

# Ultimate Guide to Patient Diagnosis and Case Studies #2

Brain Resource Guide by Simply Neuroscience



simply  
neuroscience

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# Spinocerebellar Ataxia (SCA)

## Overview:

- Group of hereditary ataxias, characterized by degenerative changes in the cerebellum (motion control), & sometimes in spinal cord.
- Caused by mutations in genes
- For some types, the gene known to cause it has been identified, while in others, the genetic cause is still unknown (about 40% to 25% of the cases).

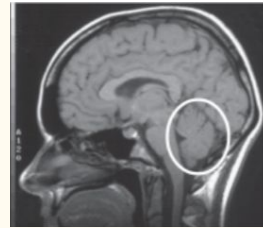
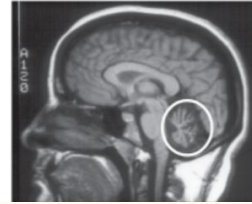


Photo courtesy of University of Washington

# Spinocerebellar Ataxia (SCA)

## Symptoms:

- Problems with coordination and balance (Poor hand-eye coordination) (ataxia)
- Uncoordinated walk
- Involuntary eye movement & vision problems
- Difficulty processing, learning, and remembering information

# Spinocerebellar Ataxia (SCA)

## **Diagnostic Tests:**

- Carrier testing for at-risk relatives and prenatal testing are possible if disease-causing mutations in family are known.
- Genetic testing is best way to confirm SCA and identify the specific type
- A diagnosis is often suspected when symptoms are present.

# Spinal Muscular Atrophy (SMA)

## Overview:

- Spinal muscular atrophy (SMA) is a disease that robs people of physical strength by affecting the motor nerve cells in the spinal cord, taking away the ability to walk, eat, or breathe.
- SMA is caused by a mutation in the survival motor neuron gene 1 (SMN1).
- It is the number one genetic cause of death for infants.

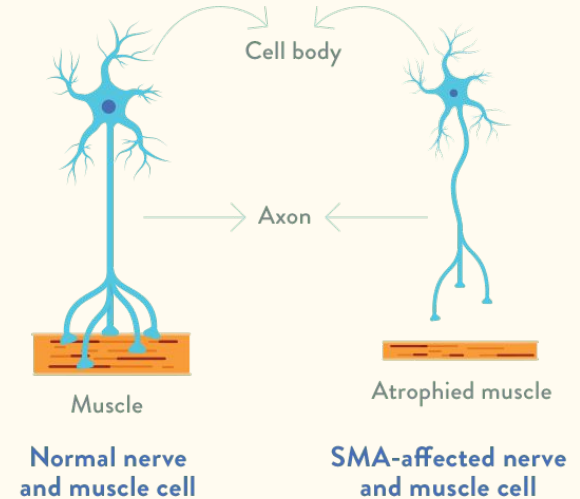


Photo courtesy of  
[https://www.togetherinsma.com/en\\_us/home/introduction-to-sma/smn1-gene.html](https://www.togetherinsma.com/en_us/home/introduction-to-sma/smn1-gene.html)

# Spinal Muscular Atrophy (SMA)

## Symptoms:

- Individuals with SMA have difficulty performing the basic functions of life, like breathing. However, SMA does not affect a person's ability to think, learn, and build relationships with others.
- Swallowing or feeding may also become difficult, and children may lose the ability to swallow safely without choking or inhaling food into the lungs (aspiration).
- Individuals with SMA lack the ability to hold their head up, to roll over, or to sit up independently.

# Spinal Muscular Atrophy (SMA)

## Diagnostic Tests:

- Doctor may order an electrical study called EMG (electromyography) or perform a muscle biopsy to confirm the diagnosis of SMA.
- Newborn screening: Although newborn screening is not yet standard practice, time to an SMA diagnosis is critical. Earlier diagnosis may help improve outcomes for children with spinal muscular atrophy.
- qPCR: Detects copy number (dosage) of the SMN1 and SMN2 genes in patient affected with spinal muscular atrophy (SMA).

