

the creation of epidemiological posts at national and regional level. We would hope that priority will be given to the further development of such a service within the Department of National Health and Population Development.

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Dangers of large doses of vitamin A during pregnancy

Vitamin A is an alcohol — retinol — which has profound effects on cell differentiation and proliferation and is an essential dietary nutrient for growth, vision, reproduction, immunocompetence and the maintenance of differentiated epithelia and mucus secretion.¹ Retinol metabolises to an aldehyde form — retinal — and an acid form — retinoic acid — both of which are members of a large class of compounds, the retinoids. The average balanced diet contains the recommended daily allowance (RDA) for adults of approximately 4 000 - 5 000 IU vitamin A.

The use of vitamin A and retinoids is increasing,^{2,3} perhaps encouraged by popular protagonists such as Linus Pauling⁴ and Adele Davis⁵ of megadose supplements. Vitamin A tablets containing 25 000 - 50 000 IU are freely available in health-food shops and pharmacies in South Africa. Marketing data in the USA have shown widespread high-dose vitamin A utilisation (IMS America Ltd, Ambler, Pennsylvania, 1983) and the consumption of megadose vitamin A appears to be encouraged by health stores in the UK.² The toxic syndrome of hypervitaminosis A can result from prolonged intake of doses in excess of 10 - 20 times the RDA.⁶

Of particular concern is the use of excessive amounts of vitamin A by women of childbearing age. Since the original report of vitamin A teratogenicity in animals by Cohlman,⁷ more than 100 studies have found various analogues of vitamin A to be teratogenic in numerous species.⁸ In humans, the teratogenic potential of the synthetic retinoic acid derivatives, isotretinoin and etretinate, used in the treatment of acne and psoriasis are now well known, typically producing craniofacial malformations such as microtia or anotia, agenesis or marked stenosis of the external ear canal, maldevelopment of skull and facial bones, micrognathia, heart defects, thymic abnormalities and central nervous system malformations such as hydrocephalus and microcephaly.⁹ The pattern of abnormalities is similar to that induced by vitamin A if given during the same period of development.⁸⁻¹⁰ The first observations of human teratogenicity with isotretinoin were reported in 1983 by Roche Laboratories. At this stage there were only 5 reports in the literature and 2 received by the Food and Drug Administration (FDA) in the USA of human

birth defects associated with excessive maternal vitamin A exposure.¹⁰⁻¹⁵ In 1984 Hall¹⁶ called vitamin A a newly recognised human teratogen and suggested it was a harbinger of things to come. Since 1984 10 more unpublished case reports have been documented by the FDA,¹⁰ and another has been documented in the literature. Twelve of the above cases had defects similar to those seen in animals and in human retinoid syndromes, such as microtia, cleft palate, and central nervous system and cardiovascular abnormalities. The mothers of malformed infants were exposed to supplements of 25 000 IU vitamin A per day or more, and all but 1 of the 18 birth defects occurred with long-term exposure continuing after conception.¹⁰ Vitamin A levels are greatly influenced by the duration of use — the vitamin is cumulative because of its long half-life.^{10,18} In the mouse, although the blastocyst appears to be resistant to the teratogenic effects of vitamin A, we have found that a large dose of the vitamin administered during the pre-implantation period exerts its toxic effect during the later more vulnerable embryonic period, which is in keeping with a prolonged maternal elimination rate.¹⁹ Patients are advised not to become pregnant for several months after discontinuing treatment with large doses of vitamin A and the retinoic acid derivative, etretinate.^{8,20}

The mechanism by which vitamin A and other retinoids interfere with normal embryonic development is not well understood. Retinoids may enter the cell, bind to a specific cytoplasmic protein, and then be transported to the nucleus where they may alter the pattern of gene action. The involvement of ear, thymus, heart and brain has raised speculation of a specific effect on neural crest cells.²¹⁻²³ Other mechanisms that have been advanced include a toxic effect on cell membranes, abnormal differentiation, interference with mucopolysaccharide metabolism and increased cell death.^{12,24-26.}

The concern of the Teratology Society regarding excess vitamin A use during pregnancy recently led to the publication of the first position paper in 13 years.³ Their important recommendations are: (i) women in their reproductive years should be informed that excessive use of vitamin A before and during pregnancy could be harmful to their babies; (ii) supplementation of 8 000 IU

vitamin A (as retinol/retinyl esters) per day should be considered the maximum before or during pregnancy; (iii) manufacturers should lower the maximum amount of vitamin A per unit dosage to 5000 - 8000 IU and identify the source of vitamin A (high dosages of vitamin A as retinol/retinyl esters (25000 IU or more) are not recommended because these dosages are not necessary as a nutrient supplement and may be teratogenic); since carotene has not been associated with embryotoxic effects, it is suggested that β -carotene be considered the primary source of these vitamins for women in their reproductive years; and (iv) labelling of products containing vitamin A supplements (as retinol/retinyl esters) should indicate that consumption of excessive amounts of vitamin A may be hazardous to the embryo/fetus when taken during pregnancy and that women of childbearing potential should consult their doctor before consuming these products.

It remains to be seen whether the authorities and/or industry take cognisance of these recommendations and limit the maximal amount of vitamin A per unit dosage. Doctors and pharmacists remain responsible not only for ensuring that pregnant patients are not prescribed megadoses of vitamin A, but that women in their reproductive years are informed of the dangers of excessive use of vitamin A shortly before and during pregnancy. However, even if health professionals fulfil their role, if control of dosage is not forthcoming, large outlets such as those through health-food stores will remain unchecked.

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Nuus en Kommentaar/News and Comment

Autotransfusion

Concern about AIDS virus transmission by blood transfusion has led to increased interest in autotransfusion, the transfer of the patient's blood back into the body. An article by Dale *et al.* (*Ann R Coll Surg Engl* 1986; **68**: 296) discusses the use of autotransfusion with a centrifugal cell washer in a series of 76 cases, 54 of which involved liver transplantation. The procedures were commonly accompanied by major blood loss and the apparatus used was the Haemonetics Cell Saver, which filters the blood and performs the centrifugal separation and cell washing. It has an efficient suction apparatus which provides immediate effective anticoagulation. One snag is the cost, about R60 000.

All the patients involved were at risk for excessive haemorrhage, but only 2 died of continued haemorrhage, 1 being an elderly patient with a ruptured aneurysm who developed disseminated intravascular coagulation. On average in these cases 64% of the estimated total blood loss was collected and about 45% of collected blood was actually processed, representing 27% of total blood loss. The authors estimate the use of this apparatus reduced the amount of blood needed in these 74 cases by about 604 units.

Malnutrition and misleading advertising

Intellectual ability and the higher education should not necessarily be equated with common sense, as a case report in the *Canadian Medical Association Journal* points out (Muir A, Kalnins D, 1987; **136**: 1274). A 6½-month-old boy was admitted to hospital with a 1-day history of increasing lethargy, vomiting and a bulging anterior fontanelle. He was the child of university-educated vegans and weighed 2580 g at birth. At 6 weeks maternal anxiety resulted in a change from breast milk to a soya-based substitute claimed in advertisements to be a 'quality substitute' for breast milk. The product was obtained from a health food store, and the general practitioner presumably did not scrutinise the accompanying brochure too closely. The result of feeding with this formula was that the child was eventually admitted to hospital with the signs of deficiency of vitamins A and D together with marasmus. A more orthodox formula together with supplies of vitamins A and D rapidly dealt with the condition. This bears out the old adage that the best place to peddle phoney wares is among the highly educated.