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 Classic)
Neurofibromatosis type 2 (Central or Acoustic)

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

Neurofibromatosis type 1
Cutaneous Manifestations

- Café-au-Lait Spots
- Axillary or inguinal Freckling
- Neurofibromas
- Plexiform Neurofibromas

Café-au-Lait Spots

Present at birth
Few millimeters to centimeters
Don’t increase in number after 2 years
Not found on scalp, palms, soles
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, Wilms' Tumor, Neurofibrosarcoma, Leukemia Rhabdomyosarcoma, 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

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
TUBEROUS SCLEROSIS

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

**SYSTEMIC MANIFESTATION**
- RENAL ANGIOMYOLIPOMA AND CYST 50-80%
- CARDIAC RHABDOMYOMA 50%, solitary, multiple
- PULMONARY LYMPHANGIOMATOSIS
- HAMARTOMA AND POLYPOSIS OF GI
- DENTAL ENAMEL PITS
- SCURVY LESION OF LONG BONE
- CYSTIC LESION OF METACARPALS AND PHALANGES
TUBEROUS SCLEROSIS DIAGNOSTIC CRITERIA

- PRIMARY FEATURES
  1. Facial angiomatosis or fohead 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

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

**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 patients have 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 hemiplegia 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, papillitis, nystagmus, cataracts.
- 8% with visual loss due to retinal detachment
- Skeletal abnormalities, hemivertebrae, accessory ribs
- Delayed dentition, pegged teeth

LINEAR SEBACEOUS 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 hemangio, tangiectases, varicosities, arteriovenous fistula, lymphangiectasis. Vascular lesions in area of limb hypertrophy. Most common finding is limb hypertrophy. Megancephaly, glaucoma

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