# ATAXIA

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## ATAXIA

- Clinical syndrome of movement incoordination that is NOT the result of muscular weakness
- From Greek αν (used as a negative prefix) + τάξις (order), meaning "lack of order".
- Also a group of degenerative diseases in which progressive ataxia is the prominent manifestation

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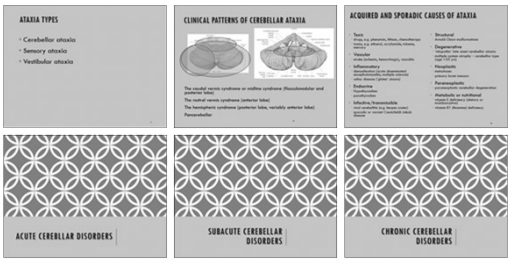


## ATAXIA TYPES

- Cerebellar ataxia
- Sensory ataxia
- Vestibular ataxia

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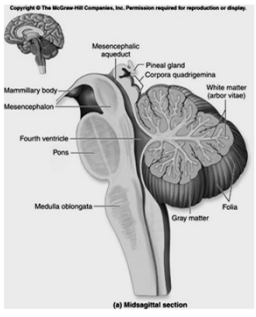
## ARNOLD-CHIARI MALFORMATION

- a downward displacement of the cerebellar tonsils through the foramen magnum (the opening at the base of the skull), sometimes causing non-communicating hydrocephalus[1]

## CEREBELLAR ATAXIA

Lesions of the cerebellum or its afferent or efferent connections in

- the cerebellar peduncles,
- red nucleus,
- pons,
- spinal cord.

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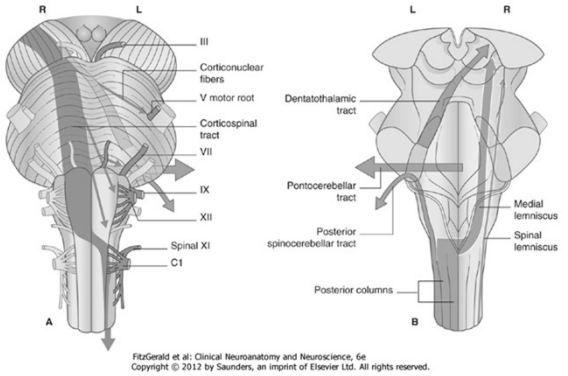



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## THE CEREBELLUM

- A coordination center that maintains balance and controls muscle tone,
- Assures the precise, temporally well-coordinated execution of all directed motor processes.
- Unconsciously

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## THE CEREBELLUM

- Receives a very large amount of general and special sensory input,
  - BUT does not participate to any significant extent in conscious perception or discrimination.
- influences motor function,
  - BUT cerebellar lesions do not produce paralysis.
- Unimportant for most cognitive processes
  - BUT plays a major role in motor learning and memory.

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## AFFERENT AND EFFERENT CONNECTIONS OF THE CEREBELLUM & CEREBELLAR ATAXIA

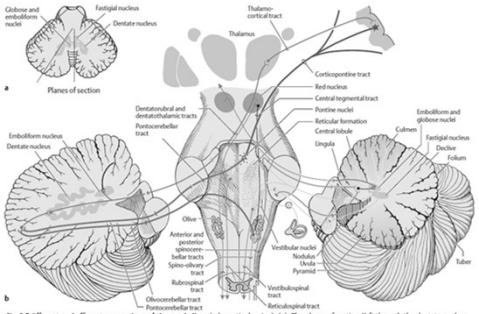

Fig. 5.5 **Afferent and efferent connections of the cerebellum** (schematic drawing). (a): The planes of section (left through the dentate nucleus, right through the vermis).

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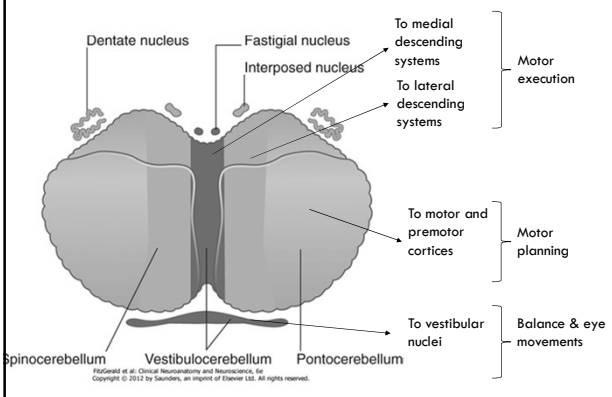



## CLINICAL SIGNS OF CEREBELLAR DYSFUNCTION

- Oculomotor disturbances:
  - Nystagmus
  - Disorders of smooth pursuit
  - Disorders of saccades
- Dysarthria
  - the muscles of voice production and speech lack coordination so that sudden irregular changes in volume and timing occur, i.e. scanning or staccato speech.
- Upper limbs:
  - ataxia and intention tremor, best seen in movement directed towards a restricted target, e.g. the finger–nose test;
- dysdiadochokinesia, i.e. slow, inaccurate, rapid alternating movements.
  - Lower limbs: ataxia → the heel–knee–shin test
- Gait and stance ataxia: heel-to-toe-walk or standing still on one leg
- Hypotonia - is not very useful in clinical practice.

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## CEREBELLAR REPRESENTATION IS IPSILATERAL

- Left cerebellar hemisphere lesion will produce
  - nystagmus which is of greater amplitude when the patient looks to the left,
  - ataxia which is more evident in the left limbs,
  - a tendency to deviate or fall to the left when standing or walking.

