Gomel State Medical University
Department of Neurology and neurosurgery

Lecture

THEME 7. INFECTIOUS AND INFLAMMATORY DISEASES. AUTOIMMUNE DISORDERS OF NERVOUS SYSTEM

The faculty of general medicine

Encephalitis is an inflammation of the brain parenchyma, sinuses and represents a diffuse and/or focal neuropsychological disfunction.

This pathology makes up to 6% of organic diseases of the CNS.

Classification of the encephalitis

Primary

Seasonal

1. Arbovirus encephalitis:

a) tick-borne encephalitis;

b) Japanese encephalitis;

c) Australian encephalitis.

2. True polioencephalitis:

The polyseasonal

a) Economo's A encephalitis;

b) enterovirus encephalitis;

c) herpes encephalitis.

Secondary encephalitis:

a) Post- and parainfectious (tuberculous, syphilitic, rheumatic, influenzal, measles, rubellar,parotitas);

b) postvaccinal encephalitis (smallpox, rabies);

c) Transmissible spongiform encephalopathy, also known as prion diseases (Creutzfeldt-Jakob disease).

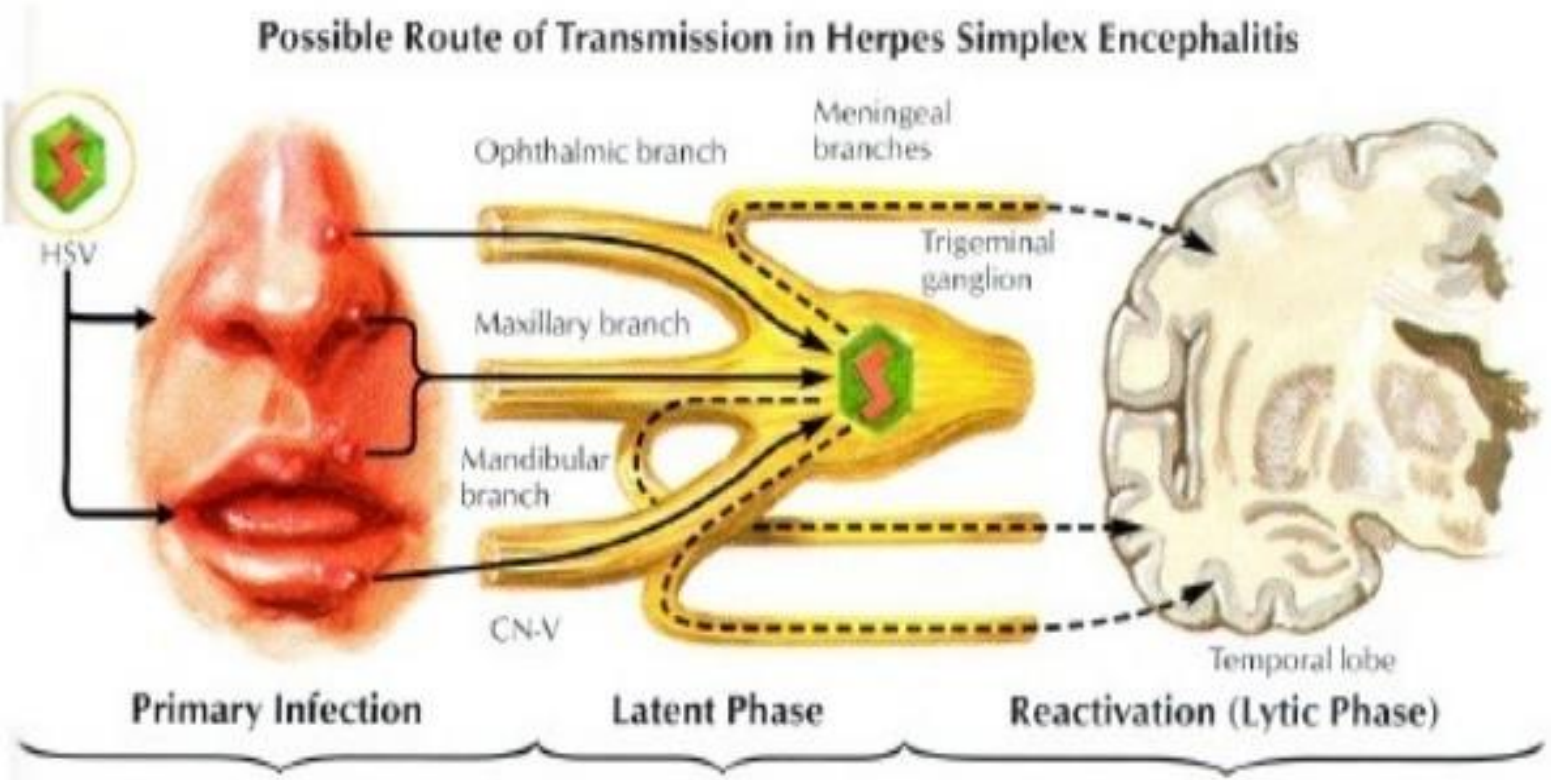
Herpes simplex encephalitis (HSE) is severe viral infection of the human central nervous system.

The majority of cases of herpes encephalitis are caused by herpes simplex virus-1 (HSV-1).

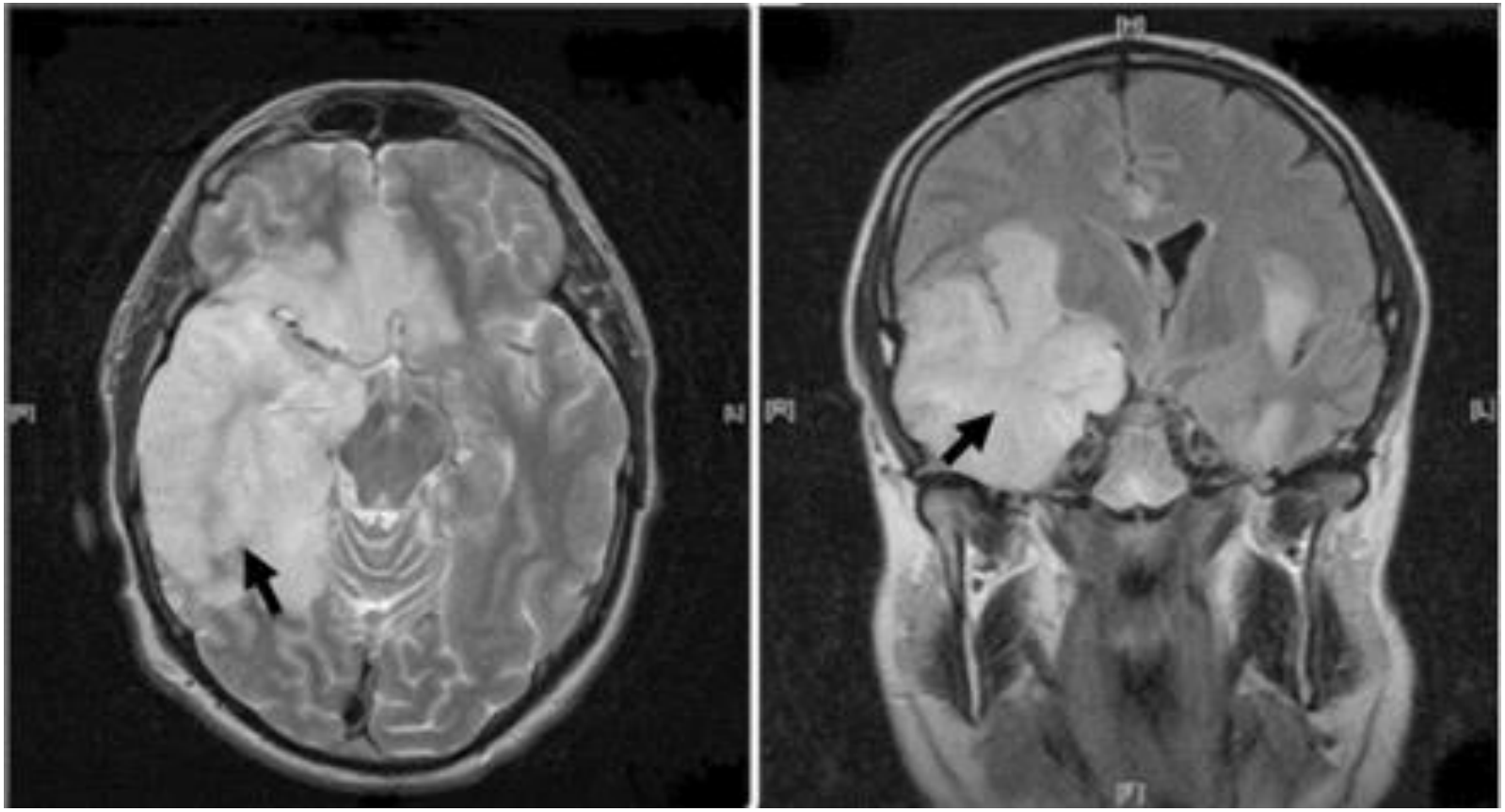
About 10% of cases of herpes encephalitis occur due to HSV-2, which is sexually transmitted virus.

