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WERNICKE_KORSAKOFF SYNDROME

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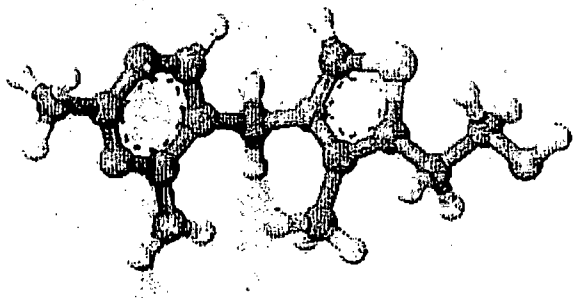
# Wernicke–Korsakoff syndrome

**Wernicke–Korsakoff syndrome (WKS)** is the combined presence of Wernicke encephalopathy (WE) and alcoholic Korsakoff syndrome. Due to the close relationship between these two disorders, people with either are usually diagnosed with WKS, as a single syndrome.

The cause of the disorder is thiamine (vitamin $B_1$) deficiency, which can cause a range of disorders including beriberi, Wernicke encephalopathy, and alcoholic Korsakoff syndrome. These disorders may manifest together or separately. WKS is usually secondary to alcohol abuse. It mainly causes vision changes, ataxia and impaired memory.[1]

**Wernicke–Korsakoff syndrome**

Synonyms Korsakoff's psychosis, alcoholic encephalopathy[1]



Thiamine

Specialty Neurology, psychiatry

Wernicke encephalopathy and WKS are most commonly seen in people who are alcoholic, and only 20% of cases are identified before death. This failure in diagnosis of WE and thus treatment of the disease leads to death in approximately 20% of cases, while 75% are left with permanent brain damage associated with WKS.[2] Of those affected, 25% require long-term institutionalization in order to receive effective care.[2]

## Contents

# Signs and symptoms

The syndrome is a combined manifestation of two namesake disorders, Wernicke encephalopathy and alcoholic Korsakoff syndrome. It involves an acute Wernicke-encephalopathy phase, followed by the development of a chronic alcoholic Korsakoff syndrome phase.[3]

## Wernicke encephalopathy

WE is characterized by the presence of a triad of symptoms;[4]

1. Ocular disturbances (ophthalmoplegia)
2. Changes in mental state (confusion)
3. Unsteady stance and gait (ataxia)

This triad of symptoms results from a deficiency in vitamin $B_1$ which is an essential coenzyme. The aforementioned changes in mental state occur in approximately 82% of patients' symptoms of which range from confusion, apathy, inability to concentrate, and a decrease in awareness of the immediate situation they are in. If left untreated, WE can lead to coma or death. In about 29% of patients, ocular disturbances consist of nystagmus and paralysis of the lateral rectus muscles or other muscles in the eye. A smaller percentage of patients experience a decrease in reaction time of the pupils to light stimuli and swelling of the optic disc which may be accompanied by retinal hemorrhage. Finally, the symptoms involving stance and gait occur in about 23% of patients and result from dysfunction in the cerebellum and vestibular system. Other symptoms that have been present in cases of WE are stupor, low blood pressure (hypotension), elevated heart rate (tachycardia), as well as hypothermia, epileptic seizures and a progressive loss of hearing.

About 19% of patients have none of the symptoms in the classic triad at first diagnosis of WE; however, usually one or more of the symptoms develops later as the disease progresses.[4]

## Alcoholic Korsakoff syndrome

KS is described as an acute onset of severe memory impairment without any dysfunction in intellectual abilities.[1][5] The DSM IV lists the following criteria for the diagnosis of alcoholic Korsakoff syndrome:

1. anterograde amnesia
2. Variable presentation of retrograde amnesia

One of:

1. Aphasia
2. Apraxia

3. Agnosia
4. A deficit in executive functions

In addition, the DSM-IV indicates that normal activities and function will be impaired by the memory deficits and that the experience of amnesia must occur outside of times where the individual is in a state of delirium, intoxification, or withdrawal. The criteria for diagnosis also maintain that there must be evidence that the amnesia is caused by the use of alcohol.[5]

Despite the assertion that alcoholic Korsakoff syndrome must be caused by the use of alcohol, there have been several cases where it has developed from other instances of thiamine deficiency resulting from gross malnutrition due to conditions such as; stomach cancer, anorexia nervosa, and gastrectomy.[6]

## Cognitive effects

Several cases have been documented where Wernicke–Korsakoff syndrome has been seen on a large scale. In 1947, 52 cases of WKS were documented in a prisoner of war hospital in Singapore where the prisoners' diets included less than 1 mg of thiamine per day. Such cases provide an opportunity to gain an understanding of what effects this syndrome has on cognition. In this particular case, cognitive symptoms included insomnia, anxiety, difficulties in concentration, loss of memory for the immediate past, and gradual degeneration of mental state; consisting of confusion, confabulation, and hallucinations.[2] In other cases of WKS, cognitive effects such as severely disrupted speech, giddiness, and heavy headedness have been documented. In addition to this, it has been noted that some patients displayed an inability to focus, and the inability of others to catch patients' attention.[7]

In a study conducted in 2003 by Brand et al. on the cognitive effects of WKS, the researchers used a neuropsychological test battery which included tests of intelligence, speed of information processing, memory, executive function and cognitive estimation. They found that patients suffering from WKS showed impairments in all aspects of this test battery but most noticeably, on the cognitive estimation tasks. This task required subjects to estimate a physical quality such as size, weight, quantity or time (i.e. What is the average length of a shower?), of a particular item. Patients with WKS performed worse than normal control participants on all of the tasks in this category. The patients found estimations involving time to be the most difficult, whereas quantity was the easiest estimation to make. Additionally, the study included a category for classifying "bizarre" answers, which included any answer that was far outside of the normal range of expected responses. WKS patients did give answers that could fall into such a category and these included answers such as 15s or 1 hour for the estimated length of a shower, or 4 kg or 15 tonnes as the weight of a car.[8]

## Memory deficits

As mentioned previously, the amnesic symptoms of WKS include both retrograde and anterograde amnesia.[3] The retrograde deficit has been demonstrated through an inability of WKS patients to recall or recognize information for recent public events. The anterograde memory loss is demonstrated through deficits in tasks that involve encoding and then recalling lists of words and faces, as well as semantic learning tasks. WKS patients have also demonstrated difficulties in preservation as evidenced by a deficit in performance on the Wisconsin Card Sorting Test.[3] The retrograde amnesia that accompanies WKS can extend as far back as

twenty to thirty years, and there is generally a temporal gradient seen, where earlier memories are recalled better than more recent memories.[9] It has been widely accepted that the critical structures that lead to the memory impairment in WKS are the mammillary bodies, and the thalamic regions.[10] Despite the aforementioned memory deficits, non-declarative memory functions appear to be intact in WKS patients. This has been demonstrated through measures that assess perceptual priming.[5]

