

Regulation of Vitamin E, a Nutritional Antioxidant

Maret G. Traber, Ph.D.

Department of Nutrition & Food Management

Linus Pauling Institute

571 Weniger Hall

Oregon State University

Corvallis, Oregon

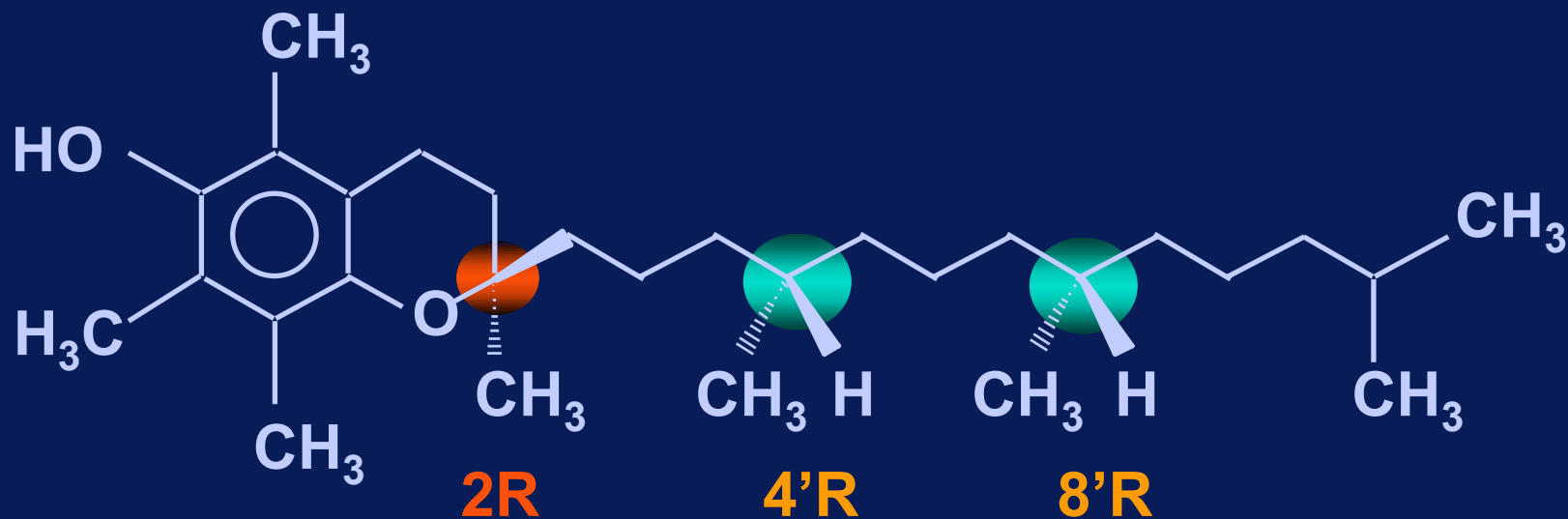
541-737-7977

Fax: 541-737-5077

Email: maret.traber@oregonstate.edu

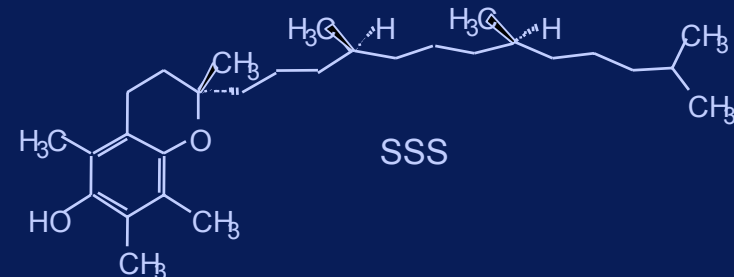
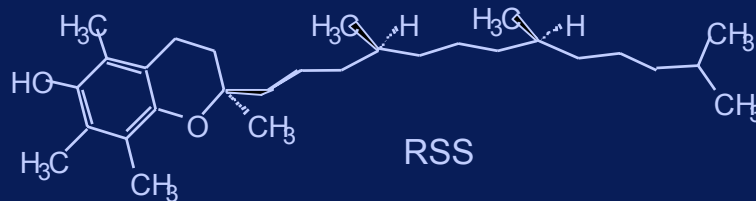
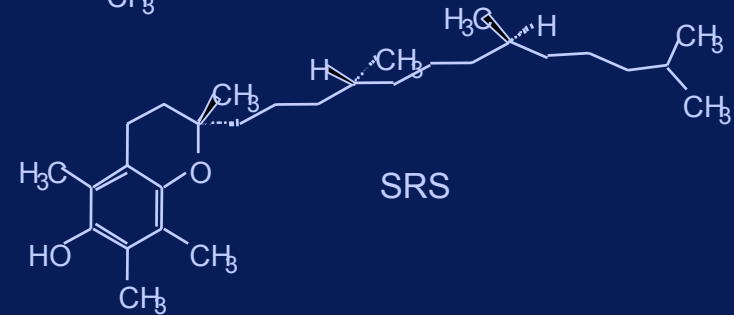
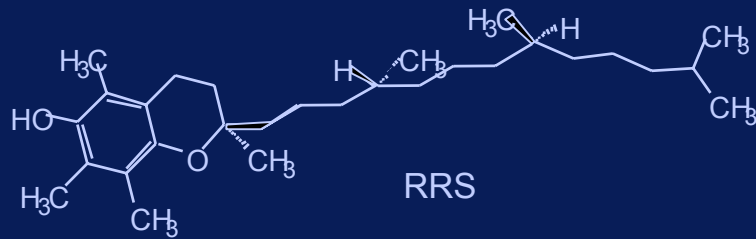
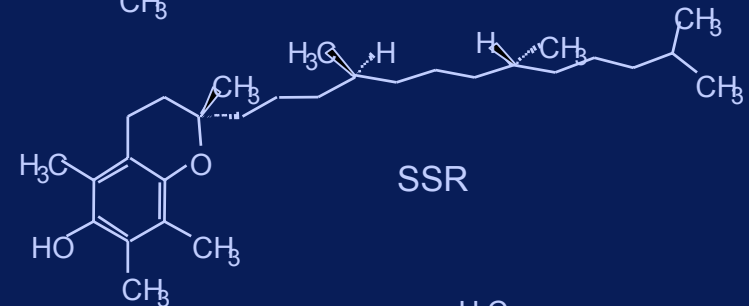
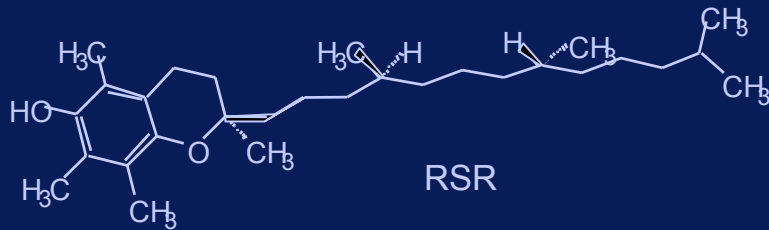
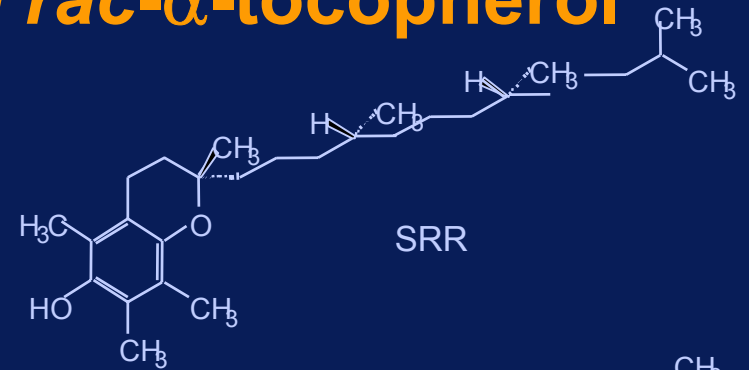
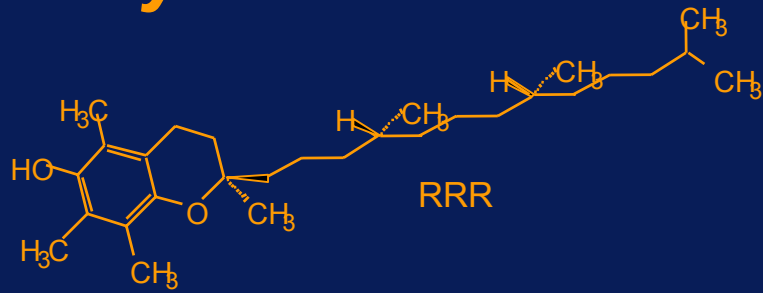


