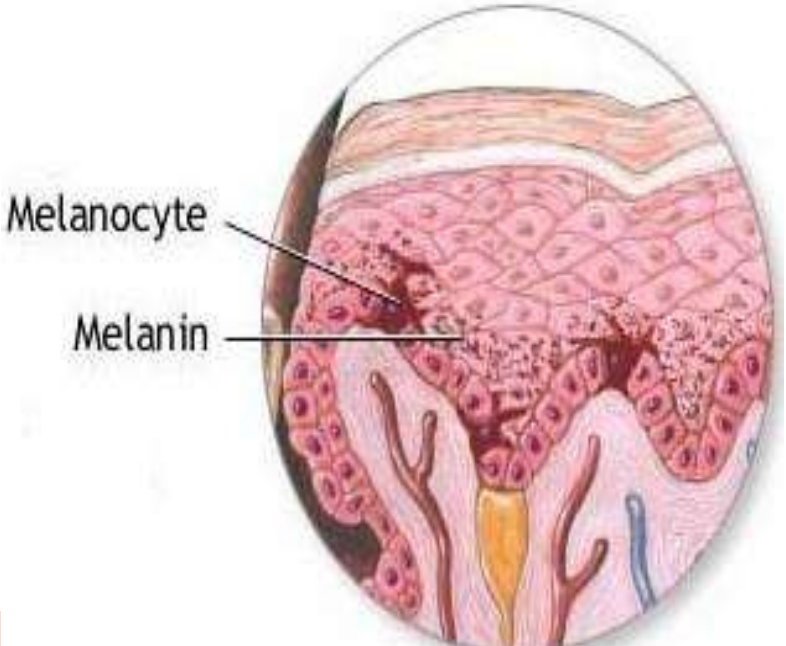
Department of Oral Medicine & Radiology
ANIL NEERUKONDA INSTITUTE OF DENTAL SCIENCES

PIGMENTED LESIONS OF ORAL MUCOSA

- Pigmentation is caused by endogenous or exogenous sources.
- Endogenous sources are hemoglobin, Hemosiderin & melanin.
- Exogenous sources are restorative materials,tattoo inks,medical metal induced & drug induced
- Melanin is a derivative of tyrosine,present in melanocytes.



Classification

- *Endogenous Pigmentation*
  - Focal Melanotic Pigmentation
    - ✓ Freckle/Ephelis
    - ✓ Oral/Labial Melanotic Macule
    - ✓ Oral Melanoacanthoma
    - ✓ Melanocytic Nevus
    - ✓ Malignant Melanoma
  - Multifocal/Diffuse Pigmentation
    - ✓ Physiologic Pigmentation
    - ✓ Drug Induced Melanosis
    - ✓ Postinflammatory(Inflammatory) Hyperpigmentation
    - ✓ Melasma(Chloasma)
  - Melanosis Associated With Systemic Or Genetic Disease
    - ✓ Hypoadrenocorticism
    - ✓ Cushing's Syndrome
    - ✓ Hyperthyroidism
    - ✓ Primary Biliary Cirrhosis
    - ✓ Vitamin B12 Deficiency
    - ✓ Peutz-Jeghers Syndrome
    - ✓ Café au Lait Pigmentation
    - ✓ HIV/AIDS Associated Melanosis

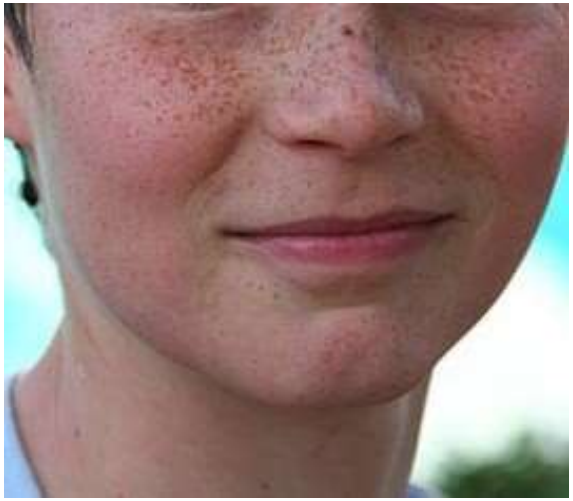
- Idiopathic Pigmentation
  - ✓ Laugier Hunziker Pigmentation
- Depigmentation
  - ✓ Vitiligo
- Hemoglobin & Iron-Associated Pigmentation
  - ✓ Ecchymosis
  - ✓ Purpura/Petechiae & Hemachromatosis

➢ Exogenous Pigmentation

- ✓ Amalgam Tattoo
- ✓ Graphite Tattoo
- ✓ Ornamental Tattoo
- ✓ Medicinal Metal Induced Pigmentation
- ✓ Heavy Metal Pigmentation
- ✓ Drug Induced Pigmentation
- ✓ Hairy Tongue

Freckle/Ephelis

- It is an asymptomatic,small,well circumscribed,tan or brown colored macule.
- Common in sun exposed areas of light-skinned individuals.
- It is developmental in origin-polymorphisms in MC1R gene & another predisposing gene mapped to chromosome 4q32-q34 have been noted
- In general,no therapeutic intervention is required.



Oral/Labial Melanotic Macule

- It is the most common benign pigmented lesions of oral cavity.
- Though the etiology is elusive,trauma has been postulated to play a role.

Clinical Features

- Common in adult females,on lower lip & gingiva.
- They tend to be <1cm,well circumscribed,oval or irregular in outline.
- Unlike a freckle,it does not increase in size on exposure to sun.

Pathology

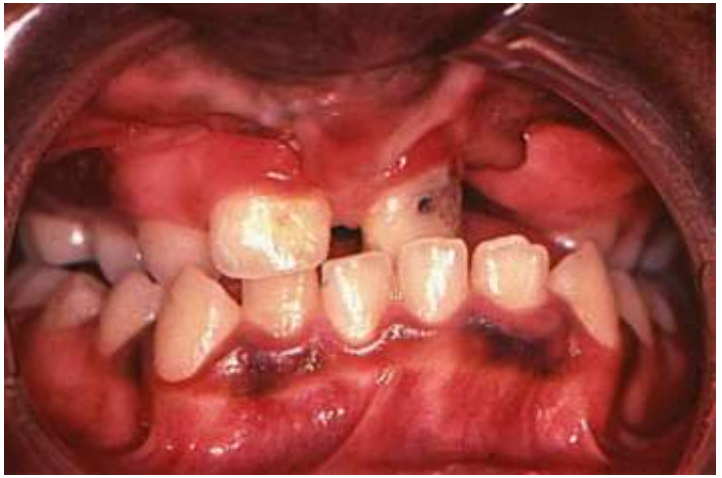
- Basal cells contain abundance of melanin pigment.
- It is accentuated at tips of rete pegs & incontinence into submucosa is common.

Differential Diagnosis

- ✓ Melanocytic Nevus
- ✓ Malignant Melanoma
- ✓ Amalgam Tattoo
- ✓ Focal Ecchymosis

Oral Melanoacanthoma

- It is an unusual,benign,innocuous melanocytic lesion.
- It is of rapid onset & reports with a history of trauma/chronic irritation.



Clinical Features

- It presents as a ill-defined,darkly pigmented,

macular or plaque-like lesion with irregular borders,in the 3rd or 4th decades of life in black females.