Neonatal HSV encephalitis usually results from acquisition of type 2 virus during passage through the birth canal of a mother with active genital lesions.

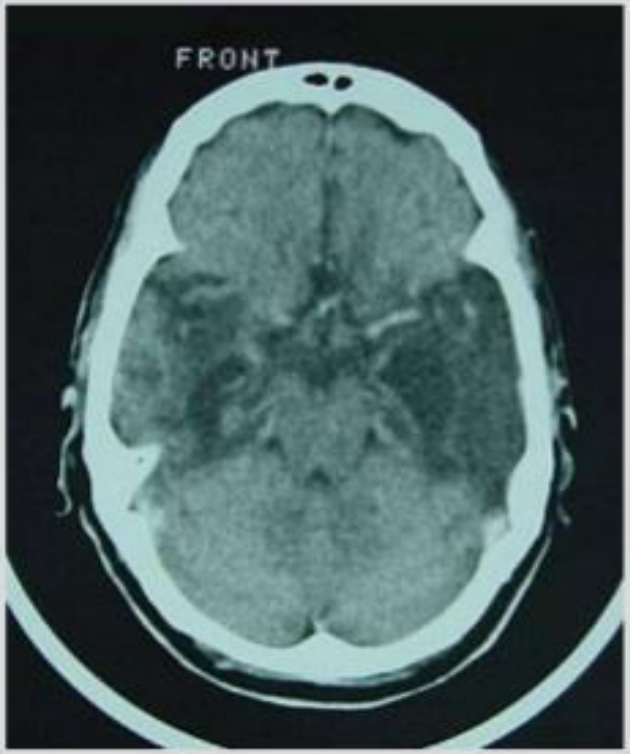
HSV Encephalitis



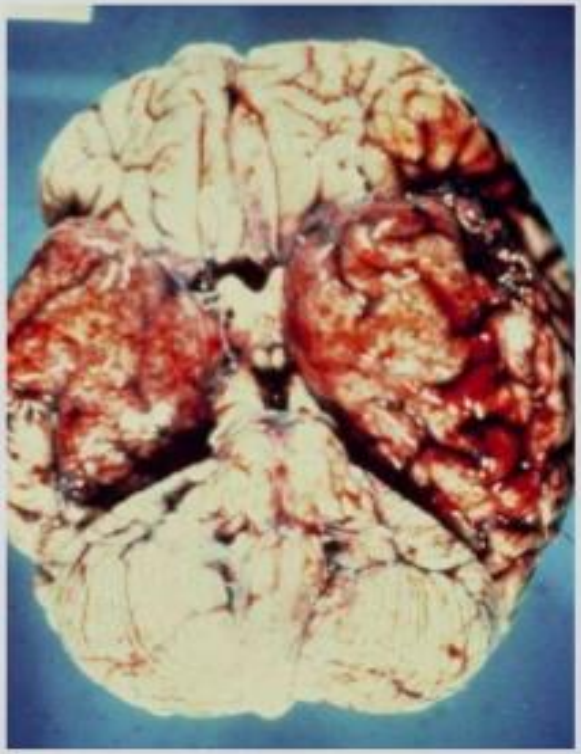
HSV encephalitis, MRI



Herpes Simplex Encephalitis



CT Scan



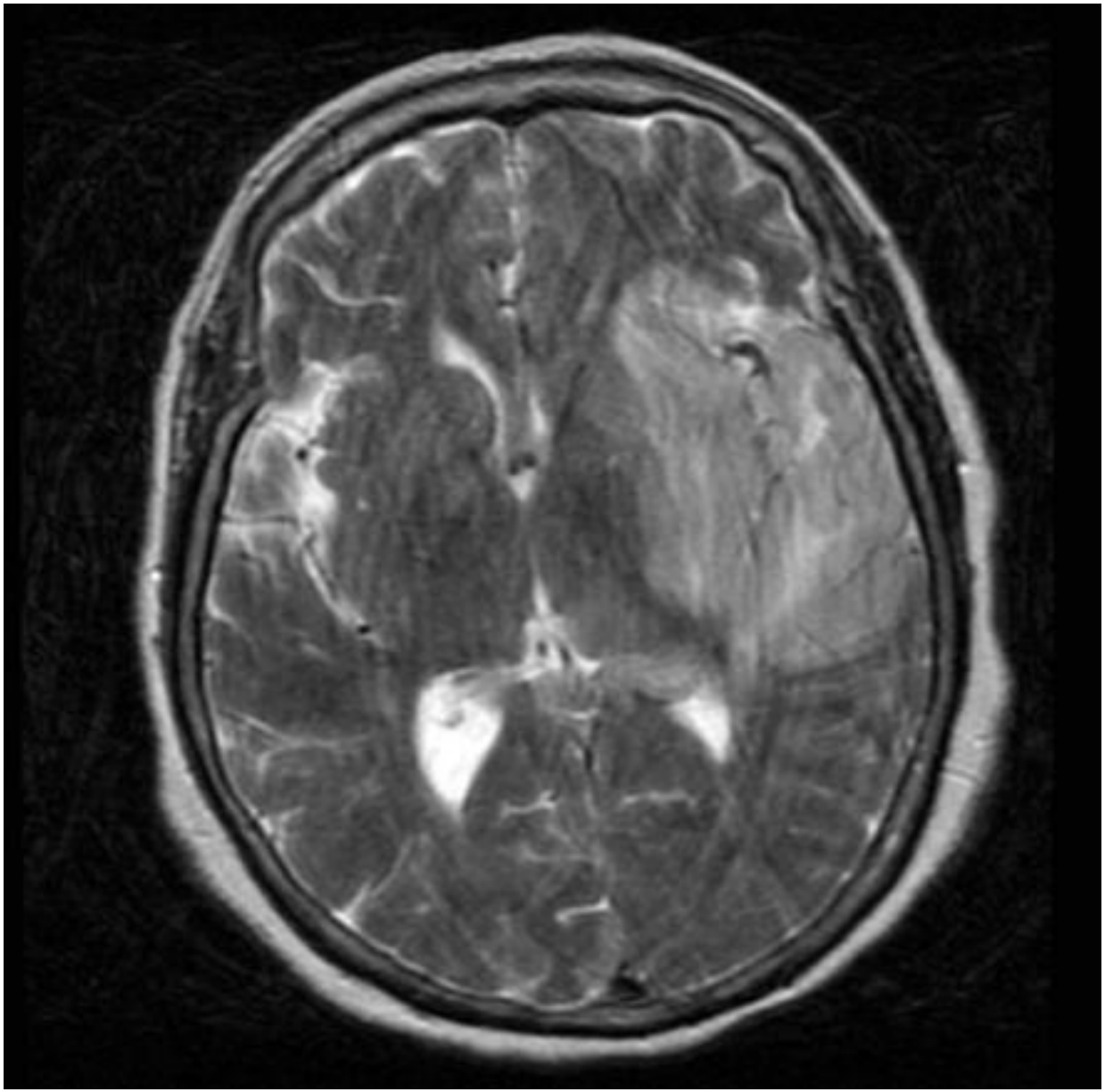
Autopsy

Symptoms and signs are the following:

- **rise of temperature;**
- **headache;**
- **stiff neck;**
- **vomiting;**
- **seizures;**
- **gustatory and olfactory hallucinations;**
- **anosmia;**
- **paresis;**
- **hyperkinetic disorder;**
- **aphasia;**
- **behavioral changes;**
- **memory loss;**
- **an altered level of consciousness;**
- **loss of consciousness, and even coma.**

CSF changes are the following:

- **increased pressure;**
- **lymphocytic or mixed lymphocytic and polymorphonuclear pleocytosis (50-500 white blood cells/mL);**
- **mild protein elevation (2-3 g/L);**
- **normal or decreased glucose;**
- **red blood cells, xanthochromia.**



HSV encephalitis MRI

Prognosis for the disease in case of acyclovir treatment is favorable. In residual period can be Korsakoff's attacks, aphasia.

