

Letter from Chicago

Grease and Greek

George Dunea

The beauty shops rang with excitement this year at the news that tretinoin cream could smooth out wrinkles and make you look young again. The telephones buzzed continuously at the local drug store, and countless customers came asking for the miracle cream. Parents raided their teenagers' supplies of acne cream; real estate agents lured prospective customers with free samples; and birthday guests came with gifts of tubes of tretinoin strapped to bottles of champagne to cure their hosts' dermatoheliosis. It was a splendid success story of grease curing Greek; and Ponce de Leon himself might have stayed at home to take the treatment rather than go looking for the fountain of youth.

Yet the initial article and the accompanying editorial were conservative enough (*JAMA*, 22-29 January, pp 527-32, 569-70). Non-dermatologists learnt that there were two types of skin aging, extrinsic and intrinsic. Extrinsic aging could be caused by wind, heat, cigarette smoke, chemical toxins, or sunlight. Only that caused by sunlight, known as dermatoheliosis or photoaging, had responded to topical tretinoin. Widely used for acne, this retinoid derived from vitamin A (retinol) prevents inflammation, keratinisation, and cell growth. It was used in a 16 week study in which 30 patients applied the cream to one forearm and one side of the face but not the other. All but one improved, their wrinkles smoothing out, their solar freckles fading, and their skin recovering some of its original smoothness and pinkness. Almost all patients (92%) had some degree of dermatitis, (redness, swelling, or smarting) but this was mild. The authors emphasized that tretinoin worked only in the extrinsic form of aging, characterized by wrinkled, yellowed, thickened, rough, telangiectatic, hyperpigmented or hypopigmented skin-and then mainly in the early and not too advanced cases. The thin, inelastic, wrinkled skin of intrinsic aging might still justify a voyage into the Caribbean sunset in search for a miracle cure.

Dermatologists under siege

Yet the impact of the article was dramatic. The drug stores ran out of cream, the price of the manufacturers' shares ran up, and dermatologists had to run away from the besieging public. They tried to explain that this was serious business, that tretinoin was a drug with side effects not just another facial cosmetic. But a nurse working for a dermatologist revealed that everybody thought that she looked 10 years younger since she had begun using the cream. In the face of such persuasive evidence interest was likely to remain high with sales booming. It was also fortunate that the news of the youth cream came at a time of growing awareness of the harmful effects of sunlight on the skin. To some extent suntans are losing their popularity as brown teenage beauties learn that they will look wrinkled sooner than need be. We are told that in parts of California suntan is out and pallor is in, though some "nouveaux pales" still hanker after a suntan, even if it has to come out of a bottle. In a work oriented society, moreover, working on a suntan could be viewed as reflecting a tendency not to work at anything else. Yet even though the glamorous suntan has not always been with us, having become fashionable somewhere around 1922 in France, it may be too early to write it off for good. But increasingly, sun

protection creams are being talked about with interest round swimming pools. Together with many other products they fall into the vague border line between cosmetics ("for cleansing, beautifying, promoting attractiveness, or altering appearances") and true drugs ("intended to affect the structure of any function of the body")—a subject of some recent controversy.

The issue has lately interested the Food and Drug Administration (FDA). Concerned with drugs, not beautification, the FDA does not particularly care if women buy exquisite creams packaged in eyedroppers and bearing exotic French names. It is accepted that most women enjoy using these chic products and do not object to the accompanying pseudoscientific blurb. But apparently some touchy competitors complained about the claim that a certain cream—"that made skin cells act young again"—had been discovered by the world renowned heart surgeon Christiaan Barnard in a Swiss laboratory. As the FDA began to look into the matter its scientific susceptibility was offended by claims that creams could rebuild the epidermis, encourage fresh cells to rise to the surface, permeate the very innermost layer of the skin, and reverse the visual signs of age on surface skin. Eventually it warned the cosmetics industry to get its advertising act together or risk "seizure and injunction." Let the ladies spend what they would, thought the FDA, especially if it was only their husbands' money. Let them think they would look sweet 16 again. But let nobody break the law by pretending that there was a scientific basis to the tomfoolery. Let nobody claim that *Crème à la Vache* activated sodium potassium cotransport or promoted calcium entry into aging cells. For this would make the cosmetic a drug, thus rendering it subject to the most rigorous evaluation.

"Miracle drug" caused 1000 spontaneous abortions

Then the FDA stumbled across another retinoid, isotretinoin (Accutane), approved in 1982 as an oral remedy for disfiguring cystic acne. Though hailed as "almost a miracle drug," it had been recognized all along as causing congenital defects if taken by pregnant women. It seems that the drug has been overprescribed; even some dermatologists would like to see tighter controls on its use. According to official reports some 62 cases of birth defects may have been associated with its use. But lately the three FDA scientists extrapolated findings from a Michigan study and announced that isotretinoin was causing 1300 birth defects and 1000 spontaneous abortions a year. The subsequent developments were predictable: a series of sensational headlines; outcries by consumer advocates that the drug should be banned, restricted, or that doctors should be made to fill in so many forms that they would think twice before prescribing it; disclaimers by the manufacturers that the extrapolation was unjustified; outraged responses from practitioners pointing out that the drug's merits outweighed the risk; and an equally outraged article in the *Wall Street Journal* about heartless bumbling bureaucrats. In late April the FDA's scientific advisory panel recommended that isotretinoin should remain on the market but that the agency should require stronger labeling as well as negative pregnancy tests on women of childbearing age. Some FDA officials wanted a photograph of a deformed infant placed on each package, but the manufacturers thought that it might be more appropriately included with the consent forms to be signed in the doctor's office. A spokesman for the agency said that there was still some "negotiating room" before final regulations would be issued.