Neurocutaneous Syndromes

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Neurocutaneous Disorders

- NEUROFIBROMATOSIS
- TUBEROUS SCLEROSIS
- STURGE WEBER SYNDROME
- INCONTINENTIA PIGMENTI
- INCONTINENTIA PIGMENTI ACHROMIANS
- LINEAR SEBACEOUS NEVUS
- NEVUS UNIS LATERIS
- KLIPPEL-TRENAUNAY-WEBER SYNDROME

NEUROFIBROMATOSIS

NEUROFIBROMATOSIS TYPE 1
(PERIPHERAL OR CLASIC)
NEUROFIBROMATOSIS TYPE 2
(CENTRAL OR ACOUSTIC)

NEUROFIBROMATOSIS TYPE1

GENETICS

- Autosomal dominant 50%
- Sporadic mutations
- Germline mosaicism in less than 1%
- Prevalence of 1 in 4000
- Chromosome 17 Band 11.2 of the long arm

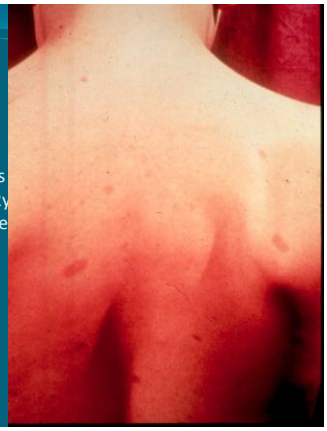
NEUOFIBROMATOSIS type 1

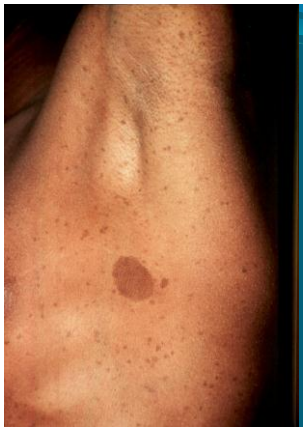
Cutaneous Manifestations

- CAFÉ-AU-LAIT SPOTS
- AXILLARY OR INGUINAL FRECKLING
- NEUROFIBROMAS
- PLEXIFORM NEUROMAS

CAFÉ-AU-LAIT SPOTS

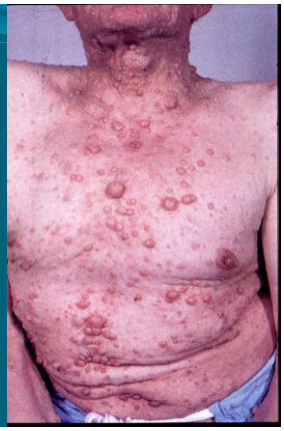
Present at birth
Few millimeters to centimeters
Don't increase in number aft 2y
Not found on scalp, palms, sole

