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Cerebral lesions and causes of death in male alcoholics

A forensic autopsy study

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Summary. Autopsies on 195 male alcoholics aged 30–64 years who died outside hospitals and nursing homes in Oslo from 1984 to 1988, were carried out at the Institute of Forensic Medicine, Rikshospitalet. In 127 cases brain tissue was examined neuropathologically, 86 (67.7%) showed abnormalities and 28 contained lesions of more than one type. Lesions associated with alcoholism were found in 61 cases (48%), 18 (14.2%) showed Wernicke's encephalopathy, 47 (37%) cerebellar atrophy, 2 central pontine myelinolysis and 1 hepatic encephalopathy. Subdural haematoma and/or cortical contusions were found in 30 cases (23.6%) and cerebrovascular lesions in 19 (15%). Of the 195 cases, 22 had a history of recurrent convulsive attacks of which 19 were examined neuropathologically and 13 had focal damage that could have caused epileptic fits. Although cerebral damage was more frequent among vagrants and other persons dependant on social support, 50% of the alcoholics living in their own homes were also affected. Alcohol-related disease was considered the cause of death in 15 of 127 cases examined neuropathologically and 9 of these died from acute Wernicke's encephalopathy all of whom were sober at death. Although the post mortem analyses included neuropathological examination of the brain, the cause of death remained unknown in 27 (21%) of the 127 cases.

Key words: Alcoholism – Alcoholic cerebellar atrophy – Wernicke's encephalopathy – Central pontine myelinolysis – Traumatic lesions – Cerebrovascular lesions

Zusammenfassung. Obduktionen an 195 männlichen Alkoholikern, welche im Lebensalter zwischen 30 und 64 Jahren in den Jahren 1984–1988 verstarben, wurden am Institut für Gerichtliche Medizin des Rikshospitalet in Oslo durchgeführt. Die Personen starben außerhalb von Krankenhäusern und von Pflegeheimen. In 127 Fällen wurde Hirngewebe neuropathologisch untersucht. 86 Fälle (67,7%) zeigten abnorme Befunde und 28 Fälle zeigten Läsionen von mehr als einem Typ. Alkoholassoziierte Läsionen wurden in 61 Fällen gefunden (48%); 18 (14,2%) zeigten die Wernicke'sche Encephalopathie, 47 (37%) eine cerebellare Atrophie, 2 eine zentrale pontine Myelinolyse und einer eine hepatogene Encephalopathie. Subdurale Hämatome und/oder Rindenprellungen wurden in 30 Fällen (23,6%) gefunden und cerebro-vasukläre Läsionen in 19 Fällen (15%). 22 der insgesamt 195 Fälle zeigten in ihrer Vorgeschichte wiederholte Anfälle. 19 hiervon wurden neuropathologisch untersucht und 13 hatten fokale Schäden, die die epiletpischen Anfälle verursacht haben konnten. Obwohl der Hirnschaden häufiger unter Obdachlosen und anderen Personen, welche von einer Sozialhilfe abhänging sind, war, waren 50% der Alkoholiker, welche in ihren eigenen Häusern lebten, ebenfalls befallen. In 15 der 127 neuropathologisch untersuchten Fälle wurde die alkoholinduzierte Erkrankung als Todesursache angesehen. 9 dieser Fälle verstarben an einer akuten Wernicke-Encephalopathie, alle waren nüchtern zum Zeitpunkt des Todes. Obwohl die postmortalen Untersuchungen eine neuropathologische Untersuchung des Hirns einbezog, blieb die Todesursache in 27 von 127 Fällen (= 21%) unbekannt.

Schlüsselwörter: Alkoholismus – Cerebellare Atrophie – Morbus Wernicke – Zentrale pontine Myelinolyse – Traumatische Läsionen – Zerebrovasculäre Läsionen

Introduction

Alcohol-related or alcohol-caused disorders form a substantial part of the work load of forensic pathologists. To our knowledge, this is the first work on cerebral lesions in middle-aged male alcoholics collected from forensic autopsies.

