

## Skin Color

Human Pigmentation and Adaptation

## Skin

- The body's largest organ
- Functions in many ways
  - Thermoregulation
  - Protection from physical and chemical injury
  - Protection from invasion by microorganisms
  - Manufactures essential nutrient

## Skin Color

- As one of the most conspicuous human polytypic variations, skin color has probably attracted more scholarly attention than any other aspect of human variability
- Skin color has served as a primary feature in most systems of racial classification

## Measurement of Skin Color

- By the latter half of the nineteenth century, while anthropologists still had no clear idea of the underlying causes of pigmentation, they began to devise measurement techniques to use skin color in racial classification
- Broca established a 34 tone scale, which was simplified by his student Topinard
- These techniques were used into the 20<sup>th</sup> century until the introduction of the reflectance spectrophotometer in the early 1950s

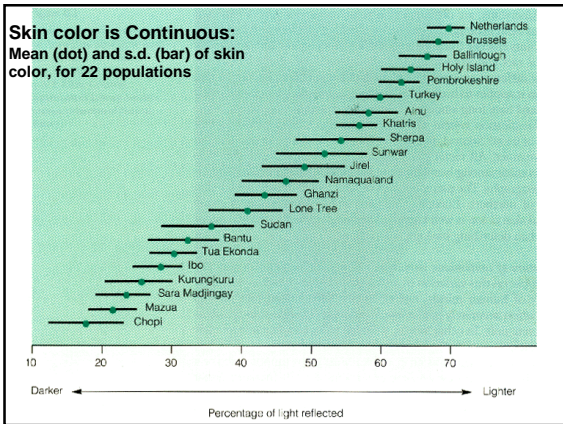
## Reflectance Spectrophotometer

- A Reflectance Spectrophotometer shines a light of a specific wave length, using a filter, and measures the intensity of light reflected by the skin
  - The technique involves alcohol wash of the skin on the inner upper arm
    - allow time for local circulation to return to normal
    - shine light and measure reflectance

## Reflectance Spectrophotometry



Reflectance Spectrophotometer from Robins (1991:100)



### Biological Determinants of Skin Color

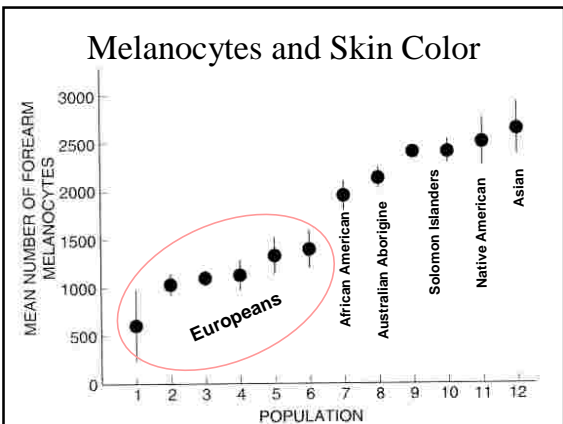
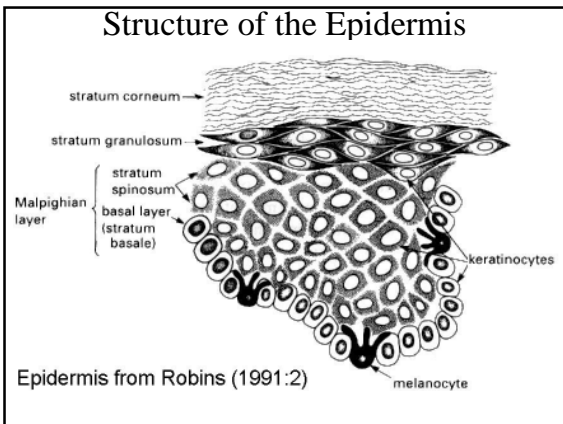
- The pigments **Carotene**, **Hemoglobin**, and **Melanin** are involved in skin color
- Carotene, the least common skin pigment results in a yellowing of skin
  - Results primarily from the over-consumption of carotene containing foods (like carrots)
  - This pigment is significant almost exclusively in pathological or abnormal skin coloration

### Hemoglobin

- Hemoglobin is the complex molecule responsible for transport of oxygen throughout our bodies
  - It is the primary protein constituent of Red Blood Cells
    - Oxygenated hemoglobin has a reddish hue
      - Produces a pinkish tint to lightly pigmented skin
    - Deoxygenated hemoglobin has a purplish color
      - Produces the bluish tint to lightly pigmented skin that is characteristic of oxygen deprivation and suffocation

