attempts are made to use oral preparations as soon as possible.

MATERIALS

The following section lists the most commonly used injectables.

Vitamin C is supplied as a colorless or faintly yellow solution. The change of color to a darker yellow is caused by transformation to the oxidized form of vitamin C which it is not desirable to administer. Ascorbic acid is always buffered to neutral pH commonly as sodium ascorbate. The usual available concentrations are 250 mg/ml and 500 mg/ml. The higher concentration of these two is irritating to the vein, usually at the site of injection but also proximally or distally. Slowing down the speed of the injections, slow finger movement or raising the arm will decrease the concentration in the venous blood outflow. Dilution is most helpful and many physicians actually prefer a slow vitamin C drip over a push. For amounts larger than several ml, preservative free vitamin C should be used. The unused portion left over in those vials is however subject to oxidization and microbial growth.

Vitamin C stored in vials at room temperature has a tendency to build up pressure and during filling the syringe can cause a messy spray. I prefer to release the pressure by inserting an unattached needle.

Intramuscular injection is painful and no significant amounts can be injected this way.

I have seen occasional cases of nausea after an i.v. injection, and a colleague has described a case of hypocalcemic tetany precipitated by hyperventilation.

The usual single dose of vitamin C is 0.5 to 50 grams i.v. With doses higher than 5 g I usually add 5 -10 ml of 10% calcium.

Thiamine Hydrochloride is a colorless liquid that turns yellow with time. Most

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commonly it comes in a multiple dose vial of 100 mg/ml. The intramuscular injection is quite painful, the intravenous is painless. Because of its very distinct taste most patients will experience a strong taste sensation shortly after i.v. use and often after i.m. use as well. The usual single dose of vitamin B1 is 10 mg to 500 mg, preferably with other B vitamins. It mixes well with most injectables and often comes in B complex mixtures.

This is one vitamin where a word of caution is necessary. As much as we like to think that vitamins are harmless, vitamin B1 for parenteral use may be an exception. It has been reported on rare occasions that injected thiamine can cause a true allergic anaphylactic reaction possibly resulting in death if untreated in the customary fashion. Such reports referred to repeated or fast administration of more than 50 mg of thiamine by itself, never as B complex. Throughout my numerous contacts with colleagues, I have not heard of any such episode.

The factors involved in such a reaction are unclear but may conceivably include impurities from the manufacturing process or deterioration by age and exposure to light. Some physicians inject a small subcutaneous test dose and wait for a reaction within 10 minutes. The validity of this test is unproven.

Until the real explanation is clear make sure to have some adrenalin on hand just in case.

Riboflavin has a very deep yellow colour and being water soluble, will appear in the urine soon after administration. The injectables contain riboflavin phosphate which is one metabolic step more available biologically than the nitrate. I usually give up to 50mg at one time, either i.m. or as B complex i.m. or i.v. Concentrated solutions by i.m. injection are painful.

Niacin is a colorless solution 100 mg/ml and is seldom supplied in combination with other injectables.

The moderate irritation of the i.m. injection is soon superseded by a marked niacin flush well known to any physicians and patients who have ever used this substance. As opposed to calcium this flush is superficial, limited to skin and more pronounced in the face and the upper torso. The

flush will stay for an average of 30 minutes regardless of the route and speed of administration.

I have given niacin slowly by i.v. and have found the flush to be greater than by i.m. or oral route. The onset is of course almost immediate. I prefer to give niacin to patients in a reclining position because of frequent dizziness and possible hypotension and have them wait for awhile after the injection. The niacin flush must be explained to every patient beforehand. The usual single dose of niacin is 50 to 500 mg.

Niacinamide is available in a colorless solution 100 mg/ml but most often in combination with other B's in multiple dose vials.

I.M. injections are somewhat painful. I.V. niacinamide may give a very mild flushing effect. It may cause some degree of nausea and most patients will taste it.

Excessive and prolonged administration of vitamin B3 will increase the need for vitamin B6.

The usual single dose of niacinamide is 10 to 1000 mg.