Vernal tick-borne encephalitis

— primary viral infectious disease involving the central nervous system

There are 4 genetic types, but the main are the following:

- **Far-Eastern;**
- **Western or**
- **Europian.**

Vernal Far-eastern tick-borne encephalitis

Causes: **tick-borne encephalitis virus (family Flaviviridae).**

Source of infection: **sick goats, rarely a cow, a sheep, dogs.**

It is transmitted by the bite of infected ticks (Ixodes scapularis, ricinus and persulcatus), or (rarely) through the non-pasteurized milk of infected and cows.

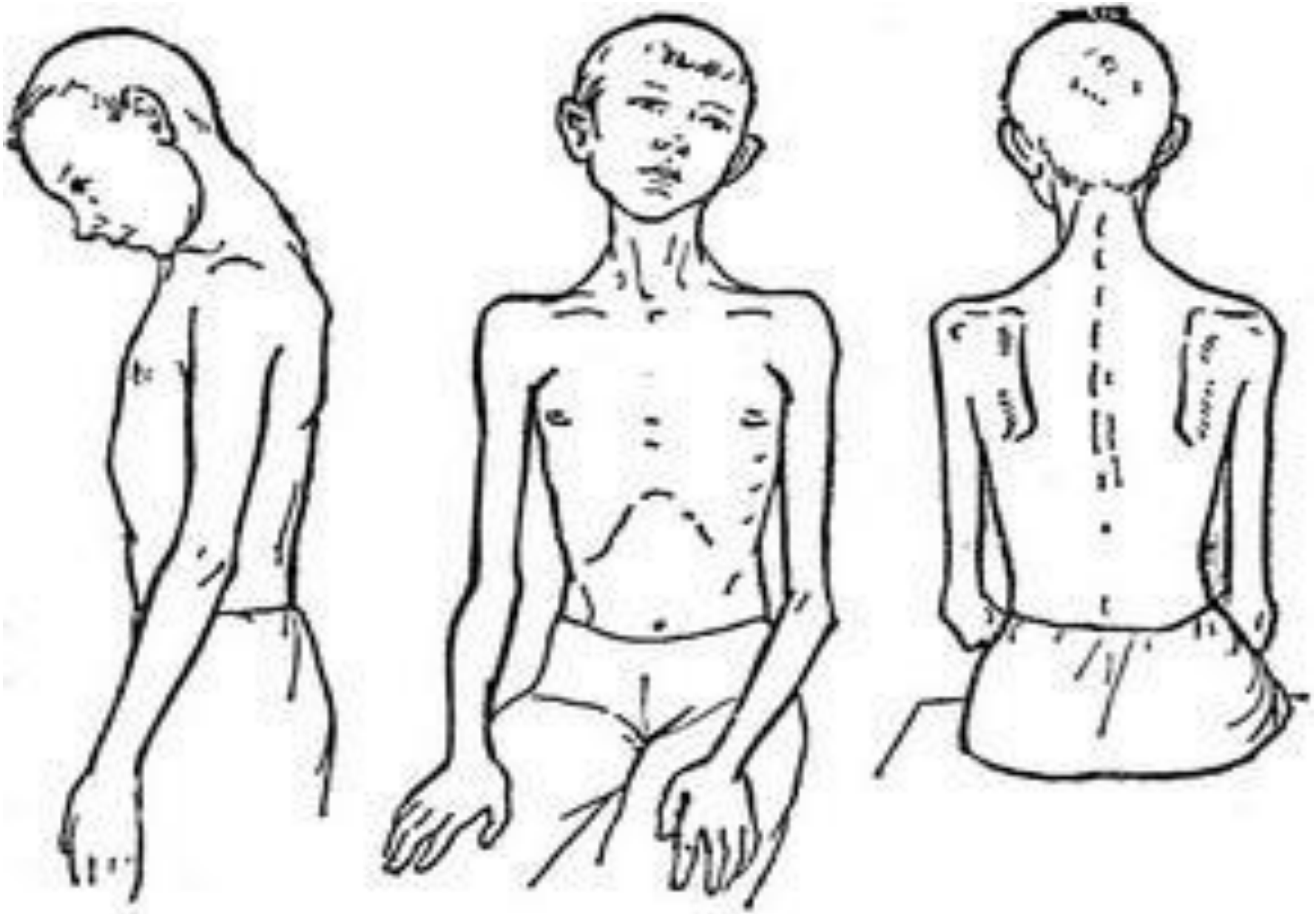
Clinical types are the following:

1. **Poliomyelitic.**
2. **Obliterated infection.**
3. **Abortive infection**
4. **Meningeal.**

Incubation period **makes up to 20 days. Shorter incubation times have been reported after milk-borne exposure(4-7 days).**

Symptoms and signs are the following:

- **acute onset of the disease;**
- **fever, malaise, anorexia, myalgia, headache, nausea, and/or vomiting;**
- **in 2 days — meningeal signs, neck muscles paralysis («drooping head»), paralysis of shoulder-girdle muscles and muscles of proximal parts of extremities;**
- **in about 5-7 days temperature decrease is marked.**