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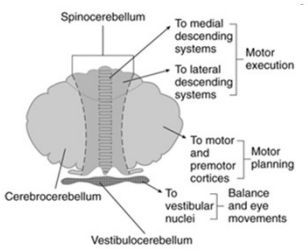


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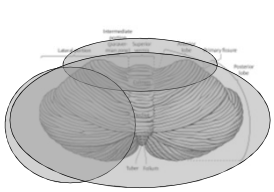
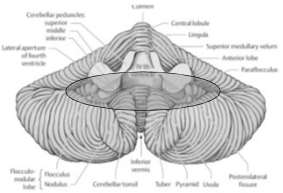
## CLINICAL PATTERNS OF CEREBELLAR ATAXIA





The caudal vermis syndrome or midline syndrome (flocculonodular and posterior lobe)

The rostral vermis syndrome (anterior lobe)

The hemispheric syndrome (posterior lobe, variably anterior lobe)

Pancerebellar

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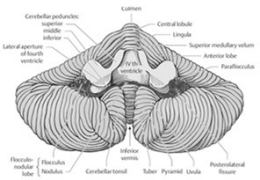
## THE CAUDAL VERMIS SYNDROME (FLOCCULONODULAR AND POSTERIOR LOBE)



Lesion in the vermis and flocculonodular lobe and their associated subcortical (fastigial) nuclei
- control of axial functions, including eye movements, head and trunk posture, stance, and gait.

Signs
- Gaze-evoked nystagmus; saccadic pursuit movements
- Stance ataxia (*astasia*) and gait ataxia (*abasia*)
- Head & trunk *titubation* (oscillation of the head and trunk)

Causes
- Tumour
- Multiple sclerosis
- Most often seen in young children

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## HEADACHES AND FALLS

A 6-year-old boy has been referred to a neurosurgeon by his physician.

- morning headaches for about 3 months

- they often are severe enough to make him vomit.

- became drowsy and increasingly unsteady on his feet,

- not able to walk without support.

Exam: his motor power and accuracy appear normal, as are his reflexes. When asked to follow the examiner's finger with his eyes, the right eye lags behind when he looks to the far right. Both eyes show nystagmus during lateral gaze in either direction. Ophthalmoscopy reveals an intense level of papilledema. When assisted to a vertical position and allowed to stand alone, he is quite stable for 10 seconds but then falls over like a pole into waiting arms.

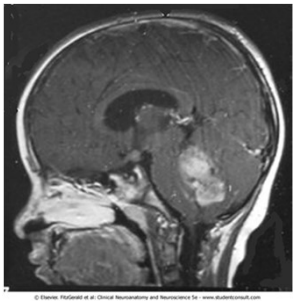
## WHAT'S YOUR OPINION ABOUT THIS CASE?

- raised intracranial pressure (headaches, drowsiness, vomiting, and papilledema)

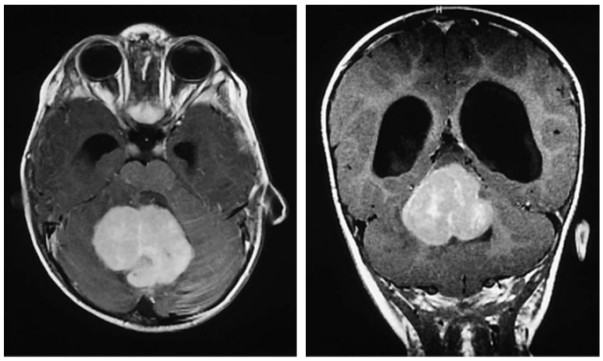
- the abducens nerve palsy (The weakness of abduction of the right eye; compression of the VI CN where it crosses the edge of the petrous temporal bone)

## CASE - HOW CAN THE FALLING BE EXPLAINED?

- The en bloc falling ➔ a sign of truncal ataxia.
- The boy is immediately taken to the neuroradiology department, where a midline mass is shown to be the problem.
- The mass has filled the fourth ventricle and is distorting the brainstem and cerebellum. The bright signal indicates a high level of vascularity.
- (Courtesy of Kamal Asaad, Ain Shams University, Cairo, Egypt. )



## MEDULLOBLASTOMA



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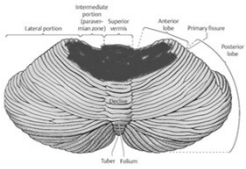
## ANTERIOR LOBE SYNDROME

Selective involvement of the superior cerebellar vermis and anterior lobe

Signs
- Gait ataxia worse than the ataxia of stance (astasia)
- **broad-based, unsteady gait** that deviates to the side of the lesion, and there is a **tendency to fall to that side**.

Causes
- alcoholic cerebellar degeneration
- Wernicke's encephalopathy
- Tumour
- Multiple sclerosis

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## CEREBELLAR HEMISPHERE PATTERN

- Cerebellar hemispheres coordinate movement and maintain tone in the ipsilateral limbs and regulate lateral gaze
- Signs:
  - Decomposition of voluntary movements
    - Ipsilateral hemiataxia, dysmetria, dyssynergia, dysdiadochokinesia and intention tremor
  - Hypotonia in acute lesions
  - Scanning dysarthria and dysartrophonia
    - Patient speaks slowly & haltingly, with poor articulation and with abnormal stress on each syllable
- Causes:
  - Infarction (ischemia)
  - Hemorrhage
  - Tumor
  - MS

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## PANCEREBELLAR PATTERN

- Signs
  - Nystagmus
  - Bilateral gaze paresis
  - Bilateral hypotonia
  - Bilateral limb ataxia
  - Gait ataxia
- Causes
  - Drug intoxications
  - Hypothyroidism
  - Hereditary cerebellar degeneration
  - Paraneoplastic cerebellar degeneration
  - Infections and parainfectious encephalomyelitis
  - Creutzfeld-Jakob disease
  - MS

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## CEREBELLAR ATAXIA - CASE

## ACQUIRED AND SPORADIC CAUSES OF ATAXIA

- Toxic
  - drugs, e.g. phenytoin, lithium, chemotherapy
  - toxins, e.g. ethanol, acrylamide, toluene, mercury
- Vascular
  - stroke (ischemic, hemorrhagic); vasculitis
- Inflammatory
  - demyelination (acute disseminated encephalomyelitis, multiple sclerosis)
  - celiac disease ('gluten' ataxia)
- Endocrine
  - Hypothyroidism
  - parathyrodism
- Infective/transmissible
  - viral cerebellitis (e.g. herpes zoster)
  - sporadic or variant Creutzfeldt-Jakob disease
- Structural
  - Arnold-Chiari malformations
- Degenerative
  - 'idiopathic' late onset cerebellar ataxia
  - multiple system atrophy – cerebellar type (age >35 yrs)
- Neoplastic
  - metastases
  - primary brain tumours
- Paraneoplastic
  - paraneoplastic cerebellar degeneration
- Metabolic or nutritional
  - vitamin E deficiency (dietary or malabsorption)
  - vitamin B1 (thiamine) deficiency