RRR- α -Tocopherol



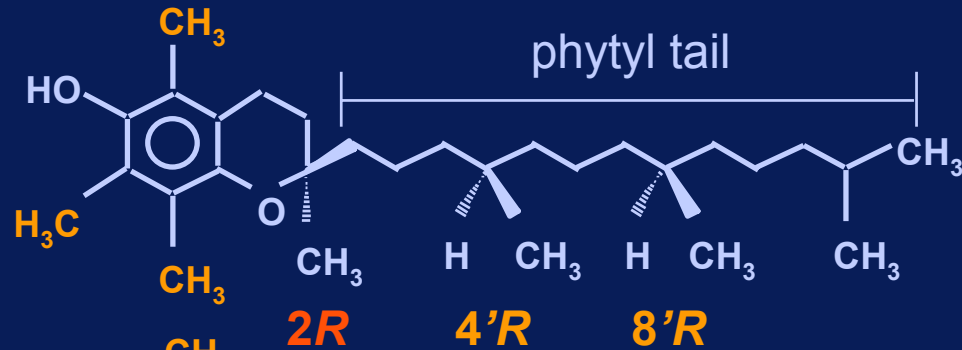
d- α -Tocopherol

Synthetic vitamin E: all *rac*- α -tocopherol

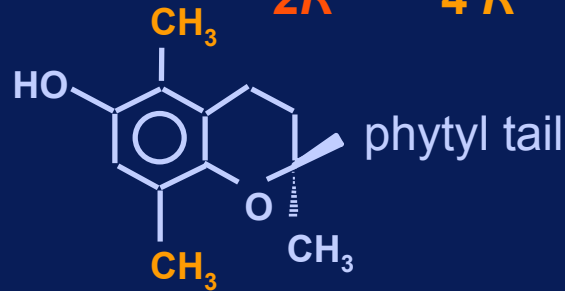


Naturally Occurring Tocopherols

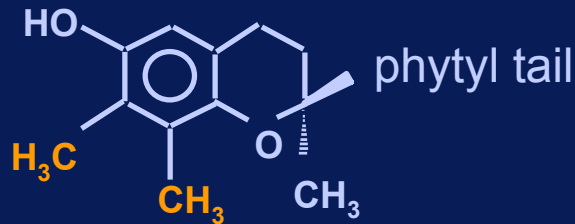
α -tocopherol



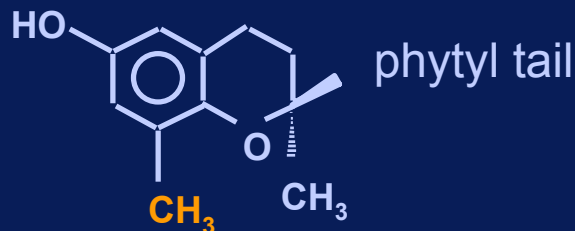
β -tocopherol



γ -tocopherol