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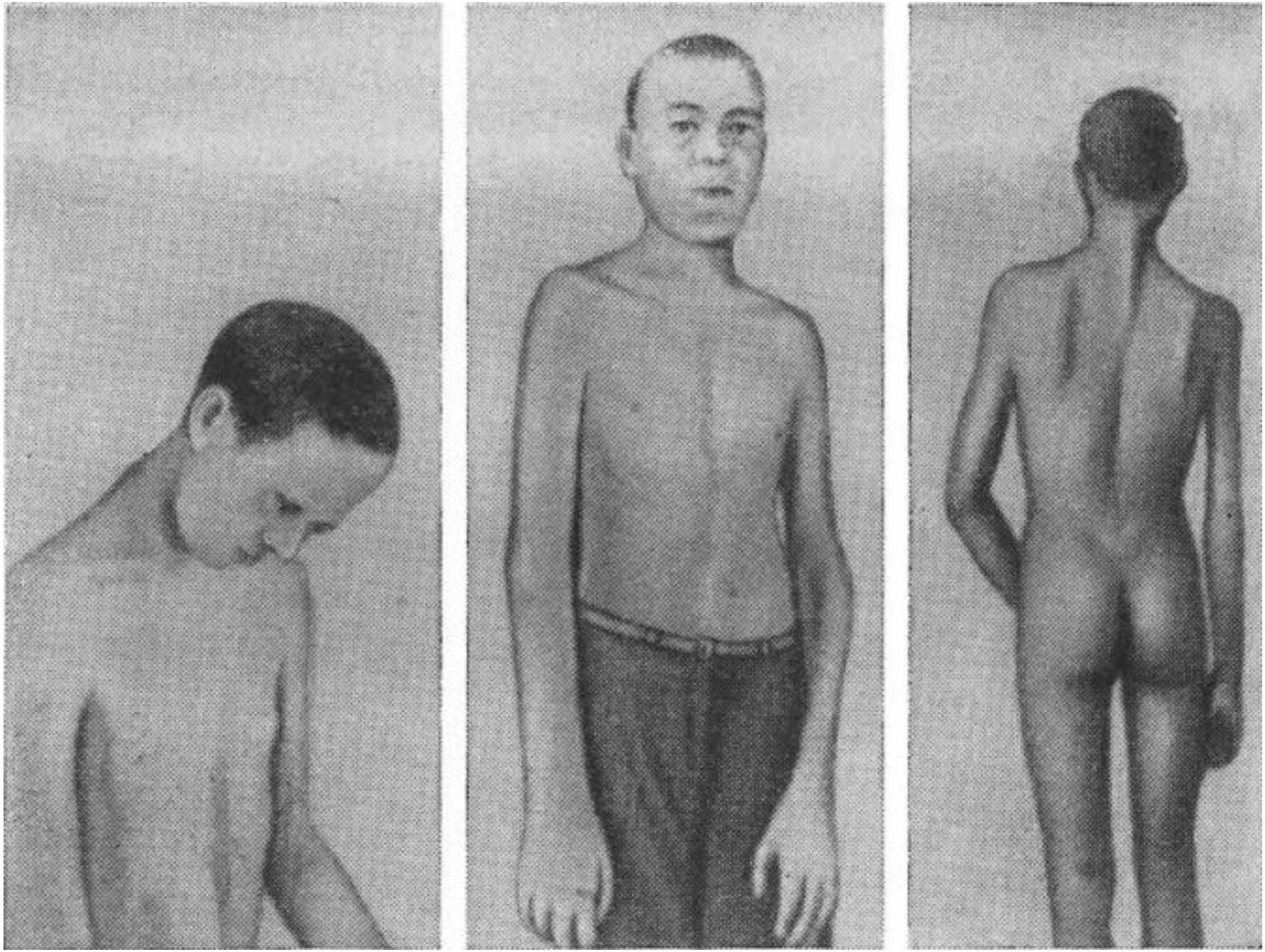
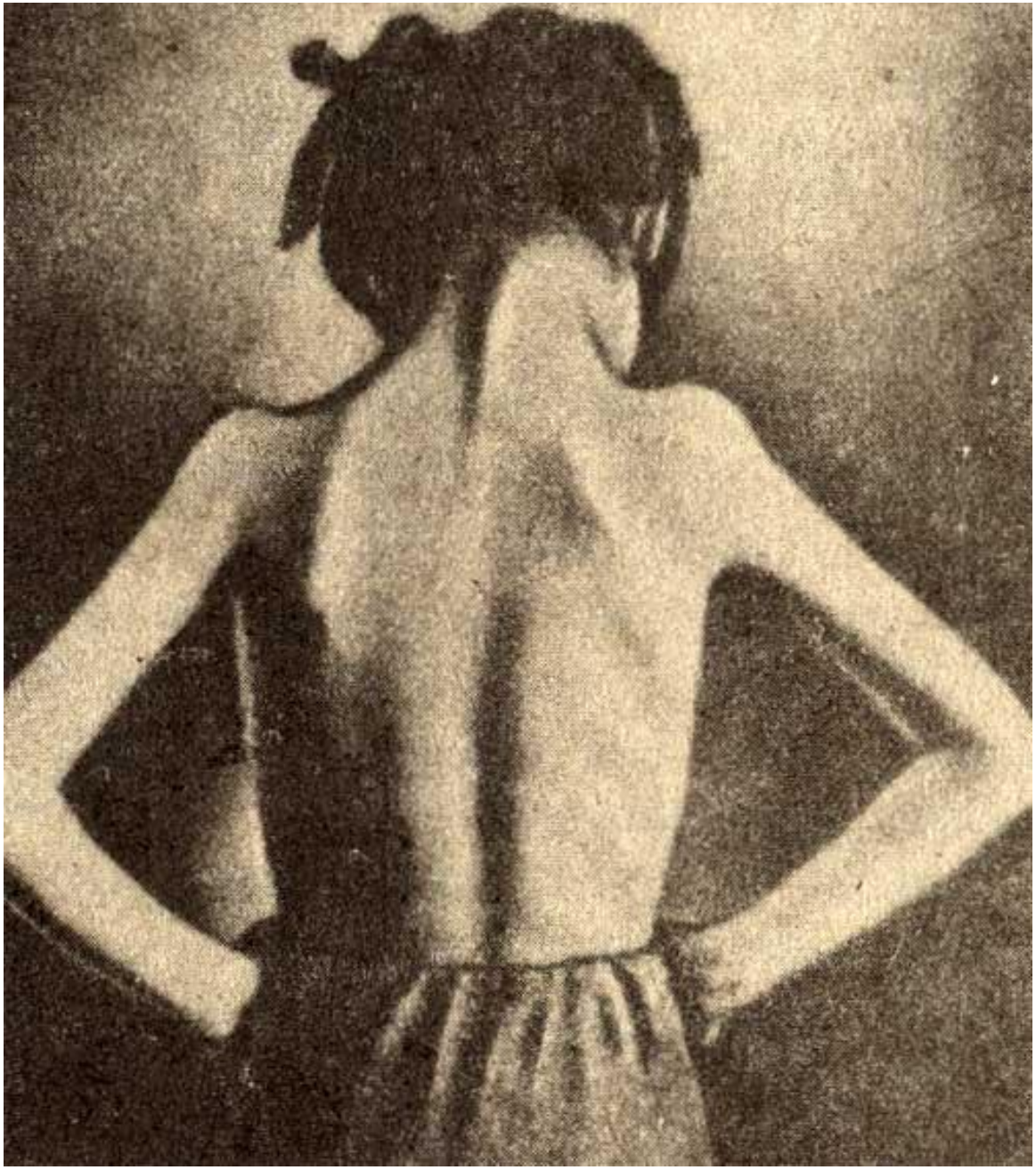




Two-wave spring-summer (Western) meningoencephalitis

Clinical types are the following:

1. **Infectious.**
2. **Meningeal.**
3. **Meningoencephalitic.**
4. **Meningoencephalomyelitic.**

Incubation period **is from 5 to 30 days.**

Symptoms and signs are the following:

- **acute onset of disease;**
- **fever, malaise, headache, vomiting, pain along a backbone;**
- **in 5-7 days temperature normalizes;**
- **in 2-3 days — second wave: temperature rise, hyperemia of face, headache, a nausea, vomiting, vertigo, wobbling, an altered level of consciousness.**

Encephalitis lethargica or von Economo disease

The virus is unknown till now.

***2 stages* of desease are known: acute and chronic.**

***Causes:* the contagious patient**

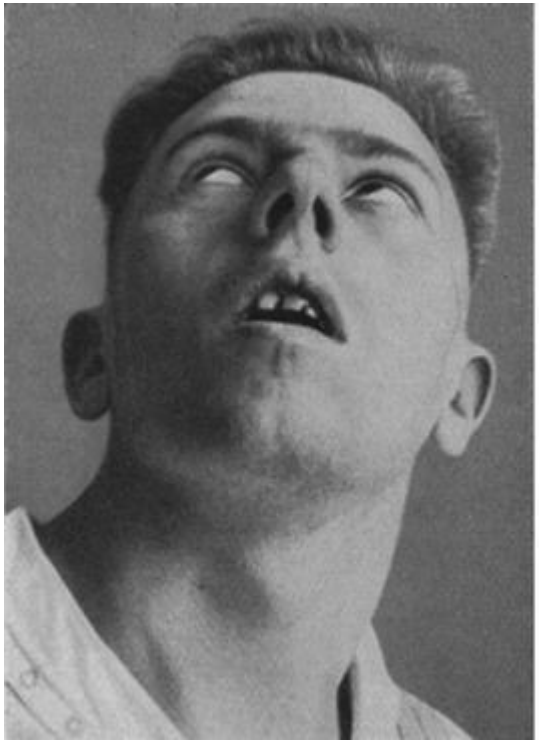
Droplet spread

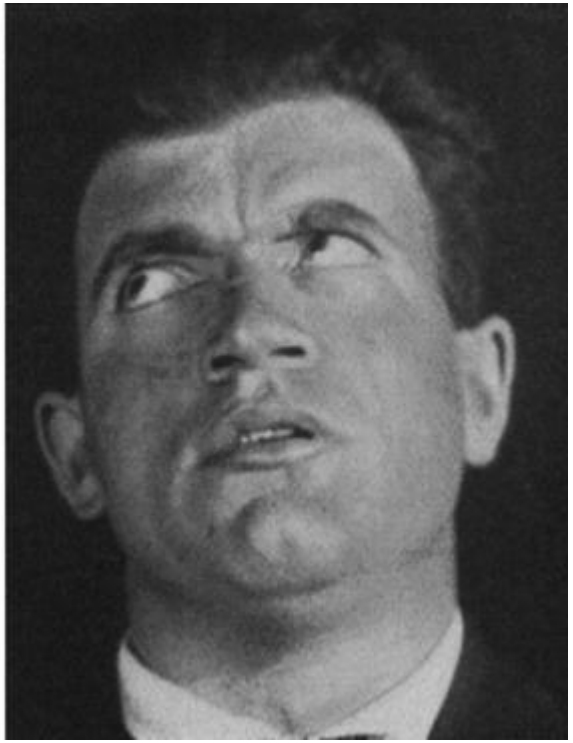
Incubation period **lasts up to 14 days.**

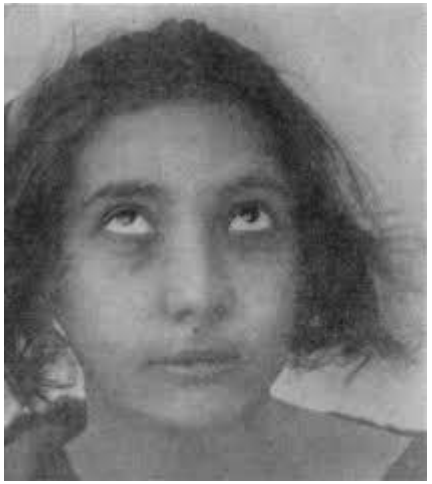
There are 3 main symptoms:

- **sleep disorders: sleepiness or sleeplessness;**
- **eye movement disorders;**
- **fever.**

Additional symptoms: headache; diplopia; mild pyrexia; hypokinesis; tremor; muscle stiffness, oculogyric crises.