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## ETIOLOGY OF CEREBELLAR SYNDROMES

- Common:
  1. drugs, especially anticonvulsant intoxication (phenytoin)
  2. alcohol, acute intoxication
  3. cerebrovascular disease
  4. multiple sclerosis
- Rare:
  1. cerebellar abscess, usually secondary to otitis media;
  2. cerebellar degeneration
     1. hereditary (e.g. Friedreich's ataxia and autosomal dominant cerebellar ataxia),
     2. alcohol induced
     3. paraneoplastic;
  3. Arnold–Chiari malformation (the cerebellum and medulla are displaced unsually low in relation to the foramen magnum);
  4. Wernicke's encephalopathy
  5. Hypothyroidism
  6. Posterior fossa tumors

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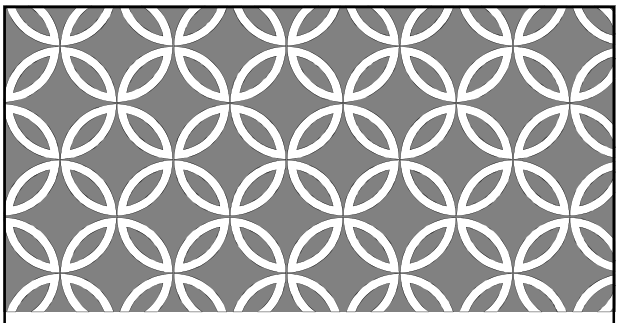
## GENETIC ATAXIAS

- Dominant
  - Autosomal dominant cerebellar ataxias
  - Dentato-rubro-pallidoluysian atrophy
  - Alexander disease
- Recessive
  - Autosomal recessive cerebellar ataxias
- Other
- 'Mitochondrial' disorders
- Fragile X-associated tremor/ataxia syndrome (age <45 yrs, male carriers of *FMR1* gene premutation)

## ATAXIA CAUSES V/S TIME COURSE

- Acute
  - Stroke – minutes
  - Wernicke's encephalopathy – hours – other features!
  - Miller Fisher syndrome - days
  - parainfectious cerebellitis – days – children
  - Intoxication
- Subacute (weeks to months)
  - paraneoplastic cerebellar degeneration,
  - Creutzfeldt–Jakob disease,
  - steroid-responsive encephalopathy with antithyroid antibodies (SREAT; previously referred to as Hashimoto's encephalopathy)
  - antiglutamic acid decarboxylase (anti-GAD)-associated cerebellar ataxia.



## ACUTE CEREBLLAR DISORDERS

## STROKE – VASCULAR CEREBELLAR ATAXIA

- Vertebro-basilar ischemia
- Cerebellar haemorrhage

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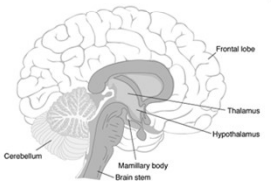
## WERNICKE'S ENCEPHALOPATHY

- Acute disorder
- Clinical triad of
  - ataxia,
  - ophthalmoplegia,
  - confusion
- Thiamine (vitamin B1) deficiency
  - chronic alcoholics,
  - malnutrition from any cause

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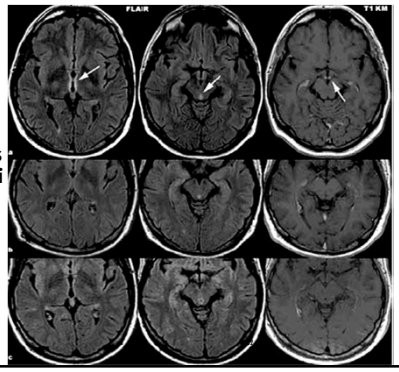
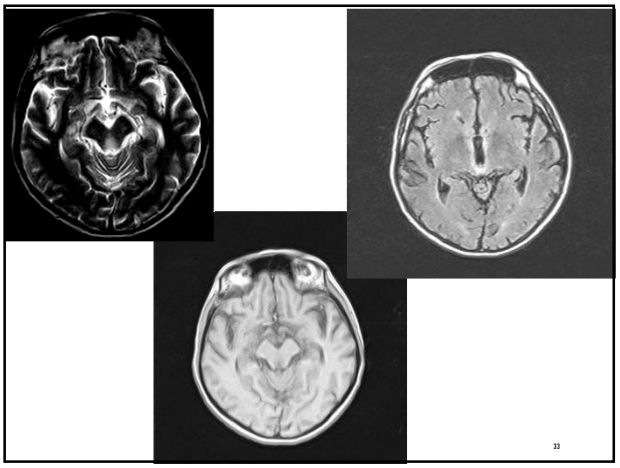
## PATHOLOGY

Punctuate haemorrhagic lesions centered around the 3rd and 4th ventricle, affect the mammillary bodies and thalamic nuclei



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## ATAXIA IN WERNICKE'S ENCEPHALOPATHY

- Both cerebellar and vestibular involvement
- Gait ataxia primarily or exclusively;
  - the legs themselves are ataxic in only about one-fifth of patients, and the arms in one-tenth.
- Dysarthria rare
- Amnestic syndrome or global confusional state,
- nystagmus
  - horizontal or combined horizontal-vertical,
- bilateral lateral rectus muscle palsies,
- absent ankle jerks.
- Caloric testing reveals bilateral or unilateral vestibular dysfunction.