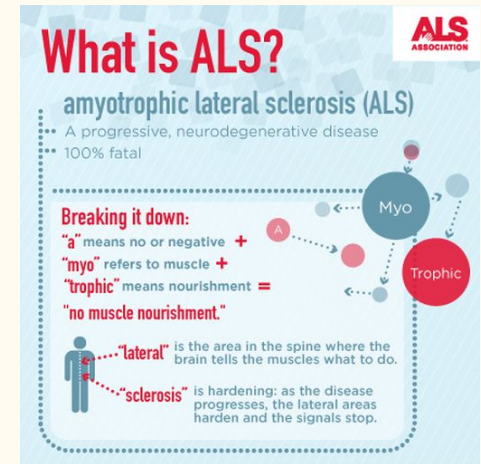


# Amyotrophic Lateral Sclerosis (ALS)

## Overview:

- ALS damages motor neurons as well as neurons responsible for cognition and behavior.
  - Motor neurons extend from the brain to spinal cord and muscles
- The cause is currently unknown, but some research suggests that it is a combination of genetic and environmental factors
- It takes an average of about 9-12 before an individual with ALS notices the first symptoms.
- The average life expectancy is 2-5 years, but many affected live longer, notably Stephen Hawking who lived with it for over 50 years.

Photo courtesy of  
<https://www.alsa-midamerica.org/about-als>



# Amyotrophic Lateral Sclerosis (ALS)

## Symptoms:

- Muscular
  - Weakness, Spasms, Loss of Muscle
- General
  - Fatigue, Tiredness
- Speech
  - Difficulty speaking
- Other
  - Drooling, constipation, shortness of breath, difficulty swallowing

### Amyotrophic Lateral Sclerosis (ALS)

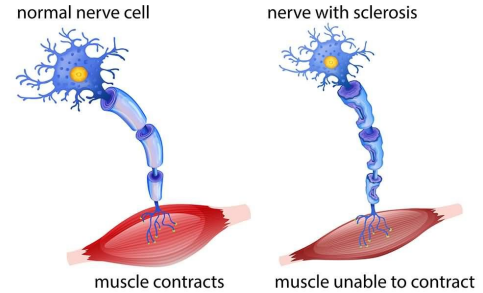


Photo courtesy of  
<https://healthella.com/als-symptoms/>

# Amyotrophic Lateral Sclerosis (ALS)

## Diagnostic Tests:

- Electromyogram (EMG)
  - A test where a doctor inserts a needle electrode that monitors the electrical activity of muscles to determine if they function properly.
- MRI
  - An MRI produces a detailed image of your brain which can reveal tumors or other conditions that may cause symptoms similar to ALS.
- Nerve conduction study
  - This study measures the ability of your body's nerves to send signals to different muscles in the body .

# Tay-Sachs Disease



## Overview:

- A disorder that causes the destruction of nerve cells → loss of muscle control
  - Occurs when the enzyme to break down gangliosides, a fatty substance isn't present and causes toxic build up in the brain
- The disease is inherited, autosomal recessive
- Symptoms begin to develop in infants about 3-6 months old
- Avg lifespan is 4-5 years in infantile form ("common" form)

# Tay-Sachs Disease

## Symptoms (in infants):

- 3-6 months
  - Muscle weakness
  - Loss of muscle tone
  - Exaggerated sensory reactions
  - Myoclonic jerks
- 6-10 months
  - Loses ability to sit, crawl, etc.
  - Decreased eye movement
- >10 months
  - Unresponsive state
  - Loss of vision
  - Seizures
  - Trouble swallowing

“Cherry spot” on retina (pictured to below) is present in all pts

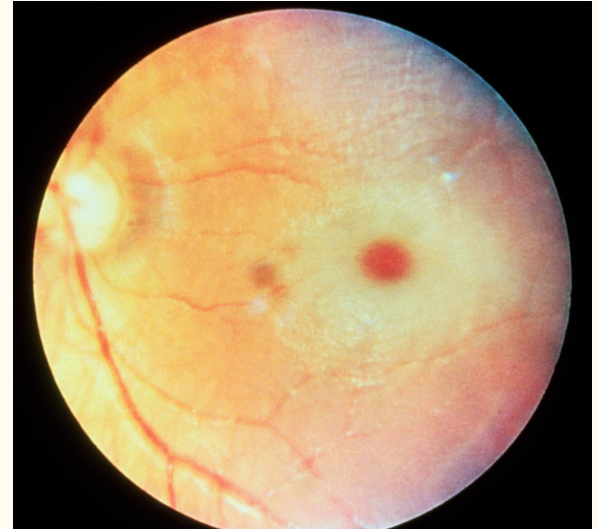


Photo courtesy of Ralph C. Eagle, Jr./Science Photo Library

# Tay–Sachs Disease

## Diagnostic Tests:

- Blood test
  - Detect the level of hexosaminidase A in the bloodstream
    - Patients with Tay Sachs disease have very low levels to no hexosaminidase A
    - Hexosaminidase A is produced by the HEXA gene → a mutation on that gene causes the disease
- Eye Exam
  - A doctor will check for a “cherry spot” on the macula
- Genetic Testing & Prenatal Diagnosis
  - Genetic testing is suggested if the disease had been known to run in the family or if it is common in the ethnicity of the parents
  - Prenatal testing options are chorionic villus sampling, amniotic fluid testing, and preimplantation genetic diagnosis

