CEREBELLAR ATAXIA

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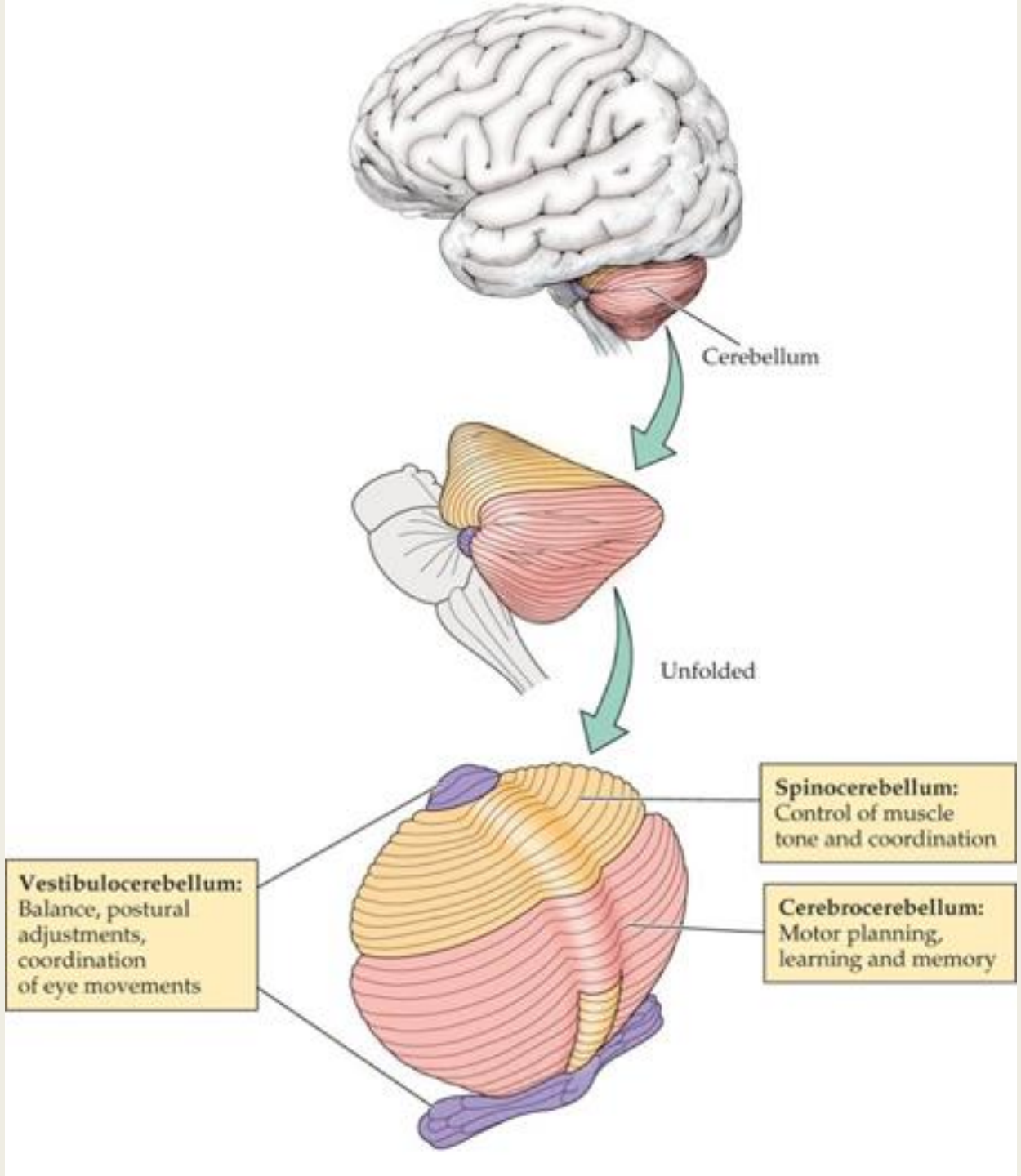
What is Ataxia?

- Derived from a Greek word, ‘A’ : not, ‘Taxis’ : orderly

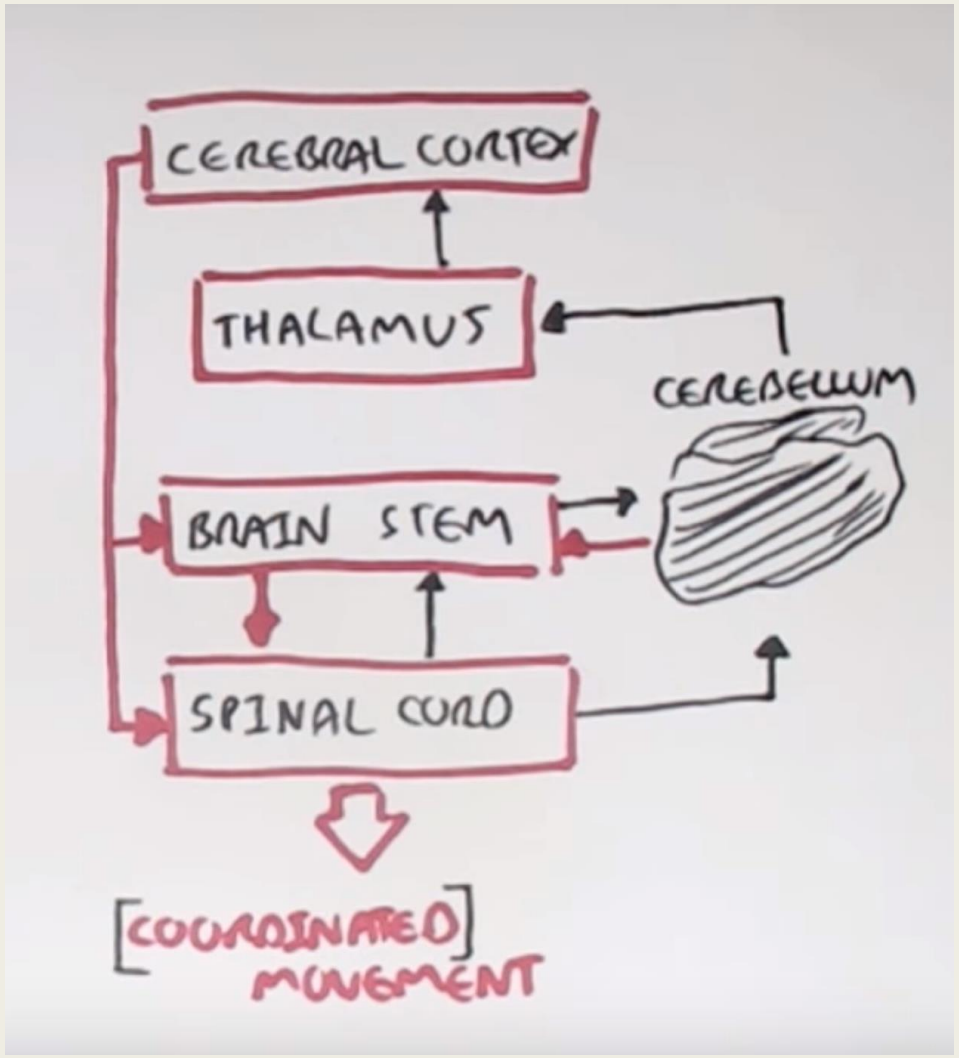
Ataxia is defined as an inability to maintain normal posture and smoothness of movement.

