



# Wernicke- Korsakoff syndrome

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AM Report

April 18, 2003

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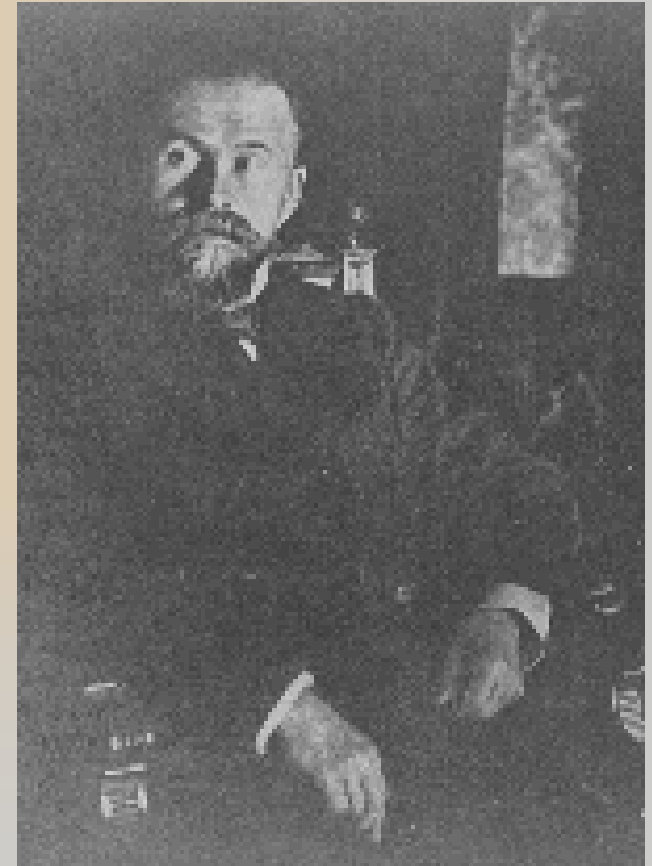


# *DR. CARL WERNICKE*

## *(1848-1904)*



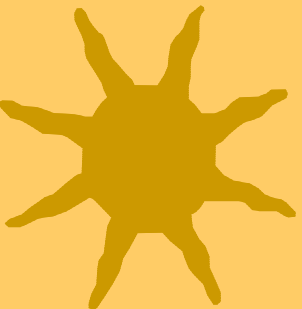
- ★ Wernicke was born in Tarnovitz, Poland. Interested in psychiatry, traditionally he studied anatomy initially and neuropathology later. He published a small volume on aphasia which vaulted him into international fame. In it was precise pathoanatomic analysis paralleling the clinical picture. He is best known for his work on sensory aphasia and poliomyelitis hemorrhagia superior.



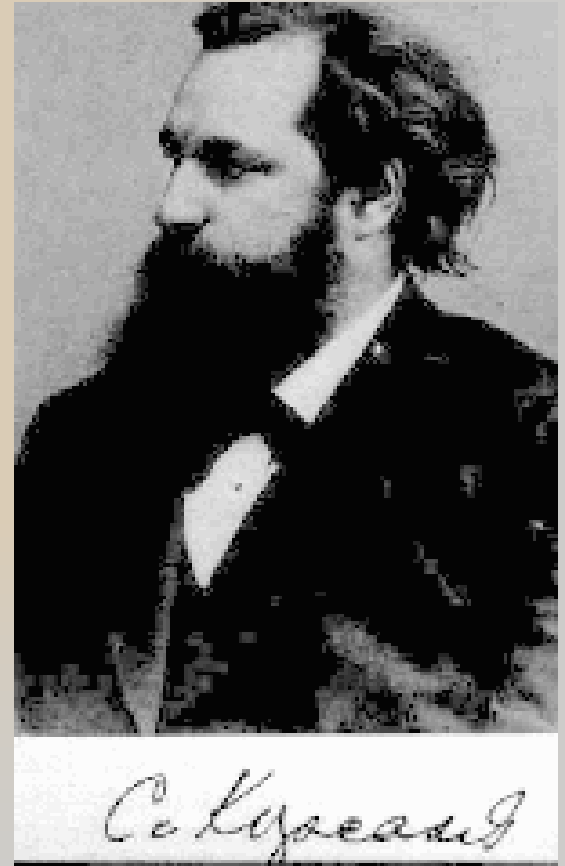


# *DR. SERGEI KORSAKOV*

## *(1853-1900)*



- ★ Korsakov was born in Russia.. Although he studied alcoholic polyneuritis with mental symptoms, his "Korsakov's psychosis" was the term used only when the mental disorder was accompanied by neuritis symptoms. Known as a humanitarian, he improved conditions in mental institutions. He was the first great psychiatrist in Russia. He is considered a "moral genius."





