Editorial

The Paradigm War Continues

The vitamin paradigm war continues to rage on even though it is clear that the new paradigm, the vitamin-as-treatment paradigm, has a firm grasp on modern medicine and will not be displaced. But there are still brush fires that have to be stamped out. A recent example is the victory of the Society for the Promotion of Nutritional Therapy (SPNT), in England with respect to vitamin B6. The skirmish began when the British Government proposed that Pyridoxine tablets should contain no more than 10 mg.

In 1997, Linda Lazarides[1] sent the following message from England.

"The officials have announced that their decision was based on the following rationale: (1) That a survey carried out more than 10 years ago by a Dr. Dalton who attributed symptoms experienced by PMS patients in her private practice to the vitamin B_6 supplements they told her they were taking, claims to have found B6 toxicity at doses as low as 50 mg per day. Virtually ignored for ten years by the scientific community, this study's methods did not follow rigorous scientific procedures and its claims have been refuted by dozens of other studies in which vitamin B6 produced no side effects at doses of 2,000 mg a day or more. (2) The toxic dose of vitamin B6 in dogs is known to be equivalent to a massive 3,000 mg per day. The government's advisers known as the Committee on Toxicity (COT) say this should be divided by a factor of 300 to arrive at a safe dose for humans of 10 mg. But leading science policy experts consider a factor of 300 to be arbitrary, not based on normal scientific practice. Why did the COT think it necessary to deviate from normal scientific practice just for vitamin supplements? Products containing up to 200 mg of vitamin B_6 have been on the UK market for decades with no reports of side effects. Even the Food Ministry's own recently completed 5-year study on the safety of dietary supplements could not turn up any adverse reactions to these products. They are sold under food law, which keeps the price down and affords the best consumer protection. Medicines do not have to be safe - only to prove that their risks do not outweigh their benefits. But foods can be taken off the market if they are found to be unfit for human consumption. Pharmaceutical licenses are primarily intended for pharmaceutical products, which is why they can cost 80,000 to several million UK pounds to obtain. The cost comes from the massive amount of data which a manufacturer must produce in order to prove that his product is a medicine. Ultimately it is the consumer who must pay the premium, in this case receiving little benefit from the added expense since vitamins are not drugs. The position of independent expert scientists is that vitamin B6 is completely safe at up to 200 mg per day, allowing for a considerable safety margin. Signs of toxicity may begin to show in a small proportion of people after taking 500 mg per day for months or years. You could help us to save our B6 by writing to our Food Minister to vouch for the safety of these products."

June 25, 1998, Lazarides outlined the report of the House of Commons Agriculture Committee.[2]

"The Agriculture Committee received written evidence from a large number of individuals and organizations, most of them questioning the scientific basis of COT's advice and, in particular, the validity of a 1987 study by Dalton and Dalton used by COT in reaching its conclusions on the toxicity of vitamin B6

The Committee's main recommendations are that: (1) in relation to dietary supplements, the Government should withdraw its proposed draft regulations to limit the level of vitamin B6 per daily dose to 10 mg.

(2) the Government should seek to introduce a voluntary limit, pending the report of the Expert Group on Vitamins and Minerals, with the industry, of 100 mg per daily dose. All dietary supplements containing vitamin B6 should display a clear warnin

that intakes above this level may carry health risks, particularly when taken over an extended period. No legislation should be considered until the Expert Group has reported. The Committees other conclusions and recommendations are as follows:

(1) We would urge that the Expert Group on Vitamins and Minerals be asked to produce recommendations for a framework for deciding whether regulation of dietary supplements is necessary at all, or whether consumer advice is sufficient.

(2) It is our view that the doubts concerning the 1987 Dalton and Dalton study are so serious that it is scientifically unjustifiable to use it as the basis for establishing a lowest observed adverse effect level in relation to vitamin B6 intake.

(3) We trust that the unfortunate row which has taken place over vitamin B6 will act as a constant reminder to [the Expert Group on Vitamins and Minerals] of the need to base its recommendations and advice on sound and substantiated scientific knowledge, and adherence to a clear definition of the role and limits of Government intervention in this area as it recommends and Parliament agrees.

(4) We recommend that, to assist in avoiding any repeat of the vitamin B6 controversy, consumer and industry interests should be able to nominate one or two independent scientific experts in nutrition and toxicology for appointment as full members of the Expert Group on Vitamins and Minerals."