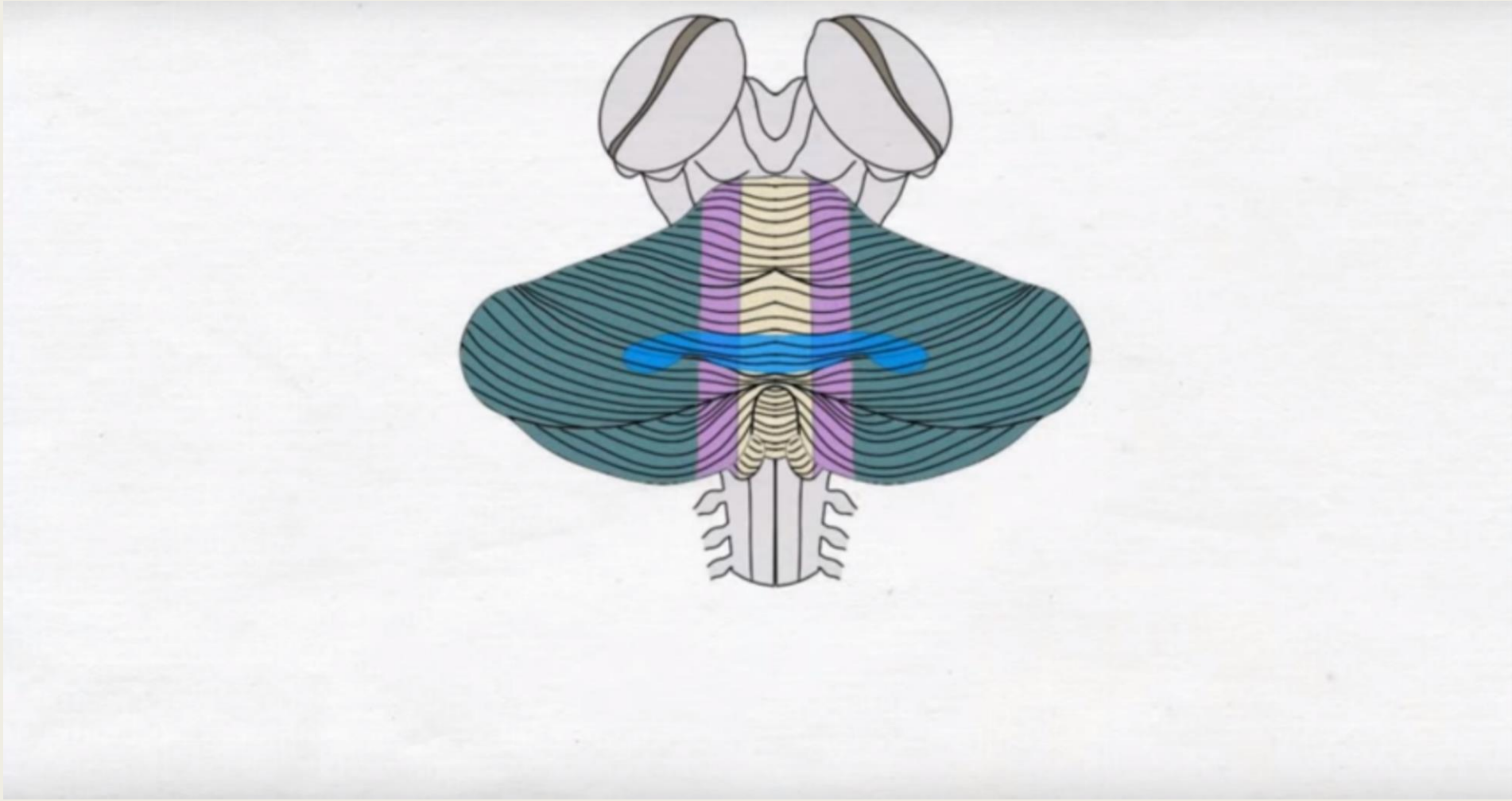
Types of Ataxia

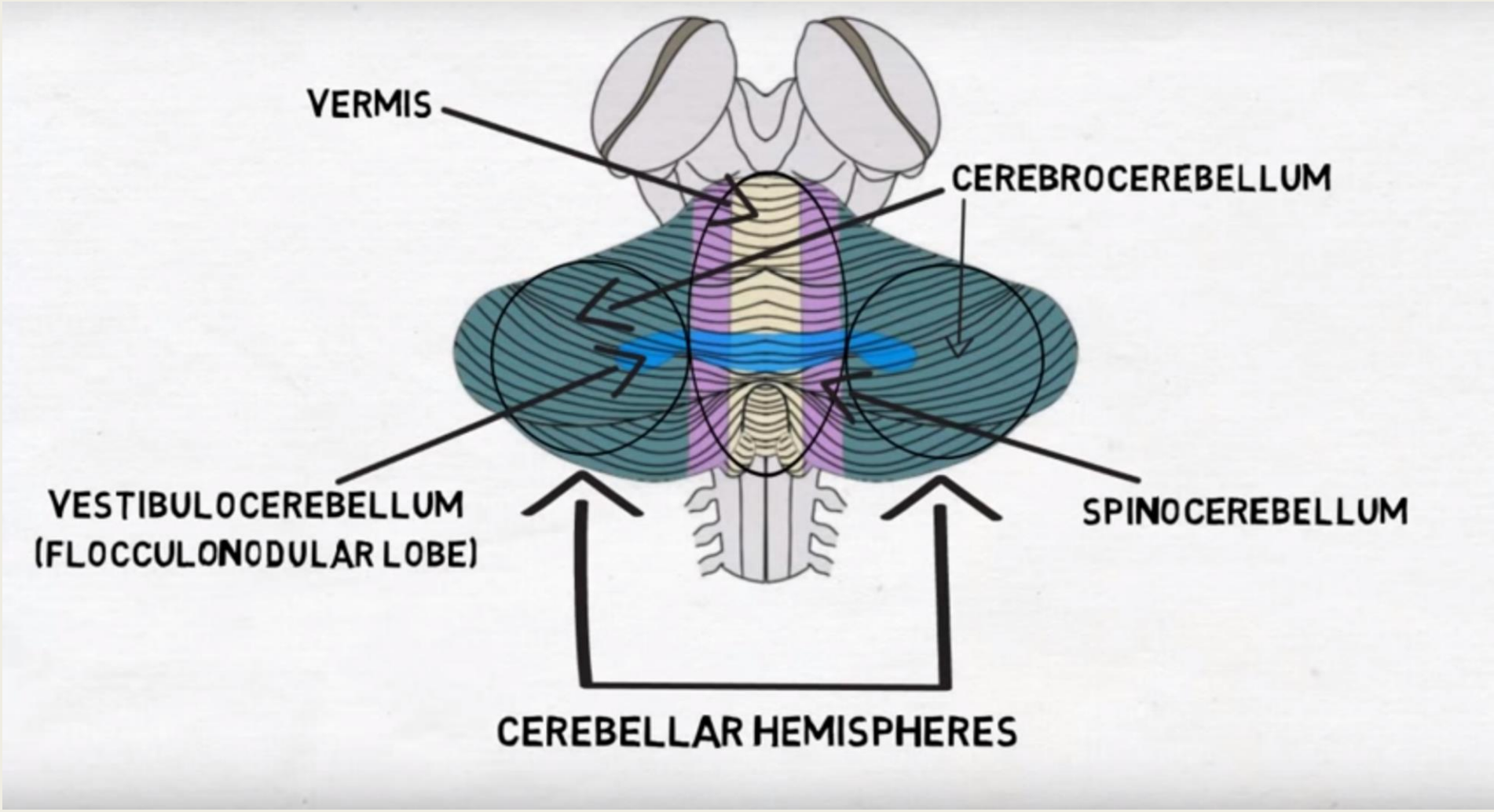
- Cerebellar Ataxia
- Sensory Ataxia
- Vestibular Ataxia



