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Computer Tomography and Magnetic Resonance Imaging in Cyanide Poisoning

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Summary. A 29-year-old chemistry student took 50 ml of a 1% potassium cyanide solution (500 mg) in an attempted suicide. He became comatose, mydriatic, and was admitted to hospital in an apneic state. He woke up after 7 h and developed Parkinsonism in the following weeks. This regressed slowly during the 2 months after the poisoning apart from dysarthria, bradykinesia of the upper limbs, and very brisk monosynaptic reflexes. At 3 weeks after the intoxication, computerized tomography was largely normal, and there was CSF-dense hypodensity in both putamina after 5 months. Sharply delimited signal elevation in T2 corresponding to the two putamina was detected by magnetic resonance imaging 8 weeks and 5 months after ingestion of the poison.

Key words: Cyanide poisoning – Basal ganglia – Computerized tomography – Magnetic resonance imaging

The brain (particularly the basal ganglia) is highly sensitive to cyanides. Cyanide salts are rapidly absorbed, and cyanide radicals inactivate cytochrome oxidase, the terminal enzyme in the respiratory electron transport chain which utilizes the oxygen derived from the dissociation of oxyhemoglobin. This finally leads to effective suspension of all cellular respiration. There is no essential difference between the neurological effects of NaCN, KCN, HCN, and CNC, and mortality is 95%. The lethal dose of KCN is 250 mg with oral intake [33], and death mostly occurs in less than 3 min from respiratory paralysis [4, 44].

Because of the rapid onset of action and the certain effect, cyanide salts are commonly used for purpose of suicide, and recently, there was a mass homicide-suicide with more than 900 fatalities [35]. The use of cyanide for disinfestation of clothes, buildings or ships, to extract gold and in galvanization, for cleaning of silver as well as an intermediate product in the chemical industry repeatedly leads to fatal accidents at work [39 zit. nach 36]. Jacobs [22] counted 104 occupational medical incipient and actual intoxications over a period of 16 years in a cyanide plant. Hydrocyanic acid gas and toxic organic cyanide also develop during the burning of polyurethane foam, with death of firemen from suffocation [1]. Rarer occurrences are intoxication by hydrocyanic acid occurring in nature, e.g., bitter almonds [17, 32], apricot kernels [28], or from administration of the product laetrile [5] containing amygdaline. Amygdaline is a glucoside which is hydrolysed to isomeric prunasine, glucose, benzaldehyde, and hydrocyanide.

Cyanide intoxications which have been survived with a blood cyanide concentration which is otherwise fatal suggest that there are individual differences in resistance to the toxin [14]. In anacidity of the gastric juice, large amounts of cyanide salts are tolerated, apart from local erosions [37]. The famous case of Grigorji Jefimowitsh Rasputin probably belongs in this category [36].

The most important antidote against cyanide intoxication is the lipid-soluble and therefore rapidly acting methemoglobin-forming 4-dimethylaminophenol. The Fe^{3+} atom in methemoglobin is able to bind cyanide and to render it innocuous [37, 47]. There is no reliance on the characteristic smell of hydrocyanic acid as a warning sign, because many people lack the olfactory sense for hydrocyanic acid for genetic reasons [8].

Because of the mostly fatal outcome of cyanide intoxication, there is little experience so far on cere-

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bral findings obtained with modern imaging techniques. Only Braico et al. [5], Finelli [15], and Jacobs [22] each published one case which had been investigated using computerized tomography (CCT). Magnetic resonance imaging (MRI) investigations after cyanide intoxication have not yet been published. In contrast to this, the CCT literature on the related carbon monoxide intoxication is already substantial [12, 21, 23, 24, 27, 31, 34, 40, 41]. It hence appears topical to report on a case surviving KCN intoxication. The patient was investigated clinically as well as by means of CCT and MRI.

Case Report

A 29-year-old chemistry student swallowed 50 ml of a 1% KCN solution with the intention of committing suicide. He was discovered in an unconscious state, and gastric lavage and intubation were carried out in the ambulance. The patient was admitted to hospital in a comatose condition, with assisted ventilation. The conjunctivae were reddened, and the pupils were mydriatic and nonreactive. Treatment was dimethylaminophenol and sodium thiosulfate. The patient was responsive again 7 h after taking the poison, and spontaneous breathing returned. There was a temporary rise in creatine kinase to 322 units/l and in leukocytes to 18,200/mm^3, and two days later, there was ulcerous reflux esophagitis, and vomiting for several days. At the end of the 1st week, there was transient oculogyria. At the beginning of the 3rd week, the patient had a swollen tongue, 3 days later, speaking was slowed down and combersome, and swallowing was impeded. In the 4th week, there were overshot trunk movements when standing up from lying down and sitting positions which had to be counteracted voluntarily. The patients gait was with a stiff trunk, with deep kneebending on climbing steps, pressing the body forward. Increasing hypokinesia, abolishing facial expression, hypersalivation, and squeaky, quiet, relatively unmodulated speech were present. On speaking, both angles of the mouth were drawn to the side, giving the impression of grinning. During eating, food could not be drawn between the teeth with the tongue and the tongue only reached the teeth when voluntarily pushed forward. Taste was not disturbed. Neck and limb rigor with cogwheel phenomenon and severe bradydiadochokinesia were observed. The patient was no longer able to play the organ. All monosynaptic reflexes were very brisk, and there were no pathological reflexes. Ear, nose, and throat findings were normal.