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## THE DIAGNOSIS OF WS

- Established by the response to administration of thiamine
- customary to give 50 to 100 mg IV or IM immediately and then 50 mg/d p.o. or IM for 3 days thereafter

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## WERNICKE'S ENCEPHALOPATHY

## RECOVERY FROM WERNICKE'S ENCEPHALOPATHY

- Ocular palsies improve first
- Ataxia, nystagmus, and acute confusion start to resolve within a few days
- Recovery may not be full

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## ACUTE DRUG INTOXICATION


- Pancerebellar syndrome
  - ethanol
  - barbiturates
  - benzodiazepines
  - Meprobamat
  - anticonvulsants (phenytoin, phenobarbital, carbamazepi
  - hallucinogens (phencyclidine ["angel dust"])
- Associated with a confusional state

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## NEUROTOXIC AGENTS - ACUTE

- Anticonvulsants
  - Acute: phenytoin, phenobarbital, carbamazepine
- Ethanol – acute

## INFECTIOUS DISORDERS

- Viral infection
  - St. Louis encephalitis
  - AIDS-dementia complex
  - Meningoencephalitis associated with
    - Varicella, mumps, polyomyelitis, infectious mononucleosis
- Bacterial infection – less common
  - 10-20% cases of brain abscess
- Acute post viral cerebellar ataxia
  - Preschool children
  - Coincides with the end of viral disease (varicella)
  - Severe gait ataxia
  - Full recovery though may take several months

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## FISHER VARIANT OF GUILLAIN-BARRÉ SYNDROME

- Signs:
  - cerebellar ataxia,
  - external ophthalmoplegia,
  - areflexia
- Symptoms develop over a few days.
- Ataxia primarily affects the gait and trunk, with lesser involvement of the individual limbs.
- Dysarthria is uncommon.

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## SUBACUTE CEREBELLAR DISORDERS

## SUBACUTE CEREBELLAR DISORDERS

- weeks to months
- Paraneoplastic cerebellar degeneration,
- Creutzfeldt–Jakob disease,
- steroid-responsive encephalopathy with antithyroid antibodies (SREAT; previously referred to as Hashimoto's encephalopathy)
- antiglutamic acid decarboxylase (anti-GAD)-associated cerebellar ataxia.

## PARANEOPLASTIC CEREBELLAR DEGENERATION (PCD)

- Immune mediated degenerative disorder of cerebellar cortex
- Remote effect of systemic cancer
- Most often associated neoplasms
  - Lung cancer (especially small-cell),
  - ovarian cancer,
  - Hodgkin's disease,
  - Breast cancer

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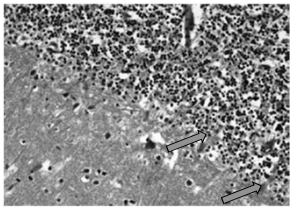
## THE PATHOGENESIS

- Diffuse loss of Purkinje cells, with secondary degeneration of the inferior olives
- Antibodies to tumour cell antigens that cross-react with cerebellar Purkinje cells
  - anti-Yo (ovarian and breast cancer),
  - antinuclear antibodies, such as anti-Hu (small-cell lung cancer)
  - anti-Ri (breast cancer)
  - Anti-Tr (Hodgkin's lymphoma)



Zanik warstwy zwojowej kory móżdżku; widać tylko pojedyncze cienie komórek Purkinjego (zaznaczono strzałkami); barwienie hematoksyliną i eozyną (powiększenie 200 ×)

## PARANEOPLASTIC ENCEPHALOMYELITIS

- The finding that patients with lung cancer and paraneoplastic sensory neuropathy harbored antineuronal antibodies led Wilkinson and **Żeromski** to hypothesize in 1965 that patients with the "encephalomyelitic form of carcinomatous neuropathy" should be investigated "for the presence of circulating anti-brain antibodies, particularly as lymphocytic infiltration is a prominent feature in these patients".

## S&S OF PCD

- Before the diagnosis of systemic cancer (but after Dx in Hodgin's lymphoma)
- Typically develop over months (subacutelly)
- Pancerebellar syndrome
- Signs:
  - Gait and limb ataxia
  - Dysarthria
  - The limbs may be affected asymmetrically
  - Nystagmus rare

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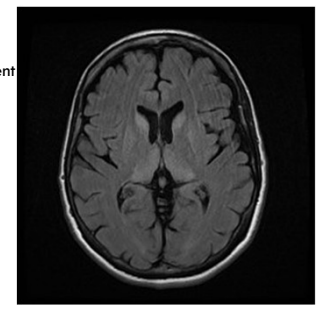
## CREUTZFELDT-JACOB DISEASE

- Prion disease that causes dementia
- Cerebellar signs are present in about 60% of pts
- In 10% ataxia is a presenting sign (ataxic variant of sCJD)
- Additionally
  - dementia,
  - pyramidal and
  - extrapyramidal signs, myoclonus
- Rapid progression
- Death in the 1st year



Case courtesy of Dr Maxime St-Amant, **Radiopaedia.org**, rID: 18712

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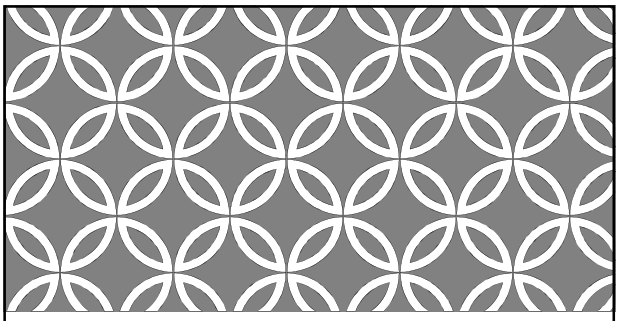

# CHRONIC CEREBELLAR DISORDERS

## CHRONIC CEREBELLAR DISORDERS

- Alcoholic cerebellar degeneration
- Posterior fossa tumors
- Hypothyroidism
- Genetic ataxias
- MS

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## ALCOHOLIC CEREBELLAR DEGENERATION (ACD)

- Chronic alcoholics,
- Result of nutritional deficiency
  - history of daily or binge drinking lasting 10+ yrs with associated dietary inadequacy.
- One of the most common forms of chronic cerebellar ataxia
- 2 autopsy studies showed prevalence of 11% and 27% in chronic alcohol users.