Other studies have shown deficits in recognition memory and stimulus-reward associative functions in patients with WKS.[10] The deficit in stimulus-reward functions was demonstrated by Oscar-Berman and Pulaski who presented patients with reinforcements for certain stimuli but not others, and then required the patients to distinguish the rewarded stimuli from the non-rewarded stimuli. WKS patients displayed significant deficits in this task. The researchers were also successful in displaying a deficit in recognition memory by having patients make a yes/no decision as to whether a stimulus was familiar (previously seen) or novel (not previously seen). The patients in this study also showed a significant deficit in their ability to perform this task.[10]

### Confabulation

People with WKS often show confabulation, spontaneous confabulation being seen more frequently than provoked confabulation.[11] Spontaneous confabulations refer to incorrect memories that the patient holds to be true, and may act on, arising spontaneously without any provocation. Provoked confabulations can occur when a patient is cued to give a response, this may occur in test settings. The spontaneous confabulations viewed in WKS are thought to be produced by an impairment in source memory, where they are unable to remember the spatial and contextual information for an event, and thus may use irrelevant or old memory traces to fill in for the information that they cannot access. It has also been suggested that this behaviour may be due to executive dysfunction where they are unable to inhibit incorrect memories or because they are unable to shift their attention away from an incorrect response.[11]

## Causes

WKS is usually found in chronic alcoholics. Wernicke–Korsakoff syndrome results from thiamine deficiency. It is generally agreed that Wernicke encephalopathy results from severe acute deficiency of thiamine (vitamin $B_1$), whilst Korsakoff's psychosis is a chronic neurologic sequela of Wernicke encephalopathy. The metabolically active form of thiamine is thiamine pyrophosphate, which plays a major role as a cofactor or coenzyme in glucose metabolism. The enzymes that are dependent on thiamine pyrophosphate are associated with the citric acid cycle (also known as the Krebs cycle), and catalyze the oxidation of pyruvate, α-ketoglutarate and branched chain amino acids. Thus, anything that encourages glucose metabolism will exacerbate an existing clinical or sub-clinical thiamine deficiency.

As stated above, Wernicke–Korsakoff syndrome in the United States is usually found in malnourished chronic alcoholics, though it is also found in patients who undergo prolonged intravenous (IV) therapy without vitamin $B_1$ supplementation, gastric stapling, intensive care unit (ICU) stays or hunger strikes. In some regions, physicians have observed thiamine deficiency brought about by severe malnutrition, particularly in diets

consisting mainly of polished rice, which is thiamine-deficient. The resulting nervous system ailment is called beriberi. In individuals with sub-clinical thiamine deficiency, a large dose of glucose (either as sweet food, etc. or glucose infusion) can precipitate the onset of overt encephalopathy.[12][13][14]

Wernicke–Korsakoff syndrome in alcoholics particularly is associated with atrophy/infarction of specific regions of the brain, especially the mamillary bodies. Other regions include the anterior region of the thalamus (accounting for amnesic symptoms), the medial dorsal thalamus, the basal forebrain, the median and dorsal raphe nuclei,[15] and the cerebellum.[16]

One as-yet-unreplicated study has associated susceptibility to this syndrome with a hereditary deficiency of transketolase, an enzyme that requires thiamine as a coenzyme.[17]

### Post-gastrectomy

The fact that gastrointestinal surgery can lead to the development of WKS was demonstrated in a study that was completed on three patients who recently undergone a gastrectomy. These patients had developed WKS but were not alcoholics and had never suffered from dietary deprivation. WKS developed between 2 and 20 years after the surgery.[18] There were small dietary changes that contributed to the development of WKS but overall the lack of absorption of thiamine from the gastrointestinal tract was the cause. Therefore, it must be ensured that patients who have undergone gastrectomy have a proper education on dietary habits, and carefully monitor their thiamine intake. Additionally, an early diagnosis of WKS, should it develop, is very important.[18]

### Alcohol–thiamine interactions

Strong evidence suggests that ethanol interferes directly with thiamine uptake in the gastrointestinal tract. Ethanol also disrupts thiamine storage in the liver and the transformation of thiamine into its active form.[19] The role of alcohol consumption in the development of WKS has been experimentally confirmed through studies in which rats were subjected to alcohol exposure and lower levels thiamine through a low-thiamine diet.[20] In particular, studies have demonstrated that clinical signs of the neurological problems that result from thiamine deficiency develop faster in rats that have received alcohol and were also deficient in thiamine than rats who did not receive alcohol.[20] In another study, it was found that rats that were chronically fed alcohol had significantly lower liver thiamine stores than control rats. This provides an explanation for why alcoholics with liver cirrhosis have a higher incidence of both thiamine deficiency and WKS.[15]

## Pathophysiology

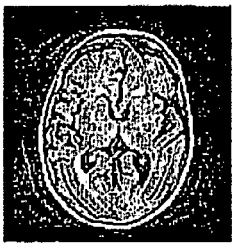
Brain atrophy associated with WKS occurs in the following regions of the brain: the mammillary bodies, the thalamus, the periaqueductal grey, the walls of the 3rd ventricle, the floor of the 4th ventricle, the cerebellum, and the frontal lobe. In addition to the damage seen in these areas there have been reports of damage to cortex, although it was noted that this may be due to the direct toxic effects of alcohol as opposed to thiamine deficiency that has been attributed as the underlying cause of Wernicke-Korsakoff Syndrome.[5]

The amnesia that is associated with this syndrome is a result of the atrophy in the structures of the diencephalon (the thalamus, hypothalamus and mammillary bodies), and is similar to amnesia that is presented as a result of other cases of damage to the medial temporal lobe.[21] It has been argued that the memory impairments can occur as a result of damage along any part of the mammillo-thalamic tract, which explains how WKS can develop in patients with damage exclusively to either the thalamus or the mammillary bodies.[5]

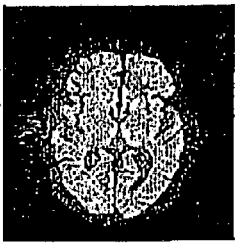
# Diagnosis

Diagnosis of Wernicke–Korsakoff syndrome is by clinical impression and can sometimes be confirmed by a formal neuropsychological assessment. Wernicke encephalopathy typically presents with ataxia and nystagmus, and Korsakoff's psychosis with anterograde and retrograde amnesia and confabulation upon relevant lines of questioning.