# Background

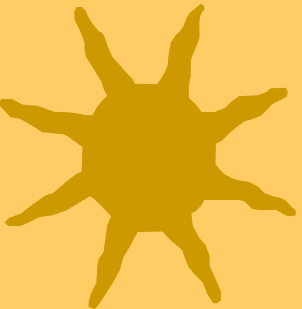
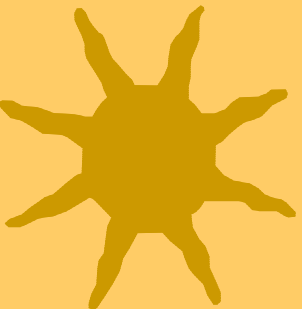


- ★ In 1881, Wernicke first described an illness in 3 pts. that consisted of triad:
  - paralysis of eye movements,
  - ataxia,
  - mental confusion
- ★ The patients:
  - 2 males with alcoholism
  - 1 female with persistent vomiting following sulfuric acid ingestion
  - All progressed to coma and death.
  - Wernicke detected punctate hemorrhages affecting the gray matter around the third and fourth ventricles and aqueduct of Sylvius. He felt these to be inflammatory and therefore named the disease **polioencephalitis hemorrhagica superioris**.



# ***Background***

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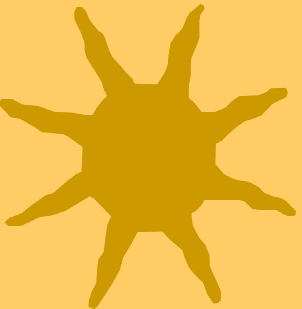


- ★ 1887-1891: Korsakoff described the disturbance of memory in the course of long-term alcoholism in a series of articles. He called this syndrome **psychosis polyneuritica**, believing that these typical memory deficits, in conjunction with polyneuropathy, represented different facets of the same disease.
- ★ The term Wernicke encephalopathy is used to describe the symptom complex of ophthalmoplegia, ataxia, and an acute confusional state. If persistent learning and memory deficits are present, the symptom complex is termed **Wernicke-Korsakoff syndrome**.



# *Pathophysiology*

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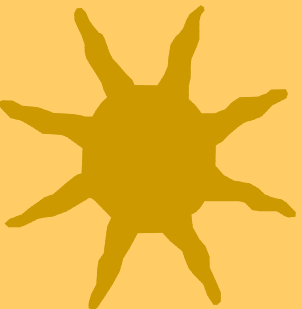


- ★ A deficiency of thiamine is responsible for the symptom complex manifested in Wernicke-Korsakoff syndrome, and any condition resulting in a poor nutritional state places patients at risk.
  - Heavy, long-term alcohol use is the most common association with Wernicke-Korsakoff syndrome. Alcohol interferes with active gastrointestinal transport, and chronic liver disease leads to decreased activation of thiamine pyrophosphate from thiamine, as well as a decreased capacity of the liver to store thiamine.
- ★ Thiamine is converted to thiamine pyrophosphate, which serves as a cofactor for several enzymes that function in glucose utilization. These enzymes include transketolase, pyruvate dehydrogenase, and alpha ketoglutarate.



# *Pathophysiology*

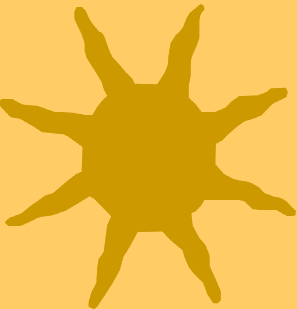
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- ★ Thiamine deficiency results in a diffuse decrease in cerebral glucose utilization. However, symptoms are attributed to focal areas of damage.
  - Ocular motor signs: lesions in the brainstem affecting the abducens nuclei and eye movement centers in the pons and midbrain.
  - Ataxia: damage to the cerebellum, particularly the superior vermis. The loss of neurons leads to persistent ataxia of gait and stance. In addition to cerebellar dysfunction, the vestibular apparatus also is affected.
  - Memory impairment: damage in the diencephalon, including the medial thalamus, and connections with the medial temporal lobes and amygdala. The slow and incomplete recovery of memory deficits suggests that amnesia is related to irreversible structural damage.