### Melanin

- The primary determinant of variability in human skin color is the amount, density, and distribution of the pigment melanin
- Melanin has a dark brown/purple/black color that is intensified by denser compaction of the melanin granules in the cells of the upper layers of the skin



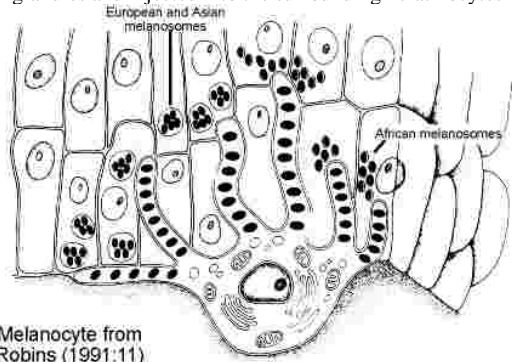
## Layers of the Epidermis

- The **stratum basale** consists of columnar cells, the keratinocytes with about 10% of the cells comprising melanocytes
  - This is the germinal level of the skin which gives rise to the outer layers of cells and the melanin granules that pigment them
    - This is also where 90% of Vitamin D synthesis takes place
- The **stratum spinosum** consists of several layers of irregular polyhedral cells (keratinocytes) flattened on their edges

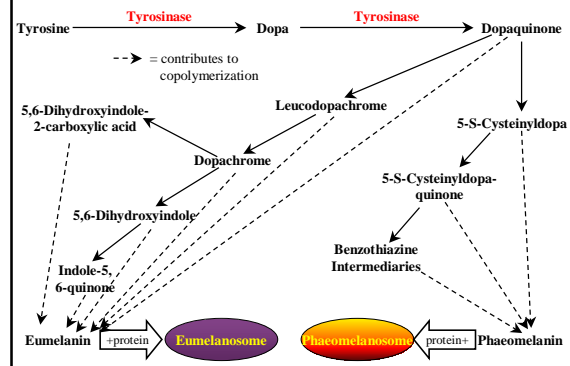
## Layers of the Epidermis

- The **stratum granulosum** consists of several layers of flattened polyhedral cells with their long axis parallel to the skin surface
  - Cytoplasm contains keratohylin
  - As the cells increase in size they die out
- The **stratum corneum** is composed of a varying number of layers of dead keratinized cells fused to one another except for the outer edge where flaking takes place

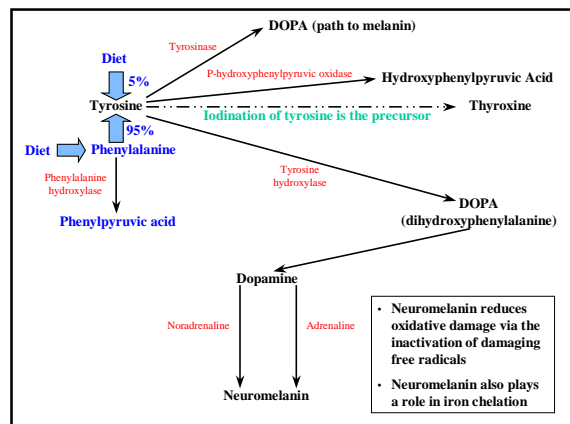
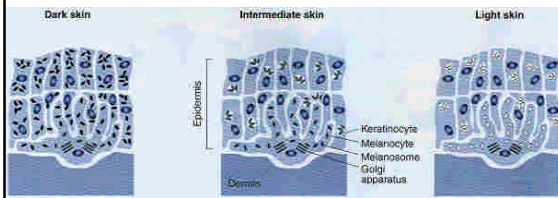
Melanocytes synthesize melanin which is combined into granules and injected into the surrounding keratinocytes



## Melanin Metabolism

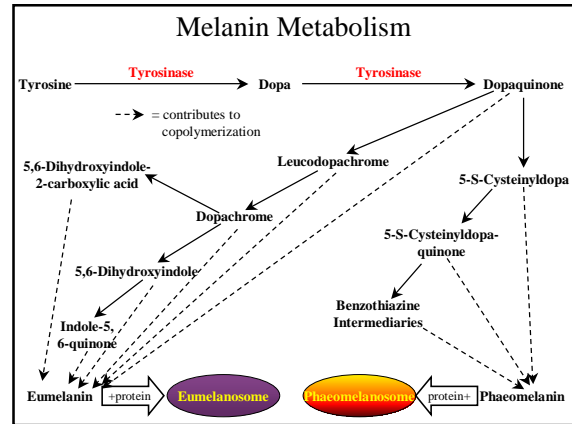


In dark skin, melanosomes accumulate eumelanin and remain as single particles, while in lighter skins they contain increasing amounts of pheomelanin and cluster in membrane bound organelles, lysosomes