Common-buccal mucosa

Pathology

- Proliferation of benign,dentritic,melanocytes through out the full thickness of an acantholytic & spongiotic epithelial layer.

Differential Diagnosis

- ✓ Malignant Melanoma
- ✓ Melanocytic Nevus
- ✓ Melanocytic Macule

Melanocytic Nevus

Classification

i. Junctional Nevi
ii. Compound Nevi
iii. Intradermal Nevi
iv. Spindle cell/Epitheloid cell Nevi
v. Blue Nevi
- Common
- Cellular

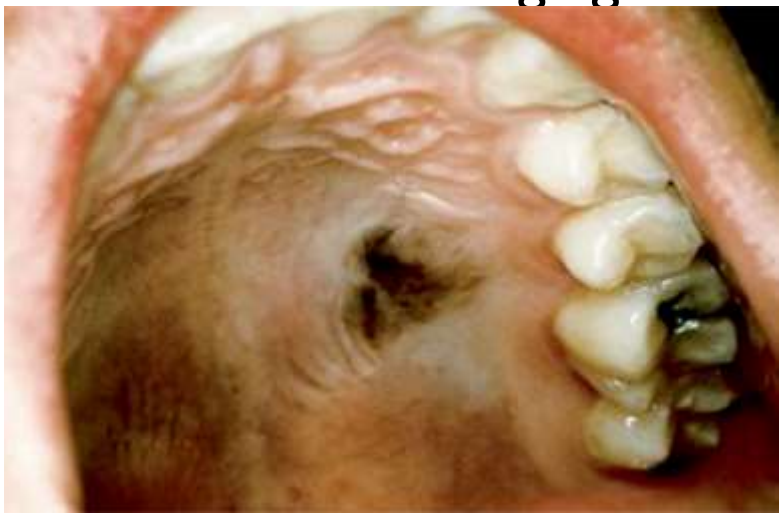
✓ They can be either congenital or acquired.Both genetic & environmental factors play a role.Seen in inherited diseases like-
✓ Carney complex
✓ Turner's Syndrome
✓ Noonan's Syndrome

Clinical Features

- Cutaneous nevi are common & present as multiple lesions,contrast to oral nevi which are rare & appear as solitary lesions.
- Oral lesions are usually asymptomatic & present as <1cm,solitary,brown/blue,well-

circumscribed nodule/macule.

- Common site is hard palate,buccal & labial mucosa & gingiva.

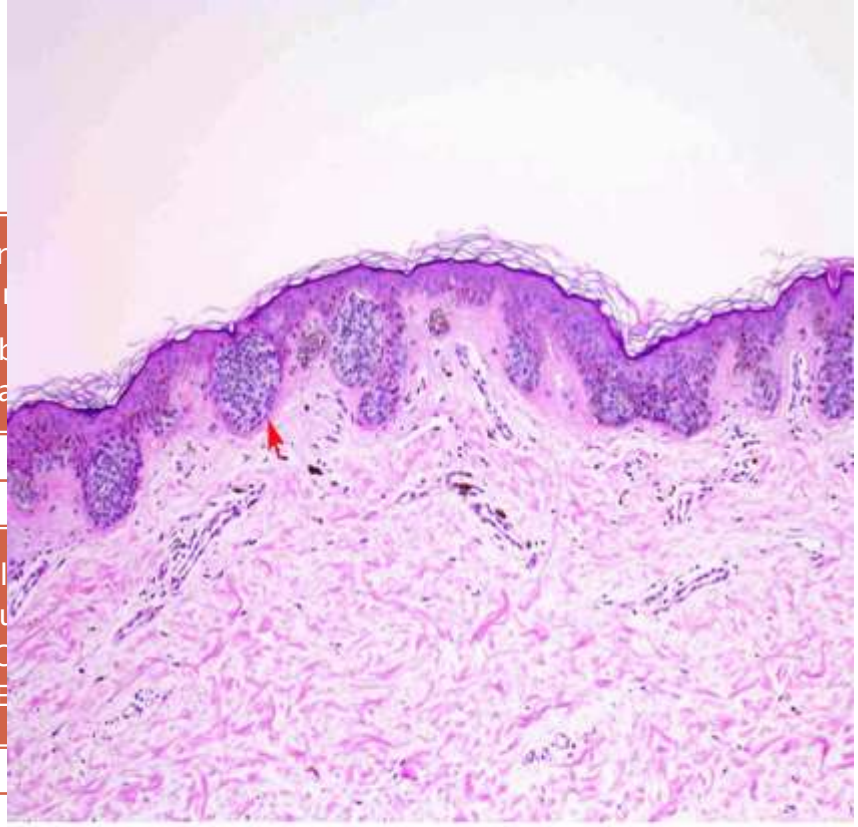


Pathology

Nevus cells localised to basal layer → Junction… <5mm,… Tan to b… appea…

Clustered melanocytes proliferate to connectivetissue → Few are still… mucosalsu… junction.(C… NE…

Nevus cells become confined to submucosal tissue (INTRAMUCOSAL NEVUS)



"nests" that are junctional (only in epidermis)

…proliferation of pigment laden,spindle shaped melanocytes

CELLULAR–submucous proliferation of both spindle shaped & large round/ovoid shaped melanocytes

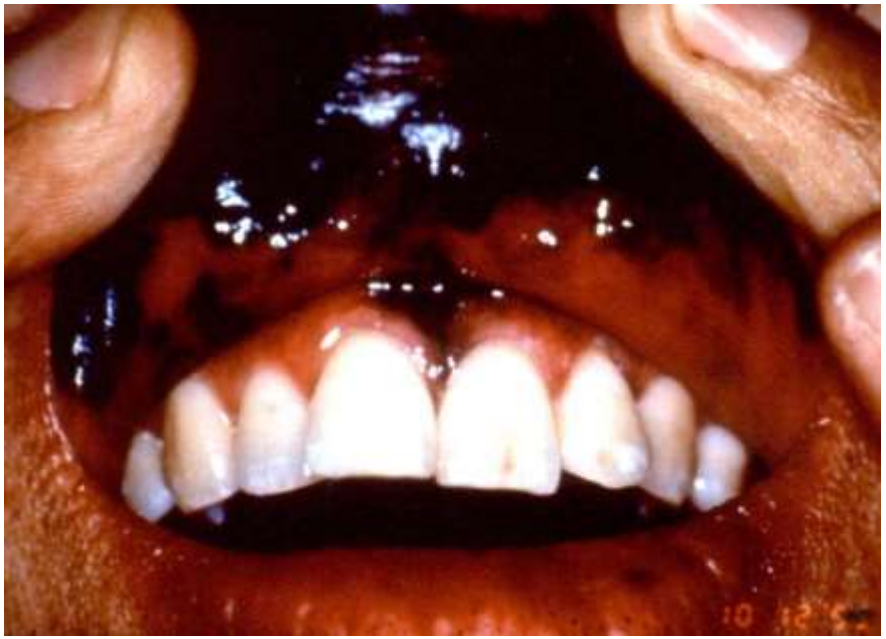
Differential Diagnosis –Malignant Melanoma

Malignant Melanoma

- Least common of all skin cancers.
- Risk Factors-
- A history multiple episodes of acute sun exposure
- Immunosuppression
- Presence of multiple cutaneous nevi
- A family history of melanoma(these families have a high incidence of germline mutations in the tumor suppressor genes,CDKNA2/p16INK4a)
- Melanomas also exhibit mutations in BRAF,HRAS & NRAS proto oncogenes.