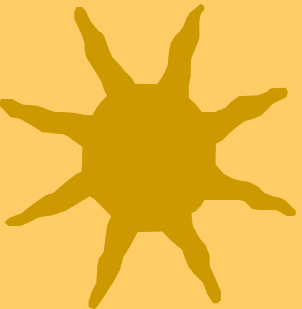
# Pathophysiology



- ★ The mechanism by which thiamine deficiency leads to damage in these specific areas is not fully understood.
- ★ Proposed mechanisms:
  - altered cerebral energy metabolism resulting from decreases in transketolase, pyruvate, and acetylcholine;
  - diminished nerve-impulse transmission at synapses;
  - impaired DNA synthesis.
  - genetic predisposition may exist in some patients?
- ★ McEntee et al (1980) have demonstrated decreased levels of a metabolite of norepinephrine (3-methoxy-4-hydroxyphenolglycol or MHPG) in the CSF of some patients with Wernicke-Korsakoff syndrome. Clonidine, an alpha-noradrenergic agonist, seemed to improve the memory disorder of their patients.
  - However, these results have not been reproduced in any large prospective study. Patients with permanent Korsakoff psychosis are not treated routinely with clonidine.



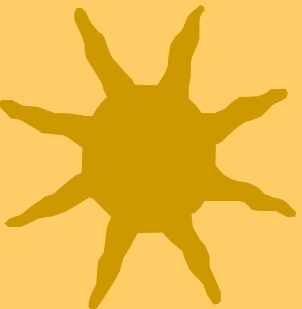
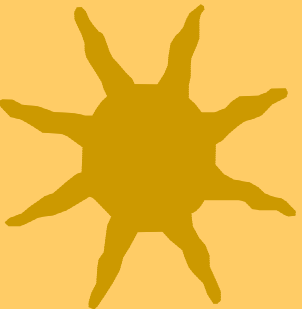
# *Epidemiology*



- ★ Long-standing alcohol use is the most common association with development of Wernicke-Korsakoff syndrome.
  - Prevalence data have come primarily from necropsy studies, with rates of 1-3%, and have indicated that prevalence at autopsy exceeds recognition in life.
- ★ The mortality rate is 10-20%. Prognosis depends on the stage of disease at presentation and on prompt treatment.



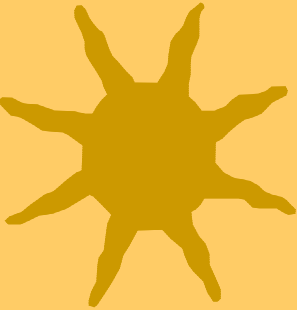
## *Epi...*



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- ★ **Race:** No racial predilection is observed.
  - ★ **Sex:** The condition affects males slightly more frequently than females.
  - ★ **Age:** Age of onset is evenly distributed from 30-70 years.



# *Physical exam signs*



- ★ Ocular abnormalities: can occur singly or in combination
  - Nystagmus, vertical and horizontal
  - Weakness or paralysis of lateral rectus muscles; Occurs bilaterally but can be asymmetric and is accompanied by diplopia and internal strabismus
  - Weakness or paralysis of conjugate gaze
  - Nonreacting miotic pupils and complete loss of ocular movements (in advanced cases)
  - Ptosis, small retinal hemorrhages, involvement of near-far focusing mechanism, and optic neuropathy (occasionally)
  - Papilledema (very rare)
- ★ Ataxia is manifested as an abnormality of both stance and gait. Vestibular paresis also plays a role in ataxia in the early stages of disease.
  - Mildest form evident on tandem walking only
  - Wide-based stance
  - Slow and uncertain short-stepped gait
  - In the most severe form, inability to walk without support
  - Abnormal results on caloric testing (indicates vestibular paresis)



# *Physical exam signs*

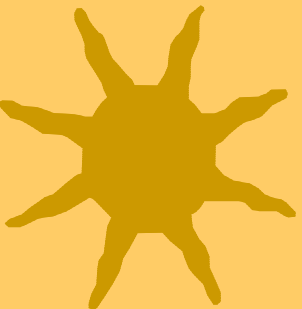


- ★ A global confusional state is the most common early manifestation characterized by apathy, inattentiveness, and indifference to surroundings. General disorientation to time, place, and purpose. Stupor or coma can be observed in more severe cases but is rare as an initial presentation. If patients remain untreated, the condition will progress to death, as in the initial cases described by Wernicke.
  - An amnestic state involves appropriate form and content with apparent loss of certain details.
  - The Korsakoff state is characterized by both anterograde (ie, learning) and retrograde (ie, memory of past events) amnesia. These gaps in memory are what lead to the characteristic feature of confabulation.
- ★ Hypothermia presents secondary to damage in temperature regulating centers.
- ★ Associated peripheral neuropathy is found in 80% of patients.
- ★ Cardiovascular dysfunction may be observed. Overt signs of beriberi heart disease are rare; The following symptoms may be observed and generally improve with administration of thiamine:
  - Postural hypotension, Tachycardia, Syncope



# *Ancillary testing*

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- ★ Wernicke encephalopathy remains a clinical diagnosis with no characteristic abnormalities in diagnostic studies of cerebrospinal fluid, brain imaging or EEGs.
- ★ MRI of the brain with contrast:
  - May show acute lesions in medial thalamic, mamillary bodies, and periaqueductal regions.