The CCT showed narrow ventricles and slight subarachnoid spaces 3 weeks after consumption of the poison (Fig. 1a). In T2-weighted MRI, there was a symmetrical signal elevation in both putamina 8 weeks after the intoxication (Fig. 2). In the course of the 2nd month, there was slow, but continuous improvement of all symptoms, the patient was receiving 6 mg biperiden per day at this time. At 5 months after the intoxication, there was still slight slowing of speech, and pronounced bradydiadochokinesia in the upper limbs. The MRI finding was unchanged. However, there was now symmetrical hypodensity corresponding to both putamina in the CCT and markedly wider ventricles and slight subarachnoid spaces compared to the first investigation (Fig. 1b). A tremor, pathological reflexes, muscle atrophy, disorders of sensitivity, or intellectual deficits had not occurred at any time.

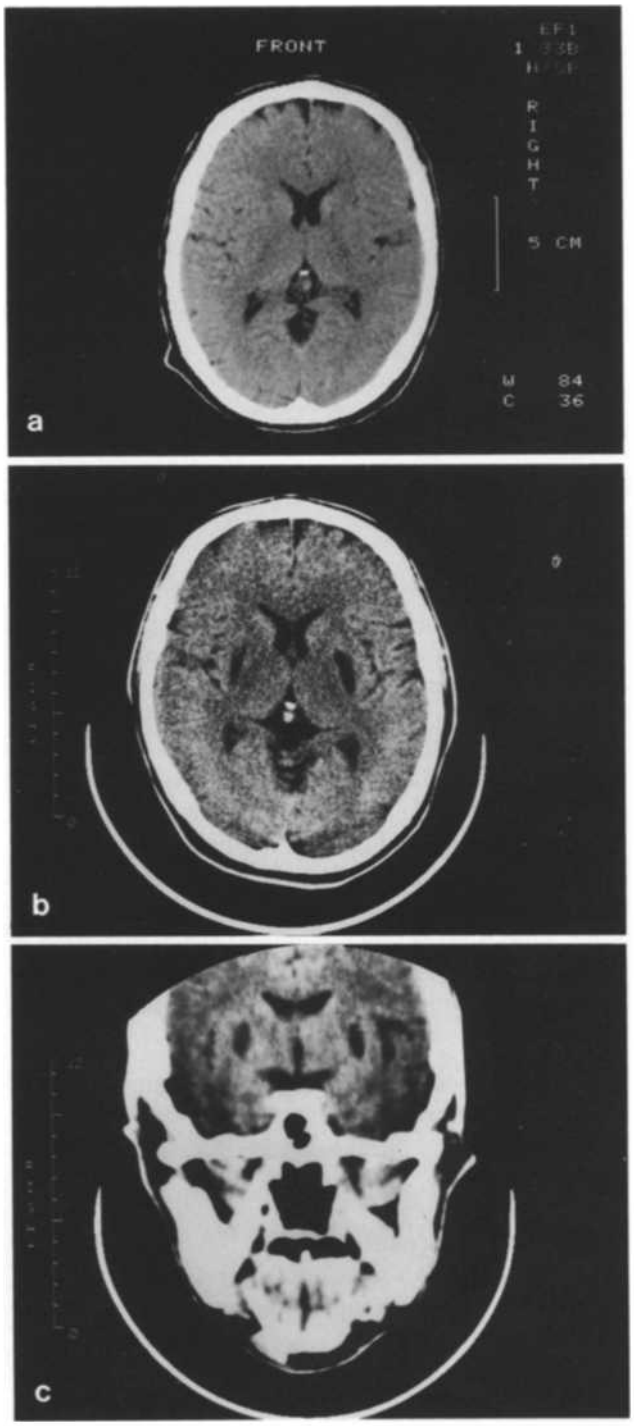

Fig. 1. a Computerized tomography (CCT) 3 weeks after intoxication. Still no abnormalities in the basal ganglia. **b, c** Horizontal and coronal section. CCT 5 months after intoxication. CSF-dense putamina. Relatively wide ventricels and pronounced subarachnoid spaces

Discussion

In the present case, there was no doubt that severe cyanide poisoning had been present, since coma, my-