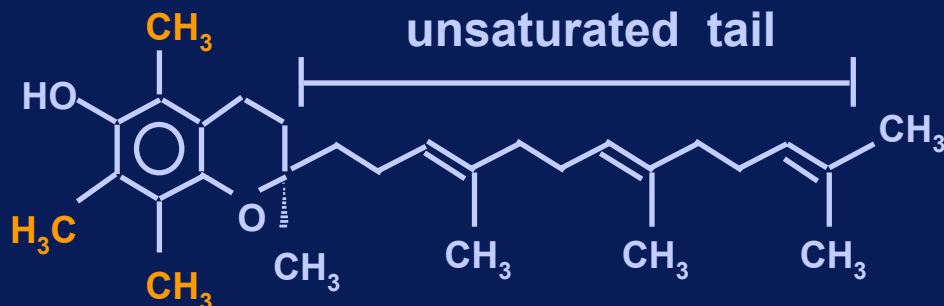


δ -tocopherol

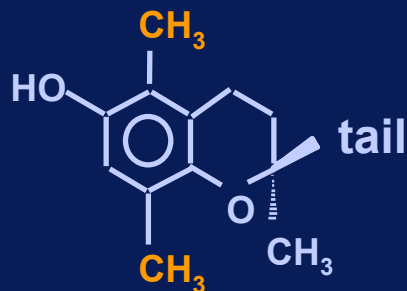


Naturally Occurring Tocotrienols

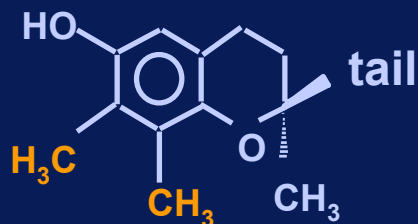
α -tocotrienol



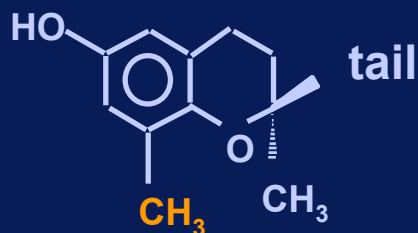
β -tocotrienol



γ -tocotrienol



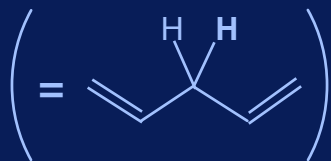
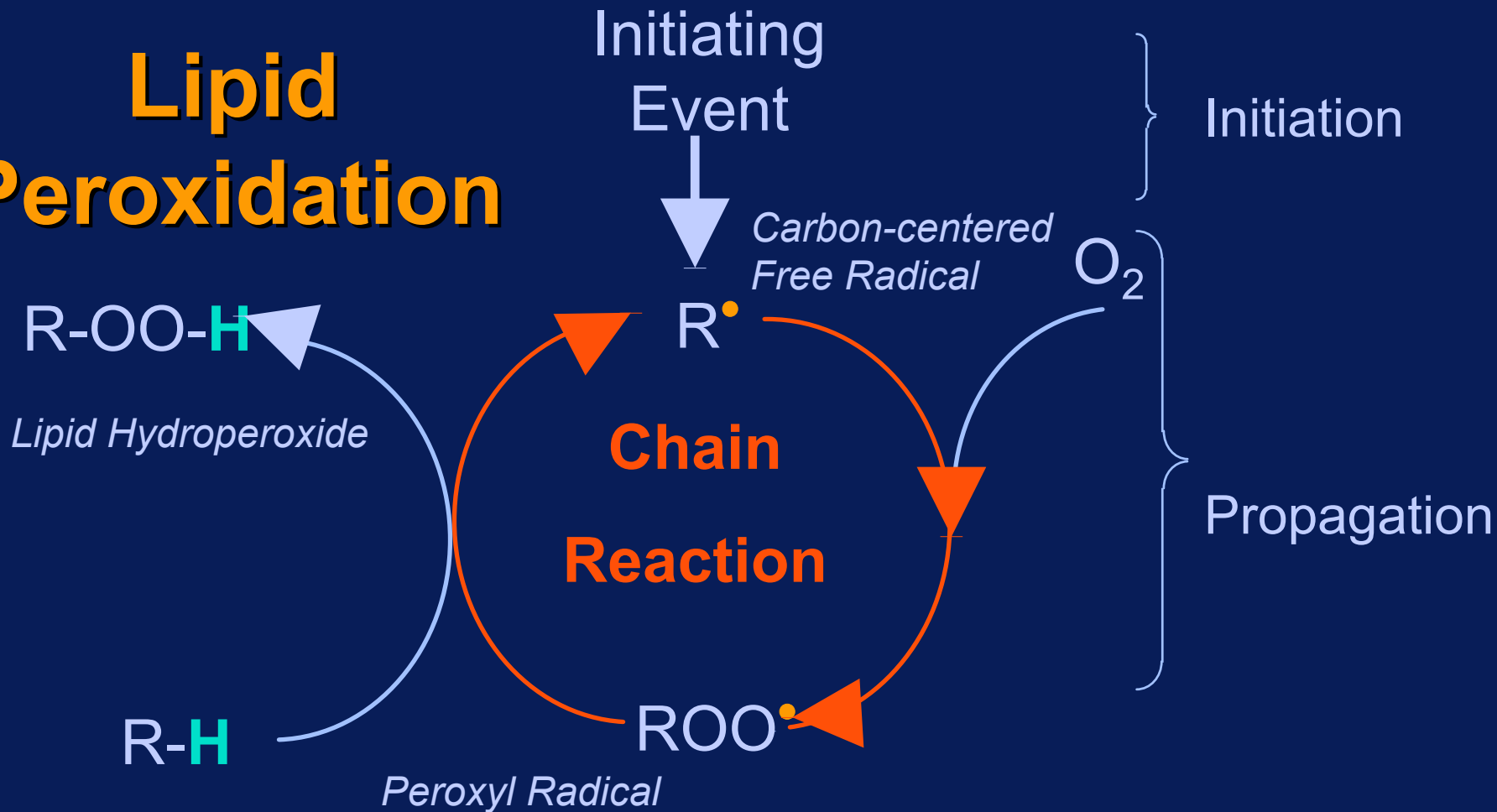
δ -tocotrienol



