Letters to the Editor

Anaerobiosis and Cancer

To the Editor:

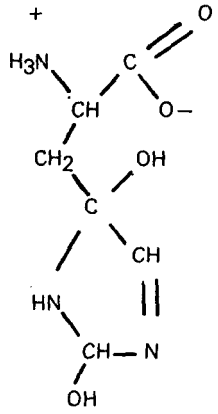
The genesis of tumors and carcinoma has been linked to many causes, such as radiation, polynuclear aromatic hydrocarbons, and many geo- and demographic factors (Smith, 1976). It is known that the so-called "Salmonella" test relates chemical potency with muta- and carcinogenicity through liver homo-genates for activation and histidine metabolite of bacteria for detection (Ames et al., 1973; McCann and Ames, 1976; McCann, 1976). The recent report of Ewing and Powers (Ewing and Powers, 1976) indicates that radiation-induced damage to bacterial spore cells is dependent on the concentration of oxygen. They note that "the exact chemical pathways through which O_2 functions as a radiation sensitizer are not known. Such information on mechanisms of oxygen-dependent sensitization on general processes leading to radiation-induced cell death is urgently needed in radiation therapy."

Singlet oxygen (Kearns, 1971; Foote, 1976) is proposed as the prime cause of cancer (and of many other degenerative and infectious ills of cells of the body). Due to the extremely short life of singlet
oxygen, even dissolved in the lipid bilayer of the cell membrane, the active molecule would have to be formed by transfer of resonance energy from pi-bonding sensitizers (Aihara, 1976) to triplet oxygen, with subsequent in-situ condensation (Foote, 1968; Hambergand Samuelsson, 1975; Porter and Funk, 1975; Pryor and Stanley, 1975; Bartlett, 1970; Wasserman et al., 1968; Ogryzlo and Tang, 1970) with unsaturated heterocyclic amino-acid nutrients, such as histidine and/or tryptophan. The resulting bicyclodioxetanes or their stereo-specific rearrangement/hydrolysis products (1) are read by m-RNA as cis-4-hydroxy-l-proline (II), a normal metabolic constituent, and are incorporated into precollagen (Witto et al., 1975; Woodhead-Galloway and Hukins, 1976) by ribosome.

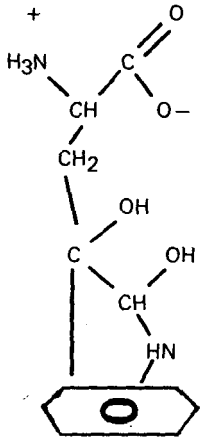
The hybrid precollagen formed condenses into defective microtubules which fail to repress cellular mitosis (Edelman, 1976). When hybridized cellular precollagen becomes incorporated into m-RNA as a mutant operator, the mis-codon eventually evolves into hybrid t-RNA and thence by recombining crossing over (Watson, 1970) into the genetic DNA (Temin, 1976). Hybridized DNA replicates without sensitivity to any normal regulating mechanisms, presumably resulting in metastasis.

I. Possible Derivatives

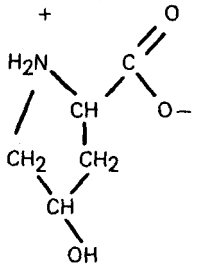
From Histidine



From Tryptophan



II. Cis-4-hydroxy-l-proline



In the case of cells exposed to radiative energy in the presence of triplet oxygen, it is believed that the hybridized precollagen formed has many more pathological derivatives, ranging from hypo- to hyperplasia, due to the great range of types of rays and of sensitivities of cells thereto.

The prime agent can be scavenged in the membrane by alpha tocopherol, cholesterol, and carotenes (Foote et a!., 1973). A high redox potential in both aqueous and lipid environments is enhanced by exposing all cells to a program of working under conditions (Cooper, 1968; Sheehan, 1975; Frisancho, 1975) of oxygen debt, whereby oxygen-dependent metabolic mechanisms revert to the more .primitive electron-transfer type (Newsholme and Start, 1973) and the airborne infectious agents cannot persist. Under these conditions, cellular synthesis of protein, RNA, and DNA remain true (unhybridized), and replication is extended through many more generations before failure of genetic codes. These mechanisms explain the doubling of number of generations of E. coli cultured with and without vitamin E (Packer and Smith, 1974) and also the relative longevity of peoples who live vigorous lives in mountainous regions of the world (Leaf, 1973).