# Locomotor Ataxia

## Overview:

- Inability to control one's own bodily movements
- Usually a symptom of tabes dorsalis
- Patients suffer from a variation of loss of coordination in movement
- Due to the degeneration of the posterior white column of spinal cord
- More frequent in males than in females

# Locomotor Ataxia

## Symptoms:

- Poor coordination
- Unsteady walk
- Difficulty with fine motor tasks (writing, eating, etc.)
- Muscle weaknesses
- Joint damage
- Vision changes
- Bladder control problems



# Locomotor Ataxia

## Diagnostic Tests:

- **Cerebrospinal fluid (CSF) analysis:** looks for conditions that affect your brain and spine
  - Series of lab tests performed on a sample of CSF that delivers nutrients to your CNS
- **Head CT, spine CT or MRI scans** of the brain and spinal cord
- **VDRL test:** assesses if you have a syphilis
  - Measures antibodies which could be produced when there are bacteria causing syphilis
  - Using a sample of the spinal fluid

# Corticobasal Degeneration

## Overview:

- A progressive neurological disorder marked by nerve cell loss and atrophy (shrinkage) of multiple brain areas
  - Damaged areas also include the **cerebral cortex** and **basal ganglia**
- Initial symptoms typically begin at/or around age 60, with cell loss and atrophy first appearing on one side of the body, but eventually affect both sides as the disease progresses
- Symptoms are similar to Parkinson disease
- Eventually, the individual becomes unable to walk

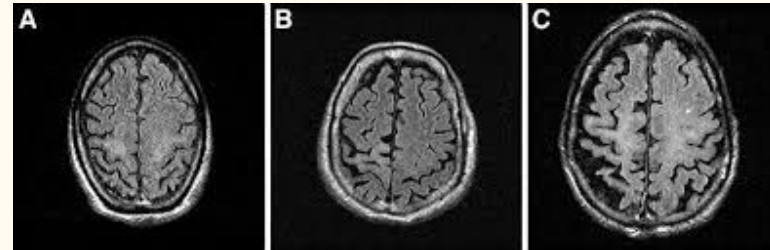


Photo courtesy of Extras Springers

# Corticobasal Degeneration

## Symptoms:

- Poor coordination
- Akinesia (an absence of voluntary movements)
- Rigidity (a resistance to imposed movement)
- Disequilibrium (impaired balance)
- Limb dystonia (abnormal muscle postures)
- Cognitive and visual-spatial impairments that can occur:
  - Apraxia (inability to make familiar, purposeful movements)
  - Hesitant and halting speech
  - Myoclonus (muscular jerks)
  - Dysphagia (difficulty swallowing)



# Corticobasal Degeneration

## Diagnostic Tests:

- There is no single test for Corticobasal Degeneration, which makes it difficult to diagnose, especially because the conditions has similar symptoms to a number of other diseases
- Diagnosis is based on the pattern of symptoms
- Brain scans (MRI, PET)
  - This is needed to rule out other conditions such as Parkinson's disease
- Neuropsychological testing
  - Involves “memory tests” designed to evaluate the full extent of symptoms
  - Assessment of: memory, concentration, understanding language, visual information processing, numbers and counting
- There is no treatment to slow the course of the disorder and associated symptoms are therapy resistant

# Infantile Refsum Disease

## Overview:

- Rare autosomal recessive disorder that occurs within the Zellweger spectrum.
- Zellweger spectrum disorders are associated with mutations in the PEX family of genes.
- Associated with deficient phytanic acid catabolism, but is different from Adult Refsum Disease.