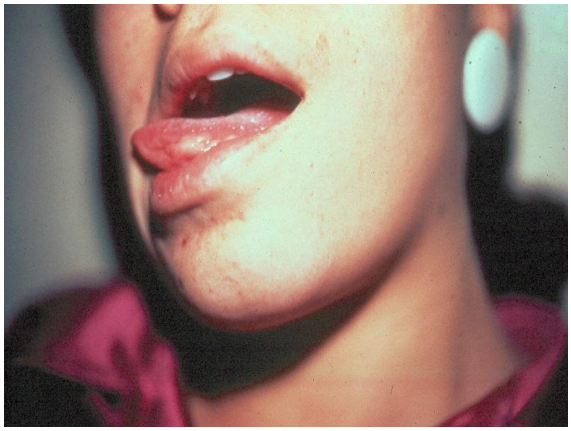




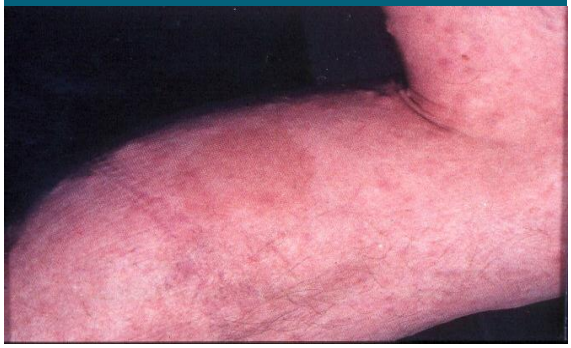
Axillary Freckling
Café-au-lait spots

NEUROFIBROMA





PLEXIFORM NEUROFIBROMA

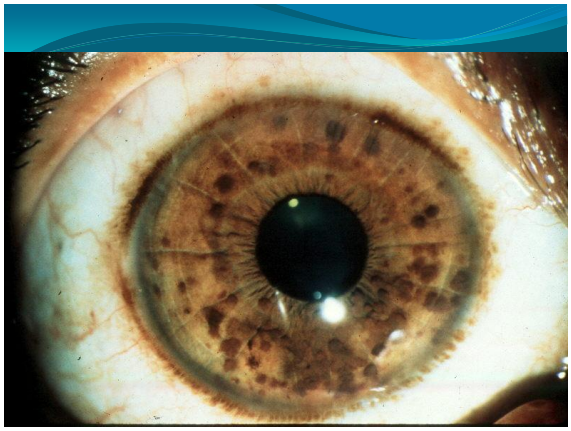


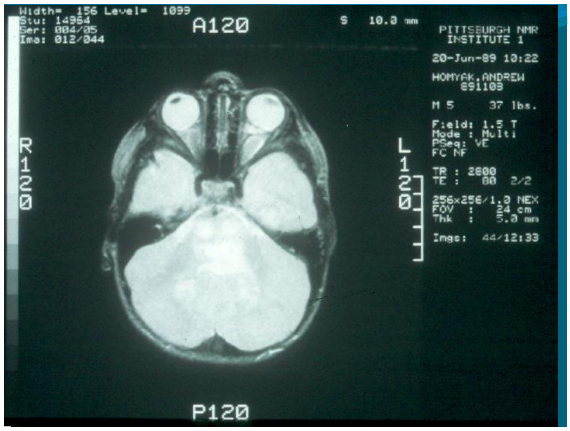
NEUROFIBROMATOSIS TYPE 1
CNS MANIFESTATIONS

- CNS Tumors
  - Optic Glioma
  - Astrocytomas
- Spinal Tumors
- Brain MRI Findings, 80% T2-signal hyperintense foci
- Learning Disability, 60%
- Seizures , 10%
- Macrocephaly
- Hydrocephalus
- Hearing Impairment

NEUROFIBROMATOSIS TYPE 1
OPHTHALMOLOGIC MANIFESTATIONS

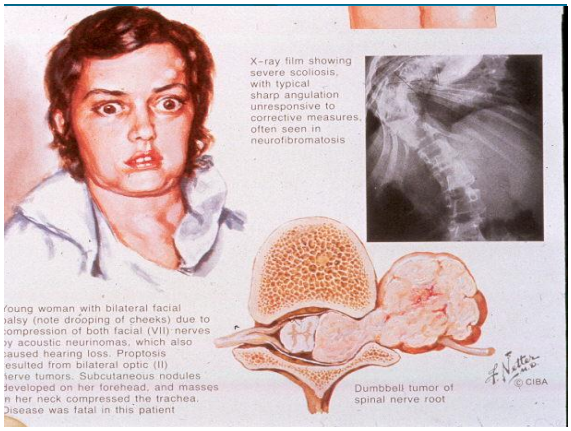
- Lisch Nodules, melanocytic hamartomas
  10% by age 6 years, 50% by age 30, 100% by 60
- Congenital Glaucoma
- Optic Glioma, 15-20%

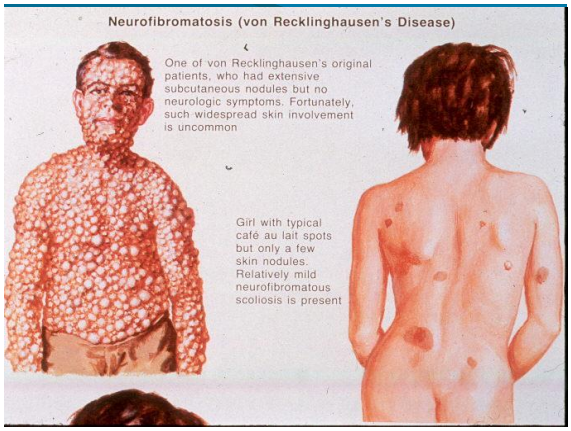




NEUROFIBROMATOSIS TYPE 1
SKELETAL MANIFESTATIONS

- Dysplasia of the Sphenoid Bone
- Pseudoarthrosis
- Dural Ectesia
- Kyphoscoliosis
- Enlargement of Long Bones
- Bone Cysts





NEUROFIBROMATOSIS TYPE 1
ENDOCRINE MANIFESTATION

- SHORT STATURE
- PRECOCIOUS PUBERTY
- HYPERPARATHYROIDISM
- HYPERTENSION

NEUROFIBROMATOSIS TYPE 1
OTHER MANIFESTATIONS

- GI
  Hemorrhage, constipation
- GU
  Bladder Dysfunction
- Increase risk for Neoplasm
  Neuroblastoma, Wilm's Tumor, Neurofibrosarcoma, Leukemia Rhabdomyosarcom, Pheochromocytoma

NEUROFIBROMATOSIS TYPE 1
DIAGNOSIS

- AT LEAST TWO OF THE FOLLOWING

1- Six or more café-au-lait spots
   a- Prepubertal > 5mm
   b- Post pubertal > 15mm
2- Two or more Neurofibroma or one plexiform Neurofibroma.
3- Axillary or Inguinal Freckling
4- Two or more Lisch nodules
5-Optic Glioma
6- Osseous lesions
7- First degree relative with NF1

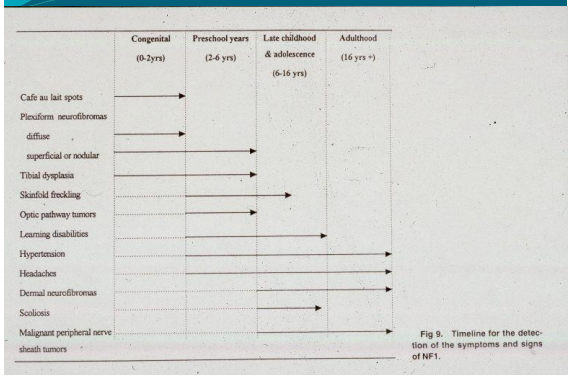


Fig 9. Timeline for the detection of the symptoms and signs of NF1.

