

To the Editor: Schaumburg et al. reported the occurrence of sensory neuropathy after prolonged daily consumption of large doses of pyridoxine (vitamin B₆), and in an editorial Rudman and Williams¹ commented on the misuse of megadoses of vitamins. Both articles stress the inappropriateness of long-term ingestion of high doses of vitamin B₆, but neither of them mentions the appropriateness of short-term (often one-time) administration of high-dose pyridoxine for life-threatening isoniazid overdose. Large intravenous doses of vitamin B₆ can rapidly reverse the disturbed consciousness and recurrent convulsions (with lactic acidosis) that result from massive ingestion of isoniazid.²⁻¹⁰ In adults, consumption of 2 to 3 g of isoniazid at one time is usually toxic, and the ingestion of 10 to 15 g produces high death rates unless appropriate therapy is given.^{2,3,6,9}

Pyridoxine is an effective antidote, in amounts approximating or exceeding the estimated number of grams of isoniazid consumed at one time.^{2,4,6,9} Smaller quantities (but still megadoses) of pyridoxine may be efficacious when administered in combination with any of several depressants or anticonvulsants (especially diazepam) that potentiate the antidotal action of vitamin B₆.^{1,6,8,9} Observations in human beings and in animals have established the safety and efficacy of large doses of pyridoxine hydrochloride (5 to 50 g for adults) in isoniazid-induced convulsions.^{2,4,7-10}

Clearly, the long-term use of very high doses of vitamin B₆ is potentially harmful, but the short-term (usually single-dose) administration of megadose pyridoxine for life-threatening acute isoniazid overdose is both safe and effective. Indeed, as stated in Poisindex (Micromedex, Englewood, Colo.), high-dose pyridoxine is the antidote for acute isoniazid toxicity.

The opinions expressed in this letter are those of the writers and do not necessarily reflect the views of the Indian Health Service.

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The above letters were referred to Dr. Schaumburg, who offers the following reply:

To the Editor: Dr. Pauling's letter underscores the confusion surrounding the terms "orthomolecular" and "megavitamin." Dr. Pauling apparently no longer advocates the consumption of large doses of pyridoxine. Others have suggested doses of up to 2 g per day.¹ I stand by my statement that "pyridoxine is a widely abused vitamin" and inform Dr. Pauling that I have now identified over 30 (not 7) such patients, several of them severely disabled. Orthomolecular psychiatrists have not contributed in the majority of these cases. Most of the patients responded to the casual suggestion to "take pyridoxine" by purchasing, and daily consuming, several of the readily available, presumably harmless, 500-mg tablets sold in health-food stores. The rationale for 500-mg tablets of pyridoxine is unclear.

It is gratifying to learn that Drs. Baker and Frank do not advocate indiscriminate use of extremely high doses of vitamins, and I am pleased that they have "produced no neuropathy." However, to my knowledge there has been no study using systematic quantitative sensory testing of large numbers of people undergoing long-term pyridoxine administration in the 200-to-500-mg range. Studies of patients with long-term low-level exposure to other neurotoxic chemicals have revealed evidence of subclinical dysfunction.²

Drs. Sievers and Herrier maintain that short-term (usually single-dose) high-dose pyridoxine is considered to be indicated in certain medical situations. This form of short-term high-dose treatment should be undertaken with caution, since in recent experiments, high-dose pyridoxine administered intraperitoneally to rodents produced vacuolation of lumbar dorsal-root ganglion cells by the second day (Krinke G; personal communication). Similar ganglion-cell vacuolation was the cardinal morphologic finding in our previous canine studies.³

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ABNORMAL T-LYMPHOCYTE SUBPOPULATIONS IN HEALTHY SUBJECTS AFTER TETANUS BOOSTER IMMUNIZATION

To the Editor: Even though changes in the OKT4/OKT8 ratio have been described by many different groups of researchers in patients with the acquired immunodeficiency syndrome (AIDS) as well as in healthy persons considered to be at risk for this disease,^{1,2} the factors leading to these changes are not well understood. Repeated immunization (alloimmunization) has been discussed as a possible contributing factor in this context.^{3,4} To study the effect of immunization on the T-lymphocyte helper/suppressor ratio we have given 11 healthy subjects (between 20 and 50 years of age, nine men and two women), who did not belong to any of the populations known to be at risk for AIDS, a widely used antigen (tetanus toxoid, T-Immun, Immuno AG, Vienna, Austria). Although OKT4/OKT8 ratios — evaluated by indirect immunofluorescence and determined on two different occasions before immunization — were comparable (means $\pm$ S.E., 1.98 ± 0.19 and 2.19 ± 0.18 , respectively), follow-up studies after booster immunization with tetanus toxoid revealed a significant decrease in the OKT4/OKT8 ratio (1.24 ± 0.1 , $P < 0.001$) (Fig. 1). In 4 of the 11 healthy volunteers, the OKT4/OKT8 ratio fell to 1 or less (0.84, 0.86, 0.9, and 1.0). Mean values for OKT4/OKT8 ratios determined in all subjects 7 and 14 days after vaccination were significantly lower than pre-vaccination values (7 days, $P < 0.005$; 14 days, $P < 0.01$). The lowest ratio, which is shown in Figure 1, appeared between Day 3 and Day 14 after vaccination and returned to normal subsequently. The decrease in the OKT4/OKT8 ratio after vaccination was due to a reduction of OKT4+ cells in the peripheral blood of these donors. If the OKT4/OKT8 ratio fell to 1 or less, an increase of OKT8+ cells could be observed in addition. However, the changes in the T-cell subpopulations were not always accompanied by changes in total lymphocyte counts (e.g., number of cells per cubic millimeter before/after, in Volunteer 10: lymphocytes, 4350/2040, OKT4+ cells, 1376/760, and OKT8+ cells, 602/760; in Volunteer 11: lymphocytes, 3332/3007, OKT4+ cells, 1617/992, and OKT8+ cells, 528/1142).