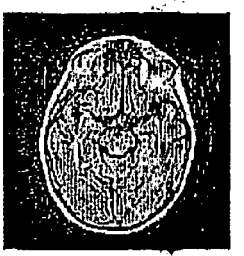
Frequently, secondary to thiamine deficiency and subsequent cytotoxic edema in Wernicke encephalopathy, patients will have marked degeneration of the mamillary bodies. Thiamine (vitamin $B_1$) is an essential coenzyme in carbohydrate metabolism and is also a regulator of osmotic gradient. Its deficiency may cause swelling of the intracellular space and local disruption of the blood-brain barrier. Brain tissue is very sensitive to changes in electrolytes and pressure and edema can be cytotoxic. In Wernicke this occurs specifically in the mammillary bodies, medial thalami, tectal plate, and periaqueductal areas. Sufferers may also exhibit a dislike for sunlight and so may wish to stay indoors with the lights off. The mechanism of this degeneration is unknown, but it supports the current neurological theory that the mammillary bodies play a role in various "memory circuits" within the brain. An example of a memory circuit is the Papez circuit.



Axial MRI FLAIR image showing hyperintense signal in the mesial dorsal thalami, a common finding in Wernicke encephalopathy. This patient was nearly in coma when IV thiamine was started, he responded moderately well but was left with some Korsakoff type deficits.



Axial MRI B=1000 DWI image showing hyperintense signal indicative of restricted diffusion in the mesial dorsal thalami.



Axial MRI FLAIR image showing hyperintense signal in the periaqueductal gray matter and tectum of the dorsal midbrain.

# Treatment

The onset of Wernicke encephalopathy is considered a medical emergency, and thus thiamine administration should be initiated immediately when the disease is suspected.[4] Prompt administration of thiamine to patients with Wernicke encephalopathy can prevent the disorder from developing into Wernicke–Korsakoff syndrome, or reduce its severity. Treatment can also reduce the progression of the deficits caused by WKS, but will not completely reverse existing deficits. WKS will continue to be present, at least partially, in 80% of patients.[22] Patients suffering from WE should be given a minimum dose of 500 mg of thiamine hydrochloride, delivered by infusion over a 30-minute period for two to three days. If no response is seen then treatment should be discontinued but for those patients that do respond, treatment should be continued with a 250 mg dose delivered intravenously or intramuscularly for three to five days unless the patient stops improving. Such prompt administration of thiamine may be a life-saving measure.[4] Banana bags, a bag of intravenous fluids containing vitamins and minerals, is one means of treatment.[23][24]

# Prevention

As described, alcoholic Korsakoff syndrome usually follows or accompanies Wernicke encephalopathy. If treated quickly, it may be possible to prevent the development of AKS with thiamine treatments. This treatment is not guaranteed to be effective and the thiamine needs to be administered adequately in both dose

and duration. A study on Wernicke-Korsakoff syndrome showed that with consistent thiamine treatment there were noticeable improvements in mental status after only 2–3 weeks of therapy.[4] Thus, there is hope that with treatment Wernicke encephalopathy will not necessarily progress to WKS.

In order to reduce the risk of developing WKS it is important to limit the intake of alcohol or drink in order to ensure that proper nutrition needs are met. A healthy diet is imperative for proper nutrition which, in combination with thiamine supplements, may reduce the chance of developing WKS. This prevention method may specifically help heavy drinkers who refuse to or are unable to quit.[4]

# Epidemiology

Internationally, the prevalence rates of WKS are relatively standard, being anywhere between zero and two percent. Despite this, specific sub-populations seem to have higher prevalence rates including people who are homeless, older individuals (especially those living alone or in isolation), and psychiatric inpatients.[25] Additionally, studies show that prevalence is not connected to alcohol consumption per capita. For example, in France, a country that is well known for its consumption and production of wine, prevalence was only 0.4% in 1994, while Australia had a prevalence of 2.8%.[28]

# History

## Wernicke encephalopathy

Carl Wernicke discovered Wernicke encephalopathy in 1881. His first diagnosis noted symptoms including paralyzed eye movements, ataxia, and mental confusion. Also noticed were hemorrhages in the gray matter around the third and fourth ventricles and the cerebral aqueduct. Brain atrophy was only found upon post-mortem autopsy. Wernicke believed these hemorrhages were due to inflammation and thus the disease was named polioencephalitis haemorrhagica superior. Later, it was found that Wernicke encephalopathy and alcoholic Korsakoff syndrome are products of the same cause.[25]

## Alcoholic Korsakoff syndrome

Sergei Korsakoff was a Russian physician after whom the disease "Korsakoff's syndrome" was named. In the late 1800s Korsakoff was studying long-term alcoholic patients and began to notice a decline in their memory function.[26] At the 13th International Medical Congress in Moscow in 1897, Korsakoff presented a report called: *"On a special form of mental illness combined with degenerative polyneuritis"*. After the presentation of this report the term "Korsakoff's syndrome" was coined.[5]

Although WE and AKS were discovered separately, these two syndromes are usually referred to under one name, Wernicke–Korsakoff syndrome, due to the fact that they are part of the same cause and because the onset of AKS usually follows WE if left untreated.

# Society and culture

The British neurologist Oliver Sacks describes case histories of some of his patients with the syndrome in the book *The Man Who Mistook His Wife for a Hat* (1985).