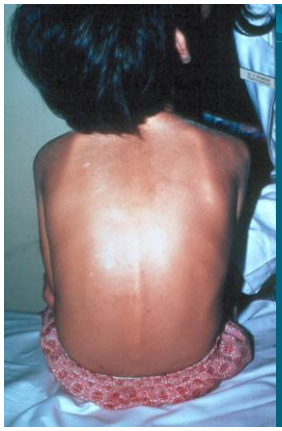
TUBEROUS SCLEROSIS
GENETICS

- Prevalence 1 per 6800
- Complete penetrance but variable expression
- 1/3 of the cases Autosomal Dominant
- 2/3 of the cases Sporadic Mutation
- TSC 1 on 9 q 34.1 encodes hamartin
- TSC 2 on 16 p 13.3 encodes tuberin

  TSC 2 gene is contiguous with the gene producing polycystic kidney disease

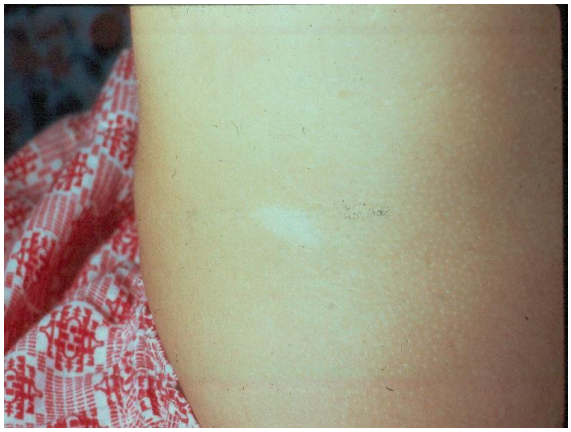
TUBEROUS SCLEROSIS
CUTANEOUS MANIFESTATION

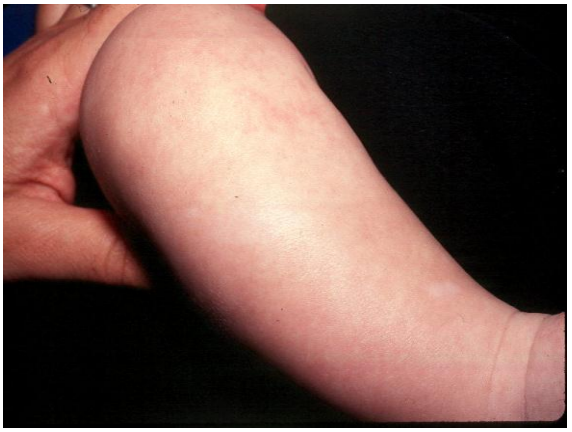
- ASH-LEAF SPOTS
- ADENOMA SEBACEUM
- SHAGREEN PATCHES
- PERIUNGULAR OR GINGIVAL FIBROMAS
- CAFÉ-AU-LAIT SPOTS
- FIBROMA OR ANGIOMA