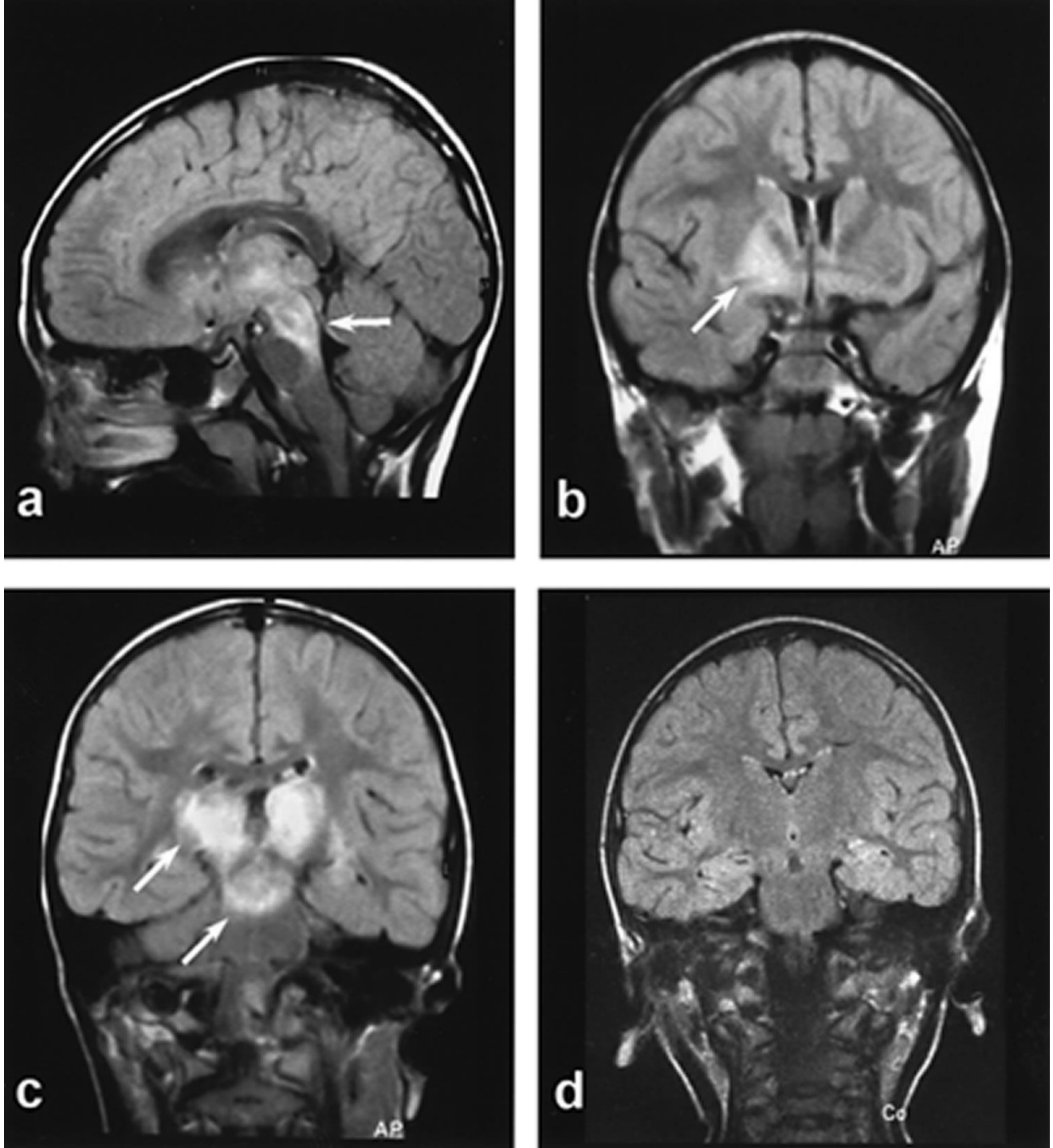






Oculogyric crises

Mandibular tic in postencephalitic parkinsonism.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AP
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Co

Symptoms regress in some months, quite often acute stage comes to an end with recovery.

In a year and more parkinsonian syndrome develops, due to the extrapyramidal system lesion.

Treatment of encephalitis is the following:

- **pathogenetic treatment;**
- **etiotropic treatment;**
- **symptomatic treatment;**
- **medical rehabilitation.**

Pathogenetic treatment is the following:

- **monitoring of breathing and heart function;**
- **dehydration;**
- **hormonotherapy;**
- **anti-inflammatory drugs;**
- **desensitization;**
- **microcirculation improvement;**
- **maintenance of homeostasis;**
- **nootropic drugs.**

Etiotropic treatment of herpes simplex encephalitis:

- **Acyclovir (Zovirax).**
- **Foscarnet (Foscavir).**
- **Ganciclovir (Cytovene).**

Symptomatic treatment

Antibiotics
Anti-seizure medications
Steroids
Sedatives
Antipyretics

Poliomyelitis

(infantile paralysis, Heine-Medin disease) — is an acute, viral, infectious disease, inflammation of the spinal cord grey matter (anterior horns).

Although a severe infection can extend into the brainstem and even higher structures, resulting in polioencephalitis.

Causal agent: **Poliovirus (genus Enterovirus), types 1, 2 and 3.**

Type 1 is commonly associated with paralytic poliomyelitis and epidemics.

This group of RNA viruses colonize the gastrointestinal tract — specifically the oropharynx and the intestine.

Fecal-oral route.

Clinical types:

1. **Subclinical (inapparent) infection: development of immunity and absence of symptoms.**
2. **Abortive infection: minor, non-specific illness-symptoms of mild infection.**
3. **Nonparalytic aseptic meningitis: more severe clinical course, characterized by the fever, headache, malaise, meningeal signs and pleocytosis in absence of paresis.**
4. **Paralytic poliomyelitis, 2 stages:**

Pre-paralytic stage: **This stage is characterized by:**

- **High fever (from 39 to 40 degree °C);**
- **severe headache;**
- **stiff neck;**
- **nausea/vomiting;**
- **general discomfort (malaise);**
- **diarrhoea.**