## See also

- Alcoholic dementia
- Dementia
- Malabsorption

## References


1. *MedlinePlus Encyclopedia* Wernicke-Korsakoff syndrome (https://medlineplus.gov/ency/article/000771.htm)
2. Thomson, Allan D.; Marshall, E. Jane (2006). "The natural history and pathophysiology of Wernicke's Encephalopathy and Korsakoff's Psychosis". *Alcohol and Alcoholism*. 41 (2): 151–8. doi:10.1093/alcalc/agh249 (https://doi.org/10.1093/alcalc/agh249). PMID 16384871 (https://www.ncbi.nlm.nih.gov/pubmed/16384871).
3. Vetreno, Ryan Peter (2011). *Thiamine deficiency-induced neurodegeneration and neurogenesis* (PhD Thesis). Binghampton University. ISBN 978-1-124-75595-7. OCLC 781626781 (https://www.worldcat.org/oclc/781626781).
4. Sechi, GianPietro; Serra, Alessandro (2007). "Wernicke's encephalopathy: new clinical settings and recent advances in diagnosis and management". *The Lancet Neurology*. 6 (5): 442–55. doi:10.1016/S1474-4422(07)70104-7 (https://doi.org/10.1016/S1474-4422%2807%2970104-7). PMID 17434099 (https://www.ncbi.nlm.nih.gov/pubmed/17434099).
5. Kyoko Konishi. (2009) The Cognitive Profile of Elderly Korsakoff's Syndrome Patients.
6. Ingram, V.; Kelly, M.; Grammer, G. "Wernicke-Korsakoff Syndrome Following Uvulopalatopharyngoplasty for Sleep Apnea". in "Abstracts Presented at the Thirty-First Annual International Neuropsychological Society Conference, February 5–8, 2003 Honolulu, Hawaii". *Journal of the International Neuropsychological Society*. 9 (2): 135–330. 2003. doi:10.1017/S1355617703920017 (https://doi.org/10.1017/S1355617703920017).
7. Thomson, Allan D.; Cook, Christopher C. H.; Guerrini, Irene; Sheedy, Donna; Harper, Clive; Marshall, E. Jane (2008). "Review: Wernicke encephalopathy revisited: Translation of the case history section of the original manuscript by Carl Wernicke 'Lehrbuch der Gehirnkrankheiten fur Aerzte and Studirende' (1881) with a commentary". *Alcohol and Alcoholism*. 43 (2): 174–9. doi:10.1093/alcalc/agm144 (https://doi.org/10.1093/alcalc/agm144). PMID 18056751 (https://www.ncbi.nlm.nih.gov/pubmed/18056751).
8. Brand, Matthias; Fujiwara, Esther; Kalbe, Elke; Steingass, Hans-Peter; Kessler, Josef; Markowitsch, Hans J. (2003). "Cognitive Estimation and Affective Judgments in Alcoholic Korsakoff Patients". *Journal of Clinical and Experimental Neuropsychology*. 25 (3): 324–34. doi:10.1076/jcen.25.3.324.13802 (https://doi.org/10.1076/jcen.25.3.324.13802). PMID 12916646 (https://www.ncbi.nlm.nih.gov/pubmed/12916646).
9. Kopelman, M. D.; Thomson, A. D.; Guerrini, I.; Marshall, E. J. (2009). "The Korsakoff Syndrome: Clinical Aspects, Psychology and Treatment". *Alcohol and Alcoholism*. 44 (2): 148–54. doi:10.1093/alcalc/agn118 (https://doi.org/10.1093/alcalc/agn118). PMID 19151162 (https://www.ncbi.nlm.nih.gov/pubmed/19151162).

10. Oscar-Berman, Marlene; Pulaski, Joan L. (1997). "Associative learning and recognition memory in alcoholic Korsakoff patients". *Neuropsychology*. 11 (2): 282–9. doi:10.1037/0894-4105.11.2.282 (https://doi.org/10.1037/0894-4105.11.2.282). PMID 9110334 (https://www.ncbi.nlm.nih.gov/pubmed/9110334).
11. Kessels, Roy P. C.; Kortrijk, Hans E.; Wester, Arie J.; Nys, Gudrun M. S. (2008). "Confabulation behavior and false memories in Korsakoff's syndrome: Role of source memory and executive functioning". *Psychiatry and Clinical Neurosciences*. 62 (2): 220–5. doi:10.1111/j.1440-1819.2008.01758.x (https://doi.org/10.1111/j.1440-1819.2008.01758.x). PMID 18412846 (https://www.ncbi.nlm.nih.gov/pubmed/18412846).
12. Zimitat, Craig; Nixon, Peter F. (1999). "Glucose loading precipitates acute encephalopathy in thiamin-deficient rats". *Metabolic Brain Disease*. 14 (1): 1–20. doi:10.1023/A:1020653312697 (https://doi.org/10.1023/A%3A1020653312697). PMID 10348310 (https://www.ncbi.nlm.nih.gov/pubmed/10348310).
13. Navarro, Darren; Zwingmann, Claudia; Chatauret, Nicolas; Butterworth, Roger F. (2008). "Glucose loading precipitates focal lactic acidosis in the vulnerable medial thalamus of thiamine-deficient rats". *Metabolic Brain Disease*. 23 (1): 115–22. doi:10.1007/s11011-007-9076-z (https://doi.org/10.1007/s11011-007-9076-z). PMID 18034292 (https://www.ncbi.nlm.nih.gov/pubmed/18034292).
14. Watson, A. J. S.; Walker, J. F.; Tomkin, G. H.; Finn, M. M. R.; Keogh, J. A. B. (1981). "Acute Wernickes Encephalopathy precipitated by glucose loading". *Irish Journal of Medical Science*. 150 (10): 301–3. doi:10.1007/BF02938260 (https://doi.org/10.1007/BF02938260). PMID 7319764 (https://www.ncbi.nlm.nih.gov/pubmed/7319764).
15. Mann, Karl; Agartz, Ingrid; Harper, Clive; Shoaf, Susan; Rawlings, Robert R.; Momenan, Reza; Hommer, Daniel W.; Pfefferbaum, Adolf; Sullivan, Edith V.; Anton, Raymond F.; Drobes, David J.; George, Mark S.; Bares, Roland; Machulla, Hans-Juergen; Mundle, Goetz; Reimold, Matthias; Heinz, Andreas (2001). "Neuroimaging in Alcoholism: Ethanol and Brain Damage". *Alcoholism: Clinical and Experimental Research*. 25 (5 Suppl ISBRA): 104S–109S. doi:10.1111/j.1530-0277.2001.tb02383.x (https://doi.org/10.1111/j.1530-0277.2001.tb02383.x). PMID 11391058 (https://www.ncbi.nlm.nih.gov/pubmed/11391058).
16. Butterworth, RF (1993). "Pathophysiology of cerebellar dysfunction in the Wernicke-Korsakoff syndrome". *The Canadian Journal of Neurological Sciences*. 20 Suppl 3: S123–6. PMID 8334588 (https://www.ncbi.nlm.nih.gov/pubmed/8334588). INIST:4778798 (http://cat.inist.fr/?aModele=afficheN&cpsidt=4778798).
17. Nixon, Peter F.; Kaczmarek, M. Jan; Tate, Jill; Kerr, Ray A.; Price, John (1984). "An erythrocyte transketolase isoenzyme pattern associated with the Wernicke-Korsakoff syndrome". *European Journal of Clinical Investigation*. 14 (4): 278–81. doi:10.1111/j.1365-2362.1984.tb01181.x (https://doi.org/10.1111/j.1365-2362.1984.tb01181.x). PMID 6434322 (https://www.ncbi.nlm.nih.gov/pubmed/6434322).
18. Shimomura, Tatsuo; Mori, Etsuro; Hirono, Nobutsugu; Imamura, Toru; Yamashita, Hikari (1998). "Development of Wernicke-Korsakoff syndrome after long intervals following gastrectomy" (http://archneur.jamanetwork.com/article.aspx?volume=55&page=1242). *Archives of Neurology*. 55 (9): 1242–5. doi:10.1001/archneur.55.9.1242 (https://doi.org/10.1001/archneur.55.9.1242). PMID 9740119 (https://www.ncbi.nlm.nih.gov/pubmed/9740119).
19. Todd, Kathryn G.; Hazell, Alan S.; Butterworth, Roger F. (1999). "Alcohol-thiamine interactions: an update on the pathogenesis of Wernicke encephalopathy". *Addiction Biology*. 4 (3): 261–72. doi:10.1080/13556219971470 (https://doi.org/10.1080/13556219971470). PMID 20575793 (https://www.ncbi.nlm.nih.gov/pubmed/20575793).