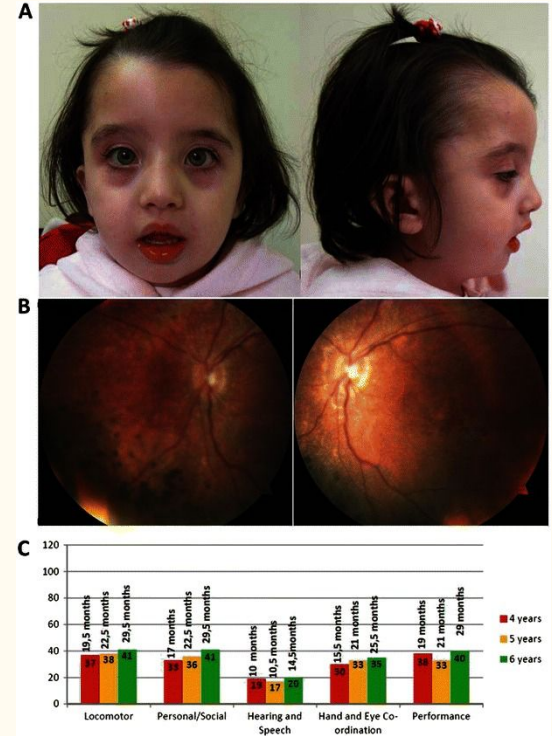


Photo courtesy of Europe PMC

# Infantile Refsum Disease

## Symptoms:

- Nystagmus
- Hypotonia
- Sensorineural Hearing Loss
- Growth Retardation
- Mild Facial Dysmorphism
- Hepatomegaly

# Infantile Refsum Disease

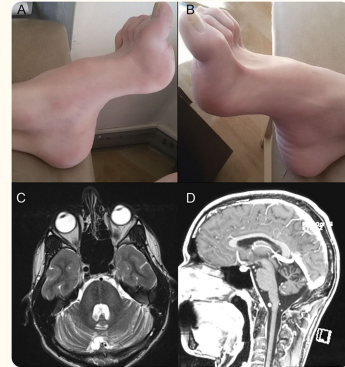
## Diagnostic Tests:

- Suspected on physical exam
- Biochemical evaluation used to confirm disease

# Autosomal recessive spastic ataxia of Charlevoix-Saguenay

## Overview:

- Autosomal recessive spastic ataxia of Charlevoix-Saguenay or ARSACS is a condition that affects muscle movement
- The condition is caused by a mutation in the SACS gene which creates the protein Sacsin
- The condition is named after the region in Quebec where it was first discovered and where it's most prevalent.



**Photo courtesy of Paula Saffie  
et al.**



# Autosomal recessive spastic ataxia of Charlevoix-Saguenay

## Symptoms:

- The first symptom that arises is an unsteady gait. The walking problems arise around the ages of 12-18 months
- Additional muscle controls such as amyotrophy, nystagmus, dysphagia and dysarthria
- Other main features of the body include scoliosis, pes cavus, hypermyelination of the retina, and recurring seizures.

# Autosomal recessive spastic ataxia of Charlevoix-Saguenay

## **Diagnostic Tests:**

- Diagnostics -traditionally- rely on MRI and CT scans in order to reveal atrophy of the cervical spinal cord, retinal examination for hypermyelination, and detection of SACS mutations.
- Differential Diagnostics include other autosomal recessive ataxias and forms of spastic paraplegia
- Antenatal Diagnostics are possible when the disease-causing mutation has been identified in the developing fetus before birth.



# Cohen-Gibson Syndrome

## Overview:

- Cohen-Gibson Syndrome describes fetal or early childhood overgrowth leading to a tall and abnormal bone structure accompanied by mild-to-severe intellectual disability
- Cohen-Gibson Syndrome is caused by a mutation to the embryonic ectoderm development (EED) gene
- There are 8 officially diagnosed patients
  - The age of diagnosis ranges from 5 to 27 years old



Photo courtesy of Journal of  
Human Genetics

# Cohen-Gibson Syndrome

## Symptoms:

- Mildly increased birth weight/height
- Tall stature
- Macrocephaly (abnormally large head)
  - *Illustrated in the image below*
- Large hands and feet
- Advanced bone age
- Mild to severe intellectual disability
- May develop scoliosis

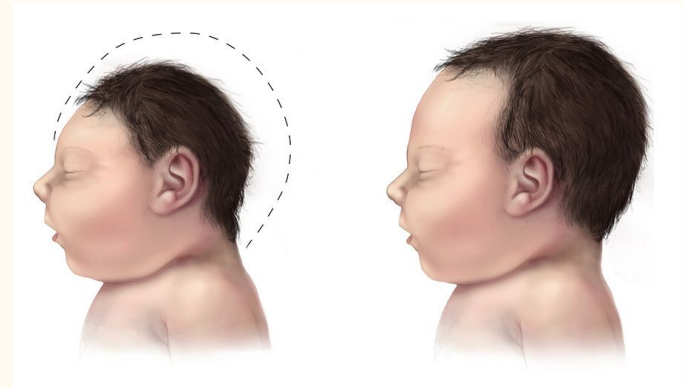
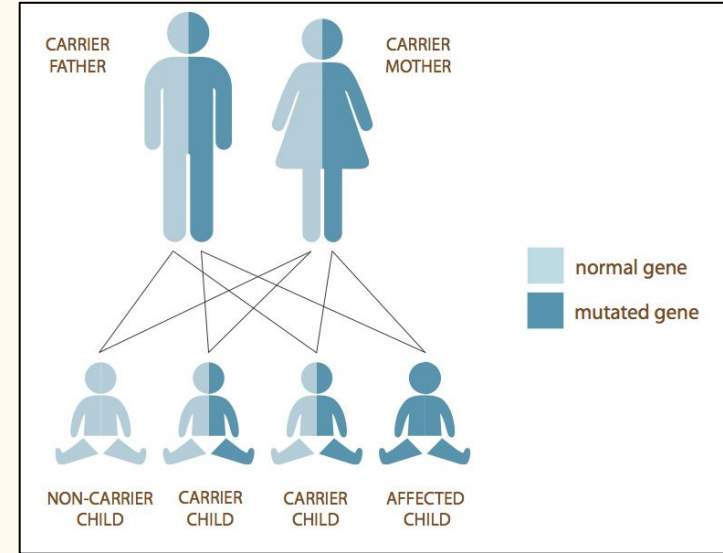