Materials and methods

The material consisted of male alcoholics aged 30–64 years who were residents in Oslo, died outside hospital and were autopsied at

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the Institute of Forensic Medicine, Rikshospitalet, during the 4-year-period 1984–1987. Cases with autolysis that prevented complete examination were not included. Those classified as alcoholics were 195 cases with a reliable history of alcohol abuse for several years, supported by findings at the scene of death and/or pathological liver changes (excessive fatty infiltration, hepatitis of alcoholic type, micronodular cirrhosis). Insufficient information was available on employment or whether the persons had been accredited disability pension or other social benefits. Therefore, the standard of residence was used as a measure of social status and the cases were classified into three groups: 1) Ordinary lodgers/house owners, 2) residents in municipal lodgings, and 3) vagrants. Both former vagrants and house owners/lodgers were present among the residents in municipal lodgings for alcoholics.

Neuropathological examination of the brain was carried out in 127 selected cases which included unknown causes of death after gross examination of all other organs, visible abnormalities of more or less uncertain origin on the cerebral surface and a clinical history of suspected organic cerebral disorder, most often seizures.

Brain tissue was fixed in buffered 8% formalin for 10–21 days and then cut in 0.5 cm frontal slices. Tissue specimens for microscopical evaluation were taken from frontal cortex (1), thalamus (1), cerebellar vermis (1), medulla oblongata (1), pons (2), and bilateral samples from the hippocampal formation and the mamillary body. Furthermore, a section of globus pallidus was taken in all cases with micronodular liver cirrhosis, as well as samples of all gross lesions of uncertain origin. Generally, a slice of mesencephalon was also available. All tissues were embedded in paraffin, and all sections were stained with hematoxylin and eosin. In cases suspected of central pontine myelinolysis the sections of pons were stained with Bodian silver impregnation and Luxol fast blue.

Cases classified as having alcoholic cerebellar atrophy showed changes restricted to the anterior and superior part of the vermis, characterized by nearly complete loss of Purkinje cells with glial response, depletion of granular cells and atrophy of the molecular layer over the entire folia.

The cerebrovascular lesions recorded were gross hemorrhages and infarcts, and microscopical lesions in sections of the cerebrum and brain stem.

Subdural hematomas and cerebral cortical contusions were the only traumatic lesions observed.

The blood alcohol level at death was measured in all 127 neuropathologically examined cases. When pure alcohol intoxication was recorded as the cause of death, the blood alcohol level was usually $\geq 3‰$.

If the cause of death remained uncertain after macroscopical examination of the organs, a general basic screening for drugs was performed. If the analysis did not reveal fatal concentrations in the blood more extensive studies including acidic drugs were done.

Because of the insufficient clinical data in the cases of lethal intoxications from alcohol and/or drugs, a further classification of these deaths into accidents and suicides was considered unreliable.

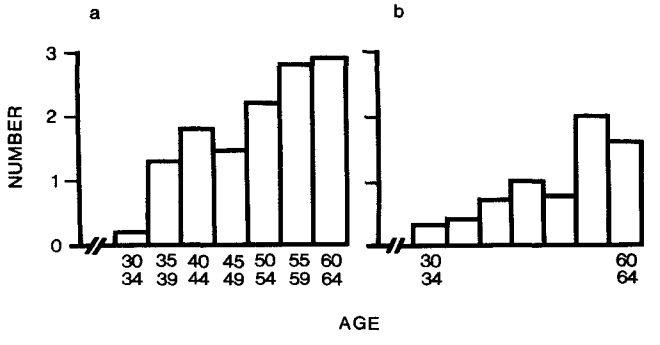

Fig. 1a, b. Age of male alcoholics examined **a** and not examined **b** neuropathologically

Results

The age distribution of the cases examined and not examined neuropathologically is shown in Fig. 1. The mean and median ages were 51.7 and 53 years, respectively. The corresponding ages among cases not examined were 52.5 and 55 years. Of the 127 examined cases, 75% were ordinary house owners/lodgers, 16% residents in municipal lodgings for alcoholics, and 9% vagrants. The corresponding numbers among cases not examined were 81, 13, and 6%, respectively.

Cerebral lesions related to alcoholism

Some of the lesions closely related to alcoholism, i.e. Wernicke's encephalopathy, alcoholic cerebellar atrophy, central pontine myelinolysis, and hepatic encephalopathy, were found in 61 (48%) of the 127 cases examined. These abnormalities were combined with traumatic and/or cerebrovascular lesions in 18 cases (Table 1).

Wernicke's encephalopathy was found in 18 cases (14.2%). Nine showed acute changes suggestive of an active ongoing thiamine deficiency, with or without astroglial response. All cases showed more or less widespread neuronal necrosis in the thalamus, and 5 had lesions in the periaqueductal gray and beneath the floor of the fourth ventricle.