Vitamin E Functions

- Specific role in a required metabolic function has not been found
- Major function appears to be as a fat-soluble, “chain-breaking” antioxidant
 - Peroxyl radical scavenger
 - Protects polyunsaturated fatty acids (PUFAs) within membranes and lipoproteins

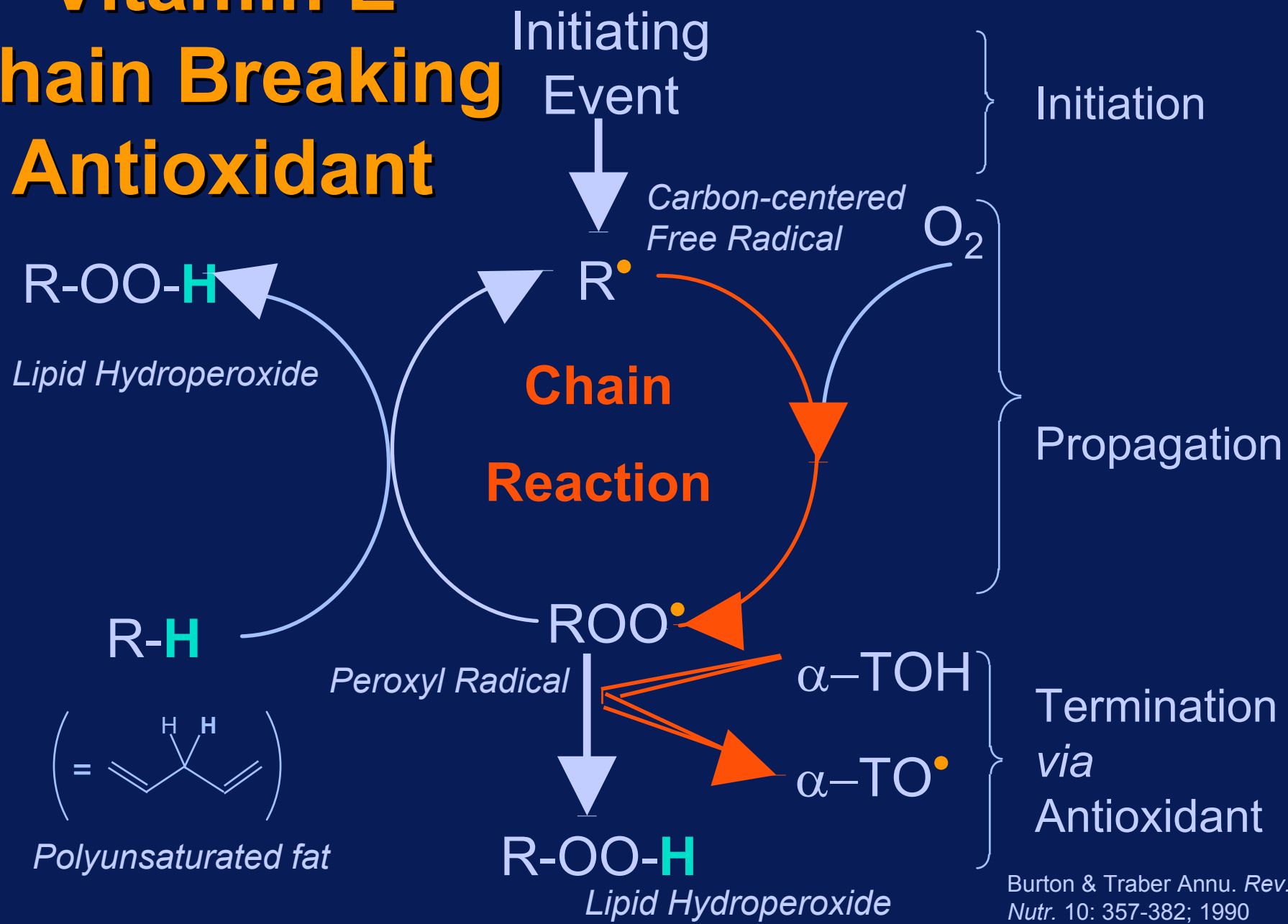
Lipid Peroxidation



Polyunsaturated fat

Burton & Traber. *Annu. Rev. Nutr.* 10: 357-382; 1990

Vitamin E Chain Breaking Antioxidant



Burton & Traber *Annu. Rev. Nutr.* 10: 357-382; 1990

Potential Cellular/Molecular Mechanisms of Vitamin E

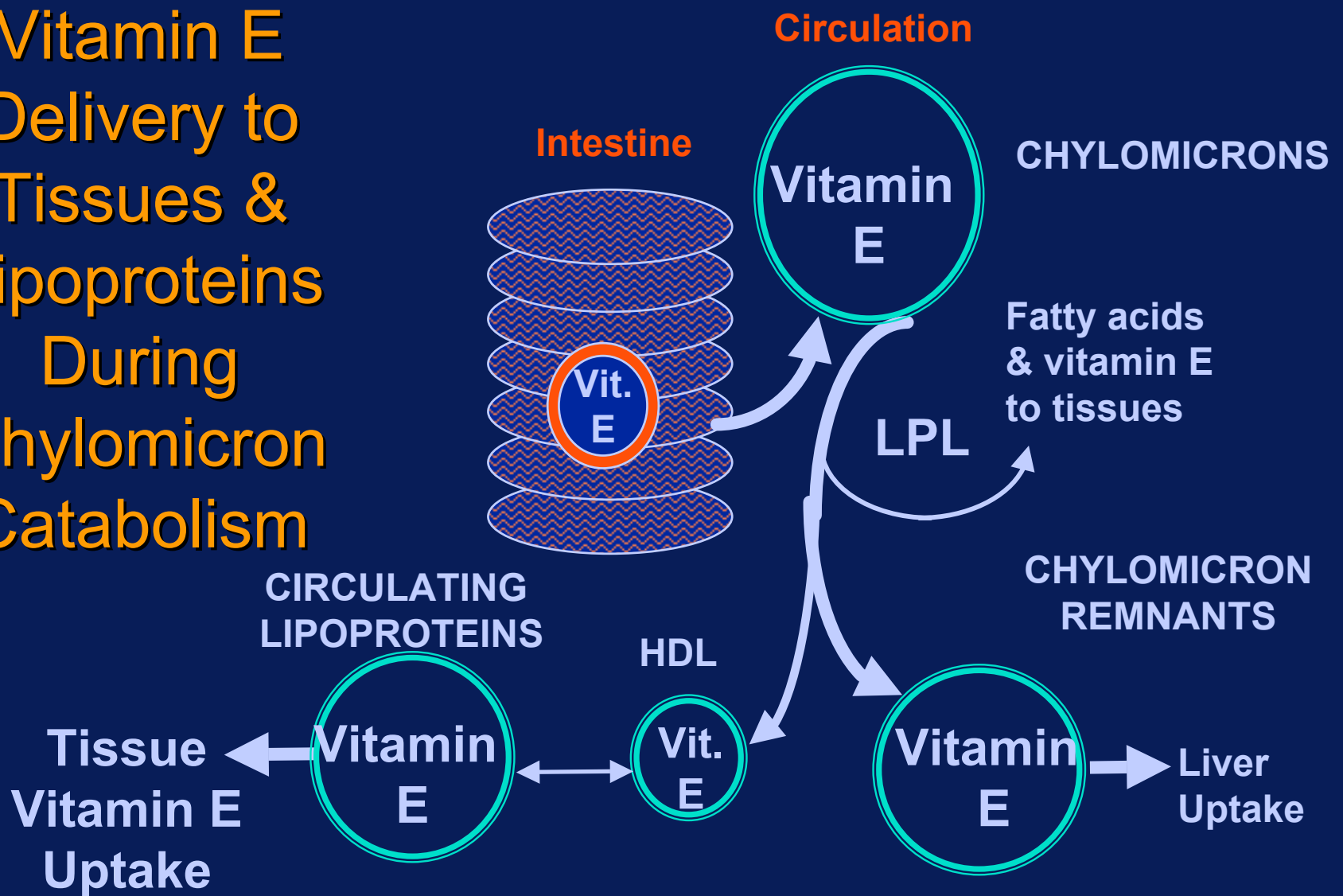
- Endothelial cells