## Phenylalanine Metabolism

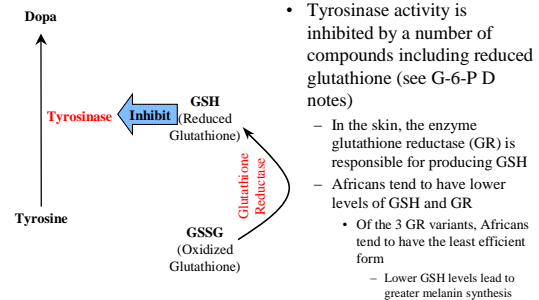
- Pleiotropy: A situation whereby several seemingly unrelated phenotypic effects are influenced by the action of a single gene
  - **Phenylalanine hydroxylase** insufficiency causes phenylketonuria: PKU
    - Growth retardation (small body, small head size), mental retardation (mean IQ between 20-30), light hair and skin
  - **Tyrosinase** deficiency causes albinism
    - Can have reproductive implications including enhanced or reduced fertility depending on mating preferences.
  - **P-hydroxyphenylpyruvic oxidase** deficiency causes tyrosinosis
    - Increased levels of circulating tyrosine and tyrosine metabolites
    - Does not abnormally increase synthesis of melanin
  - **Deficient enzymes in the iodination of tyrosine** on this pathway causes hereditary cretinism
    - Similar to iodine deficiency disease, but not treatable by diet



## Melanin Synthesis

- The metabolic pathway to melanin is extremely complicated, involving several intermediate steps
  - Starts with the amino acid **tyrosine** oxidized by the copper-containing enzyme **tyrosinase** to dihydroxyphenylalanine (dopa) and then to dopaquinone
    - A mutation to the gene for the enzyme tyrosinase that produces a protein with decreased functionality will result in a reduced production of melanin
      - In the extreme, this produces a genetic form of albinism

## Tyrosinase inhibition



- Tyrosinase activity is inhibited by a number of compounds including reduced glutathione (see G-6-P D notes)
  - In the skin, the enzyme glutathione reductase (GR) is responsible for producing GSH
  - Africans tend to have lower levels of GSH and GR
    - Of the 3 GR variants, Africans tend to have the least efficient form
      - Lower GSH levels lead to greater melanin synthesis

## Melanin Synthesis, 2

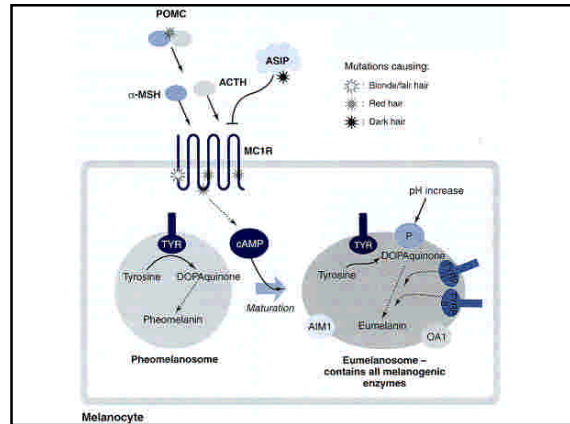
- Dopaquinone undergoes a series of non-enzymatic reactions and rearrangements forming the different molecules that are co-polymerized to make up one of the types of melanin
  - Eumelanin is the dark brown/purple/black compound found in skin and hair
  - Pheomelanin is the yellow-to-reddish-brown pigment which is present in red hair resulting from the addition of the amino acid cystine
- Both forms of melanin combine with other proteins to form the melanosome that is distributed from the melanocyte to surrounding cells

## Genetics of Skin color

- Skin color is a polygenic trait, meaning multiple genetic loci are involved in determining skin color
  - Multiple genes working together produce a continuous distribution in a “Bell Shape” curve of degrees of light to dark.
  - Early models suggested 2 or 4 major genes
    - Recent work suggests many genes working together in very complex, additive and non-additive combinations
    - The non-enzymatic conversion of dopaquinone into eumelanin and pheomelanin and their combination into melanosomes is affected by several genetic loci

