Aging skin

&

Vitamin A (retinoids)

Major Functions of Skin

Barrier

(excludes infectious agents & some chemicals; retains moisture, prevents dessication)

Temperature control

(perspiration, insulation)

Receptor of sensory stimuli

(touch, pressure, pain, temperature)

Biosynthesis

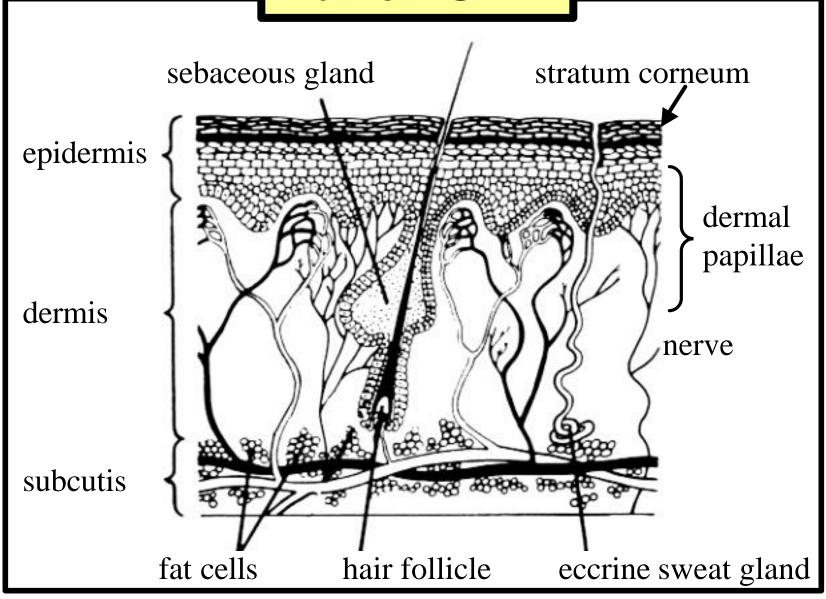
(vitamin D, melanin, estrogen)

Inflammatory/immune reactions

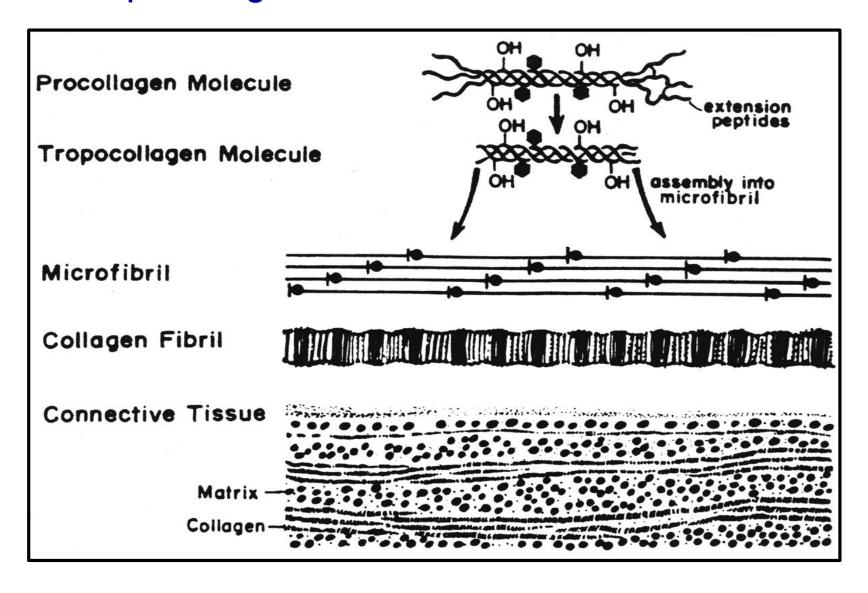
(contact dermatitis)

Excretion/secretion (sweat, milk, pheromones?)

Human Skin



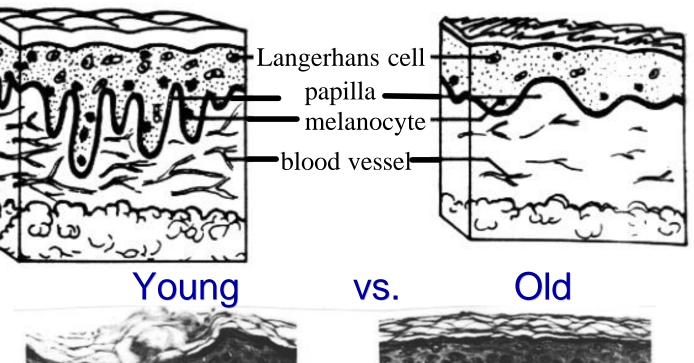
The composition of a collagen fibril and the distribution of tropocollagen molecules in connective tissue.