Panthenol is a clear liquid most often supplied in an injectable form of pantothenic acid in a multiple dose vial with a preservative. I have given it i.v. as part of a B complex in amounts up to 50 mg. Greater amounts require an i.v. drip. Such higher doses of panthenol can prolong the bleeding time. Intramuscular injection of a 250 mg/ml strength by itself is only moderately uncomfortable.

It is of interest that pantothenate is officially approved in Canada for post surgical intestinal atony. This information is, however, unknown to most surgeons and is therefore never used or taught in medical schools. The usual single dose of panthenol is 5 to 500 mg.

Pyridoxine Hydrochloride is a colorless liquid often in 100 mg/ml concentration by itself or less concentrated in B complex preparations. It is very irritating by i.m. route and if given this way to a child you will be remembered for a long time. For this reason I prefer the i.v. route which is painless. The usual dose is 10 -100 mg, but I have given up to 1000 mg at one time. I have given it to children one year old and upwards. B6 administered to a body in a state of magnesium deficiency will cause CNS irritation

which can be extreme. Treatment of choice is magnesium by any acceptable route. Prolonged B6 therapy can cause B2 responsive neuropathy. B6 mixes well and can be obtained preservative free in 1 ml ampules.

Vitamin B12 is the injectable I use most often. It is well known that B12 can have major positive effects on the patient's sense of well being despite normal serum B12 levels and seemingly normal dietary intake. The solution is deep pink and the pink color can appear in the urine after an injection, frightening the uninformed patient. B12 is supplied as very inexpensive cyanocobalamin 100 mcg/ml, 1000 mcg/ml, 5000 mcg/ml or hydroxocobalamin 1000 mcg/ml. The multiple dose vials contain preservative; preservative free ampules are difficult to come by.

B12 can be mixed with virtually anything. Vitamin B12 is most effective when administered as the co-enzyme methylcobalamin. In one country (Spain) it is the only form available. The next best form is called hydroxocobalamin even though it is normally supplied in a slightly acidic solution in which it exists in its paler aquocobalamin form. The cyanocobalamin is traditionally used most frequently because of its stability but it is biologically inferior (Reynolds, 1982).

Folic Acid is a yellow liquid available in 5 mg/ml concentration and must be protected from the light. I usually give 1 ml i.v., or s.c. by a push and have not noticed any adverse effects or pain. Folic acid solution is very alkaline and will precipitate when mixed with almost anything. It is therefore best given by itself.

Folic acid administration should not, of course, be a substitute treatment for B12 deficiency. This obvious orthomolecular fact has been overstated by those ignorant of vitamin therapies. The usual single dose of folic acid is 5 to 20 mg.

Biotin is available in a combination with B complex and vitamin C as Berocca-C by Hoffman La Roche. In some cases this i.v. injection produces a marked but temporary facial flush not unlike niacin.

B Complex comes in many varieties, just like tossed salads. It may also contain liver extract, local anesthetics, other vitamins, minerals, amino acids and preservatives. In the office I

sometimes mix B complex with another single vitamin which is needed in a higher amount than is found in the mixture. A taste sensation is often experienced after administration. For precautions, see descriptions of individual components.

Liver Extract is a dark brown liquid manufactured in different ways to preserve liver water soluble factors. It was used in the past before B12 was specifically isolated and manufactured. Since then it has been stated that the pure B12 is a superior product. This is indeed so for the B12 therapy. However, the liver extract may contain unspecified substances that have their own functions. Amounts of these substances will vary with the manufacturing process used and the source of the liver material. No standardization exists.

I use 1-3 ml of liver extract i.m often with B12, B complex or local anesthetic. I have never used it i.v. The injection is quite irritating.

Precaution must be taken with patients allergic to beef or possibly pork, whichever is the source of the material. I have not, however, come across an immediate allergic reaction, despite treating many allergic patients. It is known that ingested muscle meat has different allergic properties from organ meat such as liver.

Calcium is supplied usually as 10% calcium gluconate or 10% glucono-galacto-gluconate (Sandoz) or calcium glycerophosphate; all colorless solutions. The ampules are often preservative free; multiple dose vials have some preservative.