The remaining 9 cases affected had residual lesions in the mamillary bodies and 2 also showed neuronal loss and astrocytosis in the dorsomedial nucleus of the thalamus. None of the chronic cases showed involvement beyond this area. The age of the cases affects by Wernicke's encephalopathy ranged from 38 to 63 years, and 12 were in the sixth decade (Fig. 2). None of them were vagrants – 2 lived in municipal lodgings, and the remaining were ordinary lodgers/house owners.

Of the 47 cases (37%) that showed *alcoholic cerebellar atrophy*, 20 had additional lesions (Table 1). Figure 3 shows the number of affected cases in age-groups of 5 years and no correlation was found between frequency and age. The frequency of cerebellar atrophy among

Table 1. Combinations of lesions and number affected

Combination	Number affected
Wernicke's encephalopathy, cerebellar atrophy	6
Wernicke's encephalopathy, traumatic lesion	1
Wernicke's encephalopathy, vascular lesion	2
Wernicke's encephalopathy, traumatic and vascular lesion	1
Cerebellar atrophy, traumatic lesion	9
Cerebellar atrophy, vascular lesion	2
Cerebellar atrophy, traumatic and vascular lesion	2
Cerebellar atrophy, central pontine myelinolysis	1
Central pontine myelinolysis, vascular lesion	1
Traumatic and vascular lesion	3
Total number	28

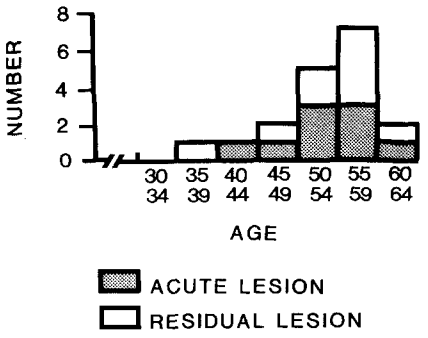

Fig. 2. Age of alcoholics with Wernicke's encephalopathy

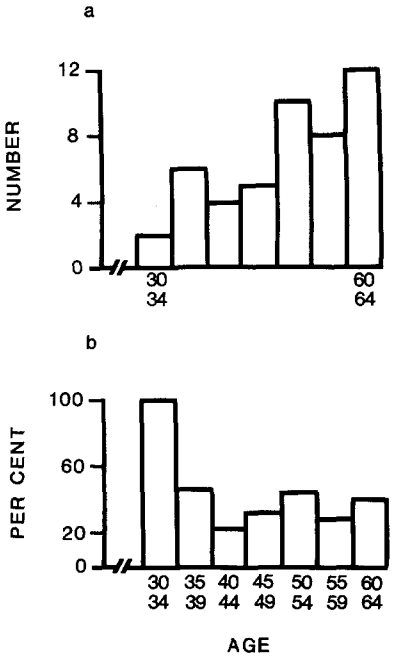

Fig. 3a, b. Alcoholic cerebellar atrophy and age. **a** Number of cases affected. **b** Proportion (%) of alcoholics examined with cerebellar atrophy

ordinary lodgers/house owners, residents of municipal lodgings and vagrants was 29, 52, and 73%, respectively.

Only 2 cases showed *central pontine myelinolysis*. The youngest (30 years) was a vagrant with cerebellar atrophy. The oldest (49 years) lived in a municipal lodging.

Hepatic encephalopathy was found in a 55-year-old lodger who died at home.

Head injuries

Of the 30 cases (24%) with subdural hematoma and/or cerebral cortical contusions, 9 showed acute damage. The remaining 21 cases had old lesions (19 contusions, 1 subdural hematoma and 1 both contusions and subdural hematoma). Sixteen of the cases with traumatic injuries showed additional abnormalities (Table 1).

Cerebrovascular lesions

Macroscopical infarcts were found in 11 cases and 6 were acute lesions. In five cases the lesions were older than one month. Four cases showed intra-cerebral hemorrhage. One was secondary to a ruptured saccular aneurysm, another was of hypertensive origin, for the other 2 the underlying cause remained unknown. Four cases showed a unilateral focal scar with loss of pyramidal neurons and gliosis in the hippocampus. Table 1 shows the additional abnormalities found in 11 of the 19 cases with cerebrovascular lesions.