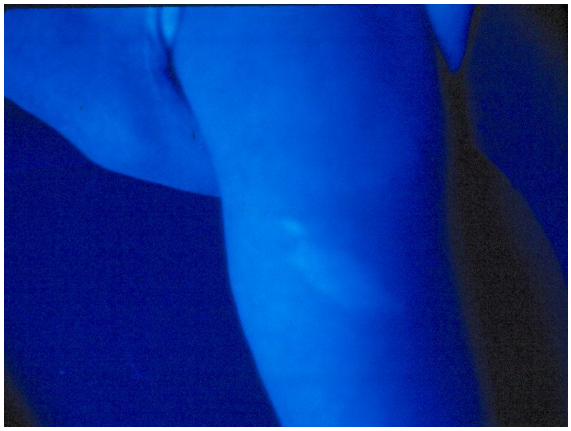


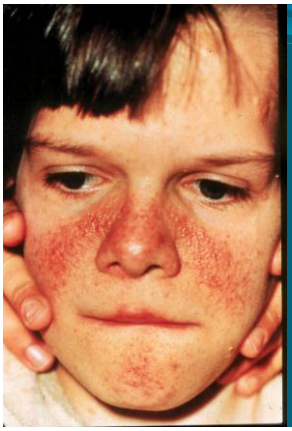
ASH-LEAF MACULE

0.4-0.8% of newborns
1 in 300-600 has TS
Reduction of melanocytes and melanin



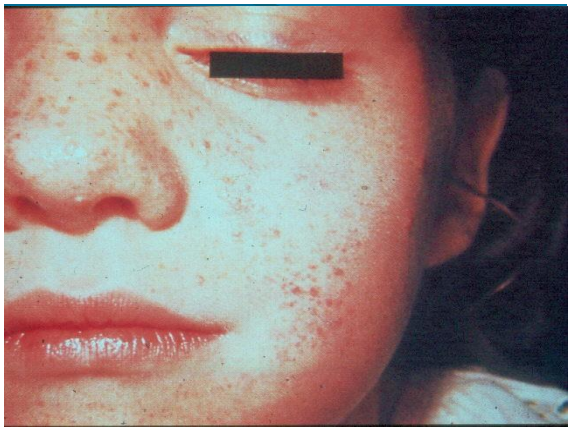


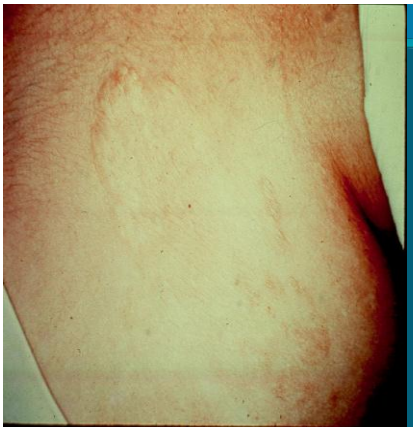




ADENOMA SEBACEUM

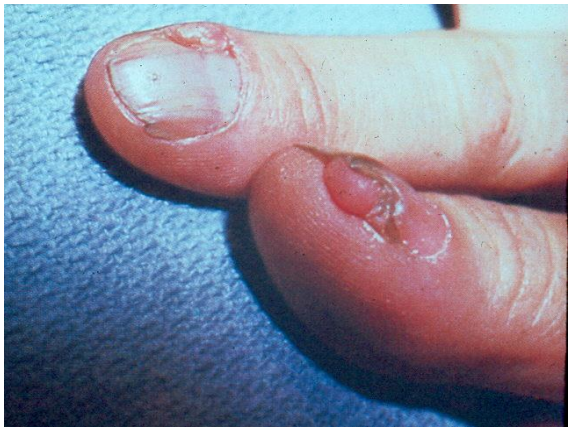
1/3 of 2 year-old patients
3/4 by puberty
Angiofibromas
Pink or red papules, patches or butterfly





Shagreen Patches

35% of patients
leathery plaque
lumbosacral area



TUBEROUS SCLEROSIS
NEUROLOGICAL MANIFESTATION

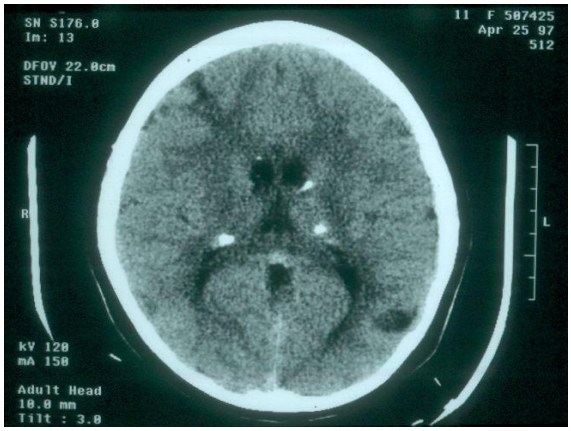
- SEIZURES 70%, INFANTILE SPASMS 1/3
- MENTAL RETARDATION, mild to severe in 47%
- TUBERS (HAMARTOMAS), calcification as early as 5 month. Number of tubers predict the severity.
- OTHERS