Photo courtesy of Contagion Live

# Cohen-Gibson Syndrome

## Diagnostic Tests:

- Cohen-Gibson Syndrome occurs because of a genetic mutation
- In order to diagnose the disease, the patient and their family undergo genetic screening
  - A sample of the patient's genes from hair, skin or blood is compared to healthy human genes to identify mutations



**Photo courtesy of Jewish Genetic Disease Consortium**

# Pontocerebellar Hypoplasia

## Overview:

- Characterized by a **small, underdeveloped cerebellum** and **pons**
- **10** different types
  - Major forms: **Type 1 (PCH1)** and **Type 2 (PCH2)**
- Causes by **genetic** factors
  - Autosomal recessive
  - 50% of cases linked to mutation in EXOSC3 gene (processes RNA molecules, crucial to development of neurons)
- Most only live into **infancy or childhood**

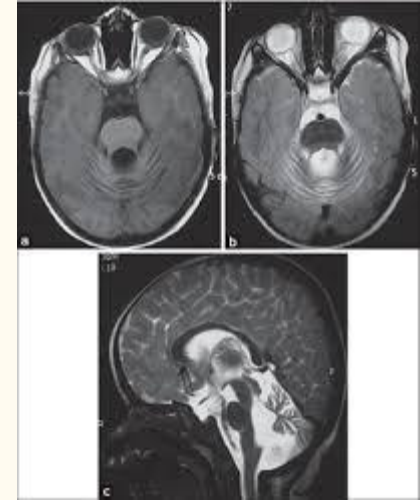


Photo courtesy of **Journal of Pediatric Neurosciences**

# Pontocerebellar Hypoplasia

## Symptoms:

- Usually **develop at birth** and become more pronounced with age
  1. Impaired brain development and delayed overall development
  2. Problems with movement
  3. Intellectual disabilities
  4. Seizures
  5. Temporary jitteriness
  6. Weak muscle tone and joint deformities
  7. Vision impairment

# Pontocerebellar Hypoplasia

## Diagnostic Tests:

- Brain imaging (MRI, CT scan)
  - Shows **cerebellum and pons size**
- Genetic testing (confirm PCH1 mutation)
- Diagnosed at birth by symptoms

## Treatment

- No cure, focused on relieving symptoms
  - Physical therapy to help with joints
  - Ventilation for breathing assistance
  - Feeding tube
  - Anti-seizure medication



# Kufor–Rakeb Syndrome

## Overview:

### What is it?

- Extremely **rare form of Parkinson disease**
- Characterized by **juvenile** parkinsonism; symptoms develop from about age 10-20; lifespan varies

### What causes KBS?

- KBS is an NBIA (neurodegeneration with brain iron accumulation) disorder; KBS is caused by mutations of NBIA genes
- ATP13A2 AKA PARK 9 is the only known gene to cause KBS; this gene's main job is to make ATPase 13A2 which transports cations

# Kufor–Rakeb Syndrome

## Symptoms:

- **Parkinsonism:** bradykinesia, rigidity, tremors
- **Oculogyric dystonic spasms:** rotating of eyeballs to fixed upward position
- **Pyramidal tract signs;** Pyramidal tract is the motor pathway between brain and spine: hyperreflexia, spasticity, paresis, Babinski sign
- **Cognitive decline:** Not much research, disease can lead to dementia
- **Visual hallucinations**



# Kufor–Rakeb Syndrome

## Diagnostic Tests:

- **MRI** (Magnetic Resonance Imaging), preference to T2 sequence type because of its sensitivity of brain iron
  - MRI can show hypointensity (dark parts) in the globus pallidus, putamen, and caudate; These parts indicate iron accumulation and usually suggest a more severe case.
- **Genetic testing** of PARK 9 gene for changes.
  - It could show no changes but that does not necessarily mean the patient does not have KRS but could be because technology is not advanced enough to find hidden changes. Important that experienced doctors confirm diagnosis.