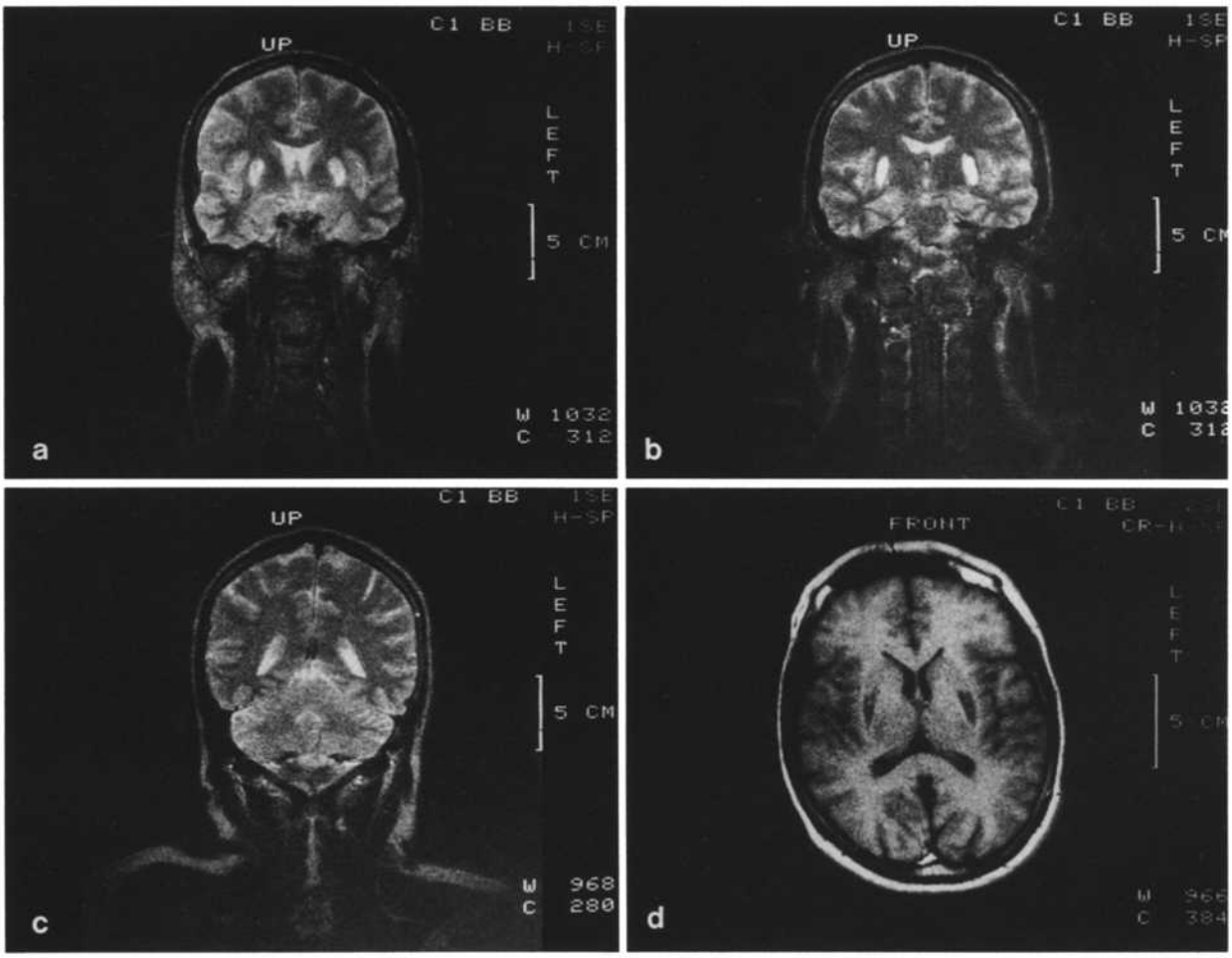

Fig. 2. a–c Magnetic resonance imaging (MRI). Coronal sections 2 months after ingestion of poison. In T2 weighting, there is symmetrically arranged signal elevation which corresponds to the putamina. **d** MRI. Horizontal section. Signal reduction in T1 weighting. These results had not altered 3 months later