Cerebellar Ataxia


CEREBRAL CORTEX
THALAMUS
CEREBELLUM
BRAIN STEM
SPINAL CORD
[COORDINATED]
MOVEMENT




VERMIS
CEREBROCEREBELLUM
VESTIBULOCEREBELLUM
(FLOCCULONODULAR LOBE)
SPINOCEREBELLUM
CEREBELLAR HEMISPHERES

Cerebrocerebellum	Spinocerebellum	Vestibulocerebellum	Vermis
Planning and initiating movements	Limb position, touch and pressure sensation	Equilibrium balance and posture	Posture, limb and eye movements
Limb ataxia, dysdiadochokinesia, Dysmetria dysarthria hypotonia		Eye movement disorders, nystagmus, VOR, postural and gait.	Truncal and gait ataxia

Gait ataxia

Types of Cerebellar Ataxia

Acute Ataxia	• Vascular • Medications and toxins • Infectious etiologies
Subacute Ataxia	• Atypical Infectious agents • Autoimmune disorders • Primary or metastatic tumors • Paraneoplastic cerebellar degeneration • Alcohol abuse and Vitamin deficiencies • Systemic disorders
Chronic Progressive ataxias	• Autosomal Dominant • Autosomal recessive • X linked • Mitochondrial • Sporadic neurodegenerative diseases

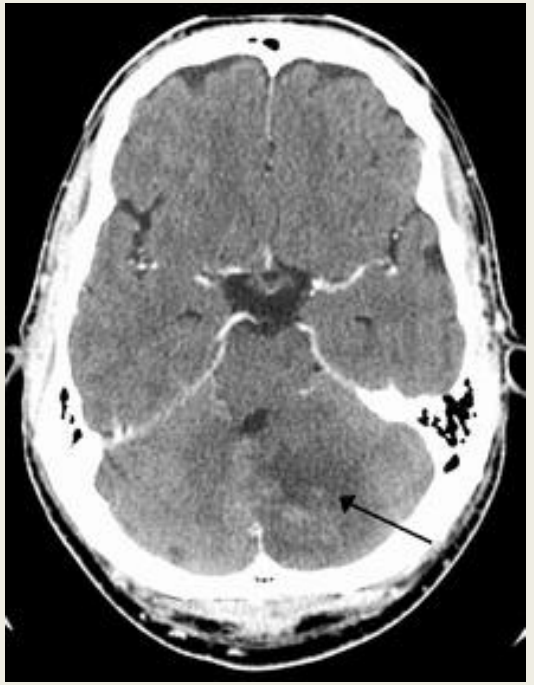
Vascular Ataxia

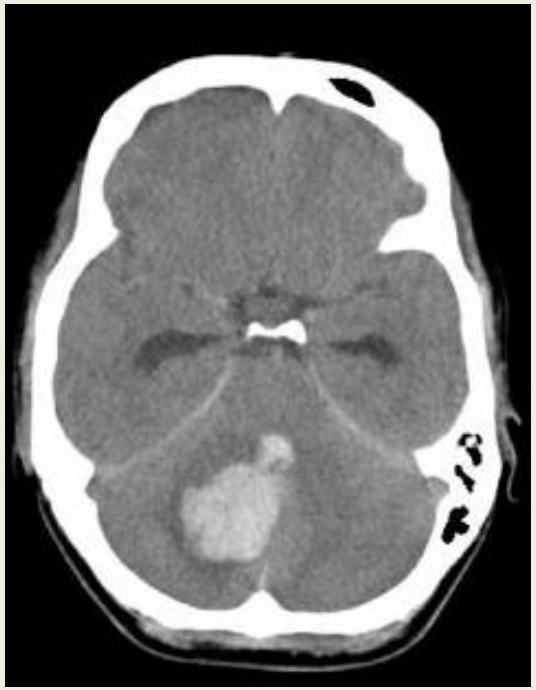
- **Benedikt Syndrome**

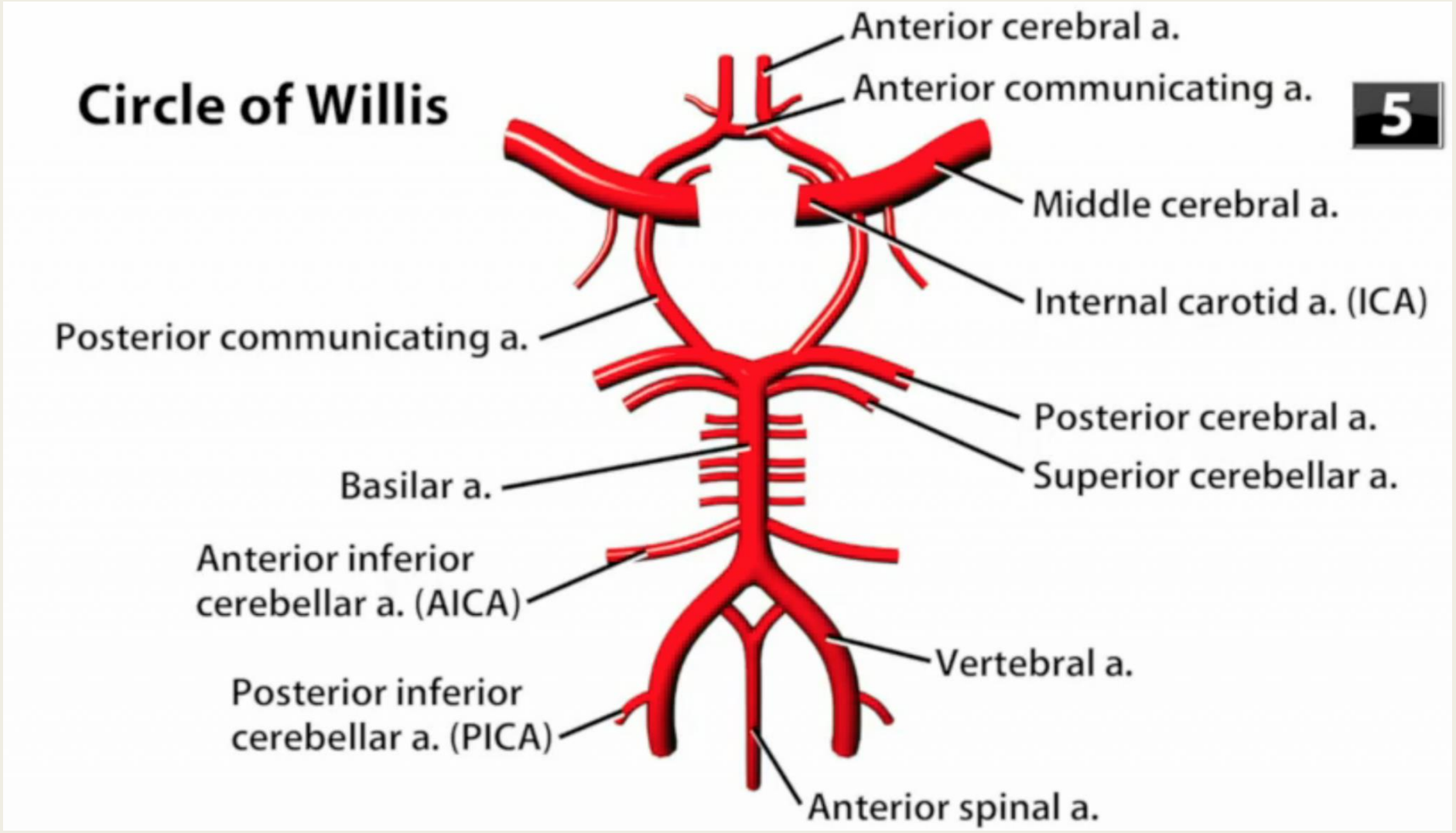
It is a rare form of posterior circulation stroke of the brain. A lesion within the tegmentum of the midbrain can produce Benedikt Syndrome. Disease is characterized by ipsilateral third nerve palsy with contralateral hemitremor. Superior cerebellar peduncle and/or red nucleus damage in Benedikt Syndrome can further lead in to contralateral cerebellar hemiataxia.