Robert T. Olsen, Ph.D.
1 Country Lane, R.R. #1, Box 48
Eastham, MA 02642

REFERENCES

SMITH, K. C, Ed.: Aging, Carcinogenesis and Radiation Biology. Plenum Press, New York, N.Y., 1976.

AMES, B. N., DURSTON, W. E., YAMASAKI, E., and LEE, F. D.: Proc. Nat. Acad. Sci. 70, 2281-5, 1973.

McCANN, J., and AMES, B. N.: Ann. N.Y. Acad. Sci. 271, 5-13, 1976.

McCANN, J.: Chem. Tech., pp. 682-7, November, 1976.

EWING, D., and POWERS, E. L: Science 194, 1049-51, December 3, 1976.

KEARNS, D. R.: Chem. Rev. 71, 395-427, 1971.

FOOTE, C. S., Chapter III in Pryor, W. A., Ed.: Free Radicals in Biology, Academic Press, New York, N.Y., 1976.

AIHARA, J.: J. Org. Chem. 41, 2488, 1976.

FOOTE, C. S.: Accounts Chem. Res. 1, 104. 1968.

HAMBERG, M., and SAMUELSSON, B.: Reported in summary by Kolata, G.: Science 190, 770, 1975.

PORTER, N. A., and FUNK, M. O.: J. Org. Chem. 40, 3614, 1975.

PRYOR, W. A., and STANLEY, J. P.: J. Org. Chem. 40, 3615, 1975.

BARTLETT, P. D.: J. Am. Chem. Soc, 3223-5, 1970.

WASSERMAN, H. H., STILLER, K., and FLOYD, M, B.: Tetrahedron Lett., 3277, 1968.

OGRYZLO, E. A., and TANG, C. W.: J. Am. Chem. Soc. 92, 5034, 1970:

WITTO, J., HOFFMANN, H. P., and PROKOP, D. J.: Science 190, 1202, 1975.

WOODHEAD-GALLOWAY, J., and HUKINS, D. W. L: Endeavour 35, 73, May, 1976.

EDELMAN, G. M.: Science 192, 218 and 457, 1976.

WATSON, J. D.: Molecular Biology of the Gene. W. A. Benjamin, Inc., Menlo Park, CA. 2nd Ed., p. 21, 1970.

TEMIN, H.: Science 192, 1075, 1976.

FOOTE, C. S., DENNY, R. W., WEAVER, L, CHANG, Y., and PETERS, J.: Ann. N.Y. Acad. Sci. 171, 139, 1970.

COOPER, D. R.: Aerobics, M. Evans and Co., New York, N.Y., 1968.

SHEEHAN, G. R.: Dr. Sheehan on Running. World Publications, Ml. View, CA, 1975.

FRISANCHO, A. R.: Science 187, 313, 1975.

NEWSHOLME, E. A., and START, C: Regulation in Metabolism. J. Wiley and Sons, New York, N.Y., 1973.

Red cells operate at a high and white cells at a low oxidation potential; in the former, pyruvate is carried through the TCA cycle to carbon dioxide and water; in the latter, pyruvate is reduced to lactic acid, which diffuses more easily through the cell membrane and which is converted in the liver to glycogen. The high redox potential necessary to achieve this conversion can be maintained by megadoses of ascorbic acid, which is also known to destroy superoxide ion (a source of singlet oxygen) in extracellular space, according to Fridovitch, I.: Ann. Rev. Biochem. 44, 147, 1975).

PACKER, L, and SMITH, J. R.: Proc. Nat'l. Acad. Sci., U.S.A., 71(121,4763-7, 1974.

LEAF. A.: Nat'l Geographic 143, 93 (1), 1973.

Role of Zinc Deficiency

To the Editor:

I have been giving a lot of thought to the possible role of zinc deficiency in the aetiology of hyperactivity and autism, hereafter termed Zn-d. (This possibly also includes manganese and chromium deficiency.) Zn-d could lead to consequent B6 and subsequent B3 deficiency and also vitamin A deficiency (see Chart 1).