TABLE 15.1: EXAMPLES OF HUMAN GENES ASSOCIATED WITH PIGMENTATION PHENOTYPES

Gene	Protein/function	Human human phenotype
<b>Melanocyte function</b>		
TYR	Tyrosinase – oxidation of tyrosine, dopa	Oculocutaneous albinism (OCA) type 1
TYRP1	P-protein, regulating pH of melanosomes	OCA2
TYRP2	Oxidation of DOPA, stabilization of tyrosinase	OCA3
SLC45A2	Membrane-associated transporter protein	OCA4
ASIP	Agouti signal protein – pheomelanogenic regulator	Association with dark hair and brown eyes
MC1R	Melanocyte-stimulating hormone (MSH) receptor	Red hair or freckles/spots
PCSK9	Pro-protein-converter (from which MSH and other endocrine hormones are produced)	Red hair with severe early-onset obesity and diabetes mellitus
CD44	G protein-coupled receptor	Striate albinism type 1
<b>Melanosome transport/signaling by keratinocyte</b>		
WDR36	Myosin VIIa motor protein	Straussler oscillans (ectodermal part) albinism
RAB27A	RAS family protein	Straussler oscillans
<b>Developmental</b>		
MITF	c-myc receptor – melanocyte migration	Piloerection
FOXP2	Transcription factor in neural tube development	Waardenburg syndrome type 2
MITF	Transcription factor	Waardenburg syndrome type 1

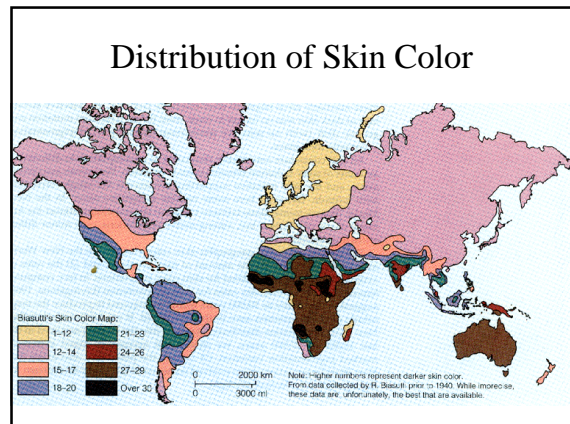
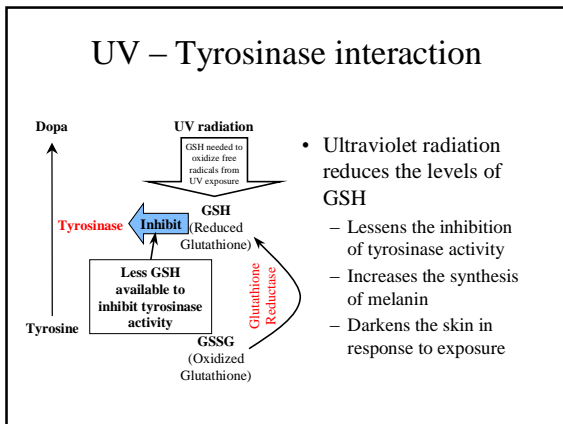


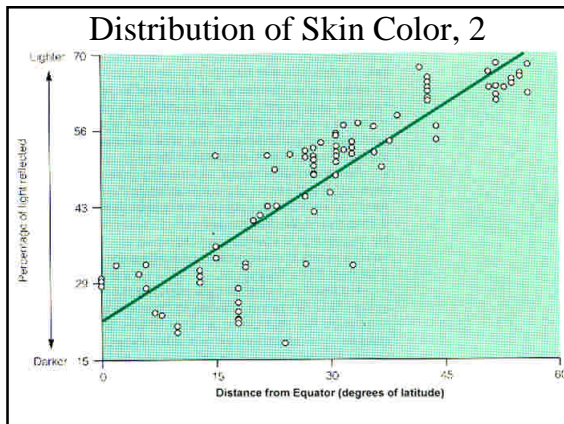
## Tanning

- Tanning is a two-stage acclimatization response of the skin to increasing levels of UV exposure
  - Immediate tanning** is the transient brownish tan following exposure to UV-A and visible light
    - Reaches a maximum within 1-2 hours after exposure
    - Fades between 3-24 hours after exposure
  - No new melanosomes formed, so the likely mechanism is the photo-oxidation of existing melanin or other epidermal elements