Clinical Features

- Cutaneous melanoma is the most common among white population.
- There is a male predilection & more common in women of child bearing age.
- Criteria-
  - *A*ssymetry
  - Irregular *B*orders
  - *C*olour Variegation
  - *D*iametre >6mm
  - *E*volution or surface Elevation



- There are 4 clinicopathologic subtypes-
- Superficial spreading melanoma
- Lentigo maligna melanoma
- Acral Lentiginous Melanoma
- Nodular Melanoma.
- Oral melanoma-
- >50 yrs of age
- Palate,maxillary gingiva
- Macular,plaque-like or mass-forming,well circumscribed/irregular,focal/diffuse areas of brown/blue/black pigmentation.
- Ulceration,pain,tooth mobility/spontaneous exfoliation,root resorption,bone loss & parasthesia/anesthesia.

Pathology

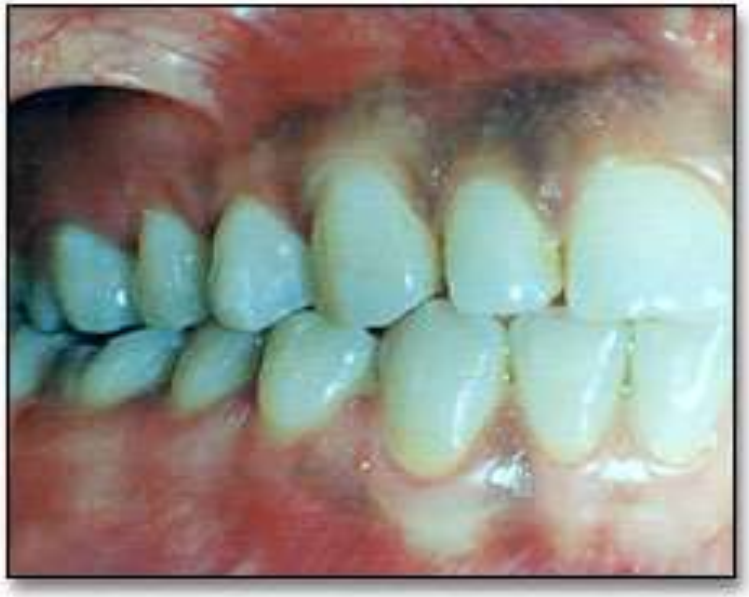
- ✓ Radial pattern of growth
- ✓ Clusters of pleomorphic melanocytes-nuclear atypia,hyperchromatism proliferate within basal cells
- ✓ Invasion on to overlying epithelium(pagetoid spread).

Management

- ✓ Ablative surgery
- ✓ Adjuvant radiation therapy

Physiologic Pigmentation

- Most common source of multifocal/diffuse pigmentation.
- Common in dark skinned individuals
- Common site - gingiva
- Common age – childhood
- Can be patchy or generalised
- ***Microscopically*** – Increases amounts of melanin pigment within the basal layer.
- ***Clinically*** - It is considered as a variation of normal,rarely it manifests as brown discoloration intraorally



Differential Diagnosis

- Idiopathic Pigmentation
- Drug Induced Melanosis
- Smoking Induced Melanosis
- Hyperpigmentation associated with endocrinopathic disorders

Management

- Gingivectomy
- Laser Therapy

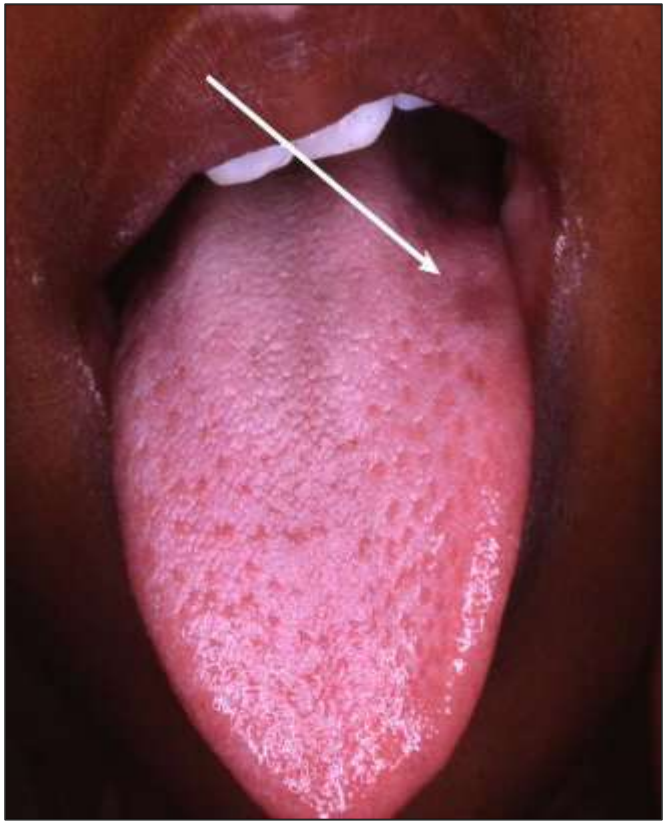
Drug-Induced Melanosis

Drugs inducing Mucocutaneous Pigmentation are-

- **Antimalarials** – Amiodarone,Chloroquine
- **Anti arrhythmic** – Amiodarone
- **Antiretrovirals** – Azidothymidine
- **Antibiotics** –Methacycline,Minocycline
- **Phenothiazines** – Chlorpromazine
- **Oral Contraceptives** – Premarin
- **Cytotoxic Drugs** – Cyclophosphamide & Busulfan
- **Misc** – Imipramine,Gold, Ketoconazole,Methyldopa

Clinical Features

- Intraorally the pigment may be diffused (multifocal or localised)
- Common site – hard palate
- Lesions are flat without any evidence of nodularity or swelling.
- Sun exposure may exacerbate cutaneous pigmentation



Pathology

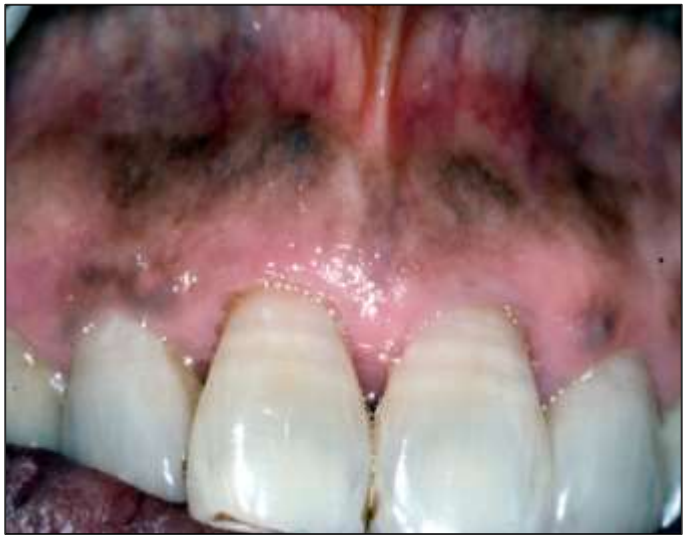
- Hemosiderin & pigmented,yellow or yellow red,drug complexes may also be identified.
- ***Mechanism***- Certain Drugs/Drug metabolites tend to stimulate melanogenesis.