## Management:

- No treatment, KBS symptoms are managed in the same way as Parkinson disease
  - carbidopa / levodopa combination, dopaminergic drugs, etc.

# Baggio–Yoshinari syndrome

Note: Research on this condition in English is very limited.

## Overview:

- Formerly called **Brazilian Lyme Disease** due to similar symptoms
  - It was renamed because the clinical and laboratory profiles differed enough for it to be classified as a novel condition.
- A **vector-borne disease**, meaning it's transmitted by vectors such as ticks and mosquitoes
- **Can be treated** with antibiotics → limits / prevents future complications



**Photo courtesy of Clipart Library**

# Baggio–Yoshinari syndrome

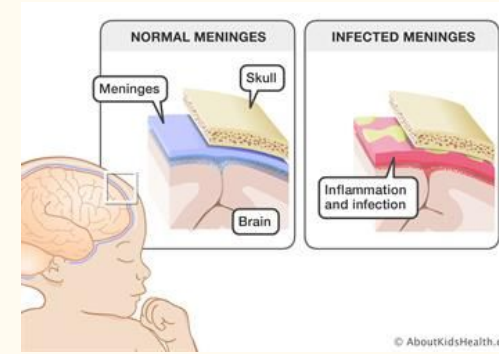
## Symptoms:

### Early Symptoms:

- **Erythema migrans** - “Migrating redness”; a spreading rash associated with tick bites

### Long-term symptoms - May appear years after the initial bite

- Arthritis
- Unilateral facial nerve paralysis
- **Radiculopathy** - pinching of nerve in the spinal column
- **Meningitis triad** - fever, stiff neck, altered mental state
- **Cranial Neuritis** - inflammation of PNS
- Vision and hearing problems



# Baggio–Yoshinari syndrome

## Diagnostic Tests:

- Standard diagnostic procedure for Lyme disease-like diseases
- Test result is positive if the patient exhibits
  - 3 major parameters OR
  - 2 major and 2 minor parameters

Table 2. Diagnostic criteria of Lyme disease-like syndrome adopted by the Discipline of Rheumatology, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo.

### Major parameters

Epidemiology (tick bite, contact with wild or domestic animals in risk areas)

Erythema migrans or systemic manifestation (arthritis, neurological abnormalities, cardiac involvement)

Positive serology for *Borrelia burgdorferi*

### Minor parameters

Recurrent episodes

Chronic fatigue, myalgia, arthralgia, cognitive disorder, paresthesia of extremities

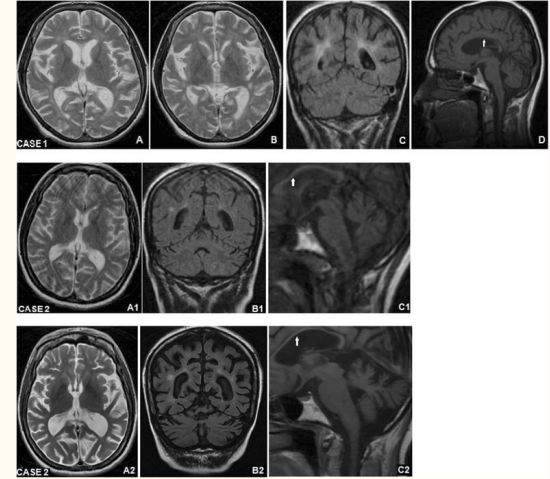
Identification of mobile spirochete-like structures by dark-field microscopy or Giemsa staining



# Kufs Disease

## Overview:

- Degenerative genetic disorder categorized under NCL (neuronal ceroid lipofuscinosis)
- Rare adult form of NCL
- Caused by a mutation in the PPT1 (palmitoyl-protein thioesterase 1)
- Usually affects people around the age of 35-40
- Affected people usually do not survive past 10- 15 years after the onset of symptoms



**Photo courtesy of BioMed Central**

# Kufs Disease

## Symptoms (which become more severe over time):

- Type A Kufs:
  - PME- progressive myoclonic epilepsy- characterized by muscle contractions and seizures.
  - Difficulty coordinating movements
  - Difficulty speaking out loud
- Type B Kufs:
  - Symptoms are similar to Type A, but Type B also can include:
    - Abnormal/involuntary movements such as tics/tremors
    - Decline in intellectual and cognitive ability
    - Changes in normal behavior
  - \*Seizures are rare in type B