 - Adhesion, NO production, superoxide production
- Smooth muscle cells
 - Proliferation
- Macrophages
 - Adhesion, invasion, signaling recruitment, ROS production
- Platelets
 - Adhesion, aggregation, clotting

Vitamin E Biologic Activity in Humans

- Absorption & Chylomicron Catabolism
 - All forms absorbed and transported to liver
- Lipoprotein Transport
 - All lipoproteins transport vitamin E
- Liver Trafficking
 - α -Tocopherol specifically secreted into plasma
- Metabolism
 - Vitamin E metabolites are NOT oxidation products

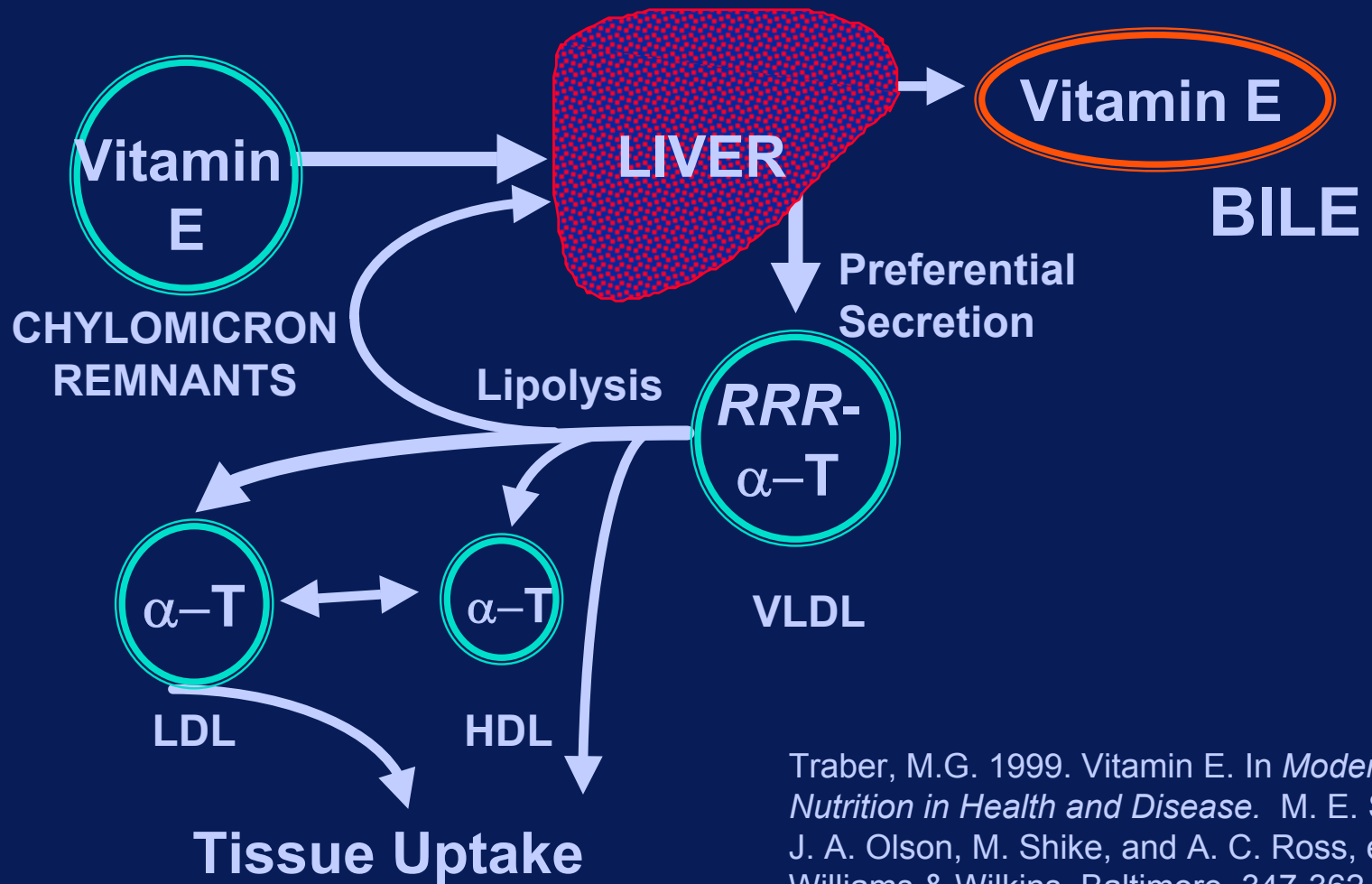
Brigelius-Flohe, R. and M.G. Traber. *Faseb J.* 13: 1145-1155, 1999.