20. He, Xiaohua; Sullivan, Edith V; Stankovic, Roger K; Harper, Clive G; Pfefferbaum, Adolf (2007). "Interaction of Thiamine Deficiency and Voluntary Alcohol Consumption Disrupts Rat Corpus Callosum Ultrastructure". *Neuropsychopharmacology*. 32 (10): 2207–16. doi:10.1038/sj.npp.1301332 (https://doi.org/10.1038/sj.npp.1301332). PMID 17299515 (https://www.ncbi.nlm.nih.gov/pubmed/17299515).
21. Caulo, M. (2005). "Functional MRI study of diencephalic amnesia in Wernicke-Korsakoff syndrome". *Brain*. 128 (7): 1584–94. doi:10.1093/brain/awh496 (https://doi.org/10.1093/brain/awh496). PMID 15817513 (https://www.ncbi.nlm.nih.gov/pubmed/15817513).
22. Victor, M; Adams, RD; Collins, GH (1971). "The Wernicke-Korsakoff syndrome. A clinical and pathological study of 245 patients, 82 with post-mortem examinations". *Contemporary Neurology Series*. 7: 1–206. PMID 5162155 (https://www.ncbi.nlm.nih.gov/pubmed/5162155).
23. Jeffrey E Kelsey; D Jeffrey Newport & Charles B Nemeroff (2006). "Alcohol Use Disorders". *Principles of Psychopharmacology for Mental Health Professionals*. Wiley-Interscience. pp. 196–197. ISBN 978-0-471-79462-2.
24. Merle A. Carter & Edward Bernstein (2005). "Acute and Chronic Alcohol Intoxication". In Elizabeth Mitchell & Ron Medzon. *Introduction to Emergency Medicine*, Lippincott Williams & Wilkins. p. 272. ISBN 978-0-7817-3200-0.
25. *Wernicke-Korsakoff Syndrome (https://emedicine.medscape.com/article/288379-overview)* at eMedicine
26. Harper, Clive; Fornes, Paul; Duyckaerts, Charles; Lecomte, Dominique; Hauw, Jean-Jacques (1995). "An international perspective on the prevalence of the Wernicke-Korsakoff syndrome". *Metabolic Brain Disease*. 10 (1): 17–24. doi:10.1007/BF01991779 (https://doi.org/10.1007/BF01991779). PMID 7596325 (https://www.ncbi.nlm.nih.gov/pubmed/7596325).


# External links

| | |
|---|---|
| **Classification** | **ICD-10**: E51.2 (http://apps.who.int/classifications/icd10/browse/2016/en#/E51.2), F10.6 (http://apps.who.int/classifications/icd10/browse/2016/en#/F10.6) · **ICD-9-CM**: 294.0 (http://www.icd9data.com/getICD9Code.ashx?icd9=294.0) · **OMIM**: 277730 (https://omim.org/entry/277730) · **MeSH**: D020915 (https://www.nlm.nih.gov/cgi/mesh/2015/MB_cgi?field=uid&term=D020915) · **DiseasesDB**: 14107 (http://www.diseasesdatabase.com/ddb14107.htm) |
| **External resources** | **MedlinePlus**: 000771 (https://www.nlm.nih.gov/medlineplus/ency/article/000771.htm) · **eMedicine**: med/2405 (http://www.emedicine.com/med/topic2405.htm) · **Patient UK**: Wernicke–Korsakoff syndrome (https://patient.info/doctor/Wernicke-Korsakoff-Syndrome) |

EVIDENCE #2

PRESS DISCOVERY OF MINALDI'S

SEVERE WKS

https://www.americanpress.com/news/local/judge-minaldi-retires-after-leave-for-alcoholism-care/article_0552f56a-77c4-11e7-9da4-dbae9652afd1.html

TOP STORY

# Judge Minaldi retires after leave for alcoholism care

The Associated Press Aug 2, 2017

FILE: A still photo from an American Press video of Judge Patricia Minaldi speaking to two members of the media Friday, April 14, 2017 at the Lake Charles Civic Center seawall. (Rick Hickman / American Press)

BATON ROUGE -- A federal judge in Louisiana has retired several months after taking medical leave for treatment of severe alcoholism, a condition that came to light only after a series of mysterious interruptions in her courtroom.

U.S. District Judge Patricia Minaldi's disability retirement took effect on Monday, said Tony Moore, clerk of court for the Western District of Louisiana.

Court records unsealed in April revealed Minaldi, 58, was required to get treatment for alcoholism so severe that a colleague asked a court to rule she cannot take care of herself.

An Associated Press investigation showed Minaldi's pattern of unusual behavior on the bench preceding her removal from a string of cases last year.

In February 2016, Minaldi was pulled off a man's fraud case following a series of mistakes in routine trial procedures. Court documents released at the AP's request showed that even basic requirements — like telling jurors the burden of proof lies with prosecutors, not the defense — weren't followed.

The next month, the district's chief judge removed Minaldi from criminal cases against a sheriff and several subordinates. No explanation was given, though the order came four days after Minaldi abruptly adjourned a hearing to accept guilty pleas by two sheriff's deputies. The two deputies wound up pleading guilty later that same day before another judge.

In December, a criminal trial in Minaldi's courtroom was cut short without explanation before a jury could be picked to hear a child pornography case. A transcript unsealed last month at the AP's request shows the proceedings ended with a defense attorney asking to speak with Minaldi privately in her chambers.

Court officials haven't explained those secretive interruptions in her courtroom. Scores of other cases originally assigned to Minaldi already have been transferred to other judges, also without a detailed explanation.

In 2014, Minaldi pleaded guilty to a drunken driving charge and was sentenced to one year of probation. Dashcam video obtained by local news organizations showed her arguing with an officer and refusing to get out of her car before police arrested her outside her Lake Charles home.

"This seems to be one of the rare instances where intervention did not come quickly enough," said University of Pittsburgh School of Law professor Arthur Hellman, an expert in judicial ethics.