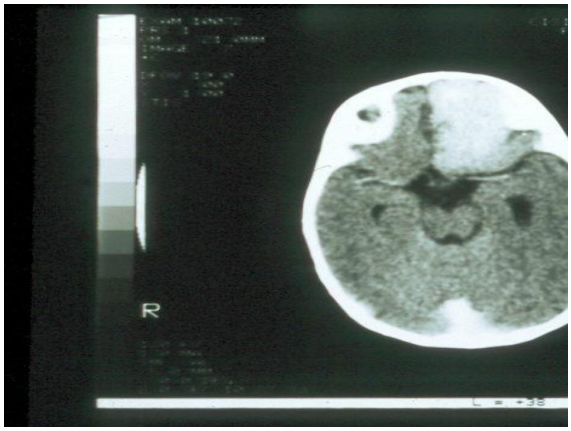
  MICROGYRIA

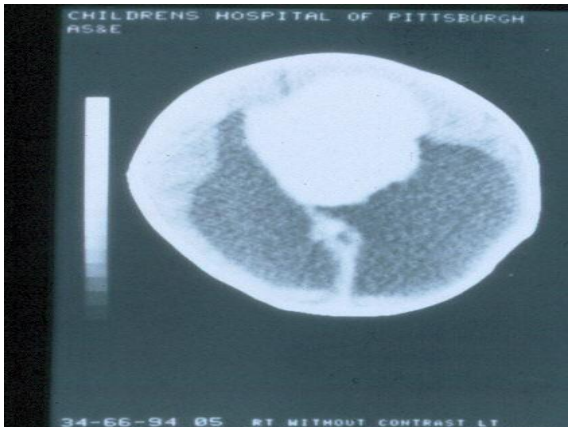
  HETEROTOPIA

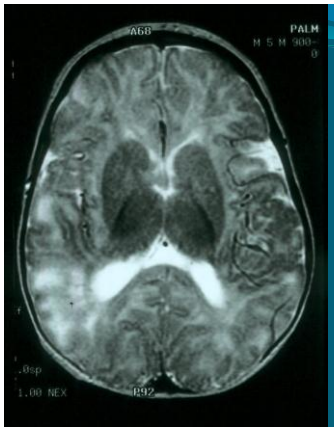
  OBSTRUCTIVE HYDROCEPHALUS

  GIANT CELL ASTROCYTOMA, 10% in periventricular

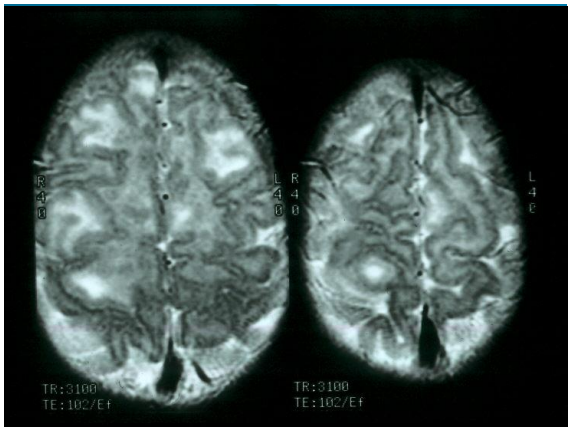






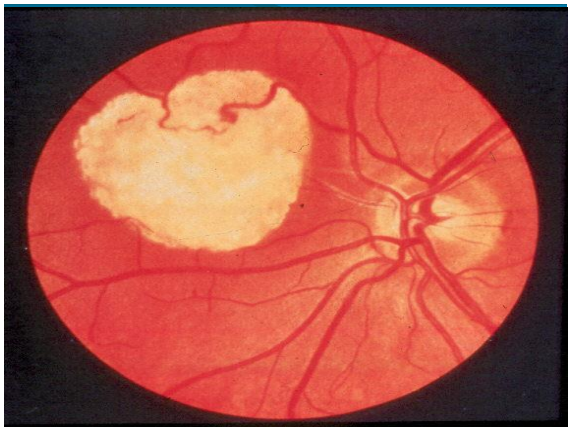


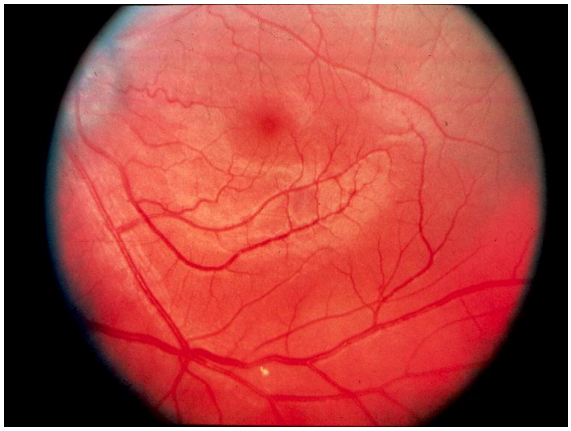
TUBERS
(HAMARTOMAS)



TUBEROUS SCLEROSIS
OPHTHALMOLOGIC MANIFESTATION

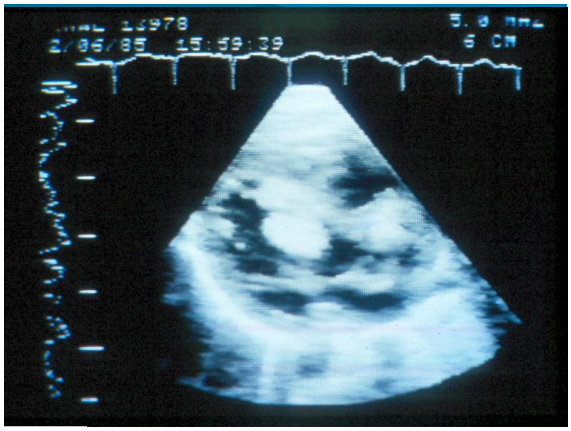
- RETINAL HAMARTOMAS (PHAKOMA)
- MULBERRY PHAKOMA
- GRAY YELLOW GLIAL PATCH
- HYPOPIGMENTED IRIS LESIONS
- CATARACTS