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## THE PATHOGENESIS OF ACD

- The toxic action of alcohol and the consequences of vitamin B1 deficiency
- Alcohol and acetaldehyde cause depression of neuronal firing by
  - interaction with GABAergic inhibitory mechanisms,
  - increased lipid peroxidation,
  - reduction of antioxidant concentrations
- good correlation between serum vitamin B1 concentrations and cerebellar volume loss in chronic alcohol users

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## ACD

- The symptoms affect gait and lower limbs more than arms and speech,
- often also with signs of peripheral neuropathy.
- The ataxia can stabilize or even improve with stopping drinking alcohol, but worsen in those who continue
- typically vermis atrophy

## ACD COURSE

- insidious in onset
- gradually progressive, eventually reaching a stable level of deficit
- No specific treatment
- Quit drinking!
- Thiamine (vit B1) supplementation

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## DEGENERATIVE CHANGES RESTRICTED TO THE SUPERIOR VERMIS

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## POSTERIOR FOSSA TUMORS

| Type | % of all | % in Adults (>20) |
|---|---|---|
| Metastases | 36 | 56 |
| Cerebellar astrocytoma | 28 | 10 |
| Medulloblastoma | 16 | 9 |
| Acoustic neuroma → Cerebello-pontine syndrome | 4 | 7 |
| Hemangioblastoma | 4 | 5 |
| Meningiomas | 4 | 5 |
| Ependymomas | 2 | 1 |

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## HYPOTHYROIDISM & ATAXIA

- mild disequilibrium and gait ataxia
  - But can have acute onset!
- Associated systemic features:
  - Fatigue, weight gain, constipation
- pathological changes in midline cerebellar structure
- Tests
  - TSH, free T4
- replacement treatment may improve the symptoms

## NEUROTOXIC AGENTS - ACUTE

- Toluene-solvent abuse syndrome
- Mercury poisoning
  - toxic to cerebellar granule cells and visual cortex
  - paresthesia, ataxia, and restricted visual fields
- Ethanol – chronic – as above

## TOLUENE-SOLVENT ABUSE SYNDROME

- Sources:
  - Toluene-containing paint thinner, paint stripper, and glue.
- Route of exposure.
  - Inhalational: huffing (inhaling soaked rags) or bagging (inhaling from bags containing solvent).
- Systemic signs.
  - Abdominal pain, anorexia, weight loss, gastritis, possible renal tubular acidosis (hypokalemia and acidosis), rhabdomyolysis, hepatitis, and solvent odour on breath.
- Neurologic manifestations.
  - Tremor of the head and extremities, ataxia, staggering gait, cognitive deficits, personality changes, optic nerve atrophy, hearing loss, loss of smell, extremity spasticity, and hyperreflexia.
- Diagnosis.
  - (1) **Laboratory**. Elevated serum toluene levels and urine hippuric acid levels confirm exposure, but may are not always detected.
  - (2) **Imaging. MRI** of the brain often shows cerebellar and cerebral atrophy. Evidence of white-matter disease can be seen with increased signal intensity on T2-weighted images in the periventricular, internal capsular, and brainstem pyramidal regions.

## MEDICATION-INDUCED ATAXIA

- Antiepileptics (AEDs)
  - phenytoin,
  - carbamazepine
  - gabapentin, pregabalin
- Metronidazole
- Amiodarone
- Chemotherapeutic Agents
  - Usually higher doses: 5-Fluorouracil (5FU), cytosine arabinoside (ara-C)

## GENETIC ATAXIAS

- Dominant
  - Autosomal dominant cerebellar ataxias
  - Dentato-rubro-pallidoluysian atrophy
  - Alexander disease
- Recessive
  - Autosomal recessive cerebellar ataxias (Fridrieich's ataxia)
- Other
- 'Mitochondrial' disorders
- Fragile X-associated tremor/ataxia syndrome (age <45 yrs, male carriers of *FMR1* gene premutation)

## SPINOCEREBELLAR ATAXIAS

- Most of the spinocerebellar ataxias are hereditary disorders—i.e., spinocerebellar heredoataxias.
- Start in childhood or adolescence and progress slowly thereafter.
- They present with varying clinical syndromes
  - common manifestations include
    - ataxia,
    - gait impairment,
    - dysarthria,
    - and reflex abnormalities.

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## FRIEDREICH'S ATAXIA

- familial, progressive degeneration of the spinocerebellar and corticospinal tracts and the posterior columns, of *autosomal recessive* inheritance.
- due to an expanded GAA trinucleotide repeat in a **noncoding** region of the **frataxin** gene on chromosome 9

From Bramwell: Atlas of Clinical Medicine

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## FRIEDREICH'S ATAXIA PATHOLOGY

Cellular pathology: Dying back of distal axons

Localization

Spinal cord
- Spinocerebellar tracts
- Dorsal columns
- Pyramidal tracts

Dorsal root ganglia: Loss of neurons

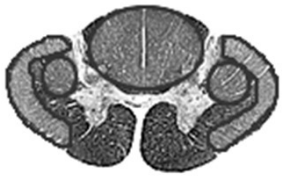
Peripheral nerves
- Loss of sensory axons: Especially large myelinated
- Axonal atrophy

Cranial nerves: Entering roots involved

Cerebellum: Dentate nucleus; Mild neuronal loss in cortex

Medulla

Cerebral cortex: Mild neuronal loss



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## FRIEDREICH'S ATAXIA

- Begins in childhood (8-15 yrs)
- Progressive gait ataxia followed by ataxia of all limbs within 2 years
- Knee & Achilles tendon reflexes lost
- Cerebellar dysarthria
- Joint position & vibration sense impaired in legs
- Weakness develops later in the course
- Babinski sign appears in first 5 years of disease

From Bramwell: Atlas of Clinical Medicine

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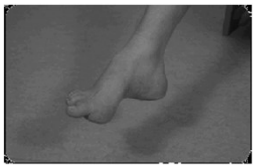
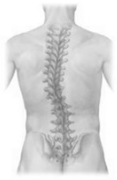
## ADDITIONAL FEATURES

- Pes cavus
- Kyphoscolisis (can be severe)
- **Cardiomyopathy**!