- **Wallenberg Syndrome**

In Wallerberg syndrome, which is also called Lateral medullary syndrome, there is dorsolateral infarction in the medulla. Damage to the cerebellum or inferior cerebellar peduncle causes ataxia.






Circle of Willis
5
Anterior cerebral a.
Anterior communicating a.
Middle cerebral a.
Internal carotid a. (ICA)
Posterior communicating a.
Posterior cerebral a.
Superior cerebellar a.
Basilar a.
Anterior inferior cerebellar a. (AICA)
Vertebral a.
Posterior inferior cerebellar a. (PICA)
Anterior spinal a.

Medications and toxins related ataxia

Format: Abstract Send to

Handb Clin Neurol. 2012;103:201-13. doi: 10.1016/B978-0-444-51892-7.00012-7.

Toxic agents causing cerebellar ataxias.

Manto M[1].

Author information

Abstract

The cerebellum is particularly vulnerable to intoxication and poisoning, especially so the cerebellar cortex and Purkinje neurons. In humans, the most common cause of a toxic lesion to the cerebellar circuitry is alcohol related, but the cerebellum is also a main target of drug exposure (such as anticonvulsants, antineoplastics, lithium salts, calcineurin inhibitors), drug abuse and addiction (such as cocaine, heroin, phencyclidine), and environmental toxins (such as mercury, lead, manganese, toluene/benzene derivatives). Although data for the prevalence and incidence of cerebellar lesions related to intoxication and poisoning are still unknown in many cases, clinicians should keep in mind the list of agents that may cause cerebellar deficits, since toxin-induced cerebellar ataxias are not rare in daily practice. Moreover, the patient's status may require immediate therapies when the intoxication is life-threatening.

PMID: 21827890 DOI: 10.1016/B978-0-444-51892-7.00012-7

[Indexed for MEDLINE]

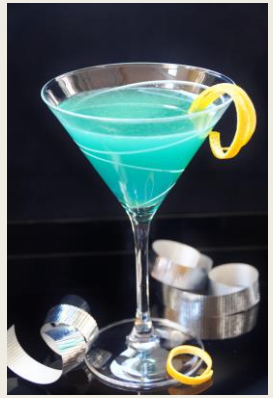
Acute Cerebellitis

- The sudden onset of ataxia following a viral infection
- It is most common in children, especially those **younger than age 3,** and usually occurs several weeks following a viral infection. Viral infections that may cause it include the following: **Varicella Zoster, Coxsackie disease** (viral infection also called hand-foot-and-mouth disease), **Creutzfeldt–Jakob disease** (a rare disease believed to be an infection that causes mental deterioration), **Lyme disease** (inflammatory bacterial disease spread by ticks), **mycoplasma pneumonia** (presents with atypical pneumonia), **Epstein–Barr virus** (Human Herpes Virus family) and **HIV.**

Wernicke’s encephalopathy

- Wernicke encephalopathy (WE) is a neurological disorder induced by thiamine, vitamin B1, deficiency.
- In long-term alcoholics, malnutrition can reduce intestinal thiamine absorption by 70%, decreasing serum levels of thiamine to between 30% and 98% below the lower level established for normal subjects
- Thiamine acts as a coenzyme in the metabolism of glucose and lipids, and, as stores of water-soluble vitamins are limited in the body, deficiency can present within 2 to 3 weeks of cessation of intake

- Without thiamine, glucose is metabolized through less efficient anaerobic pathways that produce lactic acid. Acidosis affecting periventricular structures (i.e., thalami, mammillary bodies, oculomotor nuclei, cerebellar vermis) accounts for the clinical presentation



ALCOHOL

Wernicke's Encephalopathy

IMIG

COMMON CAUSE
50 – 75% of W.E.

Alcohol
↓dietary intake
↓GI absorption
↓hepatic storage
impaired use

OTHER CAUSES

Malabsorption

Poor Intake
anorexia
hyperemesis pregn
IV feeding
fasting
GI surg
bariatric surg

Metabolic Req
systemic illness
transplant
AID

Loss of vitamins
renal dialysis

CLINICAL TRIAD: Only seen in ¼ pts
W.E. is often under diagnosed

1. ENCEPHALOPATHY (82%)

Disorientation, Indifference, Inattentiveness. 5% have ↓ed LOC

2. OCCULOMOTOR DYSFUNCTION (29%)

Nystagmus, Lateral Rectus Palsy, Conjugate Gaze Palsy, INO, Unequal Pupils, Light near dissociation, Nonreactive pupils, etc

3. GAIT ATAXIA (23%)

Primarily: Stance & gait

Unlike *Alcoholic Cerebellar Degeneration* W.E. has no upper limb ataxia

OTHER: peripheral neuropathy, hypothermia, cardiac, vestibular

Vitamin B1 (Thiamine) Deficiency

TREATMENT: *If suspected*

Thiamine & Thiamine

Thiamine BEFORE Glucose

Check Magnesium

KORSAKOFF'S SYNDROME

Chronic disease, progressed from untreated W.E.