# *Causes to consider*

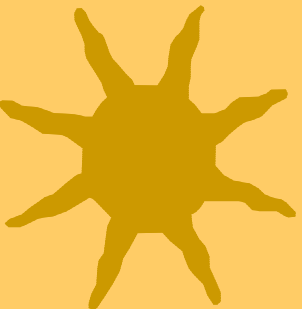
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- ★ Chronic alcoholism
- ★ Persistent emesis
- ★ **Hyperemesis gravidarum**
- ★ Gastric malignancy
- ★ Intestinal obstruction
- ★ Systemic diseases
- ★ Malignancy
- ★ Disseminated tuberculosis
- ★ Acquired immunodeficiency syndrome
- ★ Uremia/Chronic hemodialysis
- ★ Starvation/Refeeding after starvation
- ★ Anorexia nervosa
- ★ Iatrogenic
- ★ Intravenous hyperalimentation



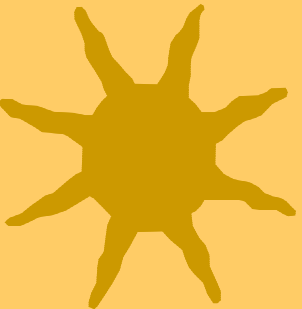
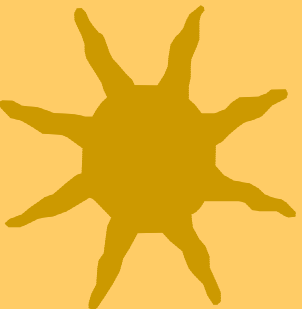
# *Hyperemesis gravidarum*



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- ★ Quite a few case reports of **Hyperemesis gravidarum** associated with Wernicke-Korsakoff syndrome
    - At UNC: case report of a primipara with Hyperemesis gravidarum admitted for MS changes at 14<sup>th</sup> week of pregnancy with ophthalmoplegia, ataxia, hyporeflexia. Pt improved quickly with thiamine administration but ataxia persisted; spontaneous abortion occurred 2 weeks later.
      - Obstetrics & Gynecology. 99(5 Pt 2): 875-7, 2002 May.



# Treatment



- ★ Wernicke encephalopathy is a medical emergency.
  - Prompt recognition of the symptom complex and a high index of suspicion are crucial.
- ★ Intravenous thiamine (50-100 mg) is the treatment of choice.
  - Early treatment can rapidly reverse the ophthalmoplegia and improve ataxia/dysequilibrium and early mental confusion, as well as prevent development of the amnestic state.
- ★ Mg, K supplements (often low in people with alcoholism).
  - Also, Mg is a necessary cofactor in thiamine-dependent metabolism.
- ★ Administration of intravenous glucose to patients who are severely malnourished can exhaust their supply of thiamine and precipitate Wernicke-Korsakoff syndrome.



# *Prognosis*

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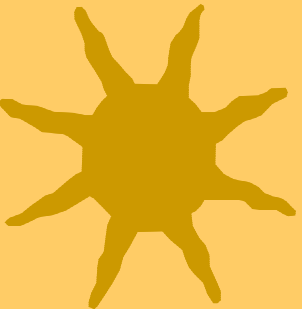
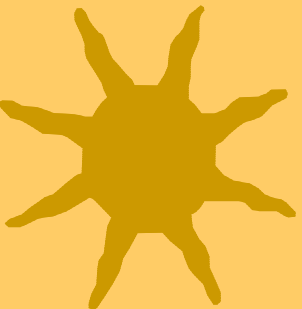
- ★ Patients with Wernicke encephalopathy have a 10-20% mortality rate.
- ★ In general, full recovery of ocular function occurs. Fine horizontal nystagmus can persist in as many as 60% of cases.
- ★ Approximately 40% of patients have complete recovery from ataxia.
- ★ Of patients surviving Wernicke encephalopathy, 80% have Korsakoff psychosis.
- ★ Of patients with Korsakoff psychosis, 25% do not recover and require long-term institutionalization.
- ★ Only about 20% eventually recover completely during long-term follow-up care.
- ★ Only 20% of patients recover completely from amnesic deficit.



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*HAPPY EASTER!*