Seizures

According to the generally scanty clinical information, 19 (15%) of the 127 cases examined neuropathologically and 3 of the 68 cases not examined suffered from recurrent convulsive attacks. Of the examined cases, 7 died during or shortly after one single or several attacks of seizures without any other discernible cause of death. Of the 19 examined cases, 11 had old cerebral cortical contusions in 4 cases combined with a unilateral focal scar in the pyramidal layer of the hippocampus, 2 and showed old cerebral cortical infarcts.

Causes of death

Toxicological analyses showed no trace of alcohol or medication in the 9 cases of acute Wernicke's encephalopathy. In 6 of these cases the general autopsy disclosed no other lethal abnormalities. The 3 remaining cases suffered from bronchopneumonia. The cerebral lesion was recorded as the cause of death in all 9. Table 2 shows the causes of death in the 9 cases with Wernicke's encephalopathy in the residual state. The causes of death in the 2 cases with central pontine myelinolysis were alcohol intoxication and intracerebral hemorrhage of unknown origin, respectively. The single case of hepatic encephalopathy died from bleeding of esophageal varices. Table 3 shows a survey of the causes of death in the 127 cases examined neuropathologically. The group of alcohol-related disease consists of deaths from acute Wernicke's encephalopathy (9 cases), acute pancreatitis (3 cases), bleeding from esophageal varices (2 cases) and delirium (1 case). The most frequent causes of death filed in "other diseases" were coronary heart disease (13 cases) and bacterial infections (13 cases), predominantly pneumonia. Severe head injury caused by a fall was the cause of death in 11 of the 14 accidental deaths. Of the 15 macroscopical intracerebral vascular lesions, 3 infarcts and 4 hemorrhages were considered to be cause of death.

Table 2. Causes of death and blood alcohol levels at death in 9 cases with Wernicke's encephalopathy in the residual state

Cause of death		Number of cases	Alcohol level (‰)
Natural	Myocardial infarct (MI)	2	0 0
	Pneumonia	1	3.2
	MI/Pneumonia	1	1.8
	Acute pancreatitis	1	0.8
Accidental	Head injury	1	2.0
Unknown		3	0 0 0

Table 3. Causes of death in 127 alcoholics examined neuropathologically

Cause of death		Number of cases with cerebral lesions	Total number of cases
Natural	Alcohol-related disease	13	15
	Other disease	20	50
Accidental		7	14
Intoxication[a]		5	17
Suicide		0	1[b]
Homicide		2	2
Unknown		14	27
Uncertain		0	1[c]

[a] Intoxications of alcohol or alcohol combined with drugs (see Material and methods

[b] Cyanide intoxication

[c] Lethal head injury and acute myocardial infarct

Table 4. Blood alcohol level (‰) at death in 127 alcoholics with and without alcohol-related cerebral lesions

Blood alcohol level (‰)	Number of cases	
	With lesions	Without lesions
0	34	38
0.1–0.5	4	3
0.6–1.0	2	3
1.1–2.0	9	8
2.1–3.0	5	8
>3.0	7	6

The intoxications include 9 cases of pure alcohol poisoning (range of blood alcohol level: 3–4.9‰), and 8 died from a combination of alcohol and drugs (blood alcohol level: 1–2.9‰). The cause of death remained unknown in 27 (21%) of the 127 cases (Table 3).

Blood alcohol levels (‰)

The blood alcohol level at death was measured in all cases examined neuropathologically. All cases with acute Wernicke's encephalopathy were sober at death; the blood alcohol level varied (Table 2) in cases with Wernicke's encephalopathy in the residual state. The distribution of blood alcohol levels in cases with and without cerebral lesions was very similar (Table 4).

Discussion

About 40% of deaths among 30–64 year-old male citizens of Oslo, Norway, occur outside hospital and other health institutions. Since 1980, medical practitioners in Norway are required by law to notify deaths of unknown origin to the police, irrespective of whether the death is considered natural or not. The new law has resulted in a gradual increase in medico-legal autopsies among deaths outside hospital in Oslo until 1984. Since then the autopsy rate has been at least 70% among 30–64 year-old men (1986: 72.7%; 1987: 76%; estimated frequency 1984 and 1985 about 70%, exact figures were not available). With very few exceptions, the medico-legal autopsies were performed at the Institute of Forensic Medicine at the National Hospital (Rikshospitalet).