Severe **retrograde & anterograde amnesia**

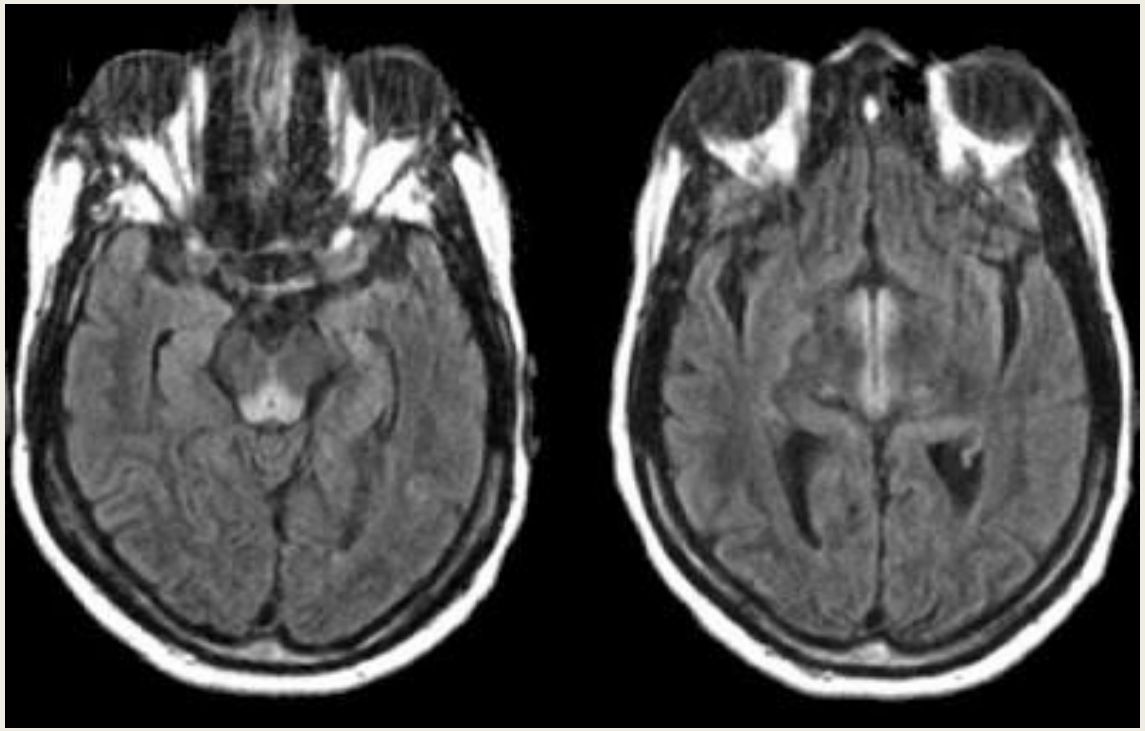
with relatively **preserved** long term memory, cognitive, and social skills

Confabulation sometimes present.

Pt **unaware** of their illness

- Alcohol abuse, AIDS, malignancy, hyperemesis gravidarum, prolonged total parenteral nutrition, iatrogenic glucose loading in a thiamine deficient patient, and other disorders associated with grossly impaired nutritional status are associated with WKS.

- Labs: Thiamine levels, high anion gap because of lactic acidosis
- MRI has high specificity so it's helpful in confirming diagnosis. Hyperintensity of periaquedal grey matter and hypothalamus.



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Immune Mediated Cerebellar Ataxia

Immune-mediated cerebellar ataxias include

1. Gluten ataxia
2. Paraneoplastic cerebellar degeneration
3. GAD antibody associated cerebellar ataxia
4. Hashimoto’s encephalopathy.

Gluten Ataxia

- Gluten ataxia is an immune-mediated disease triggered by the ingestion of gluten in genetically susceptible individuals.
- Up to 60% of patients with GA have evidence of cerebellar atrophy on MR imaging, but all patients have spectroscopic abnormalities primarily affecting the vermis.

Primary or metastatic tumors

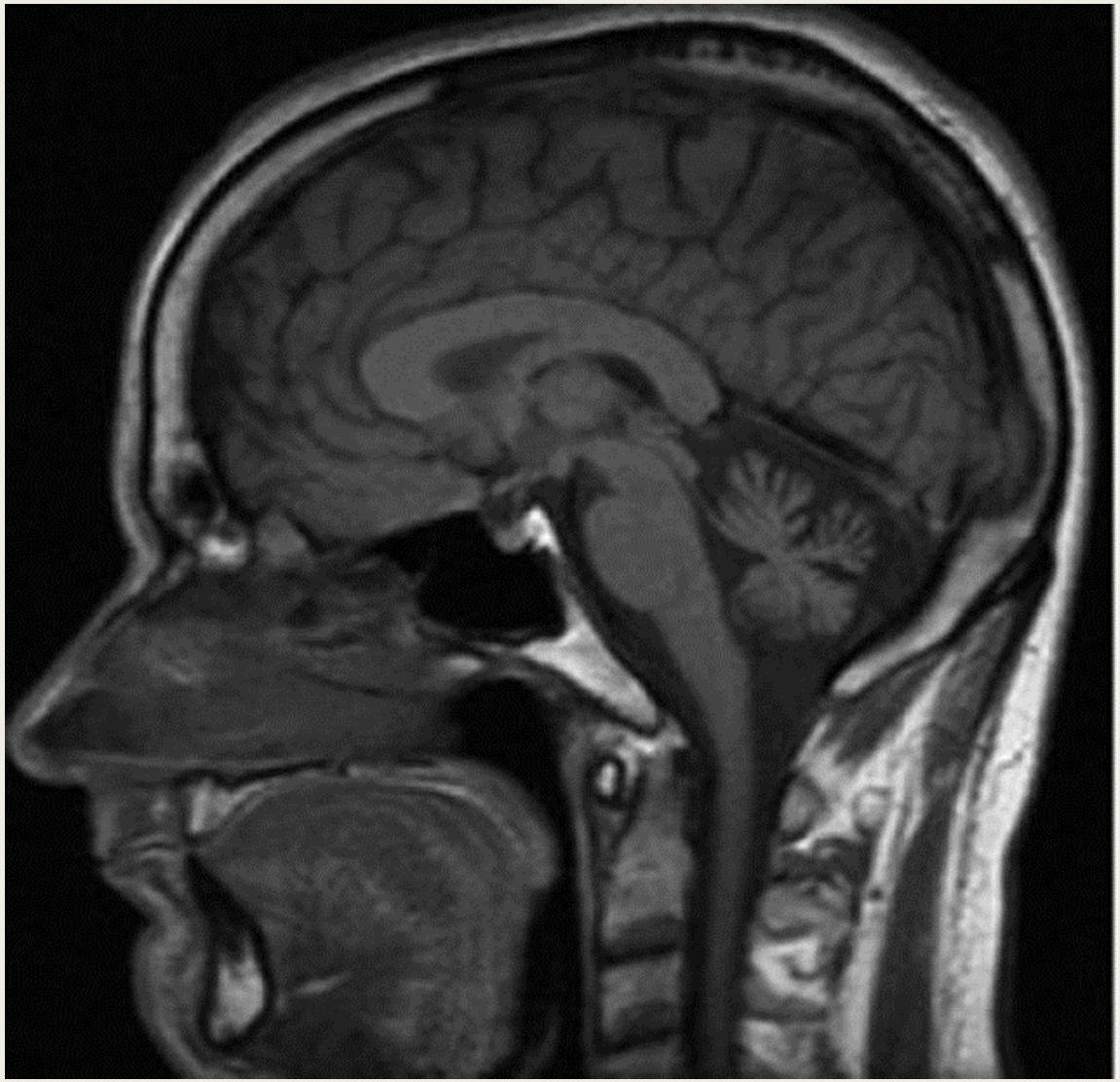
Paraneoplastic Cerebellar Degeneration

- Paraneoplastic cerebellar degeneration is a rare nonmetastatic complication of a carcinoma, typically mediated by antibodies generated against tumor antigens (proteins).
- Similar proteins are also expressed on Purkinje cells and possibly other cells within the cerebellum. The cancer-fighting antibodies mistakenly attack these normal protein cells in the cerebellum. This immune activation in the central nervous system (CNS) results in cerebellar injury and dysfunction defined as paraneoplastic cerebellar degeneration.