# Kufs Disease

## **Diagnostic Tests:**

- Diagnosis is based upon evaluation of patient's symptoms, history, physical & neurological exam, and diagnostic tests, which include:
- Biopsy can show accumulation of lipopigments in cells, which can help diagnose Kufs
- Electroencephalogram can be used to track seizures
- Genetic testing is not needed for diagnosis but can uncover genetic mutations

# Familial Dysautonomia

## Overview:

- Genetic disorder that affects the development and survival of certain nerve cells
- Caused by mutations in the IKBKAP gene
- Autosomal Recessive Inheritance
- Disrupts cells in the autonomic nervous system and can affect the sensory nervous system



**Photo courtesy of  
Dysautonomia Center**

# Familial Dysautonomia

## Symptoms:

- The most distinctive symptom is the absence of overflow tears when crying
- Older children with the disease may have delayed speech, an unsteady gait, a corneal abrasion, lowered pain and temperature perception, unstable blood pressure, etc.
- Dysautonomia crisis may also occur, which is many symptoms in response to physical and emotional stress such as vomiting, increased heart rate and blood pressure, sweating, drooling, etc.



# Familial Dysautonomia

## Diagnostic Tests:

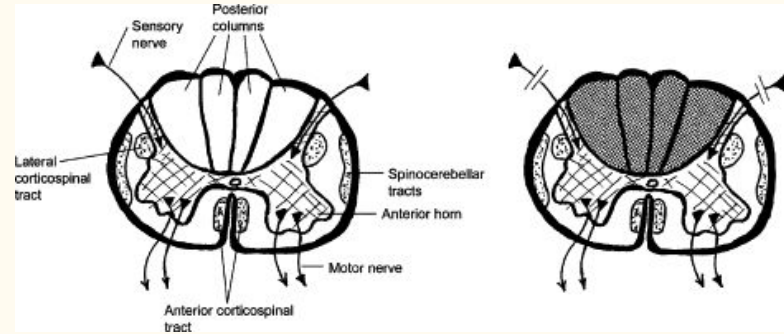
- The criteria to a clinical diagnosis of FD are: no fungiform papillae on tongue, decreased deep tendon reflexes, lack of an axon flare following intradermal histamine, no overflow tears with emotional crying
- A genetic test may be done to identify the mutation associated with FD, which is found on chromosome 9
- Preimplantation genetic diagnosis, prenatal diagnosis by amniocentesis, or chorionic villus sampling may also occur



# Tabes Dorsalis

## Overview:

- a complication of untreated syphilis that involves muscle weakness and abnormal sensations
- a form of neurosyphilis, which is a complication of late stage syphilis infection.
- When syphilis is untreated, the bacteria damages the spinal cord and peripheral nervous tissue. This leads to the symptoms of tabes dorsalis.



**Photo courtesy of Science Direct**



# Tabes Dorsalis

## Symptoms:

- Abnormal sensations (paresthesia), often called "lightning pains"
- Problems walking such as with the legs far apart
- Loss of coordination and reflexes
- Joint damage, especially of the knees
- Muscle weakness
- Vision changes
- Bladder control problems
- Sexual function problems

# Tabes Dorsalis

## **Diagnostic Tests:**

The health care provider will perform a physical exam, focusing on the nervous system.

If syphilis infection is suspected, the Serum VDRL or serum RPR (used as a screening test for syphilis infection)

If the serum VDRL or serum RPR test is positive, one of the following tests will be needed to confirm the diagnosis: FTA-ABS, MHA-TP, TP-EIA, TP-PA

# Toxic Encephalopathy

## Overview:

- Leads to an altered brain state (vision loss, memory loss, etc)
- Caused by **toxic exposure** (most often organic solvents)
- Symptoms dependent on the dose-exposure. Symptoms develop after a certain amount has accumulated.
- Lifespan will depend on the type of toxin and amount of exposure.

