

# Phacomatoses (s. Neurocutaneous Disorders, Neuroectodermal Dysplasias)

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**PHACOMATOSES** - heterogeneous genetic neurocutaneous disorders characterized by **ECTODERM-based dysplasia, hamartomas** and **neoplasia**.

- **CNS, optic system, and skin** are primarily involved – *both originate from ectoderm* (other organ systems can also be affected) – most correct term **NEUROECTODERMAL DYSPLASIAS**.

*Van der Hoeve believed that ocular findings of neurofibromatosis and tuberous sclerosis were similar and suggested that they be classified together under inappropriate term phakomatosis (Gr. phakos - lentil, mole, birthmark, mother-spot).*

### AUTOSOMAL DOMINANT PHACOMATOSES

Disorder	Gene	Main Features
<i>Neurofibromatosis type 1</i> (von Recklinghausen's disease)	NF1 (17q)	neurofibroma, low-grade gliomas (optic, brain stem, cerebellar)
<i>Neurofibromatosis type 2</i>	NF2 (22q12)	ependymoma, astrocytoma, acoustic neuroma, meningioma
<i>Tuberous sclerosis</i> (Bourneville's disease)	TSC1 (9q), TSC2 (16p13)	1. <b>Brain</b> - tubers, subependymal nodules, subependymal giant cell astrocytoma; 2. <b>Skin</b> - adenoma sebaceum in face; "ash leaf" macules; fibromas; 3. <b>Heart</b> rhabdomyomas; 4. <b>Lung</b> lymphangioliomyomatosis; 5. <b>Renal</b> angiomyolipomata
<i>von Hippel-Lindau disease</i> see p. Onc24 >>	tumor-suppressor gene (3p25-26)	1. <b>Retinal</b> angiomatosis 2. <b>Cerebellar</b> hemangioblastomas 3. <b>Various visceral</b> tumors - kidneys [ <i>renal cell carcinoma</i> , cysts, angiomas], adrenal glands [ <i>pheochromocytoma</i> ], pancreas [cysts], epididymis [papillary cystadenomas, cysts], liver [angiomas, cysts], endolymphatic sac tumors
<i>Incontinentia pigmenti achromians</i> (hypomelanosis of Ito) see p. 2997 >>	different forms of <i>genetic mosaicism</i>	asymmetrical (unilateral or bilateral) areas of <b>hypopigmented macules</b> in whorls, streaks, patches ("marble-cake"), ± epidermal nevi, alopecia, anomalies of eyes, neuro, skeleton
<i>Waardenburg's syndrome (type I)</i> see p. 98 >>	PAX3 gene (2q)	<b>Frontal patch of white hair</b> , heterochromia iridis, lateral displacement of inner canthus, cochlear deafness, synophrys
<i>Waardenburg's syndrome (type II)</i> see p. 98 >>	MITF gene (3p)	Similar to type I <i>without lateral displacement of inner canthus</i> ; deafness is more common
<i>Rendu-Osler-Weber disease</i> (hereditary hemorrhagic telangiectasia) see p. 1606 (1-4) >>		Multiple <b>angiomas</b> (skin and mucous membranes); <b>bleeding</b> from any site: nose, GI, pulmonary, GU
<i>Proteus* syndrome</i> see p. Mus9 >>		Macrocephaly, mental deficiency, seizures, hemihypertrophy (asymmetrical arms or legs), large flat feet ("moccasin feet"), thickened skin, hyperpigmented areas, <b>hemangiomas</b> and <b>lipomas</b> (subcutaneous and abdominal), bony defects, macrodactyly, hypocalcemia

\*PROTEUS - Greek god who appeared in different forms

### AUTOSOMAL RECESSIVE PHACOMATOSES

Disorder	Gene	Main Features
<i>Ataxia-telangiectasia</i> see p. Mov50 >>	ATM gene (11q22.3-q23.1)	1. Progressive <b>cerebellar degeneration</b> 2. <b>Telangiectasias</b> (bulbar conjunctivae, malar eminences, ear lobes, upper neck, antecubital and popliteal spaces) 3. Combined (T & B cell) <b>immunodeficiency</b>
<i>Chédiak-Higashi syndrome</i> see p. 1671 (8-9) >>	CHS gene (1q)	<b>Phagocyte disorder</b> (recurring infection): partial oculocutaneous albinism, photophobia, neuropathy
<i>Refsum disease</i> (phytanic acid storage disease) see p. 750 >>	PEX1 gene (7q)	<b>Disorder of α-oxidation of phytanic acid</b> - retinal pigmentary degeneration, ichthyosis, demyelinating polyneuropathy, ataxia, sensorineural deafness, anosmia, cardiomyopathy
<i>Xeroderma pigmentosum</i> see p. 3001 (9-10) >>		<b>DNA repair defects</b> → premature aging and cancer of tissues exposed to sunlight; severe neurologic and ocular changes.
<b>ROTHMUND-THOMSON syndrome</b>		1. Erythemas (in early life) → telangiectasias → atrophy, hypo- / hyperpigmentation, ectodermal dysplasia. 2. Sparse or absent body hair. 3. Juvenile cataracts, short stature, hypogonadism, saddle nose, skeletal abnormalities. 4. Normal intelligence.
<b>SJÖGREN-LARSSON syndrome</b>	FALDH* gene (17p)	Congenital ichthyosis, oligophrenia, corticospinal tract dysfunction

\*fatty aldehyde dehydrogenase gene

*Ataxia-telangiectasia* is the only **AR** disorder among "common" neurocutaneous disorders!

### X-LINKED PHACOMATOSES

Disorder	Gene	Main Features
<i>Incontinentia pigmenti</i> (Bloch-Sulzberger disease) see p. 2997 >>	X-linked dominant ( <b>lethal in males!</b> )	<b>Skin lesions</b> in 4 stages (in 3 <sup>rd</sup> stage – hyperpigmentation in bizarre configurations); ± anomalies of CNS, heart, eyes, skeleton, teeth, nails, hair
<i>Fabry disease</i> (diffuse angiokeratoma) see p. 761 >>	X-linked recessive –	<b>Endothelial accumulation of globosides</b> - angiokeratosis; vascular accidents; dorsal root ganglia neuropathy; ocular, cardiac, GI, renal disease

	GLA* gene (Xq)	
<b>RUD syndrome</b>	X-linked recessive or sporadic	<ol style="list-style-type: none"> <li>1. <b>Ichthyosis</b> (ichthyosiform erythroderma).</li> <li>2. <b>Hypogonadism</b>.</li> <li>3. Less frequent - microcephaly, dwarfism, sensorineural deafness, polyneuropathy, hypoplastic teeth and nails, acanthosis nigricans.</li> </ol>

\*α-galactosidase gene

**SPORADIC PHACOMATOSES**

Disorder	Gene	Main Features
<i>Sturge-Weber syndrome</i> (encephalotrigeminal angiomatosis)	unknown	<b>Angiomas</b> in leptomeninges, skin of face, eye

BIBLIOGRAPHY for ch. "Phacomatoses" → follow this [LINK >>](#)