Management

The discoloration tends to fade within a few months after the drug is discontinued.

Smoker's Melanosis

- Diffuse or focal melanosis of gingiva,buccal mucosa,lateral tongue,palate & floor of the mouth is occasionally seen in cigarette smokers.
- Pigmented areas are brown,flat,& irregular.
- Although the mechanism is unknown,one or more chemical compounds incorporated in within cigarettes,rather than actual tobacco,may be the causative.

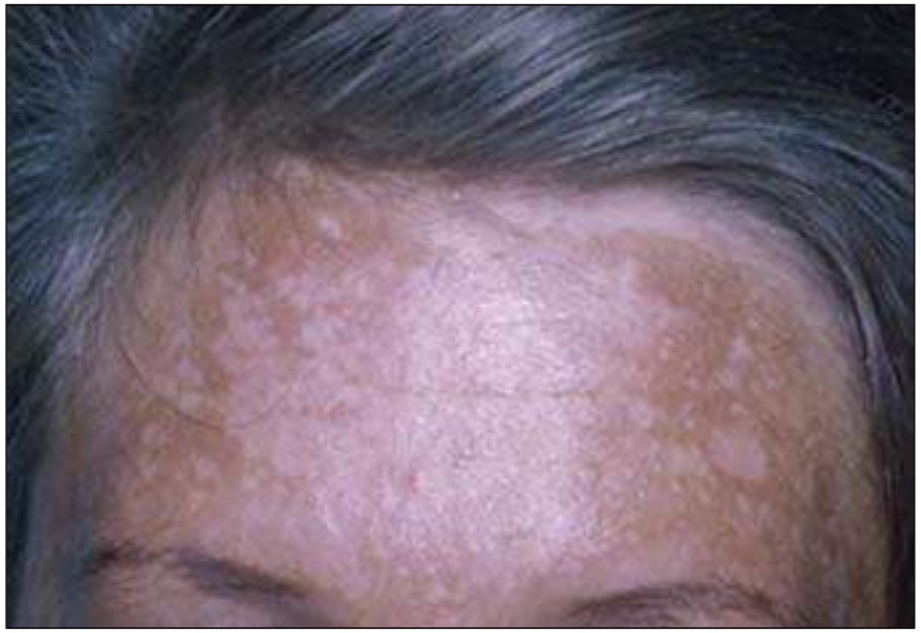


Postinflammatory(Inflammatory) Hyperpigmentation

- Common in dark-skinned individuals
- Manifests as diffuse/focal in areas previously subjected to injury/inflammation.
- The acne-prone face is more prone to this phenomenon.
- In oral cavity,the mucosa overlying a non melanotic malignancy may become pigmented

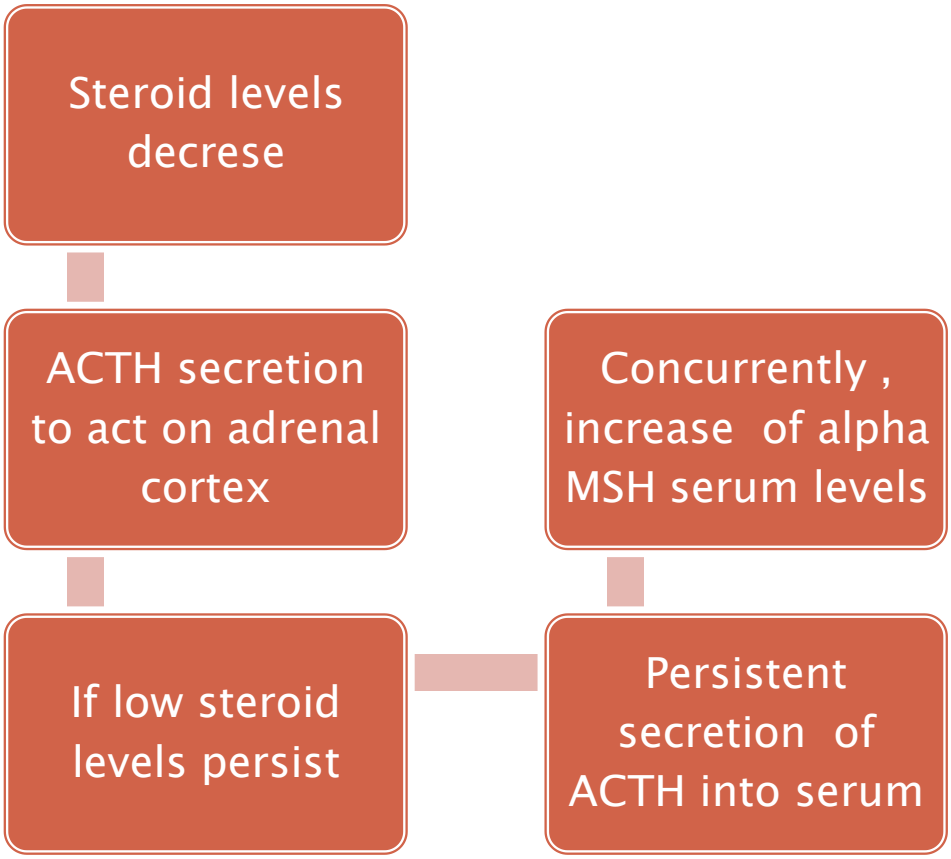
Melasma

- A relatively common,acquired symmetric melanosis developing on sun-exposed areas of skin.
- Common sites – Forehead,cheeks,upper lips & chin
- Common in females with dark skin.
- Mostly with pregnancy or ingestion of contraceptive hormones.
- It may spontaneously resolve after parturition,cessation of exogenous hormones,or regulation of endogenous sex-hormone levels.



Hypoadrenocorticism(Adrenal Insufficiency,Addison's Disease)

- It is a potentially life threatening disease,autoimmune disease being the most common cause.Other causes are,infectious agents,neoplasia,genetic etc.,
- Regardless of the cause,the end result is essentially the same,i.e.,a decrease in endogenous corticosteroid levels



Clinical Features

- In some cases,first sign of disease may be mucocutaneous pigmentation

Hallmarks-Generalized bronzing of skin & diffuse but patchy melanosis of oral mucosa(any oral surface may be involved)

Differential Diagnosis

Other causes of diffuse pigmentation including physiologic & drug induced pigmentation.