Calcium is given best intravenously 3-20 ml or more, slowly at approximately 1-4 ml per minute. The patient is explicitly warned beforehand that an internal heat sensation will be experienced starting in the throat and face and spreading along the spine down to the genital area and bladder. A sensation of voiding can occur. The patient reports to me the intensity of heat sensation and I regulate the speed of injection accordingly, avoiding unnecessary discomfort. I do not know what causes this heat sensation and why a few patients do not experience it. Occasional adverse effects include heart pounding, abdominal cramps and nausea. I have given calcium intravenously to patients from the age of six years onwards. Special consideration must be given to those who are on

cardiac medications (Digitalis, etc.). Mixing calcium and vitamin C can cause undesirable precipitation in the syringe, especially if the solutions have been refrigerated.

Results from i.v. calcium alone are sometimes very satisfying and I always prefer the i.v. use to any other parenteral route. The initial physiological effect of injected calcium, which is in ionized form, is quite different from the effect of calcium administered orally.

Effective therapy with calcium and magnesium has often been carried out despite normal serum levels.

Iron carbohydrate complexes are readily available for i.m. administration. A 4-5 cm long needle is recommended for an average size adult. After filling the syringe, use a new needle to avoid tracking the dark brown solution through the tissues. A deep i.m. injection in the upper buttock using a z-track technique (sliding the skin laterally over the muscle prior to injection) will help to avoid staining of the skin. Several other important points regarding iron administration are adequately covered in standard pharmaceutical manuals.

Magnesium is supplied usually as 50% sulfate or chloride. The colorless solution can easily crystallize because of its high concentration. It is meant primarily for intramuscular injection which is mildly to moderately painful. The pain can last for hours. Intravenous injection is easy and similar to calcium but must be very slow, not exceeding 2 ml/min of 10% solution or its equivalent. Magnesium should therefore be diluted to better control the speed with which it is injected. The heat sensation can be very pronounced.

I do not know the reason for the heat sensation which is frequently more peripheral than that of calcium i.v. The heat sensation will diminish within 1 or 2 minutes probably depending on the efficiency of the circulation system. Too fast an injection can cause nausea, lightheadedness, even a temporary loss of consciousness. Should any of this inadvertently happen, a patient should be reassured that this sensation is only temporary. Treatment of magnesium overdose is i.v. calcium.

When a small volume of concentrated solution is injected, it can remain for some

time in the distal veins. After the needle is withdrawn and the arm moves around or is lifted the whole volume can surge into the circulation causing all the symptoms which we wanted to avoid in the first place. The redness of the patient can be observed and the heat can be felt even in extremities. The i.m. injection has none of these effects, but can cause local muscular edema lasting more than 24 hours.

I usually give 0.5 to 3 ml, by i.v. push, more can be given i.m. or by i.v. drip. My usual combination is with B6, calcium, vitamin C. When mixed with other solutions precipitation can occur depending on the chemistry of other substances, pH, etc.

To conclude, I would like to encourage physicians to start using injection therapy. The technique needs practice. An easy and safe way to start is with B12 1 ml i.m. and B complex 1 ml i.m.

The next step could be calcium 10% 5 ml i.v.

Case Histories.

A 58 year old female had suffered from lower leg cramps refractory to oral mineral supplements in adequate doses along with average vitamin A, D and B complex supplements. Intravenous injection of 2 ml of magnesium sulfate 50% diluted to 10 ml gives her relief the same day and persists for weeks to a month.

A 42 year old female has immediate relief from recurrent symptoms of anxiety, insomnia and fatigue with intravenous injection of 7 ml calcium 10%, 1 ml pyridoxine and 2 ml magnesium sulfate 50% by slow push. The effect will last from one to several weeks. High oral doses of the same substances taken regularly had no noticeable beneficial effect. I have alternately omitted each one of the three items from the injection, and did not produce the same therapeutic response.

I would like to thank Dr. R. Greenberg for valuable help with the manuscript.

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Advice to Captains

A letter written by John Smith in 1626.

