Professor Hansen makes an important point that arose from my imprecise use of the word “largely” in the sentence to which he refers (1). Regrettably, I failed to note the significance of linoleic acid itself functioning in the maintenance of the water barrier in skin. In young rats, the scaly skin syndrome of omega-6 essential fatty acid (EFA) deficiency appears about 2 months after placing animals on EFA-deficient diets (2). Hansen (1) references the brilliant biochemical studies in this area by Brash and co-workers. A second feature of omega-6 EFA dietary deficiency is a failure to grow properly (3). This phenotype follows the onset of the scaly skin syndrome, that, as noted by Dr. Hansen, is partly due to dysfunction of the water barrier in skin.

Other deleterious effects of omega-6 EFA deficiency noted in the early dietary studies involve dysfunctional renal development and problems with female reproduction (2). Subsequent biochemical and genetic studies implicate defective prostaglandin (PG) formation as causal. Cyclooxygenase-2 (COX-2) knockout mice typically, although not uniformly, exhibit kidney abnormalities leading to early death. Multiple female reproductive problems of EFA dietary deficiency are associated with a lack of COX-2–mediated PG formation (3). An absence of COX-1–mediated PGF2α formation leads to failure of parturition (4, 5). Early post-partum deaths observed in EFA deficiency are caused by the absence of COX-mediated PG formation required for closure of the ductus arteriosus (6). Clearly, PGs formed primarily from 20-carbon omega-6 arachidonic acid via COXs are important mediators of life-sustaining biologic events.

References