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## CEREBELLAR ATAXIA -SPECIFIC INTERVENTIONS

- in toxic ataxia, **stopping alcohol or the offending drug;**
- in gluten ataxia and Refsum's disease, making specific **dietary restrictions;**
- in autosomal recessive ataxia with vitamin E deficiency, starting **vitamin E supplements;**
- in patients with SREAT or ataxia associated with anti-GAD antibodies, starting **corticosteroids;**
- in paraneoplastic cerebellar degeneration, **treating the underlying tumour** and starting immunomodulatory drugs;
- in cerebrotendinous xanthomatosis, giving bile acid replacement;
- in Friedreich's ataxia, prescribing **idebenone** to reduce cardiac hypertrophy
- In hypothyroidism - levotyroxine

## CEREBELLAR ATAXIA SYMPTOMATIC TREATMENT

| | |
|---|---|
| Ataxia | Low dose benzodiazepines |
| | Riluzole |
| | Buspirone |
| | Amantadine |
| | Acetazolamide |
| | 5-Hydroxytryptophan |
| Parkinsonian features | L-dopa |
| | Dopamine agonists |
| Cerebellar tremor | Propranolol |
| | Primidone |
| | Clonazepam |
| Nystagmus | Baclofen |
| | Gabapentin |
| | Clonazepam |
| | 3,4-diaminopyridine |

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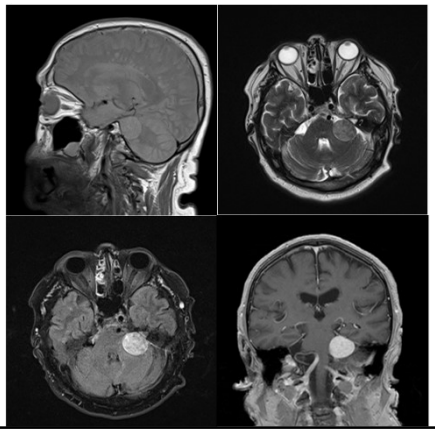
## CASE 2

- 6 months problems with taste on left tongue and numbness on the left side of face
- 6 yrs ago problems with hearing and tinnitus now patient if deaf at that side
- Exam: dissociative sensation loss of temperature with preserved touch sensation

## LEFT POSTERIOR FOSSA NEUROMA OF VIITH NERVE



## ENIGMA


- In 1932, Marian Rejewski and two fellow Poznań University mathematics graduates, Henryk Zygalski and Jerzy Różycki, joined the Polish Cipher Bureau full time and moved to Warsaw.
- Rejewski had replicas made, which he called 'Enigma doubles'.
- The method of Zygalski sheets was a cryptologic technique used by the Polish Cipher Bureau before and during World War II, and during the war also by British cryptologists at Bletchley Park, to decrypt messages enciphered on German Enigma machines.

## SENSORY ATAXIA

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## SENSORY ATAXIA

- Due to the proprioception (position sense) loss
- loss of touch sensation
  - → interferes with fine manipulative skills in the hands,
  - → with standing and walking in the case of the feet.
- Compensatory use of the eyes (→ Romberg sign)
- Clumsiness and unsteadiness are worse in the dark, or at other times when eyes closed,
  - e.g. washing face, having a shower, whilst putting clothes over head in dressing.

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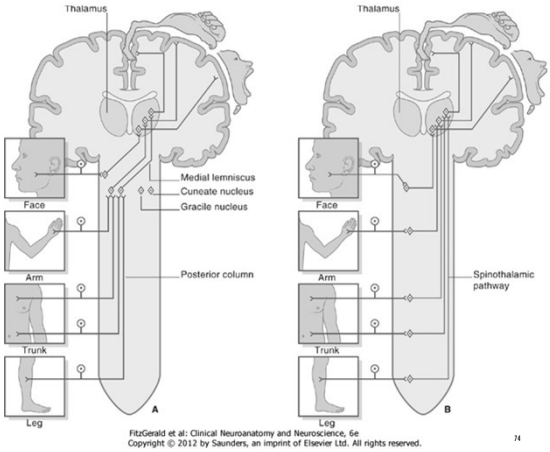


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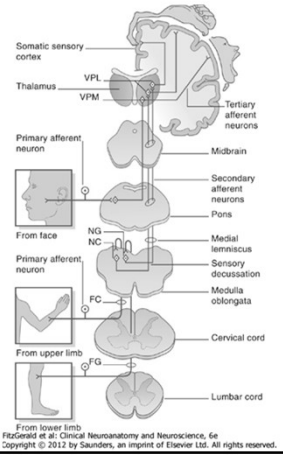
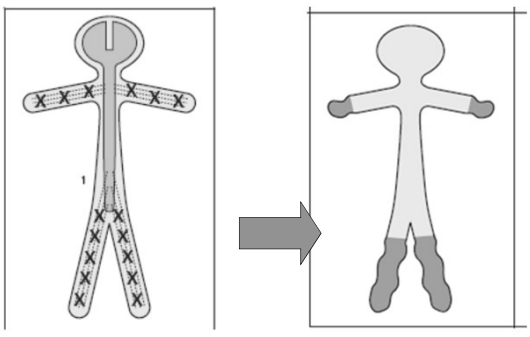




## SENSORY ATAXIA PATTERNS

## POLYNEUROPATHY AND ATAXIA

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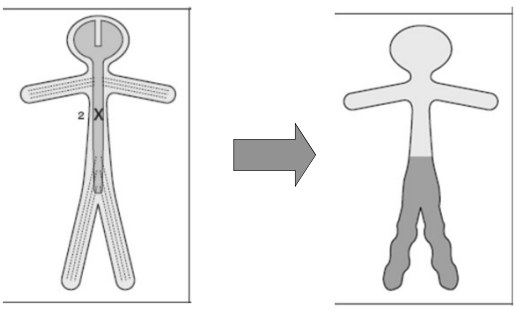
## SPINAL CORD DISEASE AND ATAXIA

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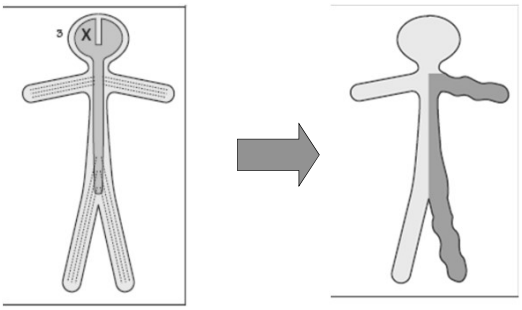
## HEMISPHERIC LESION AND SENSORY ATAXIA



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## SIGNS OF SA IN UPPER LIMBS

- Loss of touch and joint position sense in the fingers
- Pseudoathetosis
  - the patient is unable to keep his fingers still in the outstretched position.
  - appears *only* when the eyes are closed
- Clumsiness of finger movement,
  - e.g. when turning over the pages of a book singly, and when manipulating small objects in the hands, made much worse by eye closure.