## More Tanning

- Delayed tanning** is the durable brownening caused by repeated exposure, primarily to UV-B but UV-A and visible light also play a role
  - Gradual process of skin darkening starting 48-72 hours after irradiation
    - Reaches a maximum 19 days after an exposure
    - Requires 9½ months for skin to return to original melanin content
  - Melanocytes enlarge, increase dendrite density, and experience other internal changes
  - Melanosomes increase in number and melanization





### Distribution of Skin Color, 3

- The clinal nature of skin color distribution suggests an association with environmental factors varying with latitude
  - Ultraviolet Radiation, in particular, the quantity of UV rays striking the surface of the earth from the sun
  - Temperature

### Just-So Stories about Skin Color

- Noah's curse on Ham's son Canaan
- Response to the heat of the sun
- Bile theory
- Aerobic theory
- Optic theory
- Pigmentation as pathology of adverse environment
- Result of disease
- Vitamin D, Folic Acid, Cold tolerance

### Noah's curse on Ham's son Canaan

- An early explanation of dark skin comes from the biblical story of Noah's curse (Genesis Chapter 9, King James Version):
  24. And Noah awoke from his wine, and knew what his younger son had done unto him.
  25. And he said, Cursed be Canaan; a servant of servants shall he be unto his brethren.
  26. And he said, Blessed be the LORD God of Shem; and Canaan shall be his servant.
  27. God shall enlarge Japheth, and he shall dwell in the tents of Shem; and Canaan shall be his servant.
  - Nowhere does this mention darkening of the skin, although other sections of the bible, notably in Job and Isaiah associate curses with darkness

### A Biblical Account of Dark Skin Color

- Lamentations chapters 4 and 5 refer to skin color becoming dark as a result of famine
  - Ch 4, v 8: Their visage is blacker than a coal (alternate translation: darker than blackness); they are not known in the streets: their skin cleaveth to their bones; it is withered, it is become like a stick.
  - Ch 5, v 10: Our skin was black like an oven because of the terrible famine (alternate translations: terrors or storms)

### Voyages of Discovery

- By the time the slave trade was actively operating on the West African coast in the mid to late 16<sup>th</sup> century, curiosity about the cause of dark skin color was growing
- The accepted environmental explanation was that the action of the sun's heat was the cause of the differences in the complexion of Europeans and Africans

## 17th Century Developments

- Accumulating evidence made it clear that the “heat of the sun” explanation was not satisfactory
  - The skin color of the aborigines of North America in similar climates to Europeans and Africans was neither black nor white, but olive
  - Africans were found to vary in color from “black to yellow” according to sources of the day
  - Africans forced into European settings were showing no lightening of skin and those Europeans living in Africa were not appreciably darkening
- The view emerged that the African’s blackness was innate and permanent

## Thomas Browne (1605 – 1682)

- This English physician published his view in his 1646 *Pseudodoxia epidemica*:
  - “If the fervour of the Sun, or intemperate heat of climate did solely occasion this complexion, surely a migration or change thereof might cause a sensible, if not a total mutation; which notwithstanding experience will not admit. {Despite their transplantation, there remains among their descendants} a strong shadow of their Originals: and if they preserve their copulations entire, they still maintain their complexion. . . .{L}ikewise, fair or white people translated in hotter Countries receive not impressions amounting to this complexion”
  - He also dismissed the Ham’s curse explanation as a foolish tale

## Biological Differences?

- Attempts made to resolve whether differences in skin color was due to innate differences in biological structure or transient response to the sun’s heat
  - Santorio Santorio (1561-1636): 1614 *De statica medicina* skin’s complexion was determined by the presence of black bile
    - Revival of a notion from the ninth century Arabian physician ‘Ali al-Tabari in his medical compendium *Paradise of Wisdom*
  - Supported by Italian anatomist Malpighi (1687)
    - Determined that dermis and stratum corneum is colorless in both Blacks and Whites, he agreed with Santorius that the blackness of Africans must originate in the underlying mucous and reticular body—colored by bile
    - Early Eighteenth century anatomists reported the presence of black bile in the Malpighian layer

## To Bile or Not To Bile

- Scholars attempting to avoid the polygenetic implications of the bile theory clung to the work of the French surgeon Littré who failed to find a black gelatinous bile in the malpighian layer of Africans
- Monogenists began advocating a more complex view of environmental causes that harks back to Hippocrates’ *Airs, Waters, Places* focusing on the differential qualities of the atmosphere
  - This “aerobic” theory was championed by Du Bos in 1719 and picked up by others, including Blumenbach in his *Varieties of Man* in 1795