Cases included in previous Norwegian autopsy studies of alcohol-related cerebral lesions [10, 16, 17, 19], were collected from citizens of Oslo who died and were autopsied at the municipal Ullevål Hospital, where the overall autopsy rate was and still is between 70 and 80% [10, 17]. Thus, the overall autopsy rate among middle-aged male inhabitants of Oslo appears to be independent of the site of death. However, the frequencies of different lesions in this study must be considered crude estimates of the true values, as the material was neither a random sample of its subpopulation nor the autopsied cases (see Materials and methods).

In accordance with previous observations [8], the frequency of Wernicke's encephalopathy was higher among the medico-legal autopsies (14.7%) than in alcoholics hospitalized at death (10: 8.9%, 17: 12.5%). However, the difference may be artificial due to different age compositions of our material. The incidence of Wernicke's encephalopathy seems to peak in the fifth decade of life [8, 20] and previous studies in Oslo also comprised alcoholics aged from 65 to 79 years. A greater proportion of acute cases in this study supports the suggestion that the prevalence of Wernicke's encephalopathy is dependent on the age composition of the material. Altogether, the studies indicate that Wernicke's encephalopathy is a rather frequent lesion among male alcoholics in Oslo [10, 16, 17]. However, alcoholic cerebellar atrophy, which was seen in about 30% of the cases, seems to be the most frequent cerebral lesion in male alcoholics [10, 16, 19]. The pathogenesis of the alcohol-related cerebellar atrophy is uncertain. Some observations favour the cause to be nutritional factors, others attribute this to the toxic effect of alcohol [6, 11, 12, 14–17, 19, 21]. Our study gave no evidence that age is a contributory factor. Although quite a number of alcoholics with Wernicke's encephalopathy also show cerebellar atrophy [7, 16, 17, 20], there is no substantial evidence of common pathogenetic factors for Wernicke's encephalopathy and cerebellar atrophy other than the alcohol abuse. This view was supported by the very different frequency of Wernicke's encephalopathy and cerebellar atrophy among vagrants, residents in municipal lodgings, and ordinary lodgers/house owners. The frequency of cerebellar atrophy was far lower in ordinary lodgers/house owners than in vagrants. On the other hand, no vagrant showed Wernicke's encephalopathy and all but two cases affected were ordinary lodgers/house owners. A reliable explanation for the different frequency distribution has not been found.

Central pontine myelinolysis has been described both as an incidental finding [1, 7], and as a cause of unexpected sudden death [3]. In our study 2 cases with this lesion died from other causes. Central pontine myelinolysis is definitively less frequent than Wernicke's enceph-

alopathy and cerebellar atrophy in Norwegian alcoholics. The frequency of 1–2% is in accordance with previous observations [3, 13].

That only a single case showed hepatic encephalopathy indicates that this lesion is rarely found in medicolegal autopsies.

Concerning the frequency of traumatic lesions, our study confirmed the assertion that alcohol abuse increases the risk of head injuries. The frequency of old cortical contusions in this material was more than six times that (2.5%) found in a large German population [22].

Data suggest the prevalence of epilepsy among alcoholics being at least triple that in the general population, and that alcoholism may be more prevalent among epileptic patients than in the general population [5]. Most investigations on the prevalence of seizures in alcoholics have included, and some have excluded, seizures caused by alcohol intoxication and withdrawal [4, 5]. The rate of seizures ranged between 0.6 and 15% in the former, and from 2 to 9% in the latter studies [5]. Some of our cases with recurrent convulsive attacks might have had withdrawal seizures. However, more than half the cases examined neuropathologically showed structural cerebral lesions which could be responsible for epileptic fits. Thus, the frequency of structural abnormalities among cases with seizures was far above that found in an ordinary population of epileptics [9].

Concerning the causes of death, the study indicated that acute Wernicke's encephalopathy is a rather common cause in middle-aged male alcoholics who die outside hospital. In fact, it seems to be the most frequent alcohol-related cause of death in this population. Furthermore, the study provided evidence that acute Wernicke's encephalopathy is especially prevalent among alcoholics who are sober at death. That bronchopneumonia was the immediate cause of death in some of the cases was not surprising, as both alcoholism [2] and unconsciousness increase the risk of infections. The manner of death in our cases was unknown. A sudden death is not uncommon [8], and we have also seen cases of immediate death while walking. The pathophysiology of the mechanism is unknown.

Wernicke's encephalopathy in the residual state, however, was neither associated with specific causes of death nor specific blood alcohol levels.

Central pontine myelinolysis can be lethal lesion and also cause sudden death [3]. Our 2 cases with this lesion died from other causes.