- Two major patterns of antibody response have been described: anti-Hu (type IIa, antineuronal nuclear antibodies type 1) and anti-Yo (type 1, anti-Purkinje cell antibodies [APCA]). Both anti-Yo and anti-Hu antibodies label patient tumors and are believed to be elicited by tumor antigens that are cross-reactive with neuronal antigens.

- Anti Yo antibodies: Gynecologic and breast melignancies
- Anti Hu antibodies: small-cell lung cancers and most neuroblastomas, occasionally sarcomas and prostate carcinoma
- Anti Ri antibodies: Breast malignancies

- Absence of paraneoplastic antibodies does not rule out a paraneoplastic syndrome particularly in patients with known cancer and neurologic symptoms; however, the presumptive diagnosis requires the absence of the metastatic and nonmetastatic complications of the tumor.



MRI brain shows atrophy of cerebellum in advanced cases

Glutamic Acid Decarboxylase antibody associated cerebellar ataxia

- Although the pathogenic role of GAD65-Abs is unclear, studies17,18 have shown that they interfere with the γ-aminobutyric acid–ergic synaptic transmission in tissue culture systems and that these effects are reversible after removing the GAD65-Abs

- Autopsy studies reveal loss of Purkinje cells in patients with GAD associated CA.

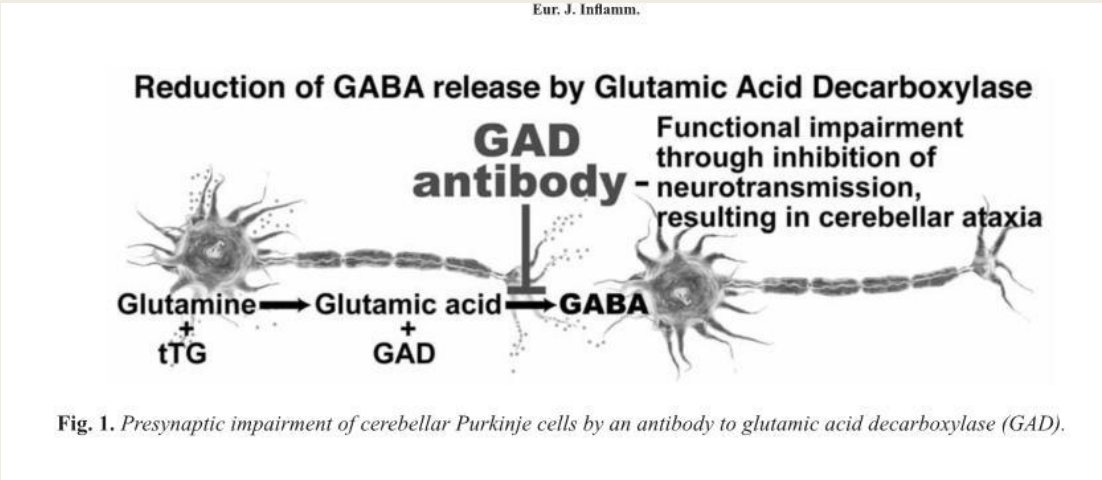


Fig. 1. *Presynaptic impairment of cerebellar Purkinje cells by an antibody to glutamic acid decarboxylase (GAD).*

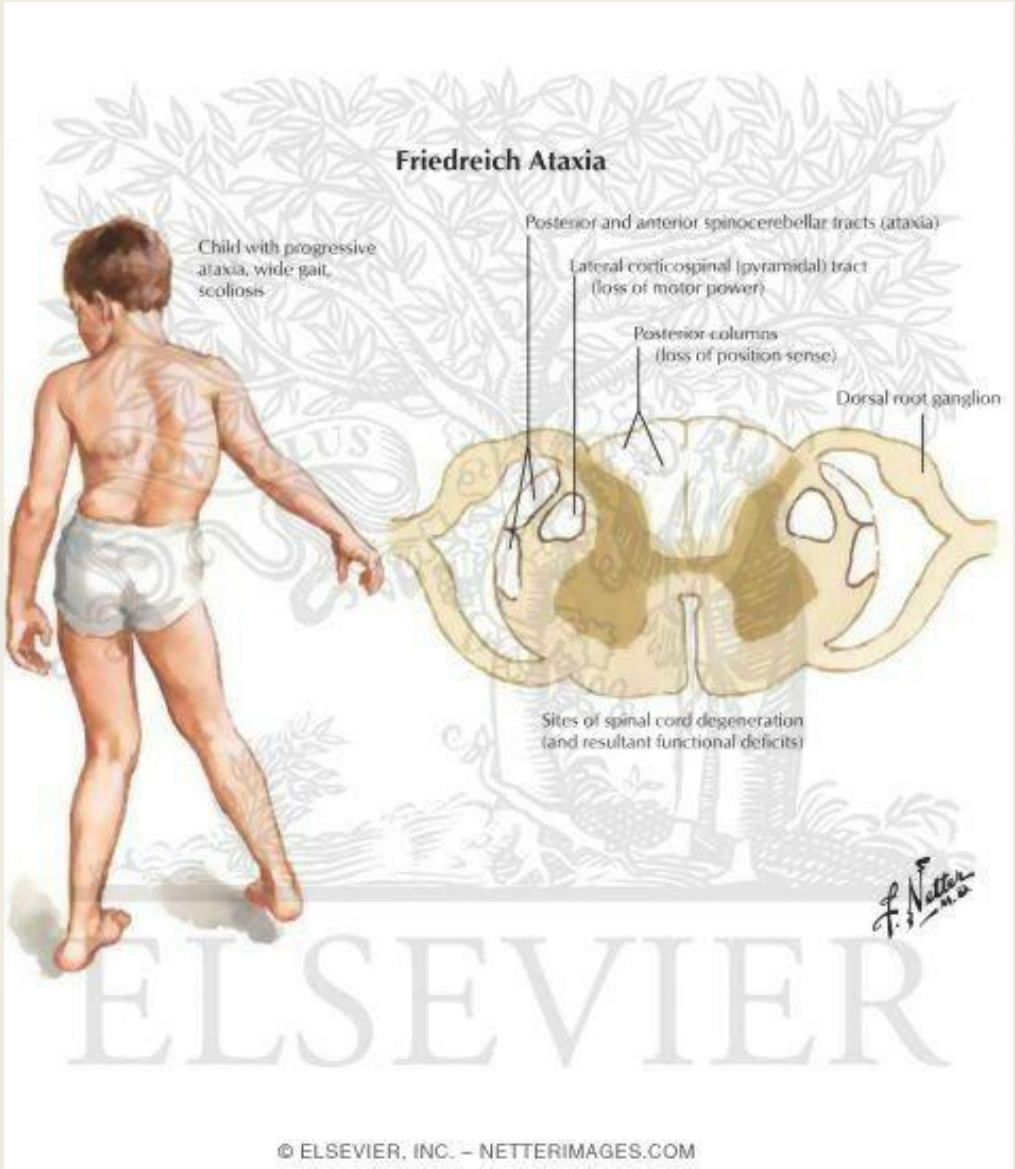
Reported first line immunotherapy for each subtype of immune-mediated cerebellar ataxias