There are many reasons why mothers may be short of zinc prior to conception, as listed by Dr. Carl C. Pfeiffer: viz; the "pill"; copper plumbing, frozen vegetables; increased use of alcohol; routine iron supplementation during pregnancy; also iron in bread and cereals; artificial fertilizers increasing phytate hazard (Oberleas, Detroit, Michigan, School of Medicine); use of copper and estrogen with fat stock. Professor Bryce-Smith, U.K., pinpoints lead in petrol, in seams of tins and industrial effluent. Cadmium from cigarettes, copper, lead, and cadmium are all antagonistic to zinc.

In **Mineral Metabolism,** edited by Comar and Bronner, pages 376 and 377, one finds all animals accumulate copper at the end of pregnancy, presumably to stimulate birth. Nature would rebalance, as human colostrum contains large amounts of zinc, 20 mg/litre at delivery (KOGA, 1935). Mature cow's milk contains 3 to 5 mg/litre. Newborns are frequently given little access to natural feeding and are fed on mature cow's milk or glucose and water. Apart from deprivation of colostrum, babies are additionally at risk due to iron supplementation of baby's milk and cereals. Disadvantages of Zn-d include:

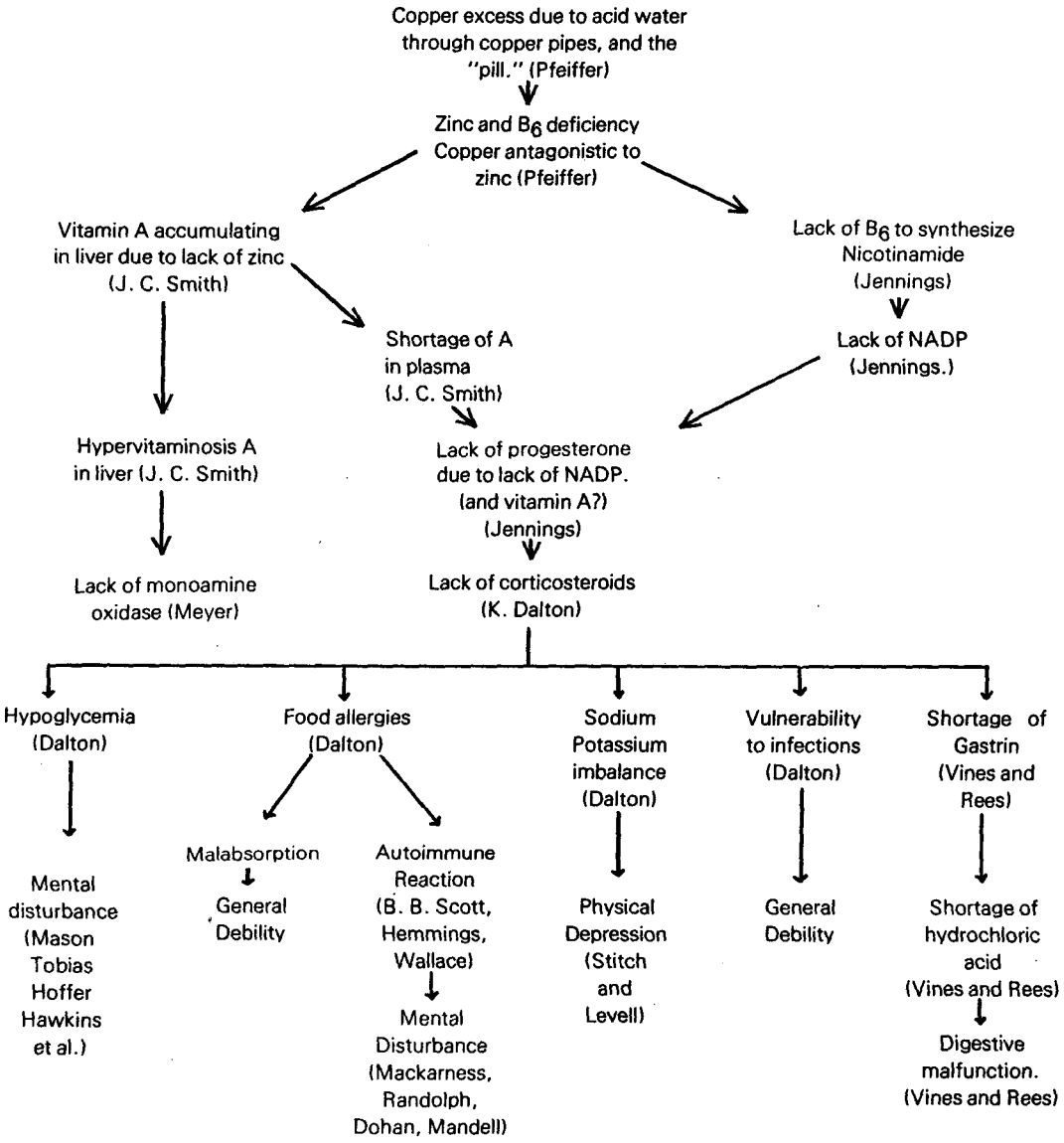
1. Those listed in Chart I.
2. Those listed in Chart II, sent to me by Dr. Pfeiffer.