Here is an excellent example of one of the major skirmishes. The vitamins-as-prevention paradigm was established slowly over a period of several decades by medical research scientists who led the field in vitamin research, against the opposition of the medical establishment. One of the leaders, Dr. Goldberg, had to inject himself and a few friends with barnyard material in order to finally prove that pellagra was not caused by an infection. But this paradigm, which proved so useful in isolating and characterizing vitamins outlived its usefulness when it became a creed promulgated by leaden of the medical establishment and the governments of United States and Canada and elsewhere. It is based upon two basic beliefs (1) that vitamins are needed only for the prevention of a few classical deficiency disease such as beri beri or scurvy; (2) that only very small, hereafter called vitamin doses, are needed. It follows that any one giving people larger doses for diseases not caused by vitamin deficiency was breaking the law. This is literally true and physicians lost their licenses by following these new ideas. This paradigm prevented treating with vitamins anything other than vitamin deficiency disease. It also prevented the proper examination of the use of vitamins in larger doses for medical conditions not believed to be deficiency disease. This had to wait until the new paradigm developed, the vitamins-as-treatment paradigm.

Paradigms in science are rather evanescent and they crumble under the weight of new evidence which it can not contain. Thus over fifty years ago several physicians found that large doses of a few vitamins were therapeutic for a number of non deficiency diseases. These included Drs. Wilfred and Evan Shute, who found vitamin E enormously useful for treating and preventing heart disease; Dr. William Kaufman, who found vitamin B3 very helpful in treating arthritis and diseases of aging, and Dr. Frederick Klenner, who found that vitamin C in enormous doses was helpful in dealing with a large number of diseases including poisonings, infections and neurological diseases. These findings were ignored and had little effect in the paradigm war.

The Saskatchewan work which showed that niacin lowered cholesterol levels was different since it is easy to measure cholesterol blood levels and also to confirm our earlier work where we showed with double blind clinical trials that vitamin B3 helped schizophrenic patients. This too was equally ignored. The cholesterol report in 1955 is

credited with being the beginning of the new paradigm. Since then it has been confirmed over and over and it is becoming common to read in medical journals, that formerly would never have published any positive articles about vitamins, now extolling their use for a large number of diseases.

But there are a few die hard resistant adherents to the old paradigm and at every opportunity they will promulgate new toxicities (invent them if necessary) and write rapturously about the dangers of vitamins. This battle in England on the surface was totally unnecessary. There have been no deaths from vitamin B_6. A few papers reported toxic reactions especially with grams doses. But these reports did not contain enough evidence to judge what really had happened. For example did the addition of Pyridoxine produce enough improvement so that patients became aware of other symptoms which had been given less attention but which now became more prominent. And in every case the subjects recovered. I have never seen a toxic reaction[3,4,5] but then my patients never take only this vitamin. They are also on other vitamins. If the English parliament decreed that only 10 mg tablets be made available it would have been a precedent that every opponent of the new paradigm would have used to try and persuade their governments to do the same. I wish they were as assiduous in banning antihistamines and aspirin, both very useful but much more toxic than vitamins. With over 122,000 patients each year dying in hospitals from the proper use of drugs in United States and Canada, I would expect that much more attention would be given to the toxic reactions of modern drugs. There have been no deaths from vitamins.

A more recent example of ongoing skirmishes was the controversy initiated by a letter to the editor of *Nature*-a journal published in England — on April 9th, 1998, The writers claimed they had evidence that vitamin C in doses greater than 500 milligrams daily increased DNA breaks, thus suggesting that in these larger than vitamin doses this vitamin was potentially carcinogenic. The report in the *New York Times* inflamed world reaction and in every country similar headlines and stories appeared. This is the second time similar reports were featured in the *New York Times.* Over 20 years ago it reported in a similar vein on a study issued by two Vancouver scientists. Irwin Stone and I rebutted this conclusion.[6]

The Vancouver team oxidized ascorbic acid with copper to the oxidized form which is toxic and then added that to cell cultures and reported genetic damage. They extrapolated from this in vitro study of oxidized vitamin C to the human and concluded vitamin C could cause genetic damage. Therefore it might cause cancer. The *New York Times,* which loves these findings, ran major headlines and the information traveled around the world. They did not point out that in the body the oxidized form seldom goes more than about three percent of the total ascorbates and only in very serious disease. As pointed out by Irwin Stone in his book, only then do these levels go much higher. The more deficient anyone is the more oxidized derivatives are found. It is corrected by giving them more.

The recent report in *Nature* was promptly criticized by many top scientists in the field including Kenneth B. Beckman, Hal J. Helbock, Bruce N. Ames, Department of Molecular and Cell Biology, 401 Barker Hall, University of California, Berkeley, CA 94720, and Balz Frei, Linus Pauling Institute, Oregon State University, 571 Weniger Hall, Corvallis, OR 97331. They concluded "that the results presented are an ex vivo artifact, given the high values obtained. In the context of the huge literature supporting the health benefits of vitamin C, the conclusions of the study are unwarranted."

