

Letters

Tissue Hypoxia and Xenobiotic Toxicity in Chronic Fatigue Syndrome

Recently this journal has published two interesting articles by Dr. Robert Buist on Chronic Fatigue Syndrome.¹² I would like to comment on each of the two hypotheses proposed (that the fatigue and aches of CFS are due to local tissue hypoxia, and that the RBC deformation responsible is due to xenobiotic toxicity) and speculate on therapeutic implications of the former.

First, there is related work describing reduced muscle tissue oxygen pressure in primary fibromyalgia by the Swedish researcher Ann Bengtsson et al.³ Since many of the symptoms of CFS mirror those of fibromyalgia, it seems noteworthy that the surface oxygen pressure of tender points in the trapezius and brachioradialis muscles of 10 fibromyalgia patients (measured by a multipoint electrode whose design obviates measurement error due to tissue trauma, pressure ischemia and variable distance from the capillary bed) differed significantly in both the distribution of readings from the electrode's multiple measuring points and the total mean oxygen pressure from 8 healthy volunteers. Although the mean age of controls is 36 vs 43 for cases and no data on smoking habits are given, these data support Dr. Buist's hypothesis that tissue hypoxia is the responsible intermediary in the myalgias and fatigue experienced by patients with CFS (and by extension, fibromyalgia).

Whether chemical exposure is the primary insult remains to be seen. I propose as an alternative hypothesis that loss of red blood cell membrane fluidity is related to widespread deficiency of alpha-linolenic acid. This would make CFS and fibromyalgia part of the "Modernization Disease Syndrome" described by Dr. Rudin in these pages and elsewhere^{4 5 6 7} and help explain the relationship between elevated lactate levels and anxiety neurosis (also an aspect of the MDS) previously described by Dr. Buist himself!⁸ I note as an aside that the mean lactate/pyruvate ratio of the

six patients in the 1989 paper² is reduced at 5.895 (converting pyruvate to mmol/l) vs 15.74 for the means of the normal ranges given (0.85/0.054) or even the extreme of $0.55/0.067 = 8.21$. Who knows what this means?

In any case, either hypothesis would help explain the well-documented clinical efficacy of potassium and magnesium aspartates, first proposed by Dr. H. Laborit in 1959 as a physiologic cure for fatigue, postulating that oxygen requirements at the cellular level were reduced by supplementation of this Krebs cycle intermediate.⁹ A total of about 3000 subjects have been studied over the years in both controlled and uncontrolled studies,^{10 11 12 13 14} giving a positive response (relief, often lasting, of both primary and post-viral fatigue) to daily doses of 1 gm of each salt in almost 90% of cases vs at most 25% of controls. While the Wyeth preparation "Spartase" is no longer available, Thorne Research (800-228-1966 in the US) makes a combination capsule containing 99 mg and 70 mg of the potassium and magnesium salts, respectively, of aspartic acid. The review by Gaby is most current.¹¹

Finally (at the risk of getting carried away), local tissue hypoxia as an etiology for CFS would suggest a possible therapeutic role for substances such as Ginkgo biloba, the extract of which has been shown to improve blood flow in the cerebral¹⁵ and peripheral¹⁶ circulations, scavenge free radicals, and inhibit platelet aggregation.^{17 18} A therapeutic trial of GBE in CFS would be most interesting.

Thus the "primary" fatigue and myalgia of CFS and fibromyalgia may be related by the common intermediary of decreased tissue oxygen pressure (perhaps especially at tender points), and the primary insult may indeed be chemical exposure, but the role of omega-3 fatty acid deficiency needs to be more fully defined. Therapeutically, both primary and secondary (post-viral) fatigue appear to respond quite well to a combination of the potassium and magnesium salts of aspartic acid, perhaps

because of an oxygen sparing effect on cellular metabolism, and the extract of Ginkgo biloba possesses properties which suggest it as a possible remedy for local tissue hypoxia due to capillary "sludging" and the effects thereof.