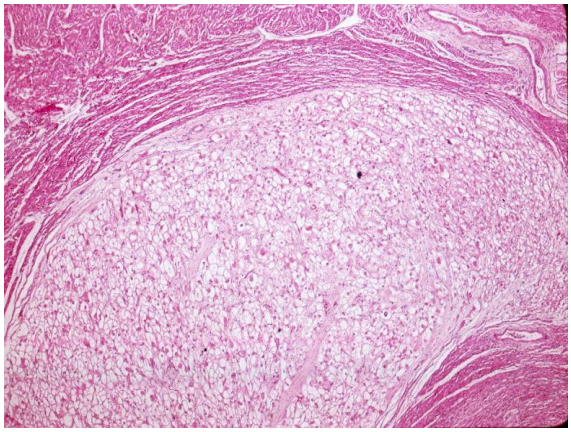


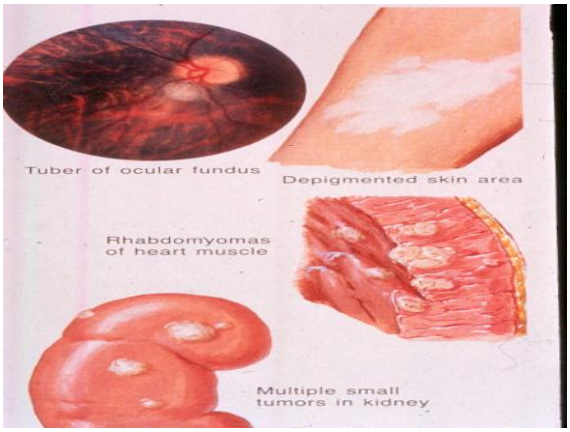


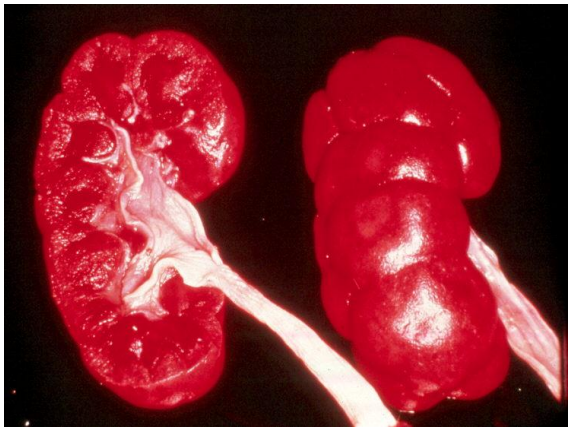
TUBEROUS SCLEROSIS
SYSTEMIC MANIFESTATION

- RENAL ANGIOMYOLIPOMA AND CYST 50-80%
- CARDIAC RHABDOMYOMA 50%, solitary, multiple
- PULMONARY LYMPHANGIOMATOSIS
- HAMARTOMA AND POLYPOSIS OF GI
- DENTAL ENAMEL PITS
- SCLEROSIS LESION OF LONG BONE
- CYSTIC LESION OF METACARPALS AND PHALANGS









TUBEROUS SCLEROSIS
DIAGNOSTIC CRITERIA

- PRIMARY FEATURES

1- Facial angiomatosis or foehead plaque
2- Nontraumatic ungual periungual fibroma
3- Multiple retinal nodular hamartomas
4- Cortical tuber, histologic confirmation
5- Subependymal giant cell astrocytoma
6- Renal Astrocytomas

SECONDARY FEATURES

1- Affected first degree relative
2- Cardia rhabdomyoma
3- Retinal hamartoma
4- Cerebral tubers, radiographic confirmation

TUBEROUS SCLEROSIS
DIAGNOSTIC CRITERIA

5- Noncalcified subependymal nodules
6- Shagreen patch
7- Forhead plaque
8- Pulmonary lymphagiomyomatosis
9- Renal angiomyolipoma
10- Multiple renal cysts

TERTIARY FEATURES

1- Hypomelanotic macules
2- Enamel pits
3- Hamartomatous rectal polyps
4- Cerebral white matter abnormality
5- Infantile spasm

TUBEROUS SCLEROSIS
DIAGNOSTIC CRITERIA

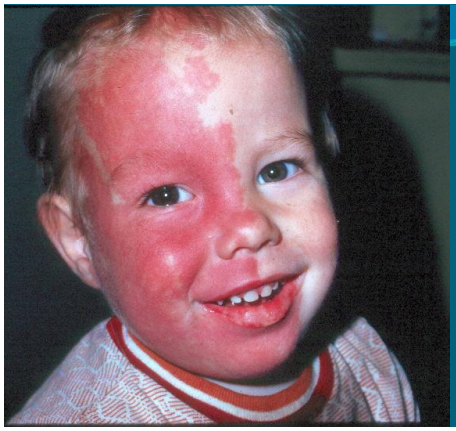
- DEFINITE TSC: Either one primary, two secondary features, or one secondary plus two tertiary features
- PROBABLE TSC: Either one secondary and one tertiary feature or three tertiary features
- Suspect TSC: Either one secondary feature or two tertiary features

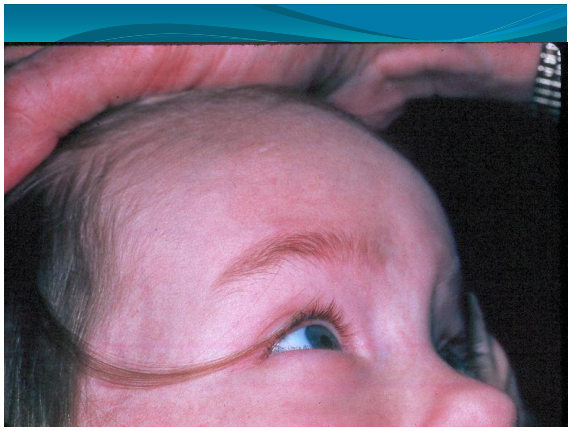
STURGE- WEBER SYNDROME
GENETICS

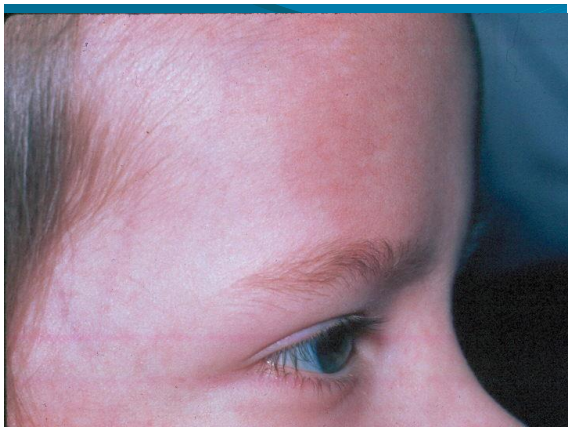
- No clear pattern of inheritance
- Incomplete penetrance