Treatment

Exogenous steroid replacement therapy

Cushing's Syndrome

- Develops as a consequence of prolonged exposure to high concentrations of endogenous/exogenous corticosteroids.
- Mucocutaneous pigmentation(mostly in↑ACTH secretion) is seen along with other systemic manifestations like moon facies,weight gain etc.,

Hyperthyroidism(Grave's Disease)

- Melanosis is common in dark skinned individuals

Primary Biliary Cirrhosis

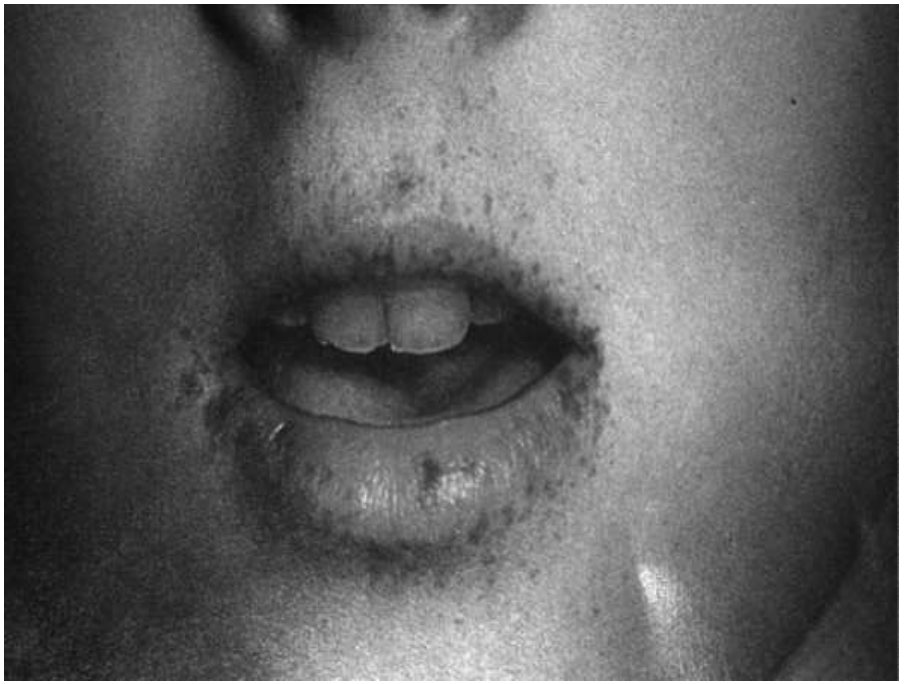
- It is an uncommon disease of unknown etiology.
- Diffuse mucocutaneous hyperpigmentation may be one of its earliest manifestations.
- Jaundice,which is it's end stage complication,caused by hyperbilirubinemia often induces a yellowish discoloration of skin,eyes & mucous membrane

Differential Diagnosis

- ✓ Carotenemia
- ✓ Lycopenemia

Peutz-Jeghers Syndrome

- It is an autosomal dominant disease that is associated with mutations in *STK*11/*LKB*1 tumor suppressor gene
- Clinical Manifestations-
- Intestinal polyposis
- Cancer susceptibility
- Multiple,small(<0.5 cm diametre) pigmented macules of lips,perioral skin,hands & feet



Differential Diagnosis

Cowden Syndrome

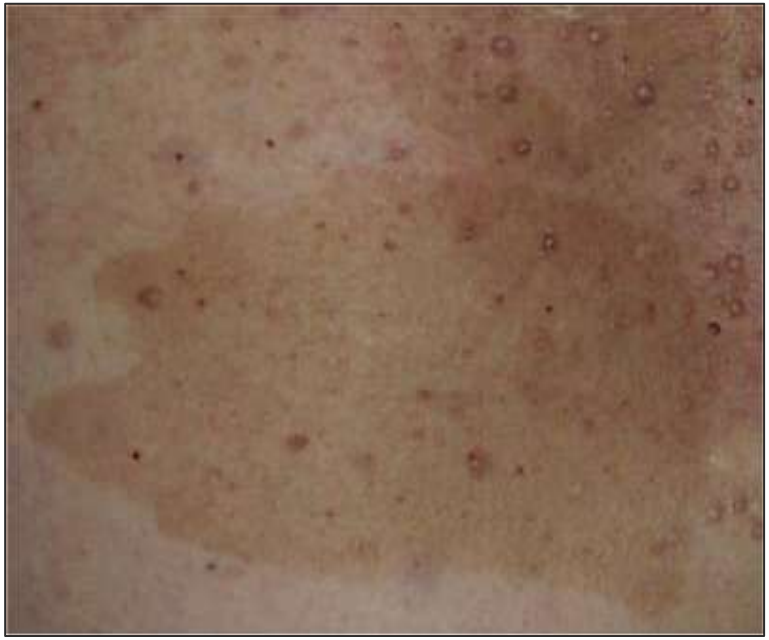
Café au Lait Pigmentation

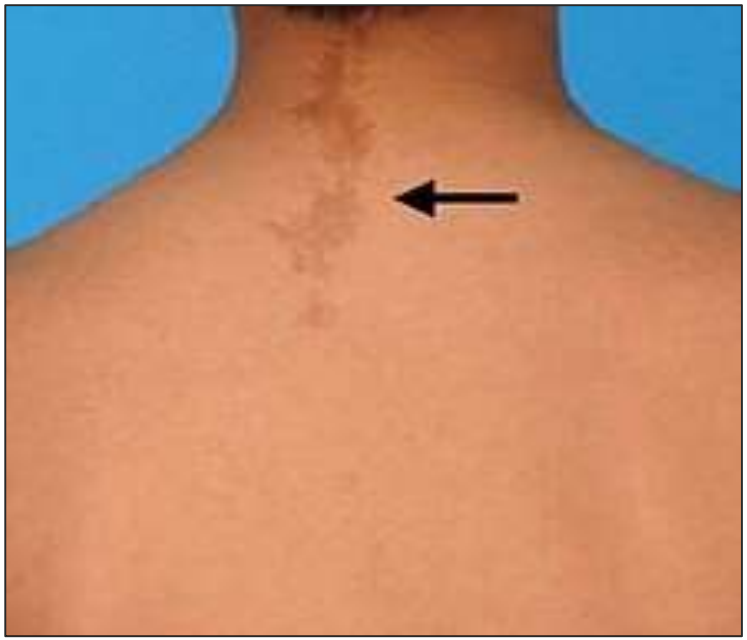
Seen in genetic diseases like-

- ✓ Neurofibromatosis Type I
- ✓ Noonan's syndrome
- ✓ Mc Cune Albright syndrome

Café au lait spots manifest as tan or brown colored,irregularly shaped macules of variable size.

- ⋆ The borders of pigmented macules in Mc Cune Albright syndrome are irregularly outlined unlike smooth in Neurofibromatosis Type I.





HIV/AIDS Associated Melanosis

- Diffuse or multifocal mucocutaneous pigmentation is seen.
- It may be related to intake of various medications(Like antifungal/antiretroviral) or due to adrenocortical destruction by virulent infectious organisms.
- It may be due to immune dysregulation associated with HIV which leads to increased secretion of alpha MSH from pituitary gland.
- The buccal mucosa is the most common site

Laugier-Hunzinker Syndrome

Etiology & Pathogenesis

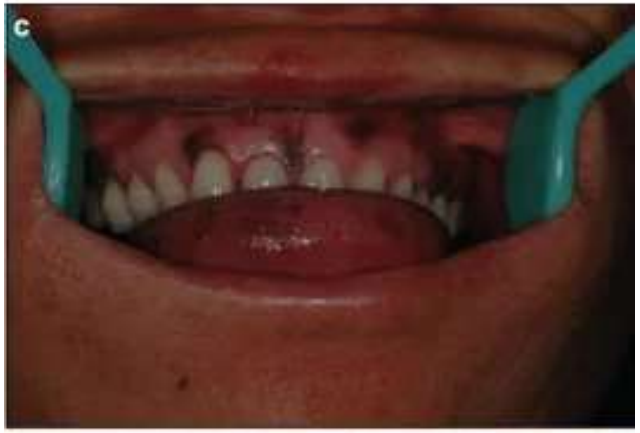
- Previoulsy described as acquired,idiopathic,macular hyperpigmentation of oral mucosal tissues,specifically lips & buccal mucosa
- 60% of the affected individuals have nail involvement,usually in the form of longitudanal melanotic streaks
- It is common in adult, light skinned individuals.