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Dr. Reading Under Fire in Australia

The following is a letter to Dr. Chris Reading, Australia, in response to his having received an ultimatum from the Royal Australian and New Zealand College of Psychiatrists (RANZCP) to cease using Orthomolecular methods.

Apparently, the Royal Australian and New Zealand College of Psychiatrists' main criticism is that, in their view, there is no scientific substantiation of the therapeutic efficacy of Orthomolecular psychiatry in the treatment of psychiatric disorders.

By doing so they are penalizing physicians and psychiatrists who have declared themselves to be Orthomolecular practitioners. The reason I make this statement is that the vast majority of physicians do use elements of Orthomolecular therapy without being aware of what they are doing.

In my opinion, there are two groups of physicians who practice Orthomolecular therapy: 1. a small group who knowingly use optimum amounts of vitamins — which may be large or small, in the same way physicians use optimum amounts of other drugs, including antibiotics; 2. the rest of the medical practitioners who practice some form of Orthomolecular therapy without knowing they are doing so.

Is, therefore, a member of the first group to be punished merely because this physician knows what he or she is doing?

The briefest definition of Orthomolecular therapy is that the physician uses optimum dosages of nutrients in order to achieve a recovery when this is possible.

These dosages usually are somewhat larger, or perhaps much larger, than the RDA doses recommended by many governments. I therefore list the following nutrients which are used in much larger quantities than RDAs — which properly are classed as Orthomolecular, and are used by most physicians. The Australian College ought to take into account these facts, because if they are going to discriminate against you on the basis of you calling yourself 'Orthomolecular', they will have to individually discriminate against every member of the profession in Australia and New Zealand. Here are some examples:

1. **Thiamine** — Used in quantities of 100 to 500 mg per day, especially for the complications of alcoholism, particularly Wernicke-Korsakoff's syndrome.
2. **Niacin, or Vitamin B₃** — Used in dosages of 3 to 9 grams per day to lower cholesterol levels and to elevate high-density lipoproteins. This is now a well-established finding used worldwide, and I would assume that most physicians who are up to date on their lipid metabolism have used, or are using, or certainly will be using within the next year or two, this particular vitamin used in very large dosages — certainly much larger than the RDAs. A second condition for which the establishment accepts the use of Vitamin B₃ is Hartnup disease, which requires up to 250 mg per day.
3. **Folic acid** — Has been used in dosages of 5 mg twice a day for the prevention of cancer of the lung and cervix. This is an establishment finding coming out of the United States.
4. **Pyridoxine** — Has been used for PMS up to 1000 mg per day, and a standard recommendation for homocystinuria is that up to 500 mg per day of B₆ should be used.
5. **Vitamin Bi₂** — This, of course, has been used for many decades in Orthomolecular dosages. The average RDA is 1 microgram per day, yet one injects 1000 times as much, that is 1 milligram, for the treatment of pernicious anemia, although the injection does not have to be given every day.
6. **Vitamin A** — This has been recommended in up to 100,000 IU injections for the prevention of xerophthalmia.
7. **Vitamin E** — Now recognized as one of the important treatments for tardive dyskinesia, using anywhere from 800 to 1600 IU per day. It is classified amongst the very important antioxidants.
8. **Ascorbic acid** — Does not have many official indications but there is one disorder for which it is recommended one use 300 to 500 mg per day — methemoglobinuria. A second application recently published in the medical literature is for ITP, that is idiopathic thrombocytopenic purpura, using anywhere between 1 to 2 grams per day.
9. **Tyrosine** — Is being used for the treatment of depression by the establishment, using 1 to 3 grams per day.
10. **Tryptophan** — Is being used now from 1 to 6 grams per day for conditions varying from depression and insomnia to manic-depressive psychosis.

I think this is a very impressive list of nutrients which are being used in large amounts, and I doubt there is any physician who has not used one or more of these modalities. They are therefore practising various aspects of Orthomolecular therapy.

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