Young gentlemen that desires command ought well to consider the condition of his ship, victual and company; for if there be more learners than sailors, how slightly soever many esteem sailors, all the work to save ship, goods and lives must lie upon them, especially in foul weather; the labour, hazard, wet and cold is so incredible I cannot express it. It is not then the number of them that here will say at home, what I cannot do I can quickly learn, and what a great matter it is to sail a ship or go to sea. Surely those for a good time will do most trouble than good. I confess it is more necessary such should go, but not too many in one ship; for if the labour of sixty should lie upon thirty, as many times it doth, they are so overcharged with labour, bruises and overstraining themselves (for there is no dallying nor excuses with storms, gusts, overgrown seas and lee shores), they fall sick of one disease or other, and then if their victuals be putrified, it endangers all.

Men of all other professions, in lightning, thunder, storms and tempests, with rain and snow, may shelter themselves in dry houses, by good fires and good cheer; but those are the chief times that seamen must stand to their tacklings, and attend with all diligence their greatest labour upon the decks. Many suppose anything is good enough to serve men at sea and yet nothing sufficient for them ashore, either for their healths, for their ease, or estates, or state. A commander at sea should do well to think the contrary, and provide for himself and company in like manner: also seriously to consider what will be his charge to furnish himself at sea with bedding, linen, arms and apparel; how to keep his table aboard, his expenses on shore, and his petty tally, which is a competent proportion according to your number, of these particulars following. Fine

wheat-flour, close and well packed, rice, currants, sugar, prunes, cinnamon, ginger, pepper, cloves, green-ginger, oil, butter, old cheese, or holland, wine vinegar, canary sack, aqua-vitae, the best wines, the best waters, the **juice of lemons for the scurvy**, white biscuit, oatmeal, gammons of bacon, dried neats' tongues, roasted beef packed up in vinegar, legs of mutton minced and stewed, and close packed up with butter in earthen pots. To entertain strangers, marmalade, suckets, almonds, comfits and such-like.

Some it may be will say I would have men rather to feast than fight. But I say the want of those necessaries occasions the loss of more men than in any English fleet hath been slain in any fight since 1588: for when a man is ill, sick, or at the point of death, I would know whether a dish of buttered rice, with a little cinnamon and sugar, a little minced meat, or roast beef, a few stewed prunes, a race of green-ginger, a flap-jack, a can of fresh brewed water with a little cinnamon, ginger and sugar, be not better than a little poor John, or salt fish with oil and mustard, or biscuit, butter, cheese or oatmeal pottage on fish days, salt beef, pork and pease, and six shillings' beer. This is your ordinary ship's allowance and good for them are well, if well conditioned, which is not always, as seamen can too well witness; and after a storm, when poor men are all wet and some not so much a cloth to shift him, shaking with cold, few of those but will tell you a little sack or aqua-vitae is much better to keep them in health than a little small beer or cold water, although it be sweet.

From *A Book of England*, Ivor Brown (Ed.) Collins, London, 1958.

Book Review

Why Your House May Endanger Your Health

**Alfred V. Zamm, Robert Gannon
Simon and Schuster, New York**

This book alerts us to the dangers in the home and tells how they can be avoided or controlled. It describes some of the health problems that can result from harmful substances in water, paint, wallpaper, floor wax, gas, kerosene, house dust and other materials as well as chemical and electrical processes that make up the environment of the modern home.

The book deals with toxins, subtoxins and allergens found in the home and stresses their important effect on the health and wellbeing of the residents. It emphasizes the dangers of allergies and reactions to various substances in the home environment. It cites English physician Dr. Richard Mackarness' claim that allergy has overtaken infection to become "the number one cause of illness in Westernized society". It also cites research by Dr. Michael Alvanja who studied 1595 women who died from urinary-tract or gastrointestinal cancer in seven New York

counties. "When he compared the water in the homes of those women, he made an alarming discovery: Those who drank chlorinated water ran a 44 percent higher chance of dying from the cancers than those who drank untreated water."

The authors provide valuable information about clothing and furnishings in the home and a section on maintaining the healthy house. They describe in non-technical terms the procedures to be followed in designing and building the healthy house. There is a checklist to identify health hazards in the home, construction drawings, manufacturers' list, informative notes and a handy index.

The book is important in that it provides information about dangers to health and ways of detecting and controlling them and helps individuals to take responsibility for their own health and safety. It emphasizes public awareness, knowledge and responsibility in health matters and stresses the need for prevention of disease rather than complete reliance on the crisis type of medical services.

I.J. Kahan