Vitamin E Delivery to Tissues & Lipoproteins During Chylomicron Catabolism



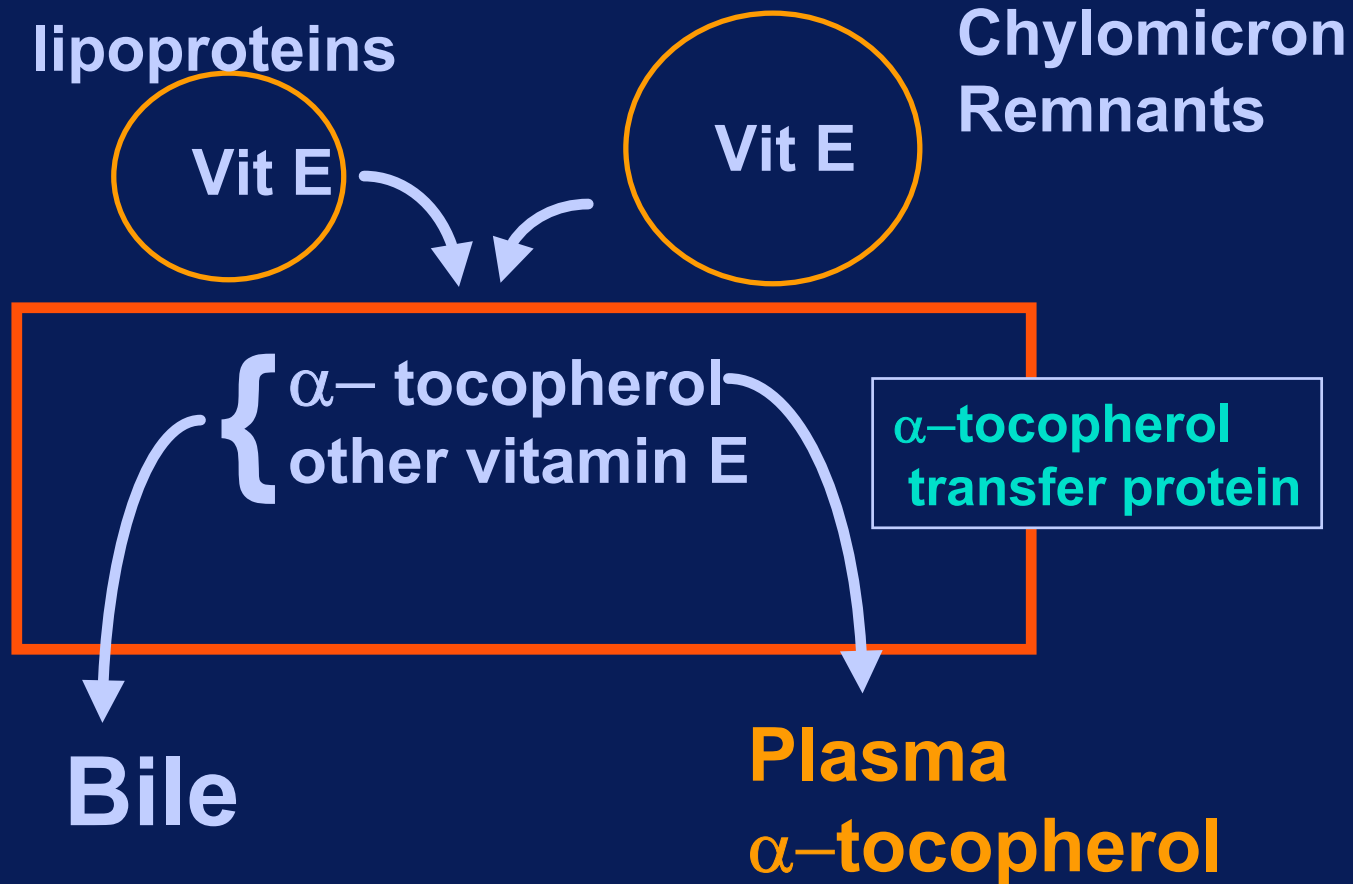
Traber, M.G. 1999. Vitamin E. In *Modern Nutrition in Health and Disease*. M. E. Shils, J. A. Olson, M. Shike, and A. C. Ross, eds. Williams & Wilkins. Baltimore. 347-362.

Preferential Secretion of α -Tocopherol in VLDL and Its Delivery to Tissues



Traber, M.G. 1999. Vitamin E. In *Modern Nutrition in Health and Disease*. M. E. Shils, J. A. Olson, M. Shike, and A. C. Ross, eds. Williams & Wilkins. Baltimore. 347-362.

Regulation of Liver Vitamin E



Kayden, H.J. and M.G. Traber. *J. Lipid Res.* 34: 343-358, 1993.