## Aerobic and Optic Theories

- Le Cat 1765 discerned black deposits he called “æthiops” in nerve tissues of animals
  - Without having any idea about the origin or role of these æthiops he was convinced that there was a relationship with the environment and he conjectured that Negroes had more of the structures than Europeans did, making them the basis of the dark complexion of the Africans
- Patot 1733 claimed that complexion differences were based on the ability of the human skin to transmit light—the “optic” theory of skin color

## A New World Perspective

- John Mitchell (1744) published the first major scientific study of skin color in the New World
  - Compared skin of colonial Whites and African slaves in Virginia
    - Concluded there was no anatomical basis for the bile theory
    - Only structural difference was thicker skin among the Africans
      - Applied Newtonian optics to suggest that skin color was based on thickness of the skin and its ability to transmit light
      - As thickness increased, the skin appeared darker
        - African’s thick skin prohibited the transmission of any color through them
    - He also conjectured that the original skin color of man was neither black nor white but something in between with Europeans and Africans represented divergent extremes caused by the degenerative influences of the environment

## Degeneration of the Primordial Type

- Buffon argued that skin color differences were reflective of the geographical degeneration of the primordial type
  - He suggests restoration of the “degenerate races to the purity and vigor of the original type” would require the transplantation of these people to a more temperate zone plus a change of diet and a long span of time

## Pigmentation as Pathology

- Laitau (1724) argues that dark skin color is a congenital malformation—already present in African fetuses
- Rush (1795) claimed the skin color of the Negro was derived from leprosy
  - He argues that Africans suffer from a congenital disease so mild that excess pigment was the only symptom
- Albinism and other depigmentation conditions among Africans were seen as reversion to the original complexion

## An “Universal Freckle”

- Samuel Stanhope Smith (1810) used the depigmentation of Henry Moss, an African American from Virginia to suggest that pigmentation was nothing more than an “universal freckle”, occasioned by environmental exposure to sunlight
- He argued that climate affected skin color
  - Evidence: the darkening and lightening of complexion with the seasons
  - Cold air “chafes the countenance and increases the ruddiness of the complexion”

## Physiology of Pigmentation

- Late in the 19<sup>th</sup> century the process of melanization in plants was discovered to be dependent on the enzyme tyrosinase
- German histochemist Bruno Bloch demonstrated in 1927 that this same pathway was involved in pigmentation of human skin *in vitro*
- By 1950 the cells where these reactions took place, the melanocytes, were identified and it was found that these cells originate embryonically in the neural crest
- By 1955 the UV protective effects of melanin in the skin were demonstrated

## 20<sup>th</sup> Century Just-So Stories

- The discovery of the interaction between melanin and UV led to a number of explanations of skin color
- The association between vitamin D synthesis, UV radiation, and skin pigmentation was suggested in the 1930s but it was largely ignored until revived by Loomis in 1967
  - Loomis proposed that the rate of vitamin D synthesis is governed by pigmentation and keratinization which affect the amount of UV penetrating to the *stratum granulosum*, making skin color responsive to UV levels

## Selection Favoring Dark Skin

- Selection favoring high levels of melanin pigmentation in areas of high Ultraviolet (UV) radiation may involve several selective agents
  - Sunburn can cause skin lesions and infections, preventing some degree of heat loss
  - Also predisposes to skin cancer
    - Highly pigmented skin provides partial protection so selection would favor dark skins in high UV areas



## Skin Cancer

- Skin cancer is found to be prevalent among light skinned individuals in tropical latitudes
- In Nigeria and Tanzania no albino over the age of 20 years was found to be free of malignant or pre-malignant skin lesions
- In Tanzania chronic skin damage was found in every albino infant by the end of the first year of life
  - This high rate and early evidence of skin damage suggests that cancer may have been a strong selective pressure in tropical areas

## Folic Acid Deficiency

- UV light causes denaturation (a chemical breakdown) of Folic Acid circulating in the blood
  - This can induce a deficiency even if the diet supplies adequate folic acid
    - Deficiency symptoms include anemia, infertility, and birth defects, especially neural tube defects
  - High melanin content in the epidermis can protect circulating Folic Acid, thereby selecting for dark skin in low latitude areas

## Immune Suppression

- Ultraviolet light is known to suppress immune function
  - It has been hypothesized that increased melanization could protect the immune system by shielding the blood borne components of the system from UV
  - A recent study demonstrated that differences in skin color were not associated with differences in UV-induced immune deficits