Minaldi had been on medical leave since late December. The mandate for Minaldi to complete at least 90 days of substance abuse treatment came from the chief judge of the 5th U.S. Circuit Court of Appeals. It's unclear when Chief Judge Carl Stewart imposed that mandate, but Minaldi arrived at a rehab facility on Jan. 4.

The court records unsealed in April were part of a lawsuit filed by a longtime friend and colleague, U.S. Magistrate Kathleen Kay. The lawsuit challenged Minaldi's physical and mental capacity to manage her personal and financial affairs.

Minaldi gave power of attorney to Kay in 2007 and then revoked it two days after Kay sued in March.

In the lawsuit, Kay said Minaldi was diagnosed with severe Wernicke-Korsakoff syndrome, a degenerative brain disorder linked to alcohol abuse. The suit said Minaldi's condition in March was so severe that she was "unable to take care of her daily activities" and "unable to safely take care of her personal needs, financial matters, or her property matters."

The records showed Minaldi moved into an assisted living facility specializing in "memory care" within three months of presiding over the trial that was cut short without explanation in December.

Minaldi began serving as a judge in the district's Lake Charles division after her nomination in 2003 by then-President George W. Bush.

Her retirement leaves the Lake Charles division without a district judge. Moore said the Western District of Louisiana, currently served by three active district judges, has three other judicial vacancies.

Federal judges who take disability retirement after at least 10 years of continuous service are entitled to continue receiving a salary for the rest of their lives.

MORE INFORMATION

Minaldi convictions challenged

WITNESS AFFDAVIT BY BRENDA LEE (KRETSER)

I can remember sitting in the court room of Judge Patricia Minaldi with my 13-year-old daughter, waiting to hear the outcome of my husband's trial, his sentencing infact. Our daughter earlier that week had written the judge a letter telling her in her own words what kind of person her daddy was, he was kind and helpful to others. She went on about how he loved his children and said that everyone makes mistakes, even her daddy. She asked the judge to please not take her daddy away from her and her baby sister. Please give him a chance she asked. When the judge came out and the jury asked her a question about how much time did a crime of this nature carry because there was a question about entrapment, she told them it was equivalent to a misdemeanor, she said it was no big deal. The judge soon started speaking rude and disrespectful (even though she saw my child sitting in the courtroom) to Karl, putting in her own personal thoughts and opinions about him such as she thought he was a disgrace and a "special kind of monster" putting his own daughter up to writing a letter to her about how her daddy was a good man. She stated several times in the court room that she thinks he had committed other crimes of this nature and just hadn't been caught yet. She told she thinks he's was a low life. She told my daughter that she was doing her, her sister and mother a favor by putting her daddy away forever. My daughter became emotional and sick to her stomach and started crying in the court room, the judge yelled at her and told her if she was going to cry to get out of her court room and don't come back in. I removed her from the court room and I returned to the room. The judge stated to Karl that she was going to use him as an example to other cops who think they are above the law. She said that cops are not above the law and will be dealt with accordingly. She told Karl he was disgusting and a nuisance to society and she was going to take him off the streets for good.

Brenda Lee (Kretser)

Brenda Lee (Kretser)

# WITNESS AFFDAVIT BY ARIKA SHAFFETT

To Whom It May Concern:

I, Arika Shaffett, wanted to provide my witness to the erratic behavior exhibited by Judge Patricia Minaldi during my father's, Karl Kretser, trial and June 2007 sentencing.

At the trial, the Jury was questioning the amount of time my father would be sentenced to, as they expressed concerned because this was an entrapment issue. The judge told the jury "his crime is equivalent to a misdemeanor, it's no big deal". However, during sentencing she processed an upward departure and she announced a verdict of 30 years.

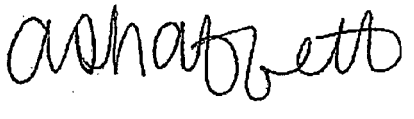
The behaviors exhibited by Judge Minaldi during sentencing were unbelievable, however I was only 14 at the time so I did not understand fully what was happening. The Judge told me directly that my father was a monster and that she was doing me a favor by taking him away from me. She scolded my father's character because I had written her a letter by my own choice asking her to please spare my father a harsh punishment, as we needed him to be a part of our family. She also stated that she was giving him an exuberant amount of time because she believed that he had committed other crimes, but had not been caught.

Seeing my father in this situation and knowing his character, I was greatly upset and started to cry. The Judge yelled at me and told me that I needed to leave the court room because I was crying.

This situation caused me to have severe PTSD. After some time, I realized that this behavior what not normal. I decided to find transcripts from the sentencing; however none of the above incidents are included.

Please do not hesitate to reach out to me if there are any other questions.

Regards,



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CURRENT MEDICAL DIAGNOSIS

AND TREATMENT 2016 Edition

WKS SYNDROME

asymptomatic, but after a variable latent period (which may be as long as several years) a myelopathy develops in some instances. The MRI, electrophysiologic, and cerebrospinal fluid findings are similar to those of multiple sclerosis, but HTLV-I antibodies are present in serum and spinal fluid. There is no specific treatment, but intravenous or oral corticosteroids may help in the initial inflammatory phase of the disease. Prophylactic measures are important. Needles or syringes should not be shared; infected patients should not breastfeed their infants or donate blood, semen, or other tissue. Infected patients should use condoms to prevent sexual transmission.

Yamano Y et al. Clinical pathophysiology of human T-lymphotropic virus-type 1-associated myelopathy/tropical spastic paraparesis. Front Microbiol. 2012 Nov 9;3:389. [PMID: 23162542]

## SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD

Subacute combined degeneration of the spinal cord is due to vitamin $B_{12}$ deficiency, such as occurs in pernicious anemia. It is characterized by myelopathy with spasticity, weakness, proprioceptive loss, and numbness, sometimes in association with polyneuropathy, mental changes, or optic neuropathy. Megaloblastic anemia may also occur, but this does not parallel the neurologic disorder, and the former may be obscured if folic acid supplements have been taken. Treatment is with vitamin $B_{12}$. For pernicious anemia, a convenient therapeutic regimen is 100 mg cyanocobalamin intramuscularly daily for 1 week, then weekly for 1 month, and then monthly for the remainder of the patient's life. Oral cyanocobalamin replacement is not advised for pernicious anemia when neurologic symptoms are present.