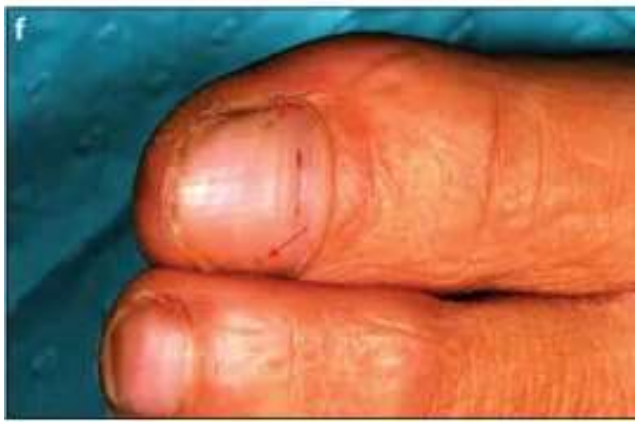
Clinical Features

- Patients present with multiple,discrete,irregularly shaped brown/dark brown oral macules.

Differential Diagnosis

- Physiologic pigmentation
- Drug induced pigmentation
- Peutz-Jeghers syndrome





Treatment

- Laser
- Cryosurgery

Treatment Of Mucocutaneous Melanosis

First line Therapy-

- Topical medicaments,i.e., bleaching creams

Single agents-Azelic acid or hydroquinone

Combinations-4% hydroquinone+0.05%retinoic acid+0.01% fluocinolone acetonide

Second line Therapy-

- Laser
- Cryosurgery

Depigmentation

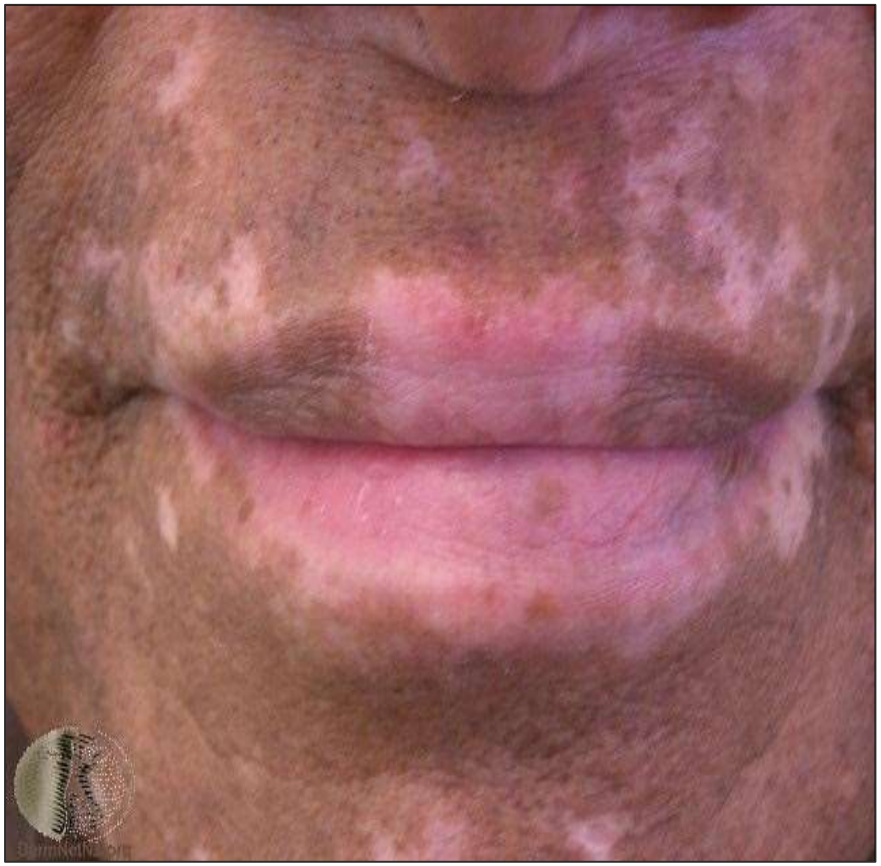
Vitiligo

It is a relatively common,acquired,autoimmune disease associated with hypomelanosis.

The pathogenesis is multifactorial,with both genetic & environmental factors likely to play a significant role.

Clinical Features

- It presents as diffuse/focal areas of pigmentation.
- The skin & hair of most of the body may lose its pigmentation(vitiligo universalis)
- Lesions present as well circumscribed,round,oval or elongated,pale or white macules that may coalesce into larger areas of diffuse pigmentation.
- It is easily apparent in dark skinned individuals
- It rarely affects the intraoral mucosal tissues.



Pathology

- Entirely loss of melanocytes & melanin pigmentation in basal cell layer.

Management

- ✓ Topical corticosteroids
- ✓ Systemic photochemotherapies
- ✓ Autologous epithelial grafts