## Selection for Depigmentation

- Selection favoring low levels of melanin pigmentation in ecosystems where there are low levels of UV radiation (primarily in the high latitudes) may also involve different factors:
  - The regulation of Vitamin D synthesis
  - Frost bite sensitivity and cold tolerance

## Regulation of Vitamin D

- Regulation of Vitamin D synthesis
  - Vitamin D in the body is derived primarily from the skin and secondarily from the diet
  - Vitamin D is synthesized in skin by the action of UV-B
    - Precursor molecule is 7-DHC or 7-dehydrocholesterol, which occurs in the strata granulosum and basale of the epidermis
    - UV-B exposure causes a photochemical (non-enzymatic) conversion of 7-DHC into previtamin D
      - High melanin content in skin reduces UV-B exposure and cuts photochemical conversion

## Regulation of Vitamin D, 2

- Previtamin D is transformed into vitamin D by a temperature dependent process over 2-3 days
- Vitamin D then diffuses into the blood vessels of the dermis
- The liver and kidney further transform the Vitamin D into 1,25-dihydroxyvitamin D which is the most active form of the vitamin
- The function of Vitamin D is to actively cause calcium absorption across the wall of the small intestine into the blood stream

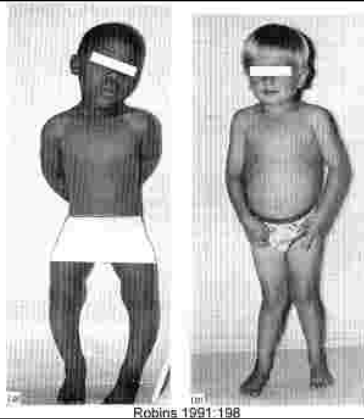
### Regulation of Vitamin D, 3

- Calcium is used for bone and tooth development as well as for nervous and muscle action
  - The skeleton serves as a calcium reservoir
  - If calcium levels in intracellular fluid drops, hormones are released to cause resorption of bone, placing calcium into circulation

### Regulation of Vitamin D, 4

- A deficiency of Vitamin D in infants and children causes Rickets, in adults a deficiency causes osteomalacia
  - Rickets refers to a defect in the calcification of growing bone so that the bones are structurally weak and unable to withstand mechanical pressure
    - Symptoms include muscle weakness, deformity of the long bones including bowed legs, knuckle-like projections along the rib cage (rachitic rosary), deformities of the pelvis that are often permanent
      - Long bone deformity impairs locomotion
      - Pelvic distortion can make childbearing dangerous--potentially killing mother and baby
  - Prior to widespread Vitamin D supplementation in the 1930s, Black women in the U.S. showed nearly 8 times greater pelvic deformity than White women