In the May 26 issue of the *Journal*, the suggestion was made that blood donors should be examined for OKT4/OKT8 ratios as well as serum immunoglobulin levels and "blood from donors with abnormal values should be rejected."⁵ The results presented in this letter demonstrate that abnormal T-lymphocyte helper/suppressor ratios

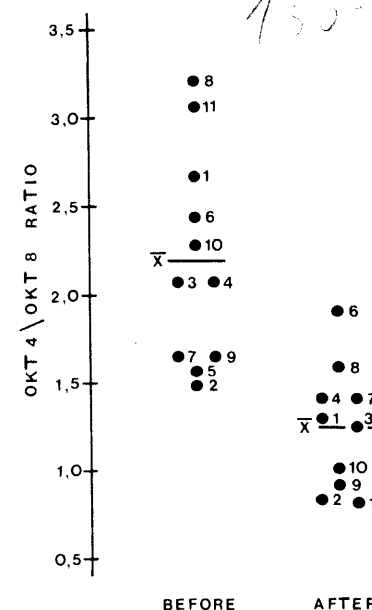


Figure 1. Comparison of OKT4/OKT8 Ratios in Healthy Subjects before and after Booster Immunization with Tetanus Toxoid.

Each dot represents the OKT4/OKT8 ratio immediately before vaccination (BEFORE) and the lowest value of serial determinations within a two-week period after vaccination (AFTER). Arabic numbers refer to individual subjects. Post-vaccination values were significantly lower ($P < 0.001$).

can be detected in healthy persons after immunization with a widely used antigen. Therefore, this test is of limited value for screening blood or plasma donors, especially for those in hyperimmunization programs.

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DIABETIC KETOACIDOSIS

To the Editor: In Foster and McGarry's well-documented review of diabetic ketoacidosis (July 21 issue),¹ there is one disturbing remark. In the discussion of complications it is stated that in a case of shock (ordinarily due to volume depletion and acidosis) not responding to treatment with fluids, "blood should be given."

In this form this statement is untrue. "Blood," which apparently

must be defined as donor red cells suspended in acid citrate (or citrate phosphate dextrose (anticoagulant) plasma, has a role in the treatment of nonhemorrhagic, hypovolemic shock in and certainly not in the management of diabetic ketoacidosis.

Whole blood contains erythrocytes, which are superfluous may even be damaging in a hemoconcentrated patient with small total red-cell mass. It contains microaggregates, which to the danger of peripheral stasis, sludging, and obstructing the microvasculature. It contains hyperosmolar, acidotic to be administered to a patient who is acidotic and hyperosmolar. Except, of course, in the case of severe blood loss, blood transfusion is contraindicated in hypovolemic patients with hypovolemia.

The aim of therapy in this case is to restore peripheral lower cardiac workload, and to accelerate the correction of the disturbances by improving the rheologic properties of the blood. This goal can be reached only by administering plasma and/or a 3 to 5 per cent solution, together with ample fluids.

Dextran is not the drug of choice in this case.² In short, a blood transfusion would do more harm than the treatment of shock caused by diabetic ketoacidosis.

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To the Editor: I much enjoyed the excellent article by Foster and McGarry on the metabolic derangements and treatment of diabetic ketoacidosis. I was, however, surprised at Dr. Foster's remark "Why does ketosis develop in a normal person after fasting, but not hyperglycemia?"

According to Dr. Foster, hyperglycemia is prevented by released by the elevated levels of both free fatty acids and ketone bodies. The evidence for this statement in the literature is convincing. There are no studies in human beings showing that free fatty acids are capable of releasing insulin, but several studies in dogs show that free fatty acids do not stimulate the human pancreas to secrete insulin.¹⁻⁸ Physiologically, this seems meaningful. During fasting, the declining insulin level stimulates lipolysis, leading to a rise in free fatty acids, which then provide energy for the brain. Hyperglycemia is, however, certainly prevented by a large amount of insulin secreted in normal subjects but not in deficient diabetics. Whether this small amount of insulin is because the lack of glucose during fasting cannot decrease secretion to zero or because the rising level of ketone bodies acts the decline in circulating insulin levels by stimulating secretion^{9,10} is not yet clear.

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