2. Possibly a paucity of zinc-dependent enzymes. These include alkaline phosphatase (transports calcium across gut wall); carbonic anhydrase (copes with carbonic acid in drinking water); lactic, glutamate, and malic dehydrogenase (it has been found helpful by some doctors to remove milk, gluten, and some fruits from the diets of autistic children); carboxypeptidase; and the pyridine nucleotide dependent metallo dehydrogenases. There are also 19 metallo enzyme complexes activated by zinc.

2. Possibly retardation of hippo-campal function (see "Zinc and Hippo-campal Function" by Crawford and Connor, Journal of Orthomolecular Psychiatry, Volume 4, Number 1, 1975) . . . "In very young rats hippocampal staining (by stained zinc) was light, diffuse, and generally unremarkable until 18 days . . . An intense burnt orange color . . . characteristic of the adult hippocampus, was fully developed at *22* days postpartum ..." The weaning age of the rat is 16 days to *22* days, so the amount of zinc present in the hippocampus may be an important factor in the maturation of behavior and/or digestive performance.

5. Disadvantages listed in a number of papers regarding Zn-d in rats by Cald well, Oberleas, and Prasad of the Lafayette Clinic, Detroit, Michigan. Rats deprived of zinc during gestation were

CHART I

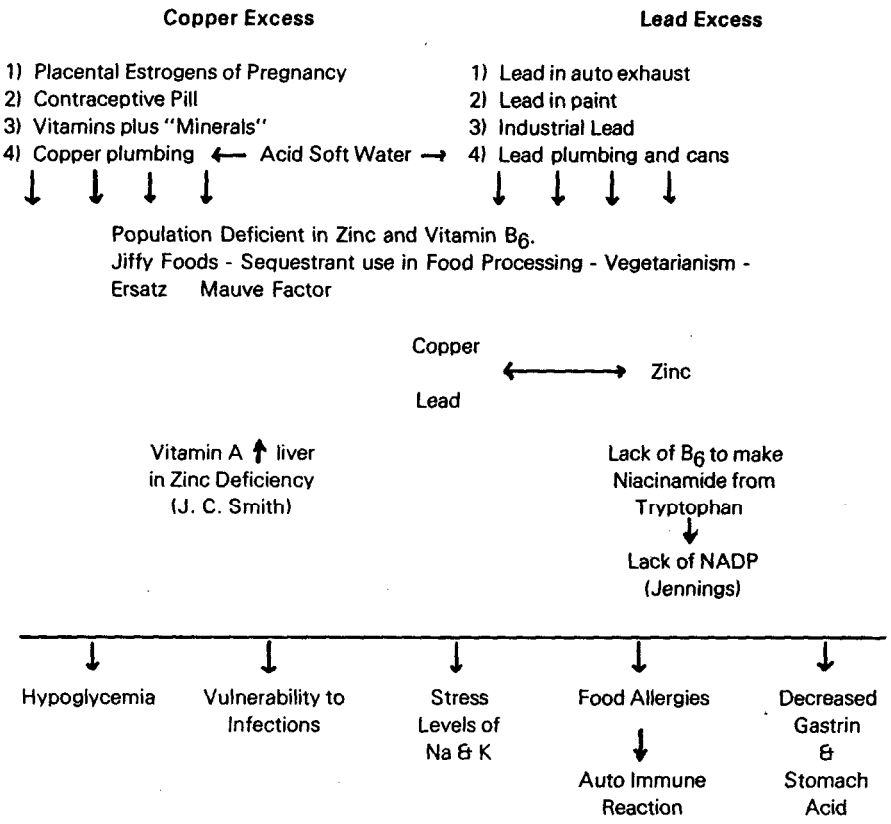


found in all tests backward mentally compared with normals.