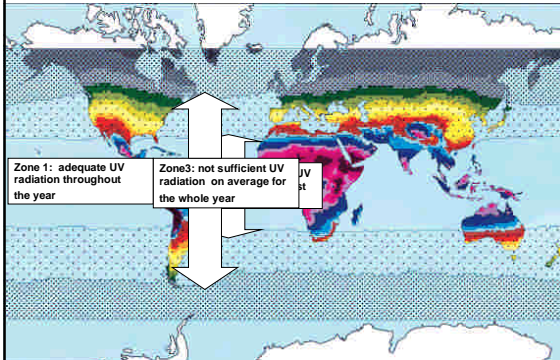
### Rickets



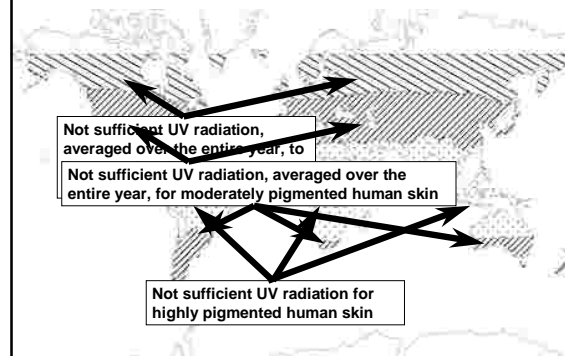
### Regulation of Vitamin D, 5

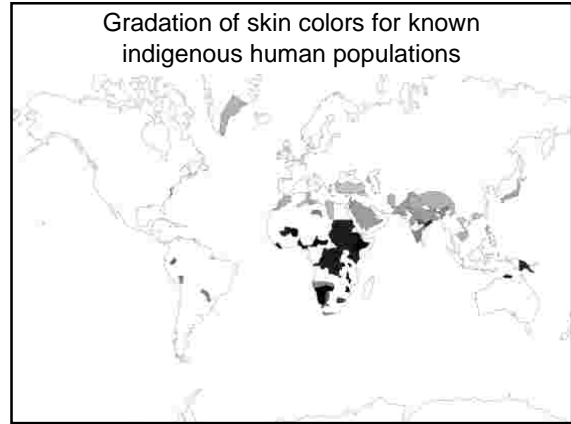
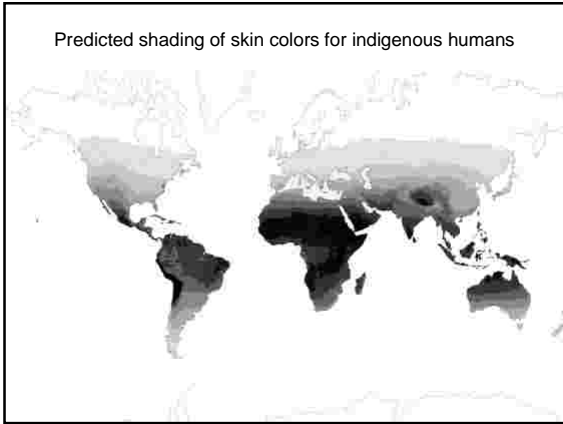
- Assuming that our ancestors had dark skin in the tropics, as hominids moved into higher latitudes there would have been substantial selection favoring lower melanin content in the skin to improve Vitamin D synthesis

### Potential for synthesis of previtamin D<sub>3</sub> in lightly pigmented human skin based on annual average UV



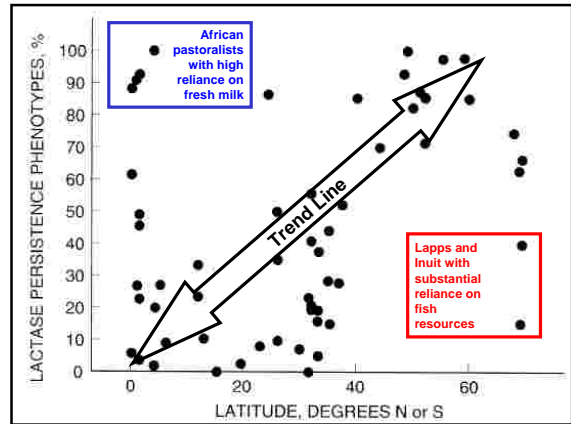
### Areas in which UV is not sufficient over the year for lightly, moderately, and highly melanized skin





Alternatives to skin production of Vitamin D for Calcium Absorption

- Lactose appears to promote the absorption of calcium
  - Human milk is 50% higher in lactose than cow’s milk, infants show better calcium absorption when nursing
  - Milk drinking increases calcium and lactose intake, may lessen selection on UV-Vitamin D
- Fish consumption increases intake of vitamin D
  - Fish eating would decrease selection for light skin color and biosynthesis of Vitamin D



Frost Bite and Cold Tolerance

- Frost bite sensitivity and cold tolerance
  - As our ancestors moved into higher latitudes they also would have been subject to colder temperatures
  - There is a great deal of anecdotal evidence and some medical record evidence (most from the Korean War) suggesting that individuals with heavily pigmented skin are more susceptible to frostbite
  - Animal studies demonstrate that melanocytes are more easily destroyed by freezing than the rest of the skin cells

Frost Bite and Cold Tolerance, 2

- Experiments with guinea pigs, cooling both dark and light skinned areas on the same animal, showed dark skin more susceptible to frost bite
- Frost bite cripples hands and feet causing survival problems, and secondary infections including gangrene may be fatal

## Sexual Selection

- Mating preference for skin color was promoted by Darwin as being one of the primary reasons for differences in skin color between the races of man
- Recently Aoki (2002) has argued that this is the primary reason for the distribution of aboriginal skin color

## Sexual selection and skin color

- Aoki argues that selection is unidirectional favoring dark skin to prevent sun burn, skin cancer, folate denaturation, etc.
  - This selection would be relaxed at higher latitudes with lower UV stress
- He suggests that there is a near universal preference for light skin in human mate selection
  - As selection lessened at higher latitudes, this intersexual selection for lighter skin color would become a stronger force driving skin color genes in the direction of less pigmentation
- The clinal distribution of skin color results from the balance between natural and sexual selection

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