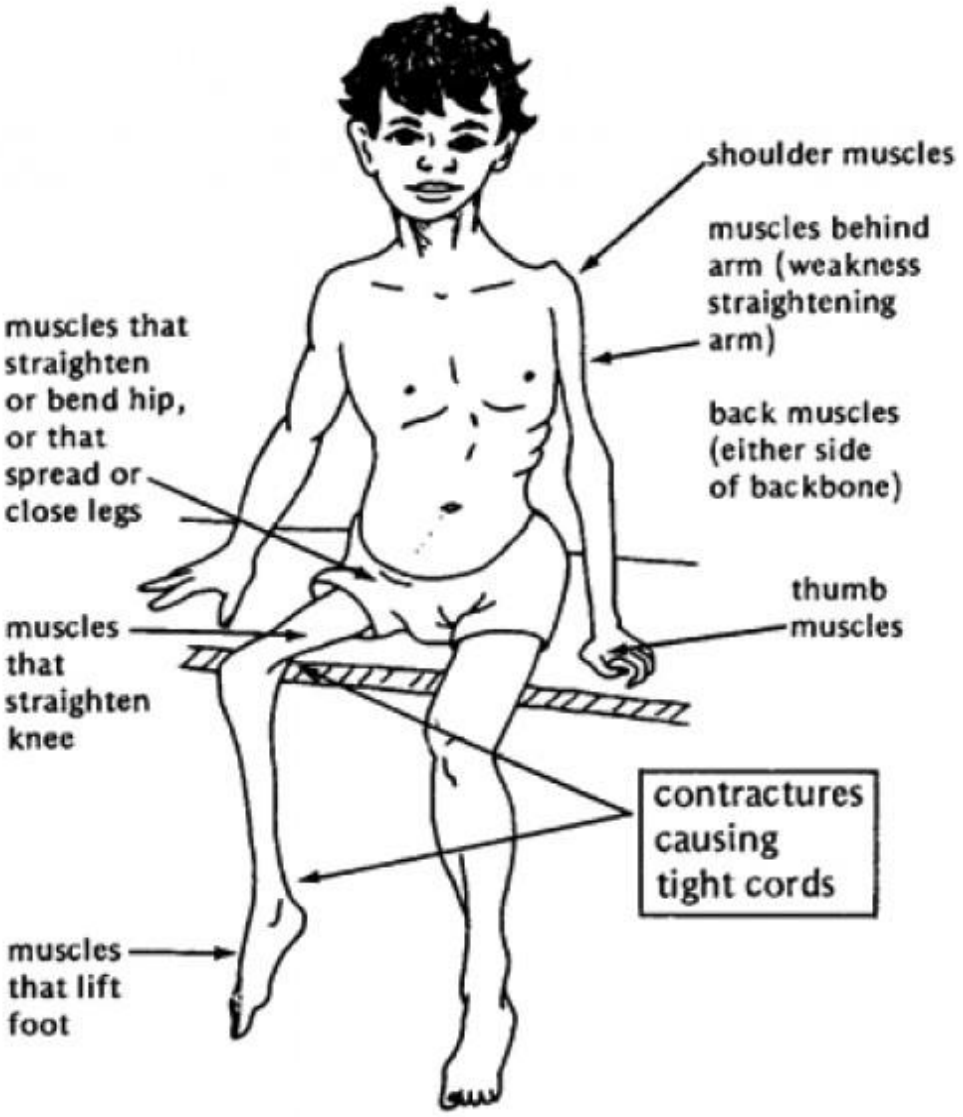
Paralytic stage: **In this stage although fever and other symptoms subside but still muscle tenderness and pain are present.**

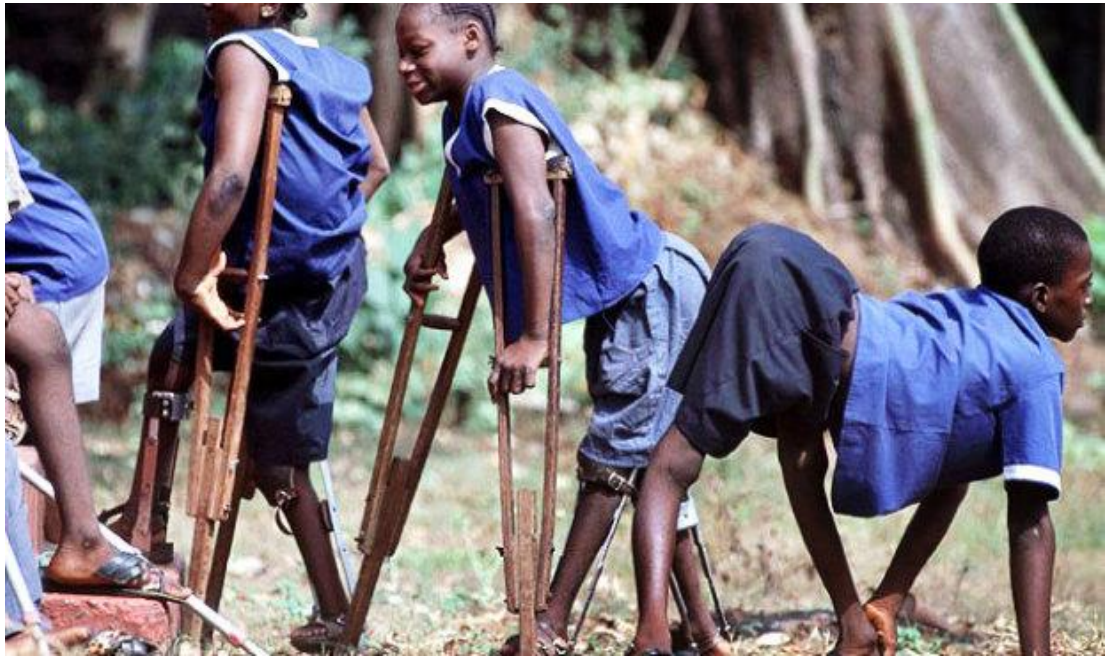
Paralysis in poliomyelitis may appear with irregular distribution. Complete paralysis spreads within 24 hours and persists for several days.

Symptoms are the following:

- **flaccid palsy with muscle atrophy;**
- **hypo- or areflexia;**
- **trophic disturbances of bones which lead to the shortening of limb.**

MUSCLES COMMONLY WEAKENED BY POLIO





Multiple sclerosis is chronic, progressing, multifactorial genetically determined autoimmune disease which affects young, able-bodied persons.

Epidemiology

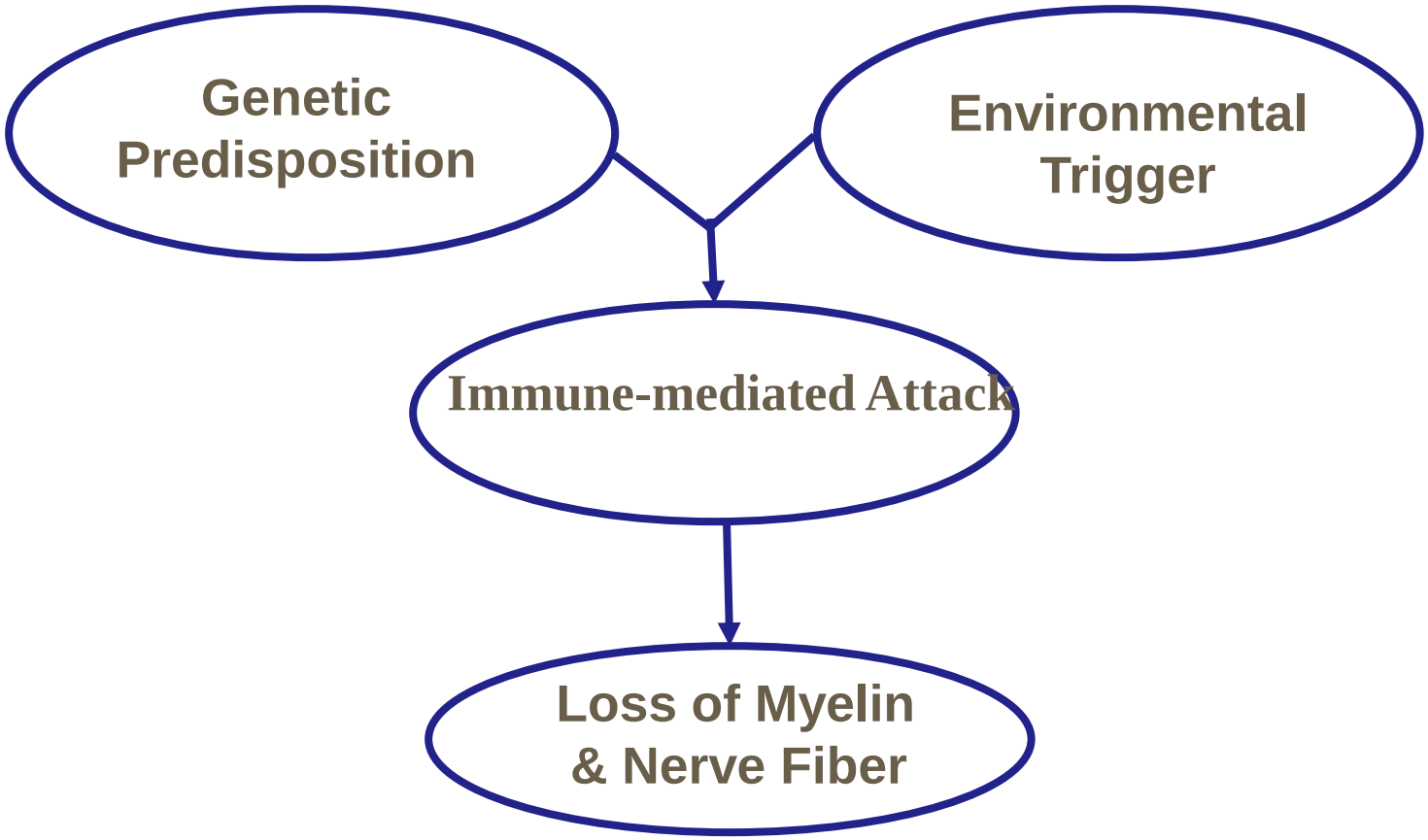
- **The risk of getting MS is approximately:**
  - **1/750 for the general population (0.1%)**
  - **1/40 for person with a close relative with MS (3%)**
  - **1/4 for an identical twin (25%)**