Vitamin E Deficiency in Humans

- Malabsorption Syndromes
 - Abetalipoproteinemia
 - Cholestatic Liver Disease
 - Cystic Fibrosis
 - Short Bowel Syndrome
 - Total Parenteral Nutrition
- Genetic Abnormalities in α -Tocopherol Transfer Protein
 - Familial Isolated Vitamin E Deficiency (FIVE)
 - Friedreich's Ataxia Variants (AVED)

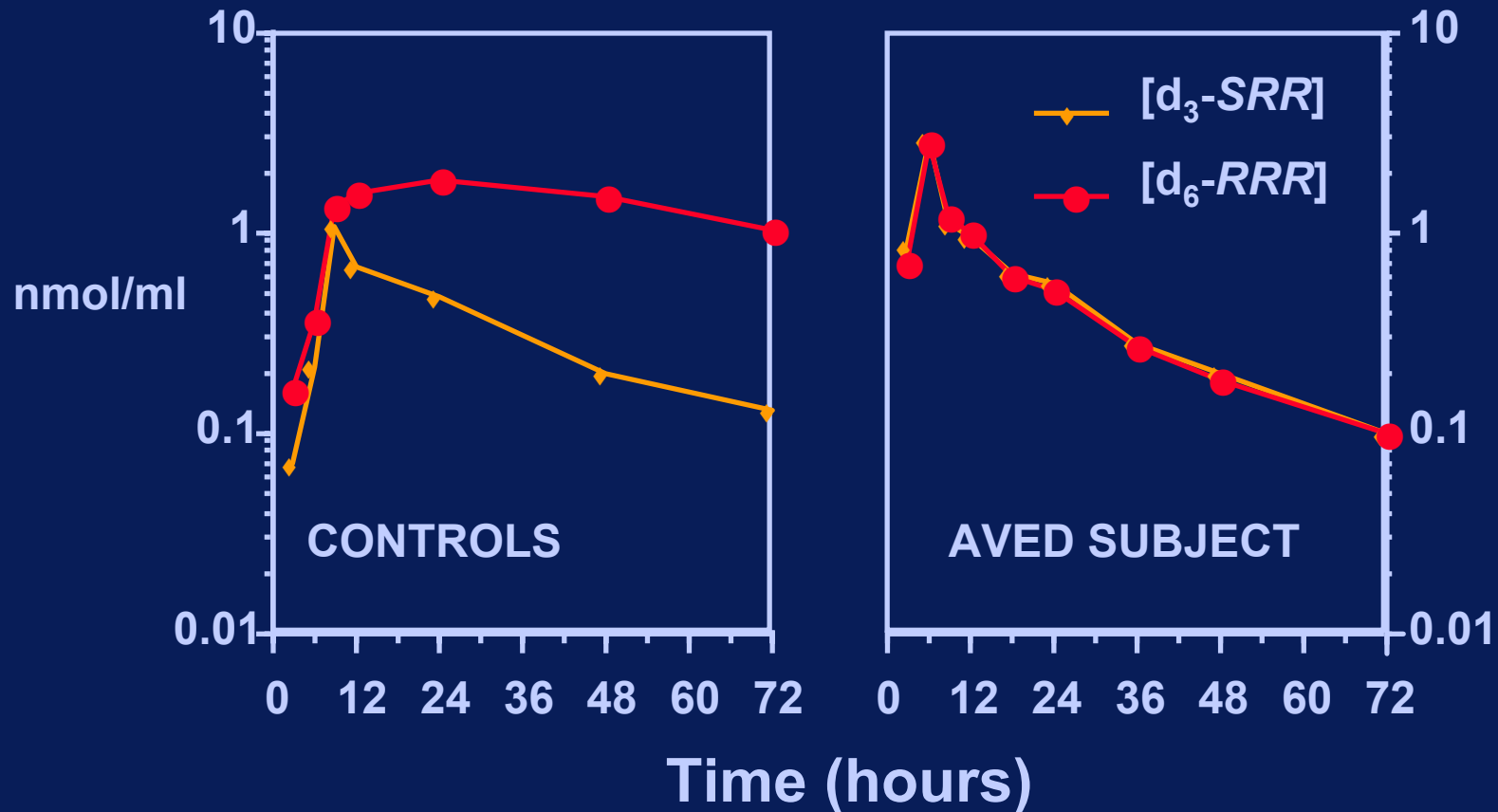
Traber, M.G. 1999. Vitamin E. In *Modern Nutrition in Health and Disease*. M. E. Shils, J. A. Olson, M. Shike, and A. C. Ross, eds. Williams & Wilkins. Baltimore. p347-362.

Clinical Features and Associated Neuromuscular Lesions in Human Vitamin E Deficiency

- Loss of Position and Vibratory Sensation
 - Peripheral Nerve
 - Posterior Columns
- Ataxia
 - Cerebellum
 - Spinocerebellar tracts
- Weakness
 - Skeletal Muscle

Traber, M.G. 1999. Vitamin E. In *Modern Nutrition in Health and Disease*. M. E. Shils, J. A. Olson, M. Shike, and A. C. Ross, eds. Williams & Wilkins. Baltimore. p347-362.

Plasma deuterated α -tocopherol concentrations in controls and subject with ataxia with vitamin E deficiency (AVED)



Traber, M.G. *et al. J Clin Invest.* 85: 397-407, 1990.