STURGE WEBER SYNDROME
CUTANEOUS MANIFESTATION

- PORT WINE NEVUS
- Present at birth
- Primarily involving V1, but can involve V2, V3
- 8% of patient has intracranial involvement in unilateral facial lesions. 24% in bilateral facial lesions





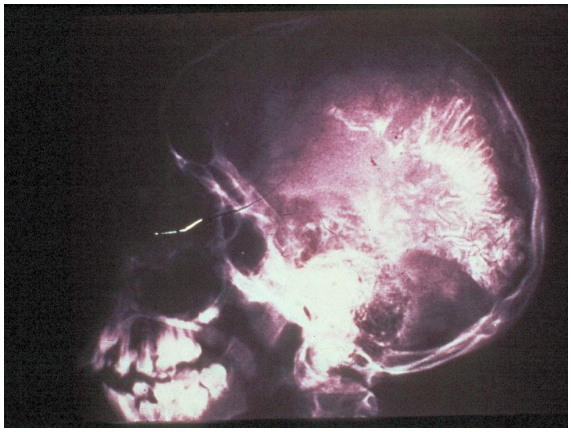


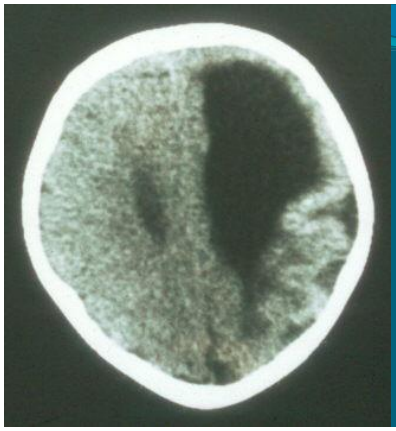
STURGE WEBER SYNDROME
OPHTHALMOLOGIC MANIFESTATION

- GLUCOMA 25%
- IRITIC HETEROTOPIA
- STRABISMUS
- DILATED RETINAL VEINS

STURGE WEBER SYNDROME
NEUROLOGIC MANIFESTATION

- Leptomeningeal Angiomatosis
- Ipsilateral port wine nevus
- Tram-trak curvilinear calcifications 100% by age 20 yr
- Seizures 75%
- Mental retardation
- Contralateral spastic hemiplagia 25-50%
- Homonymous hemianopsia





INCONTINENTA PIGMENTI

- Transmitted as an X-linked dominant trait
- Affecting females 90-97% of cases
- Most male fetuses are spontaneously aborted

INCONTINENTA PIGMENTI
SKIN MANIFESTATION

FIRST STAGE:

Vesiculobullous lesions at birth or first few weeks of life

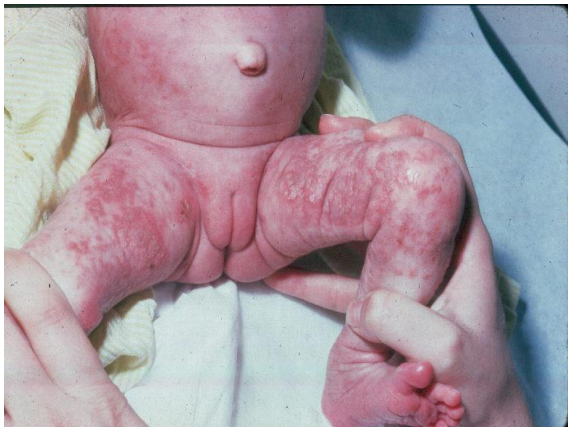
Eosinophils is found in vesicular fluid.

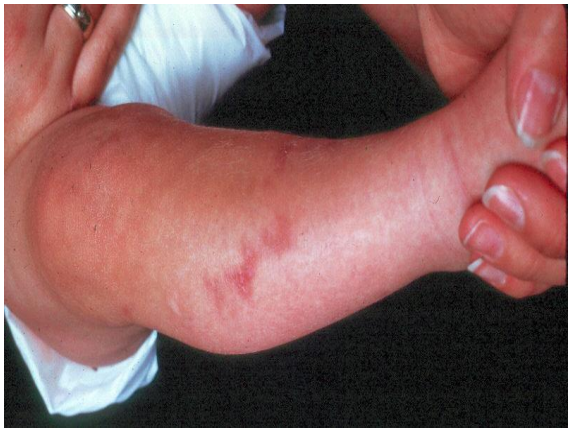
SECOND STAGE:

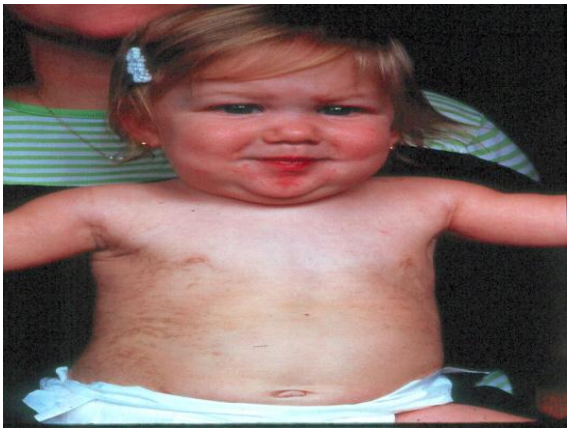
Lesions tend to heal resulting in atrophic cutaneous areas