The frequent combination of cerebellar atrophy and traumatic lesions indicate that neurological deficits from the cerebellar lesion may contribute to fall acidents with more or less severe head injuries.

The rate of lethal vascular lesions was in accordance with that in a general population of 40 to 69-year-old men from Oslo, examined at Ullevål Hospital from 1975 to 1977 [18].

Altogether, the study showed a high frequency of cerebral lesions in middle-aged male Norwegian alcoholics and that the abnormalities caused or contributed to death in a substantial number of the cases.

References

1. Adams RD, Victor M, Mancall EL (1959) Central pontine myelinolysis. Arch Neurol Psychiatr 81:154–172
2. Bergman MM, Cleckman RA (1988) Infectious complications in alcohol abusers. Hosp Pract 23:145–156
3. Bratzke H, Neumann K (1989) Zentrale Pontine Myelinolyse Morphologie und Forensische Bedeutung. Z Rechtsmed 102: 79–97
4. Brennan FN, Lyttle JA (1987) Alcohol and seizures: a review. J R Soc Med 80:571–573
5. Chan AWK (1985) Alcoholism and epilepsy. Epilepsia 26: 323–333
6. Estrin WJ (1987) Alcoholic cerebellar degeneration is not a dosedependent phenomenon. Alcoholism (NY) 11:372–375
7. Harper C (1979) Wernicke's encephalopathy: a more common disease than realised. A neuropathological study of 51 cases. J Neurol Neurosurg Psychiatr 42:226–231
8. Harper C (1983) The incidence of Wernicke's encephalopathy in Australia – a neuropathological study of 131 cases. J Neurol Neurosurg Psychiatr 46:593–598
9. Hauser WA, Kurland LT (1975) The epidemiology of epilepsy in Rochester, Minnesota, 1935 through 1967. Epilepsia 16:1–66
10. Lindboe CF, Løberg EM (1988) The frequency of brain lesions in alcoholics. Comparison between the 5-year-periods 1975–1979 and 1983–1987. J Neurol Sci 88:107–113
11. Mancall EL, McEntee WJ (1965) Alterations of the cerebellar cortex in nutritional encephalopathy. Neurology 15:303–313
12. Phillips SC, Harper CG, Kril J (1987) A quantiative histological study of the cerebellar vermis in alcoholic patients. Brain 110:301–314
13. Rogde S, Skullerud K (1982) Alkoholrelaterte hjerneskader i et rettsmedisinsk materiale. In: Voigt J, Gürtler H, Hennings K, Keiser-Nielsen S, Stentoft A (eds) 8. møde i Nordisk Rettsmedicinsk forening. Rettsmedicinsk institut, København, pp 185–188
14. Skullerud K (1985) Variations in the size of the human brain. Influence of age, sex, body length, body mass index, alcoholism, Alzheimer changes, and cerebral atherosclerosis. Acta Neurol Scand 71, (Suppl) 102:1–94
15. Tavares MA, Paula-Barbosa MM, Cadete-Leite A (1987) Chronic alcohol consumption reduces the cortical layer volumes and the number of neurons of the rat cerebellar cortex. Alcoholism (NY) 11:315–319
16. Torvik A (1987) Brain lesions in alcoholics: Neuropathological observations. Acta Med Scand (Suppl) 717:47–54
17. Torvik A, Lindboe CF, Rogde S (1982) Brain lesions in alcoholics. A neuropathological study with clinical correlations. J Neurol Sci 56:233–248
18. Torvik A, Stenwig JT (1981) Changes in frequency of cerebrovascular diseases in Oslo, Norway, 1958–1977. An autopsy study. Stroke 12:816–823
19. Torvik A, Torp S (1986) The prevalence of alcoholic cerebellar atrophy. A morphometric and histological study of an autopsy material. J Neurol Sci 75:43–51
20. Victor M, Adams RD, Collins GH (1971) The Wernicke-Korsakoff syndrome. Contemporary Neurology Series, vol 7. Blackwell Scientific Publications, Oxford
21. Adams RD, Victor M, Mancall EL (1959) A restricted form of cerebellar cortical degeneration occuring in alcoholic patients. Arch Neurol 1:579–688
22. Welte E (1948) Über die Zusammenhänge zwischen anatomischem Befund und klinischem Bild bei Rindenprellungsherden nach stumpfen Schädeltrauma. Arch Psychiatr Nervenkr 179: 243–315