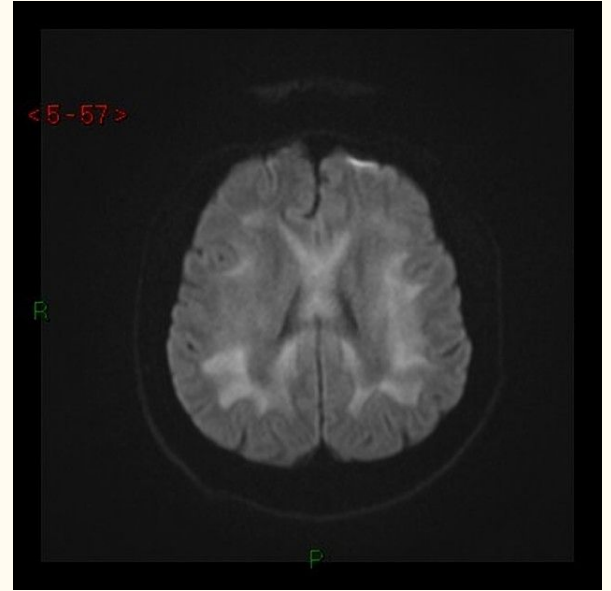


Photo courtesy of radiopedia.org



# Toxic Encephalopathy

## Symptoms:

- Acute and chronic symptoms include altered brain behaviour, which entails:
  - memory loss, personality changes, seizures, and loss of concentration.
- There can also be a decrease in psychomotor functions and learning deficits.
- Once damaged, many parts of the brain don't recover leading to a wide range of long term irreversible effects.

# Toxic Encephalopathy

## Diagnostic Tests:

- **Diagnosis of exclusion**, requiring multiple different tests
- The four following criteria are used:
  - 1) intense or prolonged exposure to a neurotoxin
  - 2) neurological syndrome known to be caused by neurotoxin
  - 3) changing symptoms over a period of time
  - 4) exclusion of other neurological diseases
- Comprehensive neurological examination is heavily required in order to rule out every other option

# Multiple System Atrophy (MSA)

## Overview:

- MSA (formerly known as Shy-Drager Syndrome), is a rare **neurodegenerative** disorder affecting **autonomic** functions
- Two types of MSA
  - MSA- P; Parkinsonian (most common)
  - MSA-C; Cerebellar
- No known cause/cure
  - Genetic? Environmental? Alpha-synuclein?
- Progresses to death (failure of respiration)
  - No remission, though progression varies
  - Avg. 7-10 years after diagnosis.

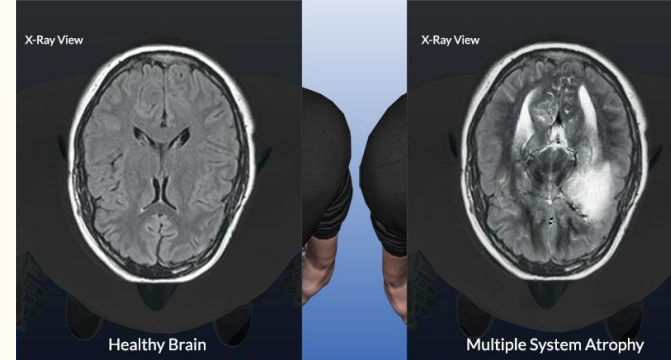


Photo courtesy of  
<https://www.startstemcells.com/>

# Multiple System Atrophy (MSA)

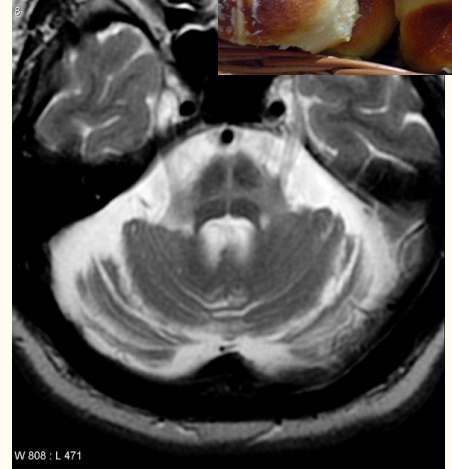
## Symptoms:

- Usually develop in people aged 50-60 yrs old
- Symptoms reflect degenerated portion of brain
  - Bradykinesia in Parkinsonian MSA (however, **tremors are rare**)
  - Ataxia in cerebellar MSA, difficulty swallowing (dysphagia), dysarthria
- Imbalances in blood pressure
  - **Orthostatic hypotension** is common (causes dizziness when standing up)
  - May have extreme hypertension when lying down
- General Symptoms
  - Incontinence, sleep disorders, sweating abnormalities, psychiatric disorders

# Multiple System Atrophy (MSA)

## Diagnostic Tests:

- Physician orders MRI and PET scan
  - Often misdiagnosed with Parkinson's/Lewy Body Dementia
  - Test for orthostatic hypotension, sweat test, EKG, CBC will help with correct diagnosis
- Radiology: “hot-cross bun” appearance of the pons in MRIs
- PET visualizes organs/metabolic function
  - DaT scan will visualize abnormal dopamine signaling
- May get diagnosed when L-dopa treatment for PD does not alleviate symptoms
- Biopsy: Characterized by inclusions in oligodendrocytes with fibrillar  $\alpha$ -synuclein



Images courtesy of  
<https://radiopaedia.org/>