The risk is higher in any family in which there are several family members with the disease

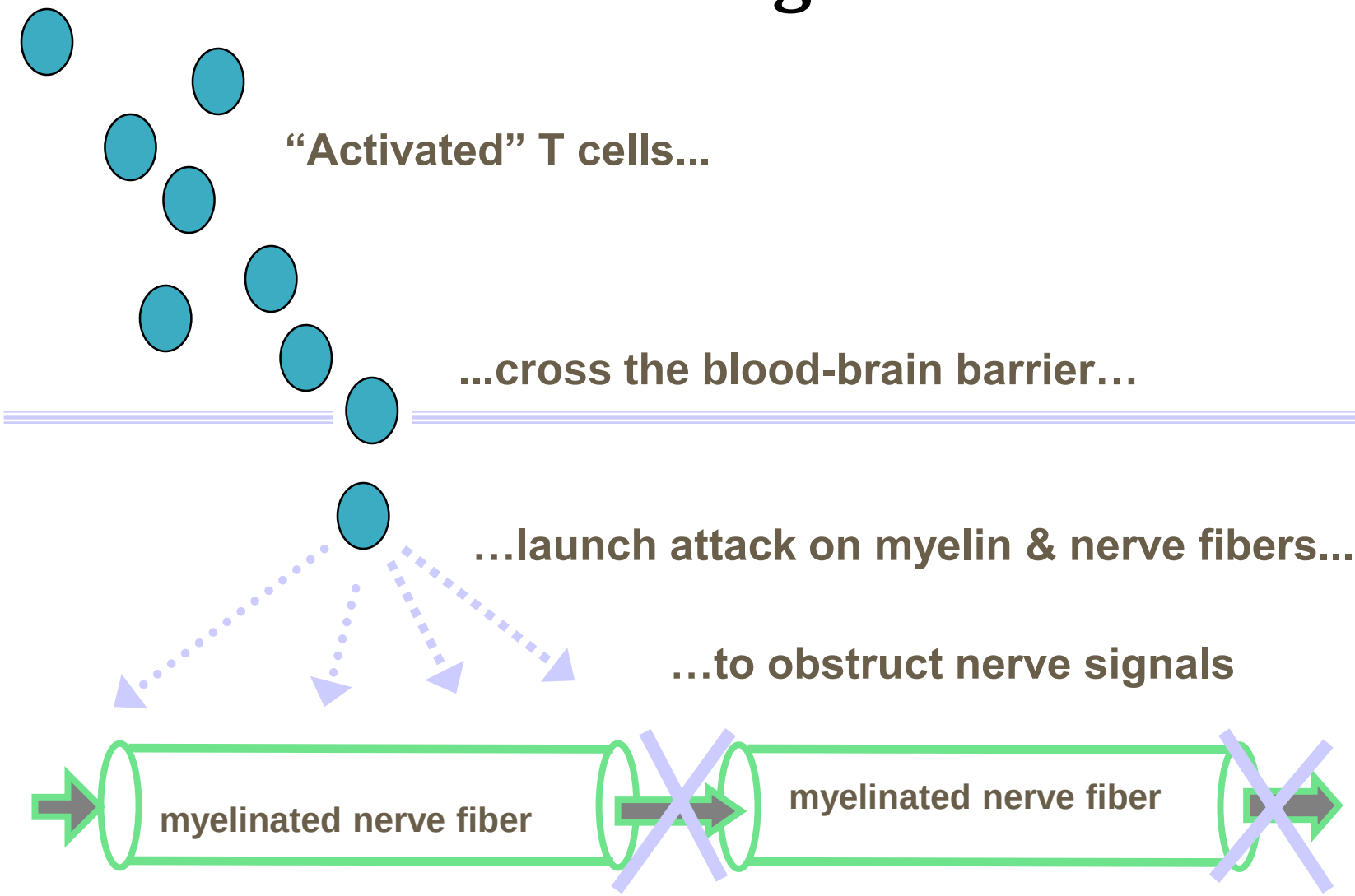
MS involves an immune system attack against the central nervous system (brain, spinal cord, and optic nerves).

As part of the immune attack on the central nervous system, myelin is damaged, as well as the nerve fibers themselves. The damaged myelin forms scar tissue (sclerosis), which gives the disease its name.

Pathogenesis



Pathogenesis



Pathogenesis

Clinical courses

- **Clinically isolated syndrome (CIS)**
- **Relapsing-remitting MS (RRMS)**
  - **About 85% of people are diagnosed with RRMS**
- **Primary progressive MS (PPMS)**
  - **About 15% of people are diagnosed with this course**
- **Secondary progressive**
  - **Most people diagnosed with RRMS will eventually transition to SPMS**

Clinically Isolated Syndrome (CIS)

- **A first neurologic event suggestive of demyelination**
- **Individuals with CIS are at high risk for developing clinically definite MS if the neurologic event is accompanied by multiple, clinically silent (asymptomatic) lesions on MRI typical of MS**

Symptom and signs

Phenomenon of «symptom's dissociation»

1. Visual acuity decrement without eye-ground changes

optic neuritis – is the acute onset of any of the following: blurred vision, graying of vision, blindness in one eye (usually).

2. Visual field defects without eye-ground changes.

3. Vestibular disorders without auditory dysfunction.

4. Loss of vibration sensation without other sensory disorders.

5. Hyperreflexia, clonus without decrement of muscle strength.

6. Combination of spastic paralysis and muscle tone increase in one muscle groups and decrease — in another.

7. Muscle tone increase when patient is in vertical position and decrease when he is in horizontal position. The result is spastic gate.

8. Loss of superficial reflexes in absence of other pyramidal signs.

9. Babinski's sign

10. Emotional Changes: euphoria, apathy, worried depression.

11. Pain (neurogenic; musculoskeletal)

12. Cognitive difficulties (memory, attention, processing)

13. The symptom of «a hot bath»: after 10 mines of staying in a bath with temperature 38°C extremities weakness is aggravated.

14. Bladder dysfunction can be the first symptom of MS in 5% of cases.

15. Pathological fatiguability in young age.

16. Menstrual cycle disorder, impotence
17. Gait, balance, and coordination problems
18. Speech/swallowing problems
19. Tremor

Diagnostics

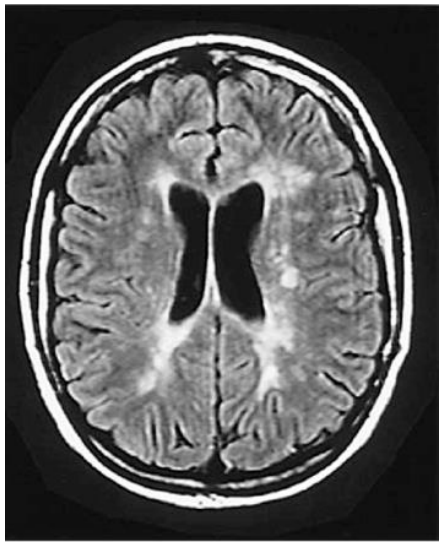
- **MS is a clinical diagnosis:**
  - **Signs and symptoms**
  - **Medical history**
  - **Laboratory tests**
- **Requires "dissemination in time and space":**
  - **Space: Evidence of scarring (plaques) in at least two separate areas of the CNS**
  - **Time: Evidence that the plaques occurred at different points in time**
- **There must be no other explanation**