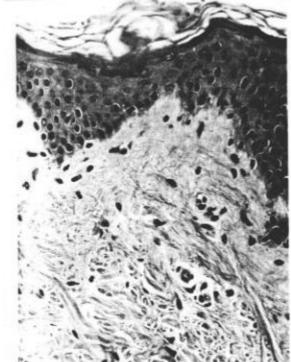
stratum corneum epidermis

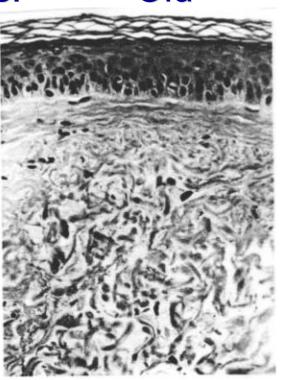
dermis

subcutis



Aging Skin





Changes in Aging Skin

Events

Epidermis

cell production, melanocytes, Langerhans cells

Dermis

density, #cells, blood vessels

Other

sweat, sebaceous glands, hair follicles

Functional consequences

wound healing, immunity, tanning, elasticity, clearance of foreign substances, thickness

blisters, infection, roughness, dryness, cancer, fragility, insensitivity

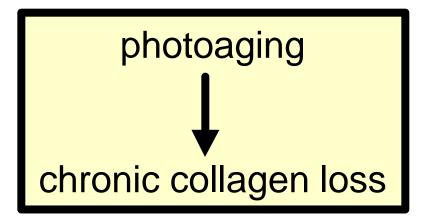
Photoaging



UV (ultraviolet) radiation

affects gene expression in skin

(↑collagenase ↓collagen)



acute collagen loss imperfect repair microscars

Treatments for photoaged skin

antioxidants

a-hydroxyacids

Retinoids (vitamin A metabolites and analogs)

"Of these three approaches only topical retinoids, particularly retinoin (all-trans-retinoic acid), have a well documented ability to repair photoaged skin at the clinical, histological and molecular level. Furthermore, the use of topical retinoids may actually prevent photoaging."

C.E. Griffiths, "Drug treatment of photoaged skin", Drugs and Aging 14, 289-301 (1999).

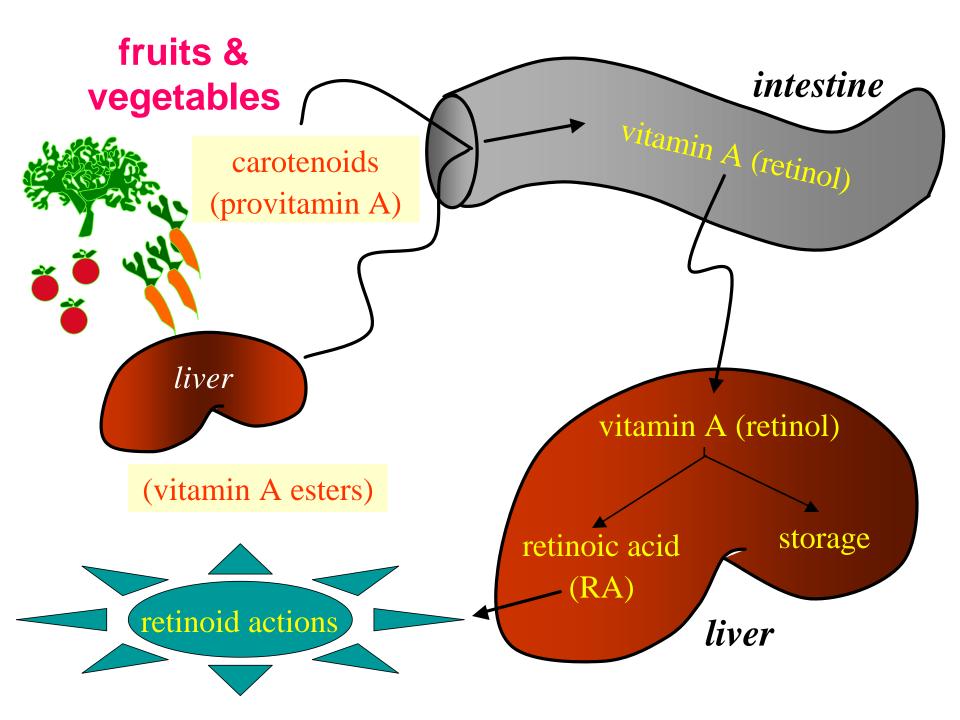
Vitamin A (retinol) is the parent retinoid

vision (nyctalopia)

development, growth, reproduction

epithelia (skin, trachea, digestive system)

immune system, nervous system



Cells (keratinocytes) convert vitamin A (retinol) into all-trans-retinoic acid (atRA).