Hemoglobin & Iron Associated Pigmentation

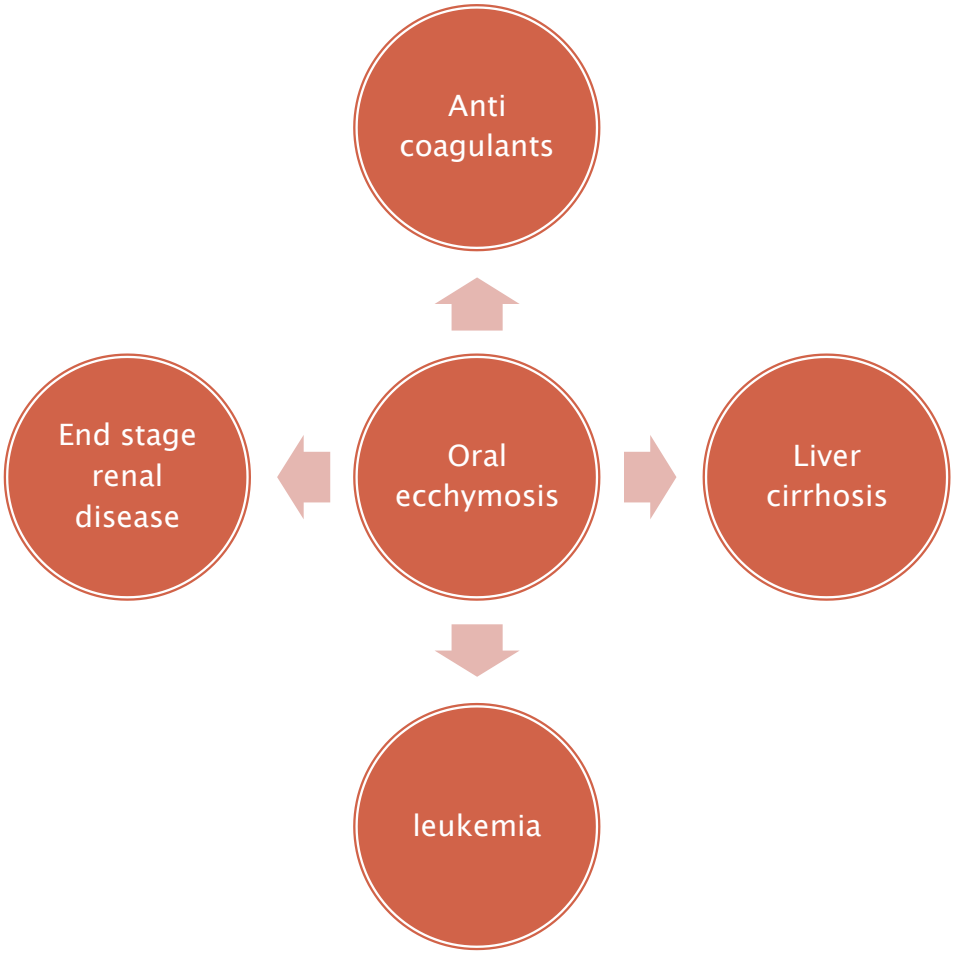
Ecchymosis

It is the skin discoloration caused by the escape of the blood into the tissues from the ruptured blood vesssels.

It is common on the lips & face

Immediately following the traumatic event,the submucosa will appear as a bright red macule or as a swelling.

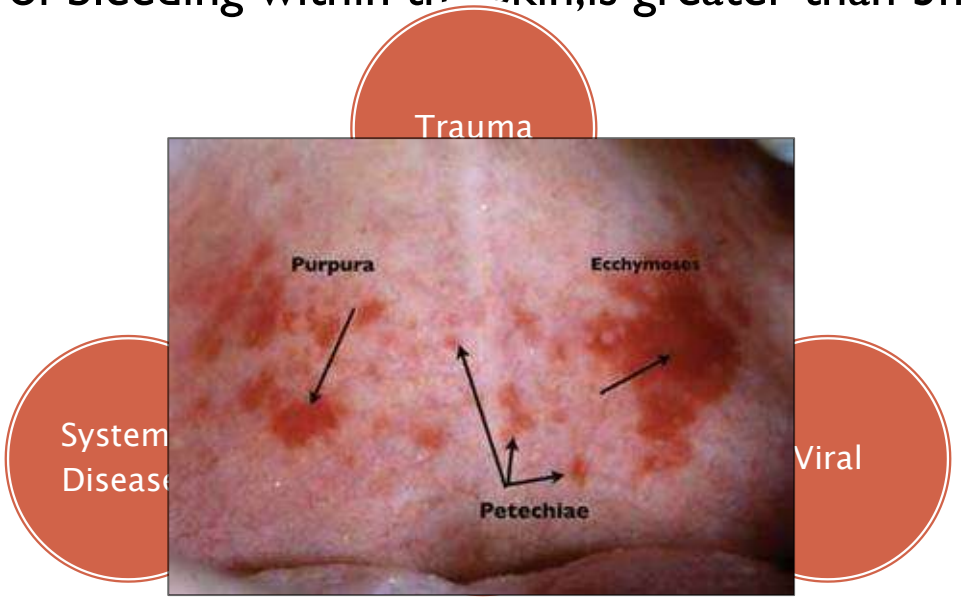
Seen in patients taking anticoagulants


Anti coagulants
End stage renal disease
Oral ecchymosis
Liver cirrhosis
leukemia

Purpura & Petechiae

Petechiae is a pinpoint flat round red spots under the skin caused by intradermal hemorrhage.

Purpura is a area of bleeding within the skin,is greater than 3mm in diametre.



Hemochromatosis

- It is a chronic,progressive disease that is charecterized by excessive iron deposition in liver & other organs & tissues
- ✓ Cutaneous pigmentation is seen in 90% of individuals.Oral pigmentation is often diffuse brown to gray in appearance

Exogenous Pigmentation

Amalgam Tattoo

- It is the single most common source of solitary/focal pigmentation in oral mucosa
- These are iatrogenic in origin & typically a consequence of the inadvertent deposition of amalgam restorative material into the submucosal tissue

Clinical Features

Lesions are bluish-gray / black

Common sites-gingiva,alveolar mucosa,buccal mucosa & floor of themouth.

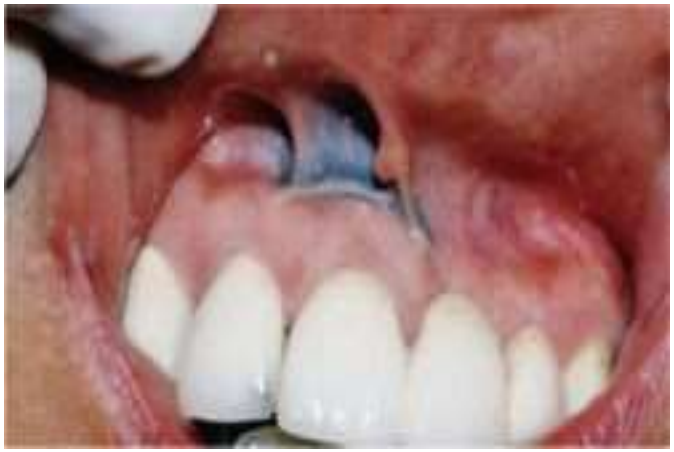
Often found in the vicinity of –

The teeth with large amalgam restorations

Crowned teeth that had amalgam

Around the apical region of endodontically treated teeth with retrograde restorations

Or with obturated points In & around healed extraction sites



Mangement

Since they are innocuous,removal is not always neccesary

Sometimes,focal argyrosis may compromise aesthetics,thus surgical removal may be warranted

Graphite Tattos

- Most common on palate & represent traumatic induction of graphite particles from a pencil
- Lesions present as solitary gray / black

Ornamental Tattoos

- Mucosal tattoos in the form of lettering or intricate artwork are becoming increasingly common phenomena
- Laser therapy is used