## WERNICKE ENCEPHALOPATHY & KORSAKOFF SYNDROME

Wernicke encephalopathy is characterized by confusion, ataxia, and nystagmus leading to ophthalmoplegia (lateral rectus muscle weakness, conjugate gaze palsies); peripheral neuropathy may also be present. It is due to thiamine deficiency and in the United States occurs most commonly in patients with alcoholism. It may also occur in patients with AIDS or hyperemesis gravidarum, and after surgery for obesity. In suspected cases, thiamine (100 mg) is given intravenously immediately and then intramuscularly on a daily basis until a satisfactory diet can be ensured. Intravenous glucose given before thiamine may precipitate the syndrome or worsen the symptoms. The diagnosis is confirmed by the response in 1 or 2 days to treatment, which must not be delayed while awaiting laboratory confirmation of thiamine deficiency from a blood sample obtained prior to thiamine administration. Korsakoff syndrome occurs in more severe cases; it includes anterograde and retrograde amnesia and sometimes confabulation, and may not be recognized until after the initial delirium has lifted.

Isenberg-Grzeda E et al. Wernicke-Korsakoff-syndrome: under-recognized and under-treated. Psychosomatics. 2012 Nov-Dec; 53(6):507–16. [PMID: 23157990]

# STUPOR & COMA

## ESSENTIALS OF DIAGNOSIS

- Level of consciousness is depressed.
- Stuporous patients respond only to repeated vigorous stimuli.
- Comatose patients are unarousable and unresponsive.

## General Considerations

The patient who is stuporous is unresponsive except when subjected to repeated vigorous stimuli, while the comatose patient is unarousable and unable to respond to external events or inner needs, although reflex movements and posturing may be present.

Coma is a major complication of serious central nervous system disorders. It can result from seizures, hypothermia, metabolic disturbances, or structural lesions causing bilateral cerebral hemispheric dysfunction or a disturbance of the brainstem reticular activating system. A mass lesion involving one cerebral hemisphere may cause coma by compression of the brainstem. All comatose patients should be hospitalized and referred to a neurologist or neurosurgeon.

## Assessment & Emergency Measures

The diagnostic workup of the comatose patient must proceed concomitantly with management. Supportive therapy for respiration or blood pressure is initiated; in hypothermia, all vital signs may be absent and all such patients should be rewarmed before the prognosis is assessed.

The patient can be positioned on one side with the neck partly extended, dentures removed, and secretions cleared by suction; if necessary, the patency of the airways is maintained with an oropharyngeal airway. Blood is drawn for serum glucose, electrolyte, and calcium levels; arterial blood gases; liver and kidney function tests; and toxicologic studies as indicated. Dextrose 50% (25 g), naloxone (0.4–1.2 mg), and thiamine (100 mg) are given intravenously without delay.

Further details are then obtained from attendants of the patient's medical history, the circumstances surrounding the onset of coma, and the time course of subsequent events. Abrupt onset of coma suggests subarachnoid hemorrhage, brainstem stroke, or intracerebral hemorrhage, whereas a slower onset and progression occur with other structural or mass lesions. Urgent noncontrast CT scanning of the head is appropriate if it can be obtained directly from the emergency department, in order to identify intracranial hemorrhage, brain herniation, or other structural lesion that may require immediate neurosurgical intervention. A metabolic cause is likely with a preceding intoxicated state or agitated delirium. On examination, attention is paid to the behavioral response to painful stimuli, the

interest. Some states require physicians to report injuries caused by abuse or suspected abuse to police authorities.

Buckley P et al. Psychopharmacology of aggression in schizophrenia. Schizophr Bull. 2011 Sep;37(5):930–6. [PMID: 21860038]

Johnson DM et al. Cognitive behavioral treatment of PTSD in residents in battered women's shelters: results of a randomized clinical trial. J Consult Clin Psychol. 2011 Aug;79(4):542–51. [PMID: 21787052]

Rees S et al. Lifetime prevalence of gender-based violence in women and the relationship with mental disorders and psychosocial function. JAMA. 2011 Aug 3;305(5):513–21. [PMID: 21813429]

## SUBSTANCE USE DISORDERS

The term "dependency" was previously used to describe a severe form of substance abuse and drug addiction characterized by the triad of: (1) a psychological dependence or craving and the behavior involved in procurement of the drug; (2) physiologic dependence, with withdrawal symptoms on discontinuance of the drug; and (3) tolerance, ie, the need to increase the dose to obtain the desired effects. The terms "dependency" and "abuse" were dropped in *DSM-5* in favor of the single term "substance use disorder," ranging from mild to severe. Many patients could have a severe and life-threatening abuse problem without ever being dependent on a drug.

There is accumulating evidence that an impairment syndrome exists in many former (and current) drug users. It is believed that drug use produces damaged neurotransmitter receptor sites and that the consequent imbalance produces symptoms that may mimic other psychiatric illnesses. "Kindling"—repeated stimulation of the brain—renders the individual more susceptible to focal brain activity with minimal stimulation. Stimulants and depressants can produce kindling, leading to relatively spontaneous effects no longer dependent on the original stimulus. These effects may be manifested as mood swings, panic, psychosis, and occasionally overt seizure activity. The imbalance also results in frequent job changes, partner problems, and generally erratic behavior. Patients with PTSD frequently have treated themselves with a variety of drugs. Chronic abusers of a wide variety of drugs exhibit cerebral atrophy on CT scans, a finding that may relate to the above symptoms. Early recognition is important, mainly to establish realistic treatment programs that are chiefly symptom-directed.

The clinician faces three problems with substance use disorders: (1) the prescribing of substances such as sedatives, stimulants, or opioids that might produce dependency; (2) the treatment of individuals who have already abused drugs, most commonly alcohol; and (3) the detection of illicit drug use in patients presenting with psychiatric symptoms. The usefulness of urinalysis for detection of drugs varies markedly with different drugs and under different circumstances (pharmacokinetics is a major factor). Water-soluble drugs (eg, alcohol, stimulants, opioids) are eliminated in a day or so. Lipophilic substances (eg, barbiturates, tetrahydrocannabinol) appear in the urine over longer periods of time: several days in most cases, 1–2 months in chronic marijuana users. Sedative drug determinations are quite variable, amount of drug and duration of use being important determinants. False-positives can be a problem related to ingestion of some legitimate medications (eg, phenytoin for barbiturates, phenylpropanolamine for amphetamines, chlorpromazine for opioids) and some foods (eg, poppy seeds for opioids, coca leaf tea for cocaine). Manipulations can alter the legitimacy of the testing. Dilution, either in vivo or in vitro, can be detected by checking urine-specific gravity. Addition of ammonia, vinegar, or salt may invalidate the test, but odor and pH determinations are simple. Hair analysis can determine drug use over longer periods, particularly sequential drug-taking patterns. The sensitivity and reliability of such tests are considered good, and the method may be complementary to urinalysis.