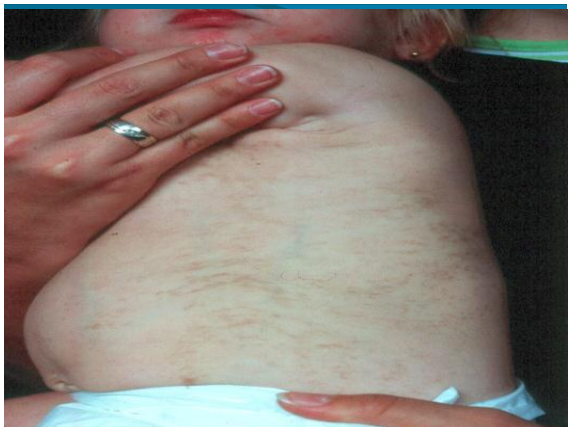
THIRD STAGE:

Hyperpigmented brown or grey-brown macular lesions have a splashed-on appearance



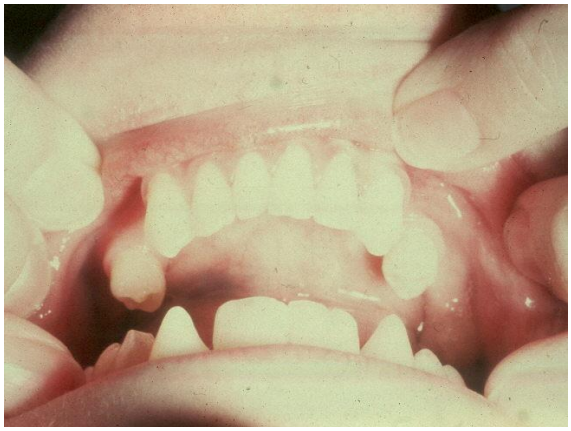






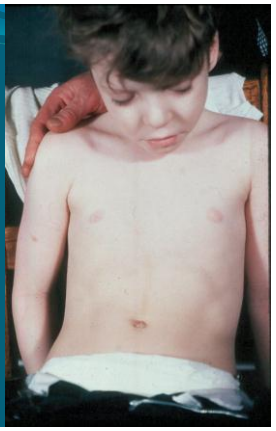
INCONTINENTA PIGMENTI

- 30-50% have developmental retardation and corticospinal tract dysfunction, seizure.
- 30% have ocular abnormalities, optic atrophy, papilitis, nystagmus, cataracts.
- 8% with visual loss due to retinal detachment
- Skeletal abnormalities, hemivertebrae, accessory ribs
- Delayed dentition, pegged teeth

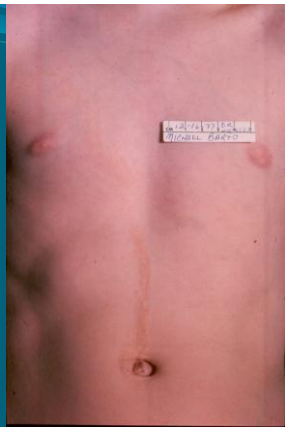


LINEAR SEBACIOUS NEVUS

Yellow-brown, hairless, waxy plaque
localized to midline or near midline
Scalp or face, trunk
Present at birth or early childhood
Tumor change in later life
60% mental retardation and seizures
MRI abnormalities, Schizencephaly, heterotopia of grey matter.

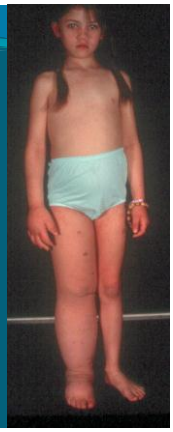


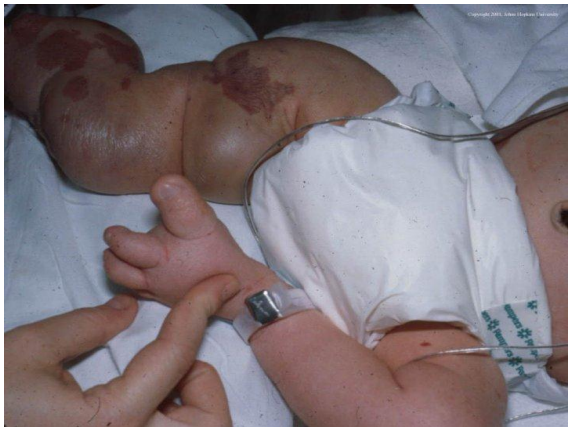
LINEAR SEBACIOUS NEVUS



KLIPPEL-TRENAUNAY-WEBER SYNDROME

Skin lesions at birth, capillary hemangioma, tangiectasias, varicosities, arteriovenous fistula, lymphagiectasis.
Vascular lesions in area of limb hypertrophy
Most common finding is limb hypertrophy.
Megancepaly, glucoma





HYPOMELANOSIS OF ITO

- Sporadic mutations and chromosomal mosaicism.
- Streaky, patchy, whorl-like or linear hypopigmented macules, palms, scalp and soles of feet are not affected
- Lesion start at birth small hypopigmented or white macules that merge to form large patches.
- 30-50% of patients may have
  Seizures
  Mental retardation
  Hearing abnormalities

HYPOMELANOSIS OF ITO