Vitamin E Definition

- Recommended intakes limited to the 2*R*-stereoisomer forms of α -tocopherol
 - *RRR*- α -tocopherol
 - Half of the stereoisomers in *all rac*- α -tocopherol
 - No other forms such as γ -tocopherol or tocotrienols meet vitamin E requirement
- All forms of supplemental α -tocopherol used to establish the UL(upper limit)

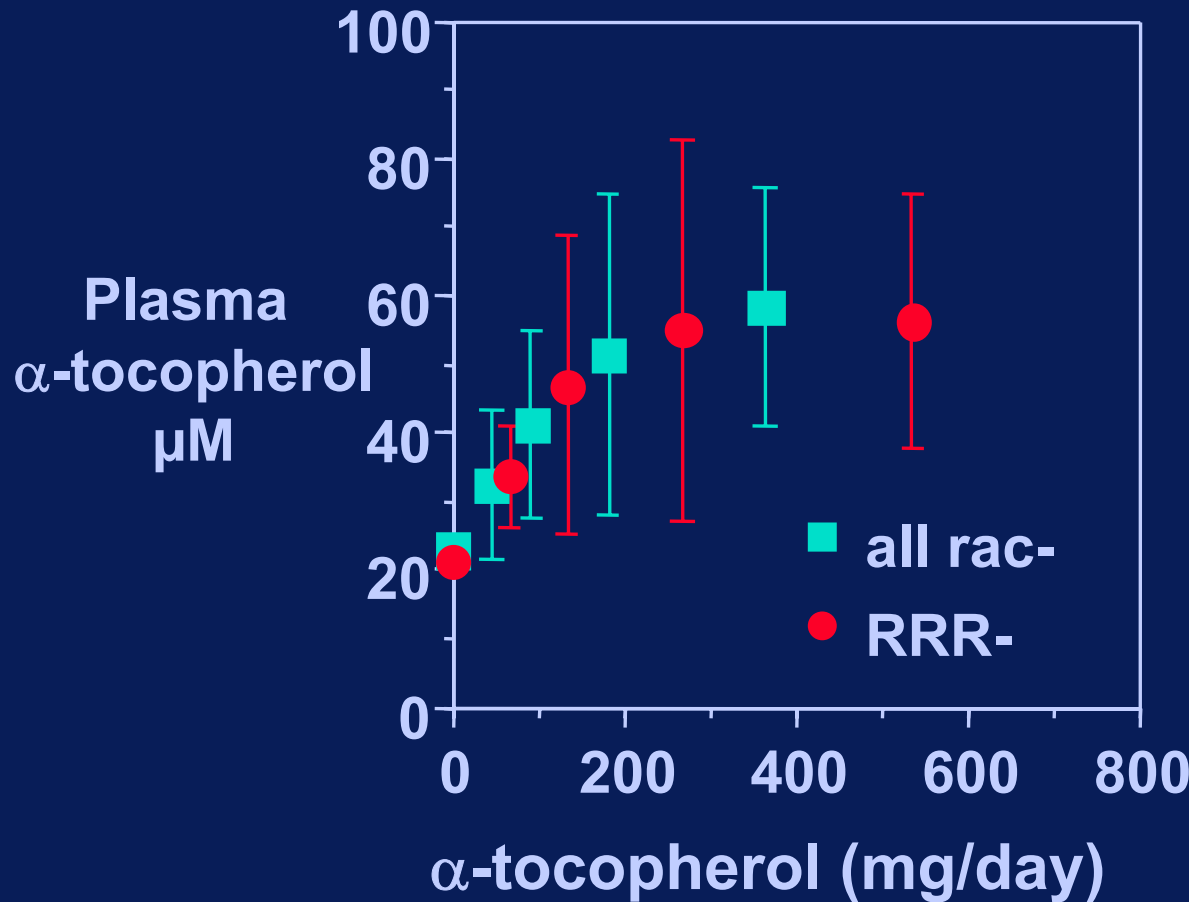
Food and Nutrition Board and Institute of Medicine. 2000. *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. National Academy Press. Washington, DC.

Estimated Average Requirement (EAR) and Recommended Daily Allowance (RDAs) for α -Tocopherol (mg/day)

<u>Life Stage</u>	<u>EAR</u>	<u>RDA</u>
19+ yrs, M	12	15
19+ yrs, F	12	15
Pregnancy	12	15
Lactation	16	19

Food and Nutrition Board and Institute of Medicine. 2000. *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. National Academy Press. Washington, DC.

Plasma α -Tocopherol in Response to Vitamin E Supplements



α -tocopherol (α -T) and α -tocopheryl acetate (α -TAC) from supplements:
 1 IU *RRR*- α -TAC divided by 1.36 equals mg *RRR*- α -TAC
 1 IU *all rac* α -TAc divided by 2 equals mg *2R*- α -TAC

400 IU Vitamin E =
 294 mg *RRR*- α -TAC
 or 268 mg *RRR*- α -T

200 mg *2R*- α -TAC
 Or 182 mg *2R*- α -T
 Devaraj *et al. Arterio Thromb Vasc Biol* 17:2273, 1997

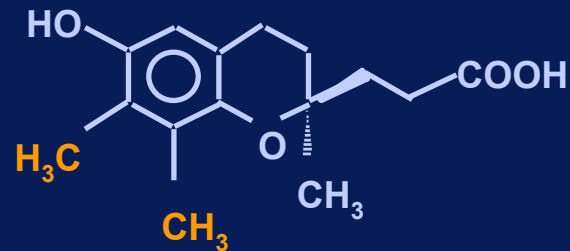
Vitamin E Metabolites

α -tocopherol
metabolite,
 α CEHC



2,5,7,8-tetramethyl-2(2'-carboxy-ethyl)-6-hydroxychroman

γ -tocopherol
metabolite,
LLU α



2,7,8-trimethyl-2(2'-carboxy-ethyl)-6-hydroxychroman

Schultz, M. *et al.* *Am J. Clin. Nutr.* 62: 1527S-1534S, 1995.

Wechter, W.J. *et al.* *Proc. Natl. Acad. Sci. USA.* 93: 6002-6007, 1996.

Summary

- Vitamin E requirement in humans limited to α -tocopherol
- Liver controls plasma vitamin E concentrations
 α -TTP facilitates α -tocopherol secretion into plasma
- Vitamin E deficiency results from genetic defects in α -TTP
- Vitamin E metabolism may be important in regulating liver vitamin E