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## SIGNS OF SA IN LOWER LIMBS

- Marked Rombergism.
  - The patient immediately becomes unsteady in the standing position when the eyes are closed.
- When walking the patient looks at the ground and at his feet.
- Loss of touch and joint position sense in the feet and toes.

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## VITAMIN B12 (CYANOCOBALAMIN) DEFICIENCY

- Pernicious anemia (impaired absorption by the gastrointestinal tract)
  - Antibodies to parietal cell 90%
- Gastrointestinal surgery
- Sprue
- infection with fish tapeworm;
- strictly vegetarian diet

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## SCD - COURSE

At onset – weakness and paresthesias of the hands and feet.

vibration and position sense lost

Gait ataxia

Weakness gets worse and spasticity of the limbs appears.

Time course vary from weeks to months

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## VITAMIN $B_{12}$ DEFICIENCY PATHOLOGY

- Neurologic signs caused by impaired myelin production

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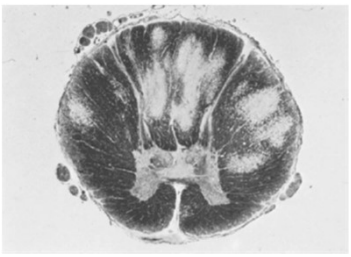
## SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD – MYELIN LESIONS

Dorsal column

Lateral corticospinal tract



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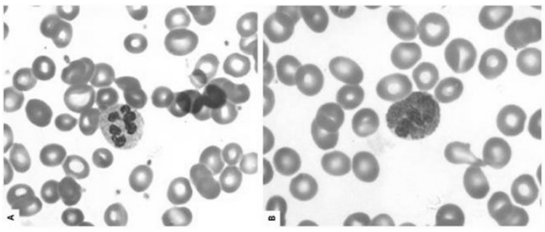
## PERIPHERAL-BLOOD SMEAR (WRIGHT'S STAIN)



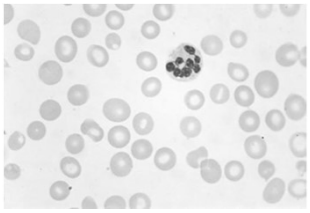
Marks, P. W. et al. N Engl J Med 2004;351:1333-1341

The NEW ENGLAND JOURNAL of MEDICINE

## MACROCYTIC MEGALOBLASTIC ANEMIA IN B12 DEFICIENCY

May not be present !

Oval Macrocytes and Hypersegmented Neutrophils in Vitamin B12 Deficiency



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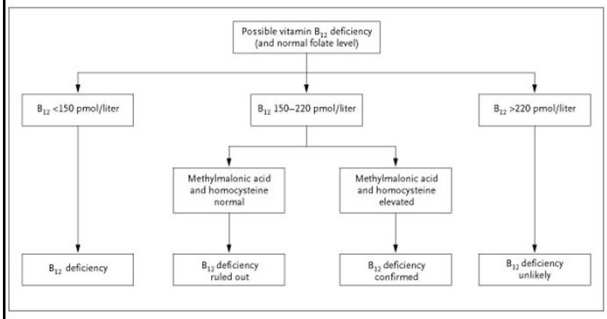
Diagnostic Algorithm for Vitamin B12 Deficiency

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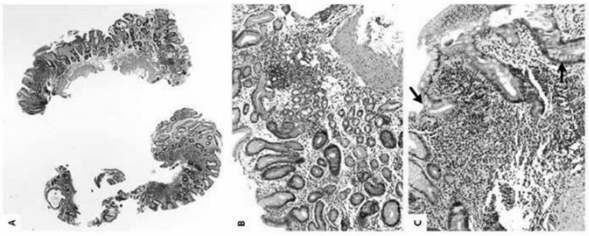

Marks, P. W. et al. N Engl J Med 2004;351:1333-1341

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## OTHER SIGNS OF SCD

- Optic nerve atrophy and centrocecal scotoma
- Peripheral neuropathy
- Behavioral and psychiatric changes

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## LABORATORY

- The definitions of Cbl (vitamin B12) deficiency are as follows:
  - Serum Cbl level <150 pmol/L on two separate occasions

  OR
  - serum Cbl level <150 pmol/L AND total serum homocysteine level >13 µmol/L OR methylmalonic acid >0.4 µmol/L (in the absence of renal failure and folate and vitamin B6 deficiencies)

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## B12 DEFICIENCY TREATMENT

- Treatment with vitamin B12 *im*
  - 1000 µg/d for 1 week,
  - then 1000 µg/wk for 1 month.
  - Then 1000 µg/mo until the cause of deficiency is corrected, or for life in the case of pernicious anemia.

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## POLYNEUROPATHIES

- Involving thick myelinated sensory fibers
  - **Diabetes**
  - **Paraneoplastic sensory neuropathy**
  - Immune-mediated PN
  - Taxol
  - Pyridoxine
  - Isoniasid

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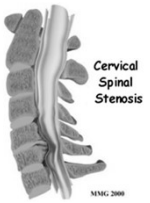
## MYELOPATHY INVOLVING POSTERIOR COLUMNS

- Acute transverse myelitis
- AIDS
- MS
- Compression due to
  - Tumor
  - Spondylosis (osteophytes)
- Vascular malformations

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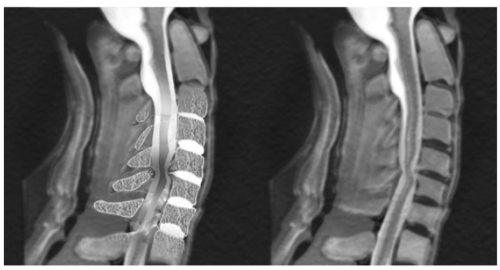
## SPINAL STENOSIS & SPINAL CORD COMPRESSION



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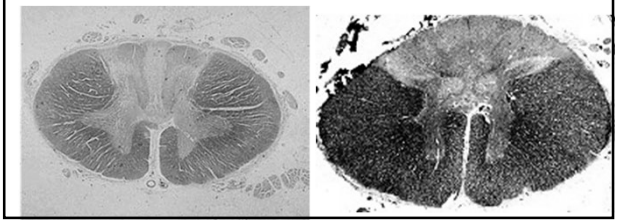
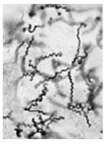
## TABES DORSALIS