Gluten ataxia
Induction and maintenance therapies: strict gluten-free diet
(In case of no improvement and negative gluten related antibodies, immunosuppressants or IVIg)
Paraneoplastic cerebellar degeneration
Quick removal of neoplasm must be the first objective of treatment
Induction therapy as soon as possible: mPSL, IVIg, immunosuppressants, or/and plasma exchange
Discussion according associated Abs
Maintenance therapy: continuous oral PSL, IVIg, immunosuppressants
Anti-GAD Abs associated cerebellar ataxia
Induction therapy: mPSL, IVIg, immunosuppressants, plasma exchange, or/and rituximab
Maintenance therapy: continuous oral PSL, IVIg, immunosuppressants, or/and rituximab

Abs antibodies, *mPSL* intravenous methylprednisolone, *oral PSL* oral prednisolone, *IVIg* intravenous immunoglobulins

Friedreich ataxia

- Friedreich ataxia is an autosomal recessive ataxia resulting from a mutation of a gene locus on chromosome 9 leading to fraxatin (iron chaperone) gene mutation
- Excessive mitochondrial accumulation of iron affects cytosolic iron levels leading to generation of oxygen free radicals.
- The posterior columns and corticospinal, ventral, and lateral spinocerebellar tracts all show demyelination and depletion of large myelinated nerve fibers. The dentate nuclei exhibit mild to moderate neuronal loss and the middle and superior cerebellar peduncles are reduced in size.


Friedreich Ataxia
Child with progressive ataxia, wide gait, scoliosis
Posterior and anterior spinocerebellar tracts (ataxia)
Lateral corticospinal (pyramidal) tract (loss of motor power)
Posterior columns (loss of position sense)
Dorsal root ganglion
Sites of spinal cord degeneration (and resultant functional deficits)
F. Netter M.D.
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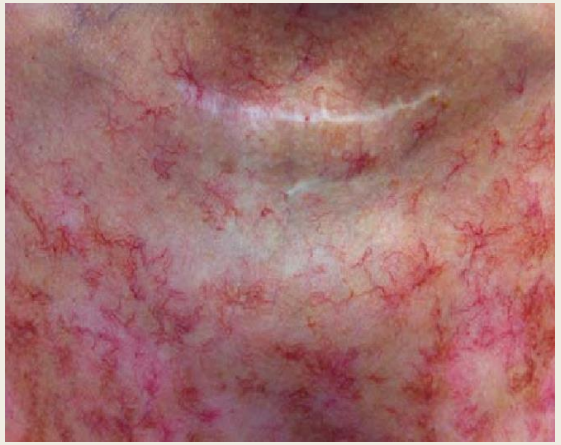
- Magnetic resonance imaging (MRI) is the study of choice in the evaluation of the atrophic changes seen in Friedreich ataxia. MRI of the brain and spinal cord in patients with FA consistently shows atrophy of the cervical spinal cord with minimal evidence of cerebellar atrophy.

- Treatment: 5-Hydroxytryptophan, Coenzyme Q (buffer free radical formation)

Ataxia Talengiectasia Syndrome

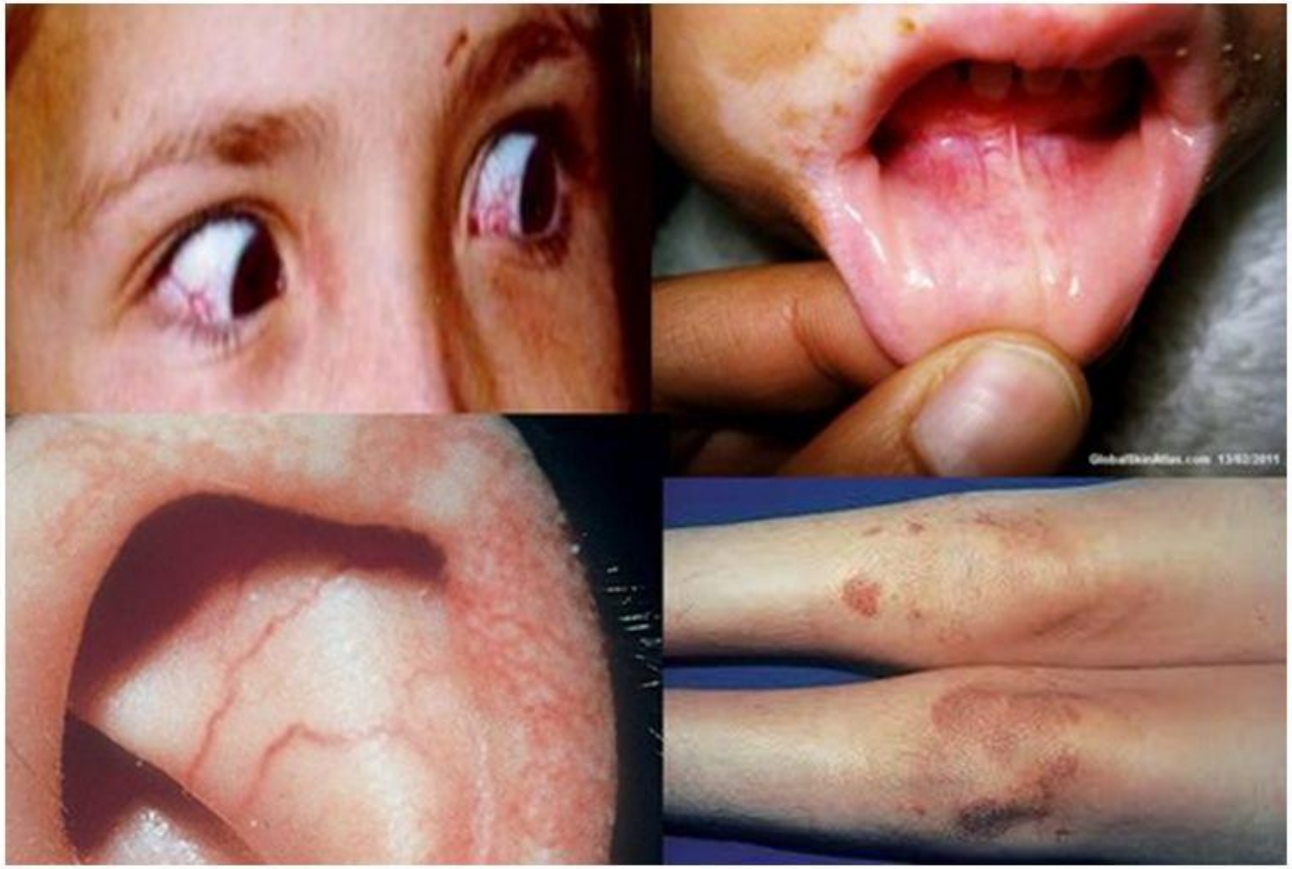


- Ataxia-telangiectasia (A-T) is an autosomal recessive, complex, multisystem disorder characterized by progressive neurologic impairment, cerebellar ataxia, variable immunodeficiency with susceptibility to sinopulmonary infections, impaired organ maturation, x-ray hypersensitivity, ocular and cutaneous telangiectasia

- The ATM gene encodes the protein kinase ATM, which is the key regulator of cellular response to double-strand breaks in DNA.