Extensive clinical evidence did not support the conclusion that vitamin C was carcinogenic. These studies, on the contrary, found that vitamin C was preventative and curative. The results of the large scale clini-

cal study I published with Linus Pauling in this journal and my continuing examination of high dose (12 grams daily) on nearly 1,000 patients treated since 1976 are entirely contrary since my patients live much longer than do the control group who do not take vitamin C. If vitamin C is carcinogenic why do my patients live longer? I now have 35 ten year survivors from an original group of about 100, almost all late stage cancers. From the control group only one survived one year.

Here we have another attempt to blow up an obscure report in a science journal to the status that it became a world wide attack on the new paradigm. It could even have led to the government in England to prohibit the sale of vitamin C tablets larger than 50 mg. Will Lazarides once more have to enter the fray and save vitamin C and the English public?

This raises the problem of how one should evaluate whether chemicals, xenobiotics and Orthomolecular chemicals, should be freely available. In considering the clinical worth of chemicals one must examine (1) the toxicity and (2) its efficacy. The ratio of the dose which is toxic divided by the dose which is therapeutic is the therapeutic index. If the index is very high the compound is relatively safe and if it is low it is relatively dangerous.

But there is another factor and that is whether the compound can be replaced by anything else. Thus insulin is very toxic but so far, it cannot be replaced and therefore because it is therapeutic it is used freely. Diabetic patients can purchase insulin freely as well as the needles they require. Thus toxic Orthomolecular chemicals, like insulin, are tolerated since there is no replacement.

When a number of compounds are equally effective, one must use the one which is the least toxic. If we have a dozen tranquilizers for the treatment of schizophrenia we must use the one which is the least toxic provided they have equal efficacy. Vitamins are not replaceable. No compound can do for the body what vitamin B3 will do, It is the only substance which can prevent and treat pellagra. Therefore even if it were relatively toxic it would still be permissible to use it. However even slight degrees of toxic reactions are undesirable and in some cases the vitamin molecule may be so modified that it becomes much less toxic. Thus niacin causes flushing because it is a vasodilator But its derivative inositol hexaniacinate, which is equally active, is not a vasodilator.

The point of this editorial is that one cannot apply the rules used in judging the therapeutic properties of xenobiotics for judging the therapeutic value of vitamins. The fight in England was not scientific. It was an attempt by a few physicians to prevent the further development of the new paradigm. Fortunately the most educated people in England were able by their determination and will to prevent this from occurring. Recently Jack Challem sent me the gist of a report which has appeared in the British Medical Journal.

The double standards that exist in judging orthodox and alternative medicine should be challenged, and reliable tools that can validate both approaches need to be found. The call came last week in London at a conference on integrated medicine which was organized by the Prince of Wales.

Dr Ian Chalmers, the director of the UK Cochrane Centre and a vociferous proponent of systematic reviews, told delegates: "Critics of complementary medicine often seem to operate a double standard, being far more as-siduous in their attempts to outlaw unevaluated complementary medical practices than unevaluated orthodox practices."

He said: "These double standards might be acceptable if orthodox medicine was based solely on practices which had been shown to do more good than harm, and if the mechanisms through which their beneficial elements had their effects were understood, but neither of these conditions applies."

It is thought that more than 60% of or-

thodox treatments have not been scientifically proved. Dr Chalmers added that the aim should not be to indulge in "data free" arguments, but to find a range of reliable tools to assess the effectiveness and safety of any healthcare intervention, be it orthodox or complementary.

The call was backed by the Prince of Wales who, as president of the Foundation for Integrated Medicine, opened the conference. "We need to commit ourselves to a rigorous but open minded evaluation of practice in all aspects of health care, and to finding ways of translating ideas into action in the most effective manner," he said. Prince Charles also urged national funding and educational bodies to increase research and awareness in the field.

For his part the health secretary, Frank Dobson, announced that a further £25,000 ($40,000) had been earmarked to continue developing a regulatory framework for complementary and alternative medicine practitioners. "I believe that what works is what counts and what counts is what works," he said.

Congratulations to Linda Lazarides, to her many coworkers, and friends.

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1. Society for the Promotion of Nutritional Therapy UK Visit our web site on http://visitweb.com/spnt
2. The Report is available from The Parliamentary Bookshop or The Stationery Office, London, England, price £20.50 (ISBN 010 2401985).
3. Marks, J. *Vitamin Safety,* Hoffmann-LaRoche, Basel, Switzerland. 1989; 10
4. Berger I, Beerger MR, Schmahl D: *The role of vitamins in the prophylaxsis and therapy of cancer,* Institute for Toxicology and Chemotherapy. German Cancer Research Center, Heidelberg, Germany. 1988; 14.
5. Vitamin Basics, B_6 *Vitamin Information Centre,* Don Mills, Ont, Canada, 1988
6. Stone I, Hoffer A: The Genesis of Medical Myths. *JOrthomolPsychiatl976;* 5:163-168.