I have compared accepted hyperactive and autistic behavior patterns with those of experimental animals with Zn-d and found 37 analogues (i.e., toe walking is common in autistics. Toewalking tenses the buttocks, knees, and thighs; posterior column disease causes weakness of the hindquarters in zinc-deficient mice. Swayback is a similar affliction in Zn-d sheep.) I am hoping to interest somebody in my list who may look into this problem.

For prevention I believe the following ideas might be helpful: 1. Prepregnancy clinics, where couples hoping to conceive might have trace mineral and vitamin levels assessed and readjusted before conception. Drinking water from homes of potential parents could be tested at tap flow for excess copper, lead, and carbonic acid, and alternative water supplied where indicated. 2. Women should be helped to breast feed. Hospitals could give more suckling time in the first few days. The optimal diet for lactation should be studied; also whether

CHART II



the "pill" inhibits milk production. Family allowances and home help schemes should be very generous for nursing mothers. 3. When this fails, researchers could study the possibility of making an artificial colostrum, or at least zinc supplementation for the baby might be studied. 4. Lead should be removed from gasoline, and lead seams in food cans made illegal. 5. The long-term detrimental effects of artificial fertilizers should be researched with the phytate hazard in mind. 6. The use of copper and estrogens with livestock should be closely investigated, with human zinc needs in mind. 7. The use of pesticides, which destroy the microscopic life of the top soil (which renders the trace minerals available to plants) should be banned. 8. The beneficial/detrimental effects of mass iron supplementation in this era of copper plumbing could be reassessed.

With children already afflicted with hyperactivity or autism, hair analysis such as that carried out by Dr. Elizabeth Lodge Rees of California would probably reveal much in every case. The numbers are rising all the time for hyperactive and dyslexic children. I do hope these preventive measures can be considered.

Belinda Barnes,
Woodhurst, Hydestile,
Godalming, Surrey, England.

ORTHOMOLECULAR PSYCHIATRY, VOLUME 6, NUMBER 3, 1977, Pp. 257-262

Hyperkinetic Behavior

To the Editor:

An excellent paper confirming the association of hyperkinetic behavior with the use of aniline food dyes has been published in Pediatrics. It is a cautiously designed experiment which is intended to control the large number of possible factors which influence this type of study.

The measures of behavior were made by parents and teachers on 15 children during their regular diet, during a complicated placebo diet, and during the diet free of salicylates and food additives. Behavior was significantly improved on the special diet in the evaluation of the teachers, but not that of the parents. This is the same finding as occurred with hyperkinetic children and the beneficial effects of dextroamphetamine. There were five chances in 1,000 that this conclusion was the result of chance.

In their discussion of the results the authors suggest that a smaller subgroup of hyperkinetic children are the ones who get the major benefit from withdrawal from salicylates and aniline dyes. This is the same conclusion that Dr. Clyde Hawley and I came to in our report which dealt with sublingual drop testing of hyperkinetic children. We found that only 35 to 40 percent of these children had behavior changes following the sublingual drop test.

It is our opinion that this test should be automatically included in the evaluation of emotionally disordered children. We need not maintain that aniline dyes are the sufficient and only cause of a complicated disorder. These chemicals can increase the behavior disorders which are already present.

Robert E. Buckley, M.D.
Levine Hospital Bldg.
22455 Maple Court, #406
Hayward, CA 94541

REFERENCES

CONNERS, C. Keith, Ph.D., GOYETTE, C. H., Ph.D., SOUTHWICK, D. A., M.A., LEES, J. M., M.D., and ANDRULONIS, P. A., M.D.: Food Additives and Hyper-kinesis: A Controlled Double-Blind Experiment. Pediatrics 58(2): 154-166, August, 1976.

HAWLEY, C, M.D., and BUCKLEY, R. E., M.D.: Hyper-kinesis and Sensitivity to the Aniline Food Dyes. Orthomolecular Psychiatry 5(2): 129-137, Second Quarter, 1976.