Marlatt GA. Update on harm-reduction policy and intervention research. Annu Rev Clin Psychol. 2010 Apr 27;6:591–606. [PMID: 20192791]

## ALCOHOL USE DISORDER (Alcoholism)

### ESSENTIALS OF DIAGNOSIS

- Physiologic dependence as manifested by evidence of withdrawal when intake is interrupted.
- Tolerance to the effects of alcohol.
- Evidence of alcohol-associated illnesses, such as alcoholic liver disease, cerebellar degeneration.
- Continued drinking despite strong medical and social contraindications and life disruptions.
- Impairment in social and occupational functioning.
- Depression.
- Blackouts.

### General Considerations

Alcohol use disorder is a syndrome consisting of two phases: at-risk drinking and moderate to severe alcohol misuse. At-risk drinking is the repetitive use of alcohol, often to alleviate anxiety or solve other emotional problems. A moderate to severe alcohol use disorder is similar to that which occurs following the repeated use of other sedative-hypnotics and is characterized by recurrent use of alcohol despite disruption in social roles (family and work), alcohol-related legal problems, and taking safety risks by oneself and with others. The National Institute on Alcohol Abuse and Alcoholism formally defines at-risk drinking as **more than 4 drinks per day or 14 drinks per week for men or more than 3 drinks per day or 7 drinks per week for women.** A drink is defined by the CDC as 12 oz of beer, 8 oz of malt liquor, 5 oz of wine, or 1.3 oz or a

"shot" of 80-proof distilled spirits of liquor. Individuals with at-risk drinking are at an increased risk for developing or are developing an alcohol use disorder. Alcohol and other drug abuse patients have a much higher prevalence of lifetime psychiatric disorders. While male-to-female ratios in alcoholic treatment agencies remain at 4:1, there is evidence that the rates are converging. Women delay seeking help, and when they do they tend to seek it in medical or mental health settings. Adoption and twin studies indicate some genetic influence. Ethnic distinctions are important—eg, 40% of Japanese have aldehyde dehydrogenase deficiency and are more susceptible to the effects of alcohol. Depression is often present and should be evaluated carefully. The majority of suicides and intrafamily homicides involve alcohol. Alcohol is a major factor in rapes and other assaults.

There are several screening instruments that may help identify an alcohol use disorder. One of the most useful is the Alcohol Use Disorder Identification Test (AUDIT) (see Table 1–7).

## Clinical Findings

### A. Acute Intoxication

The signs of alcoholic intoxication are the same as those of overdosage with any other central nervous system depressant: drowsiness, errors of commission, psychomotor dysfunction, disinhibition, dysarthria, ataxia, and nystagmus. For a 70-kg person, an ounce of whiskey, a 4- to 6-oz glass of wine, or a 12-oz bottle of beer (roughly 15, 11, and 13 grams of alcohol, respectively) may raise the level of alcohol in the blood by 25 mg/dL. For a 50-kg person, the blood alcohol level would rise even higher (35 mg/dL) with the same consumption. Blood alcohol levels below 50 mg/dL rarely cause significant motor dysfunction (the legal limit for driving under the influence is commonly 80 mg/dL). Intoxication as manifested by ataxia, dysarthria, and nausea and vomiting indicates a blood level greater than 150 mg/dL, and lethal blood levels range from 350 to 900 mg/dL. In severe cases, overdosage is marked by respiratory depression, stupor, seizures, shock syndrome, coma, and death. Serious overdoses are frequently due to a combination of alcohol with other sedatives.

### B. Withdrawal

There is a wide spectrum of manifestations of alcoholic withdrawal, ranging from anxiety, decreased cognition, tremulousness through increasing irritability and ctivity to full-blown delirium tremens. Symptoms hdrawal, including tremor, elevated vital signs, gin within about 8 hours after the last drink ve passed by day 3. Generalized seizures first 24–38 hours and are more prevalent ave a history of withdrawal syndromes. s an acute organic psychosis that is usu- 24–72 hours after the last drink (but 10 days later). It is characterized by nor, sensory hyperacuity, visual hal- nakes, bugs, etc), autonomic hyper- ydration, electrolyte disturbances (hypokalemia, hypomagnesemia), seizures, and cardiovascular abnormalities. The acute withdrawal syndrome is often completely unexpected and occurs when the patient has been hospitalized for some unrelated problem and presents as a diagnostic problem. Suspect alcohol withdrawal in every unexplained delirium. The mortality rate from delirium tremens has steadily decreased with early diagnosis and improved treatment.

In addition to the immediate withdrawal symptoms, there is evidence of persistent longer-term ones, including sleep disturbances, anxiety, depression, excitability, fatigue, and emotional volatility. These symptoms may persist for 3–12 months, and in some cases they become chronic.

### C. Alcoholic (Organic) Hallucinosis

This syndrome occurs either during heavy drinking or on withdrawal and is characterized by a paranoid psychosis without the tremulousness, confusion, and clouded sensorium seen in withdrawal syndromes. The patient appears normal except for the auditory hallucinations, which are frequently persecutory and may cause the patient to behave aggressively and in a paranoid fashion.

### D. Chronic Alcoholic Brain Syndromes

These encephalopathies are characterized by increasing erratic behavior, memory and recall problems, and emotional instability—the usual signs of organic brain injury due to any cause. Wernicke-Korsakoff syndrome due to thiamine deficiency may develop with a series of episodes. Wernicke encephalopathy consists of the triad of confusion, ataxia, and ophthalmoplegia (typically sixth nerve). Early recognition and treatment with thiamine can minimize damage. One of the possible sequelae is Korsakoff psychosis, characterized by both anterograde and retrograde amnesia, with confabulation early in the course. Early recognition and treatment of the alcoholic with intravenous thiamine and B complex vitamins can minimize damage. Excessive alcohol consumption in men has been associated with faster cognitive decline compared with light to moderate alcohol consumption.

### E. Laboratory Findings

Ethanol may contribute to the presence of an otherwise unexplained osmolar gap. There may also be elevated liver function tests, increased serum uric acid and triglycerides, and decreased serum potassium and magnesium. The most definitive biologic marker for chronic alcoholism is carbohydrate deficient transferrin, which can detect heavy use (60 mg/day over 7–10 days) with high specificity. Other useful tests for diagnosing alcohol use disorder are gamma-glutamyl transpeptidase measurement (levels greater than 30 units/L are suggestive of heavy drinking) and mean corpuscular volume (more than 95 fL in men and more than 100 fL in women). If both are elevated, a serious drinking problem is likely. Use of other recreational drugs with alcohol skews and negates the significance of these tests. Concomitant elevations of high-density lipoprotein cholesterol elevations and gamma-glutamyl transpeptidase concentrations also can help identify heavy drinkers.