- The mechanisms responsible for neurologic disease, thymus aplasia, telangiectasias, growth retardation, and impaired organ mutation have not been elucidated, but most likely, they are linked to accelerated telomere loss.

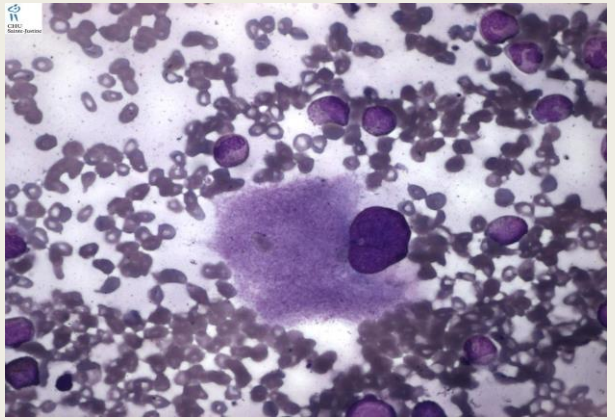
A-T has symptoms of ataxia, telangiectasia, and radiation sensitivity



Sphingolipidoses

- Niemann-Pick disease (NPD) is a lipid storage disorder that results from the deficiency of a lysosomal enzyme, acid sphingomyelinase.
- The enzymatic defect results in pathologic accumulation of sphingomyelin (which is a ceramide phospholipid) and other lipids in the monocyte-macrophage system, the primary site of pathology in patients with NPD. Additional progressive deposition of sphingomyelin in the CNS results in the neurodegenerative course observed in **NPD type A**, which shares systemic disease manifestations with NPD type B

The pathologic hallmark in Niemann-Pick disease (NPD) types A and B is the histochemically characteristic lipid-laden foam cell, often termed the Niemann-Pick cell, on bone marrow examination.

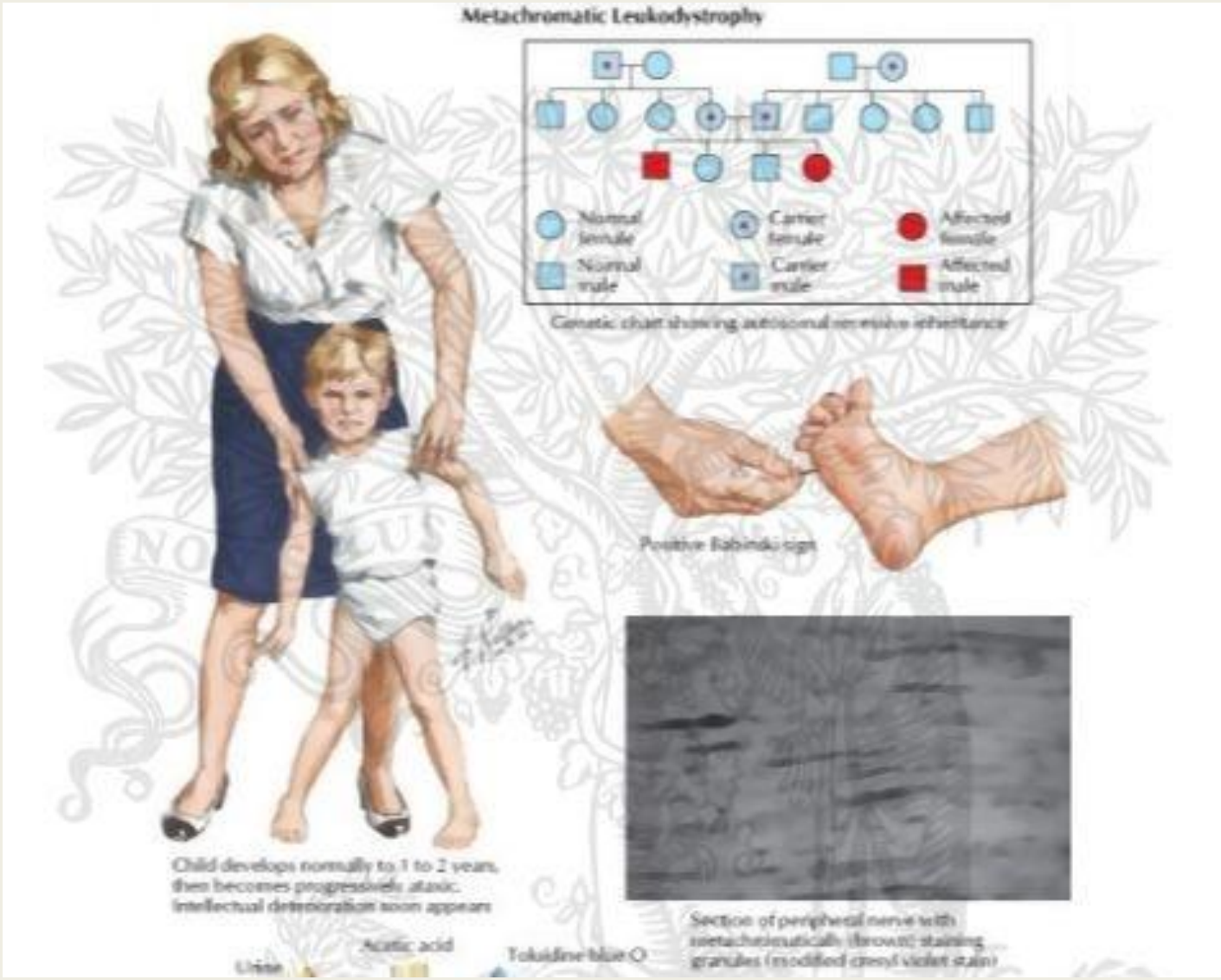


- At present, no specific treatment is available for patients with any Niemann-Pick disease (NPD) type A, and treatment is symptomatic.

Meta chromatic leukodystrophy

- All forms of the disease involve a progressive deterioration of motor and neurocognitive function.

- A deficiency in the lysosomal enzyme sulfatide sulfatase (arylsulfatase A) is present in metachromatic leukodystrophy. Defects result in the accumulation of sulfatide compounds in neural and in nonneural tissue, such as the kidneys and gallbladder.



Rx: Recombinant human arylsulfatase A (rhARSA) enzyme is available in Europe

Leigh disease, ***also known as subacute necrotizing encephalomyelopathy (SNEM), is a progressive neurodegenerative disorder and invariably leads to death in childhood.***

Clinical presentation

Typically, symptoms become evident before the age of 2, with the presentation in later childhood (juvenile form) or adulthood (adult form) being uncommon. Symptoms include:

psychomotor delay/regression

superimposed signs of basal ganglia and brainstem dysfunction

- ***ataxia***
- ***opthalmoplegia***
- ***dystonia***
- ***respiratory rhythm disturbance***
- ***cranial nerve palsies***

Approach to Ataxia