- Fibrosis & Inflammation
  - Posterior roots & meninges
  - Especially lumbosacral
- Sensory ganglia: Degeneration of neurons
- Posterior columns of spinal cord: Axonal loss



## ONSET

- 10 to 30 years after initial, often untreated, infection
- May occur in adults or children



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## CLINICAL FEATURES I

- Lightning pains:
  - Especially lower extremity & abdomen
- Sensory
  - Joint position & Vibration sense: absent/reduced
- Hitzig zones
  - Regions of reduced sensation
  - Locations: Central face; Nipples; Ulnar forearms; Peroneal legs
- Analgesia:
  - Leads to painless ulcers & Joint damage (Charcot's joints - Neurogenic osteoarthropathy)

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## CLINICAL FEATURES II

- Hyporeflexia
- Pupil disorder:
  - Argyll Robertson pupils irregular (Light-near dissociation)
- Autonomic:
  - Impotence; bladder dysfunction (flaccid bladder)
- Optic atrophy
- Systemic: Aortitis

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## TESTING

- Serum
  - Rapid Plasma Reagin (RPR)
  - VDRL
  - Above sensitive in primary and secondary syphilis, less sensitive in tertiary
  - Serum studies for T. pallidum-specific antibodies
    - Fluorescent treponemal antibody absorbed (FTA-ABS) test
    - T. pallidum hemagglutination (TPHA) test
    - Microhemaaglutination assay-T. pallidum (MHA-TP) test
- CSF
  - Early & Active disease
    - Cells: 10 to 200/µl
    - Protein: <200 mg/dl
    - IgG: High
  - Late: May be normal
- Also test for HIV

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## TREATMENT

- H**igh-dose intravenous aqueous penicillin G**
  - at a dose of 2 million to 4 million units every 4 hours for 10 to 14 days.
  - If there is a penicillin allergy then doxycycline at a dose of 200 mg twice a day for 28 days and ceftriaxone at a dose of 2 g intravenously per day for 14 days are administered.
- **CSF** studies should be **reexamined** after the completion of therapy with an improved drop in white blood cell count, protein, and IgG synthesis.

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## FRONTAL LOBE ATAXIA

- Because of the crossed connection between the frontal cerebral cortex and the cerebellum, unilateral frontal disease can also occasionally mimic a disorder of the contralateral cerebellar hemisphere.
- Involvement of the frontopontocerebellar tract (Arnold's bundle)

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## ATAXIA IN FRONTAL LOBE LESION (AKA „GAIT APRAXIA")

- Due to lesion of cortico-cerebellar tracts (eg. Fronto-ponto-cerebellar tract)
  - Neoplasms of frontal lobe
  - Anterior cerebral artery syndrome
  - Hydrocephalus
    - Gait ataxia +
    - Memory disturbance
    - Urinary incontinence
- Ataxic gait (frontal lobe gait)
- Frontal release signs (deliberation signs)

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## GAIT APRAXIA

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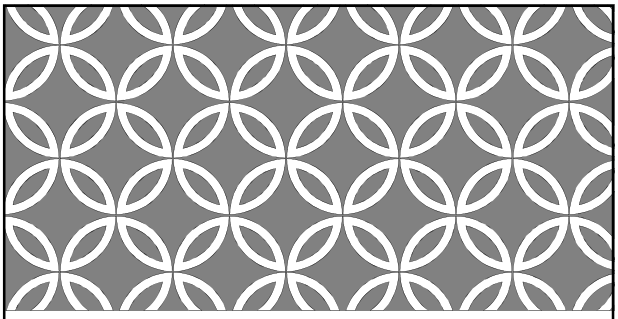
## ATAXIA IN SUBCORTICAL LESIONS

- *Status lacunaris* (lacunar state) – ataxia of gait
  - Multiinfarct
  - Ataxia
  - Emotional instability
  - Increased jaw reflex & other reflexes
- Ataxic hemiparesis
  - Lacunar stroke of internal capsule or pons

105



## VESTIBULAR ATAXIA

## ATAXIA IN VESTIBULAR DISEASE

- Vestibular inputs are vital to cerebellar function
- disorders of the vestibular system can produce ataxia, especially of gait.

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## ATAXIA IN VESTIBULAR DISEASE – 2

- Recognized by
  - the presence of prominent vestibular symptoms and signs like vertigo and rotatory nystagmus
  - by the absence of other cerebellar, brainstem and sensory signs
- Acute and unilateral
  - associated with prominent vertigo, nausea and vomiting.
- In slow-onset, chronic bilateral cases of vestibular dysfunction,
  - Above characteristic manifestations may be absent,
  - and dysequilibrium may be the sole presentation.

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## DIZZY WHEN IN BED

- Female patient 60 yrs old
- Complains on dizziness which is provoked by head movements, especially when lying down back
- Symptoms for 4-5 weeks
- Symptoms last about ½ minute, disappear spontaneously and can reoccur several times a day

## DIZZY WHEN IN BED - EXAM

- General and classic neurological examinationsis normal
- What is the most appropraiete test to do?

## DIX-HALLPIKE MANOUVER

(BRONSTEIN &LAMPERT „DIZZINESS" CAMBRIDGE UNIVERSITY PRESS )

## POSTERIOR CANAL BENIGN PAROXYSMAL POSITIONAL VERTIGO

- Brief attacks (<30 s) provoked by turning in bed, laying down, sitting up from lying, head extension or bending over
- Symptomatic episodes from weeks to months
- Remission for years
- Mainly torsional Ny beating towards the ground in lateral head-hanging position
- 90% of positional vertigo

## DIX-HALLPIKE POSTIONAL TESTING

- Mainly torsional nystagmus, fast-phase directed towards ground (+smaller upward component) when positioned on symptomatic side
- Reversal of nystagmus on sitting up

## BPPV TREATMENT – EPLEY MANOUVER

## RIGHT BPPV NYSTAGMUS

(BRONSTEIN &LAMPERT „DIZZINESS" CAMBRIDGE UNIVERSITY PRESS )