atRA regulates gene expression through nuclear hormone receptors and thereby controls cell differentiation/function.

atRA (tretinoin) = Retin-A[®], Renova^a
Accutane[®]

Effects of atRA (Renova®) on photoaged skin

18 months topical treatment once daily



before after

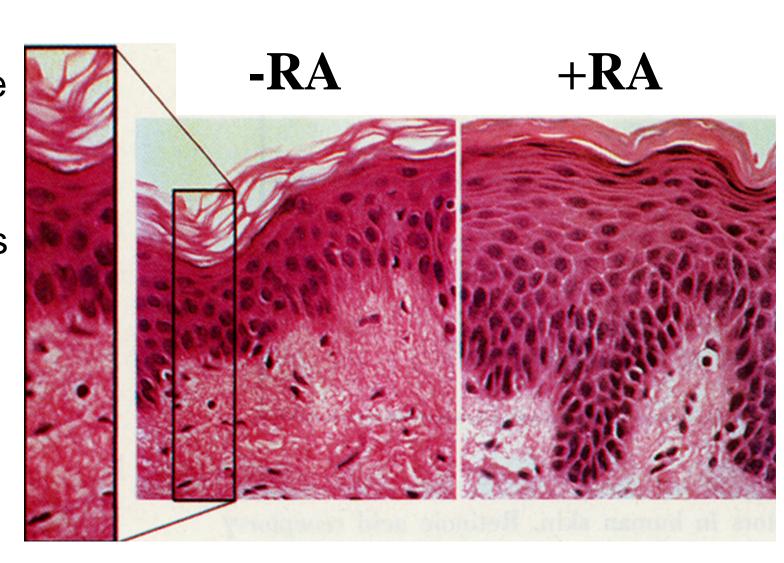
C.N. Ellis, et al., J. Amer. Acad. Dermatology 23, 629-637 (1990).

Effects of retinoic acid on human skin

protective barrier

epidermis

dermis



Retinoids and cystic acne





Systemic dosing of RA and cystic acne





before

after RA

Severe Darier's disease

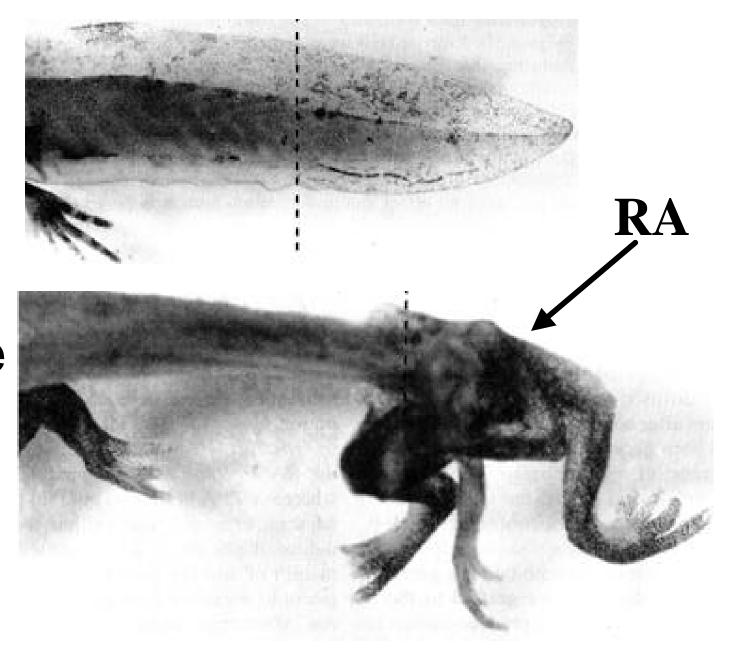


Retinoids and psoriasis vulgaris



before after RA

RA
effects
on a
tadpole
tail



Vitamin A toxicity

Single dose—100-fold > DRDA in adults, 20-fold > in children

Chronic intake—10-fold > DRDA

RA is teratogenic!

Retinoids and over-thecounter skin products