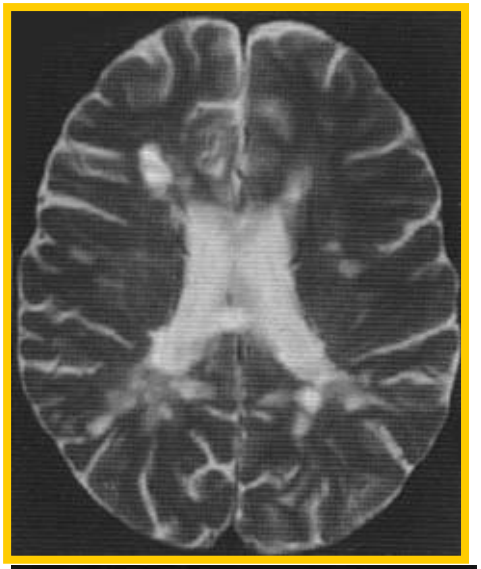
Diagnostics

- **Magnetic resonance imaging (MRI)**
- **Visual evoked potentials (VEP)**
- **Lumbar puncture**

Conventional MRI in MS

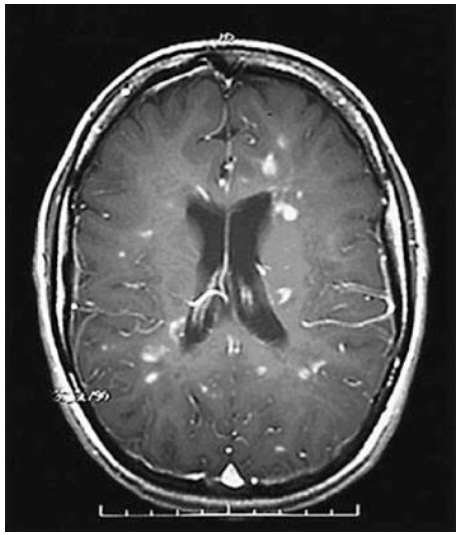
FLAIR

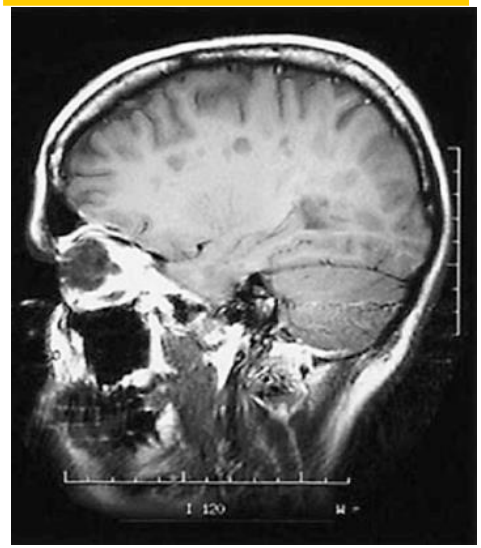




T2
BOD*

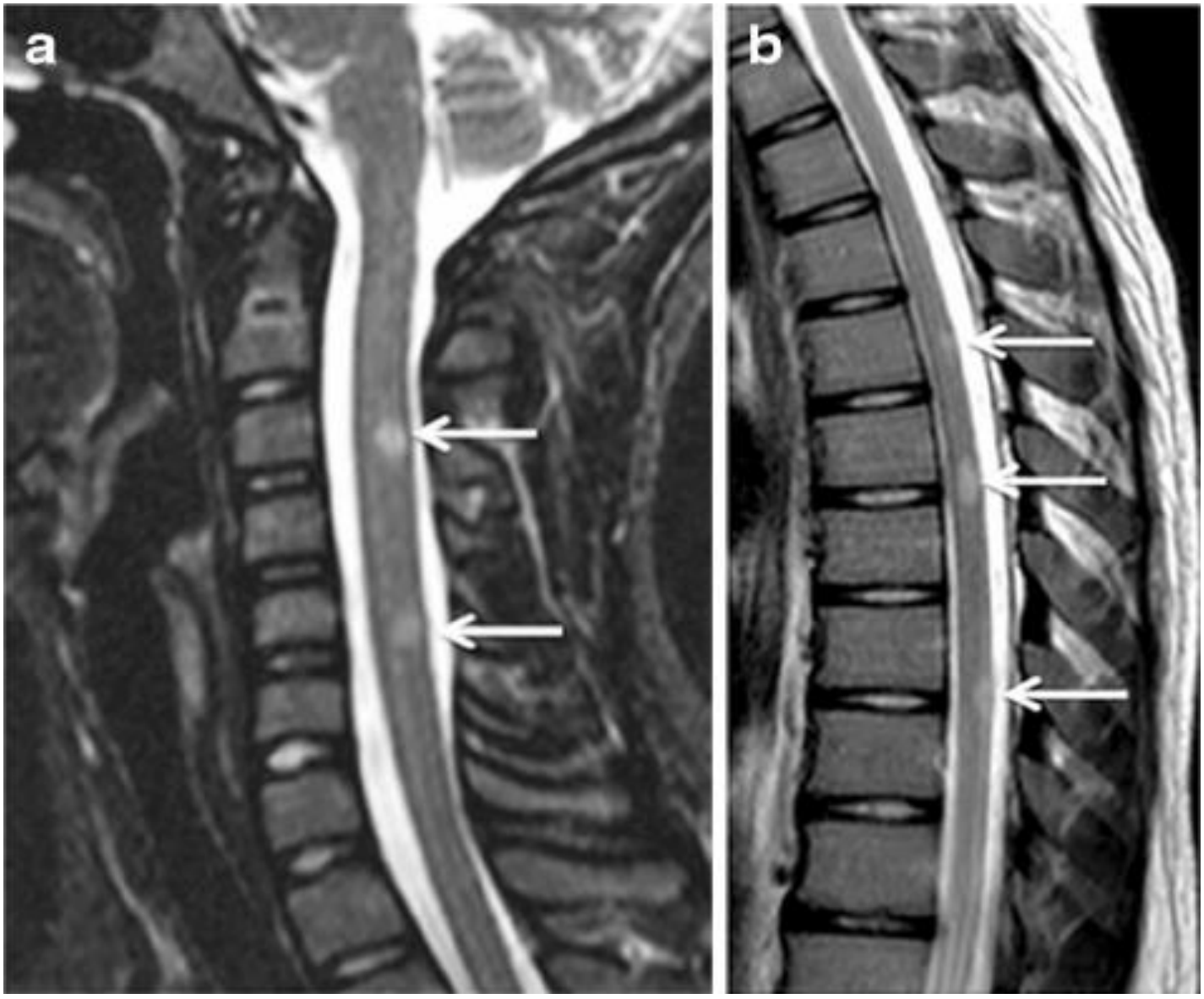
T1 Gd
postcontrast
Disease Activity†





T1
precontrast
Black Holes†

The strongest correlation with progression of disability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Treatment strategies

- **<u>Management of MS falls into five general categories:</u>**
  - **Treatment of relapses (exacerbations, flare-ups, attacks—that last at least 24 hours)**
  - **Symptom management**
  - **Disease modification *(reduce attack frequency and severity, reduce scarring on MRI, and probably slow disease progression).***
  - **Rehabilitation (to maintain/improve function)**
  - **Psychosocial support**

Treatment of relapses

- **3-5 day course of IV methylprednisolone 500mg/ 1g—with/without an oral taper of prednisone**
- **Plasmapheresis**
- **Rehabilitation to restore lost function**
- **Psychosocial support**

Disease modification

- **More than a dozen disease-modifying therapies are FDA-approved for relapsing forms of MS:**
  - **daclizumab (Zinbryta®) [inj]**
  - **glatiramer acetate (Copaxone®; Glatopa® - generic equivalent) [inj.]**
  - **interferon beta-1a (Avonex®, Plegridy®, Rebif®) [inj.]**
  - **interferon beta-1b (Betaseron® and Extavia®) [inj.]**
  - **dimethyl fumarate (Tecfidera®) [oral]**
  - **fingolimod (Gilenya®) [oral]**
  - **teriflunomide (Aubagio®) [oral]**
  - **alemtuzumab (Lemtrada®) [inf]**
  - **mitoxantrone (Novantrone®) [inf]**
  - **natalizumab (Tysabri®) [inf]**
  - **ocrelizumab (Ocrevus®) [inf]**
- **Ocrelizumab has also been approved for primary progressive MS**