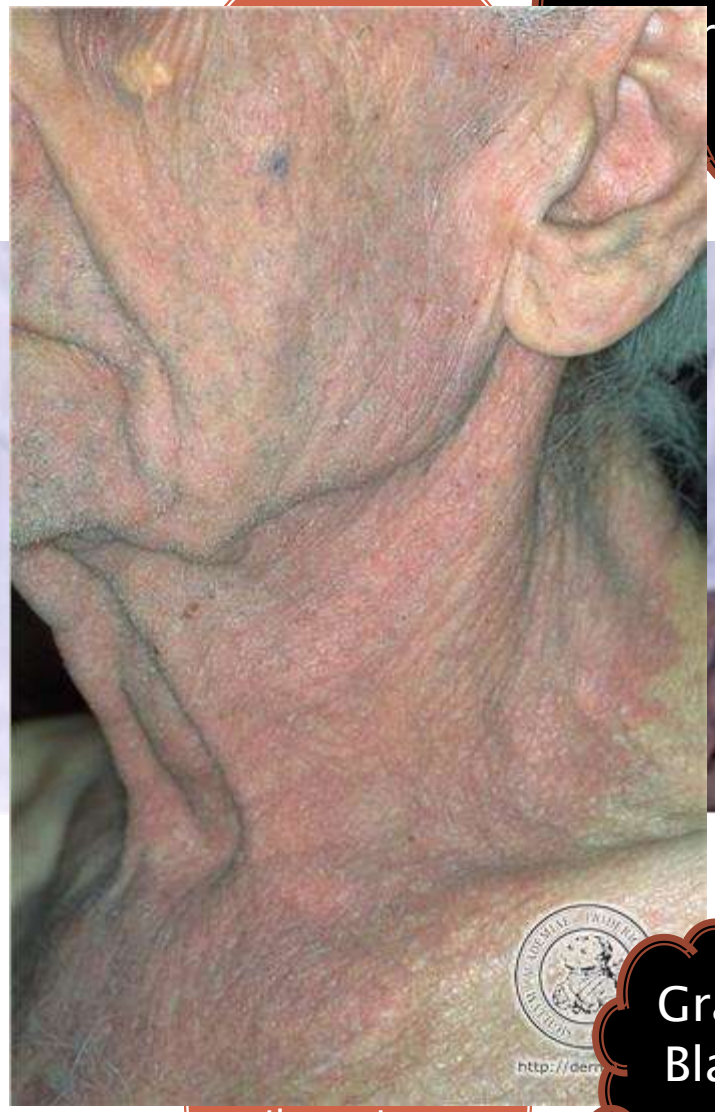
Blue gray–
gyria

Blue gray
or
purple:Chry
siasis

Black
hairy
tongue

Bismuth
subsalicyla

Gold

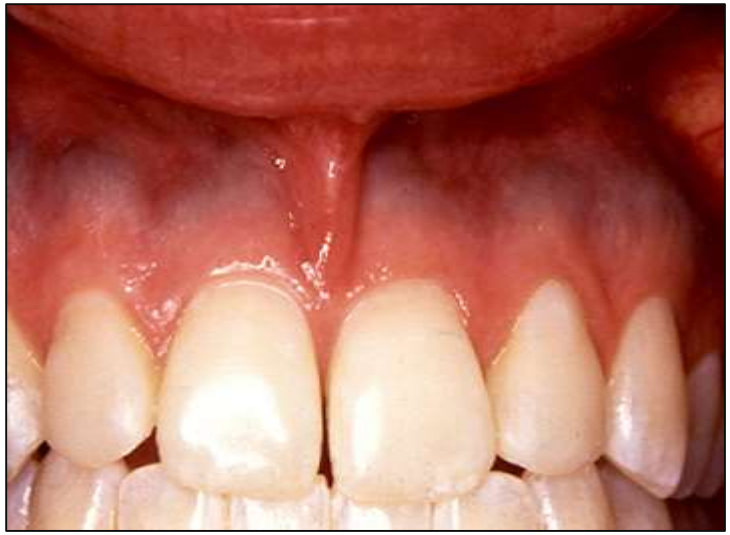


silver nitrate

Gray–
Black

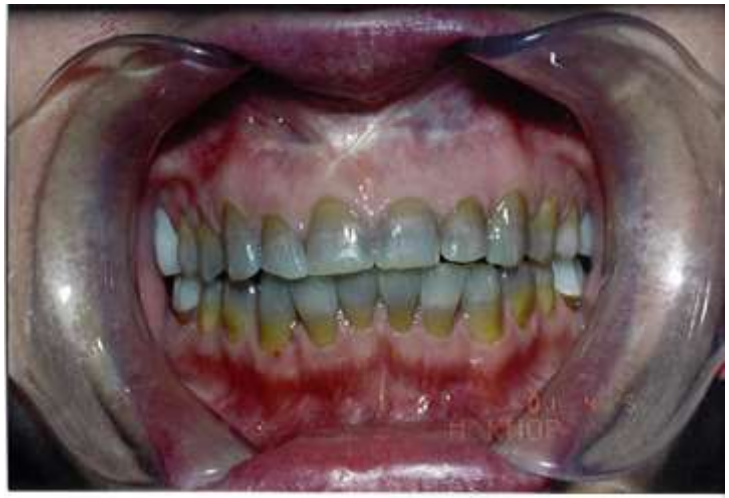
Heavy Metal Pigmentation

- **Lead,mercury,bismuth & arsenic** have been shown to be deposited in oral tissue
- The pigmentation is found on the free marginal gingiva
- This metallic line appears black/gray



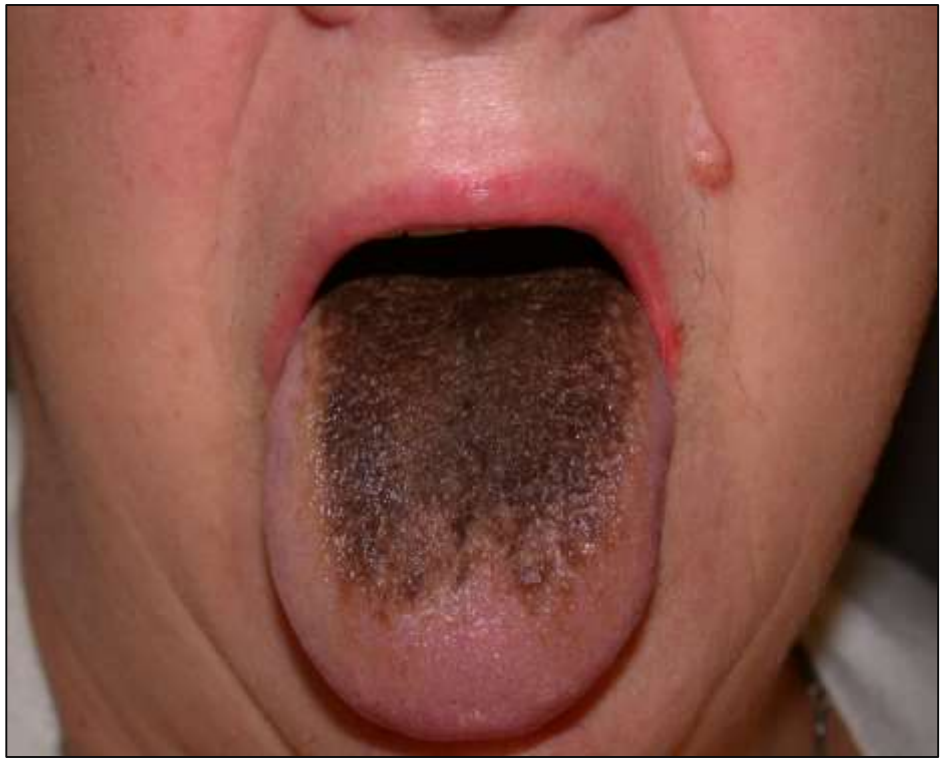
Drug Induced Pigmentaion

- Minocycline,a derivative of tetracycline is a common drug causing drug induced non melanin associated oral pigmentation
- It also causes pigmentaion of the developing teeth
- **Clinically** it may appear gray,brown or black
- The discoloration often subsides within months after dicontinuation of the drug



Hairy Tongue

- It is a relatively common condition of unknown etiology
- The change in the oral flora associated with chronic antibiotic therapy may be causative
- The middle & posterior 1/3rd of the dorsal tongue is involved
- The filiform papillae is elongated & the hyperplastic papillae then become pigmented by colonization of chromogenic bacteria which can impart white,green,brown or black colors
- ***Treatment*** consists of having the patient brush the tongue,or use a tongue scraper & limit the ingestion of color forming foods & drinks until the discolration resolves



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