driasis, and apnea were already present on commencement of intensive therapy. The degree of severity was much the same as in Finelli's case of the same age of calcium cyanide intoxication [15]. Like ours, Finelli's patient recovered rapidly and also presented the symptoms: brisk monosynaptic reflexes, bradydiadochokinesia of a hand, little objective evidence for organic brain damage, or physical disability after 4 months. After 16 years, he was completely normal mentally and only had slightly dysarthric speech and a slight athetoid movement disorder of the left upper limb. The left hand was clumsy in rapid pursuit movements, the gait was normal. The case presented bilateral lesions in the globus pallidus and a lesion in a cerebellar hemisphere in contrast to the present case. The other patient investigated by CCT [5, 22] involved laetrile intoxication in an 11-month-old baby which died 7h after the intoxication. In the CCT, the baby had a ventricular dilatation, but infarct-like lesions in the lateral putamina and fresh hemorrhages in the cerebellum were revealed at autopsy. Jacobs' patient [22] with occupational medical hydrocyanic acid intoxication had a normal CCT after 3 days and did not develop any neurological signs. Without using CCT, Uitti et al. [45] described in great detail an 18-year-old male patient with severe KCN intoxication who had major features of Parkinsonism. However, unlike idiopathic Parkinson's disease, the pathological disorder mainly involved the globus pallidus and putamen. This patient also had difficulty in expressing himself in the first weeks. He spoke slowly and hesitantly, had a wild-eyed staring appearance, infrequent blinking, and reduced facial expression. He tended to fall backwards easily. After 4 months, the patient developed generalized rigidity and bradykinesia, intermittent resting and postural tremor in the arms, unstable posture, anteropulsion and retropulsion. He died 19 months later after an overdose of imipramine and alcohol. Postmortem examination revealed major destructive

changes in the globus pallidus and putamen. The authors concluded that this was the first clinical pathological report of Parkinsonism resulting from cyanide poisoning. However, Schwab and England [43] reported Parkinsonism after cyanide intoxication as early as 1968. As has been known for a long time, Parkinsonism also occurs after carbon monoxide poisoning [23, 26, 38, 43] and after manganese intoxication [9, 43].

It is noteworthy that in the cases of methanol intoxication reported by McLean et al. [29] and Aquilonius et al. [2, 3], there were bilateral putamen lesions on CCT. The case we have described is thus the first case of cyanide intoxication with Parkinsonism and exclusive lesions of both putamina which has been investigated by CCT and MRI. In terms of the symptomatology, the cases known so far have akinesia, bradydiadochokinesia of the upper limbs, and dysarthria in common. The two latter symptoms can evidently last longest. The CCT only becomes positive after a few weeks, as proved by the case of Braico et al. [5] and our own case. Only our case had an unequivocally positive result on MRI after 8 weeks, as no MRI investigations had previously been carried out.

Human pathological brain findings in cyanide intoxication are few and far between [36]. Schmorl's case [42], which was examined histologically by Edelmann [13], displayed bilateral necroses in the globus pallidus which led the author to imply parallels to carbon monoxide intoxication, Salvarsan intoxication, and Wilson's disease. Ule and Pribillas' case [46] also had elective parenchymal necroses in the globus pallidus on both sides but also in both putamina. The case of cyanide intoxication following treatment with sodium nitroprusside described by Kim et al. [25] presented bilateral pallidum malacia. On the other hand, pertinent animal experimental literature, which describes brain findings in dogs [18, 30], cats [16], and rhesus monkeys [6, 19, 20] with very similar findings to those in humans, is more abundant.

In the cases reported in the literature and our own case, which have been investigated histologically and/or with CCT or MRI, as the main finding only the putamen was affected in two cases, putamen and globus pallidus in two cases, and only the globus pallidus in two cases. Accordingly, these two nuclei are likely to be especially vulnerable to cyanides. It cannot be decided whether the lesion of only one nuclear area or of both nuclear areas reflects the concentration of the poison, the symptomatology, or the prognosis, in view of the small number of cases which can be reviewed and the varying standard of detail in the case reports. Intoxication with poisons which result in functional or morphologial elimination of specific nuclear areas of the brain are experiments of nature. They can be used for the study of clinical manifestations of functional loss. With modern imaging techniques, the pathomorphology can be well-recognized even while the patient is alive, and the course can be followed and related to clinical manifestations. The effects in humans of the functional loss of the putamina, which are regarded as resonators for a major proportion of the activity of the cerebral cortex, and damage which leads to dedifferentiation of motor activity and disturbance of fine movements [10, 11] can be studied in detail. This can be compared for example with the effects of related poisons (carbon monoxide, manganese, methanol). The common denominator for these relationships is likely to be the cytotoxic hypoxydosis which these poisons cause in connection with the high iron content and the major oxygen requirement of the structure. As a rule, the histopathology in cases which have died quickly is characterized by circulation-dependent findings in the tissue besides the topospecific cytotoxic effects of the poison, i.e., multifarious lesions. This impedes pathogenetic discrimination [6, 7]. In view of the rarity of survivors of cyanide intoxication, CCT and MRI should become a valuable aid in diagnosis of the localization of the lesion and an important tool in research on brain damage of toxic origin.

References

1. Anderson RA, Oliver IS, Thomson I, Harland WA (1978) Cyanide exposure in fires. Lancet II:91–92
2. Aquilonius SM, Askmark H, Enoksson P, Lundberg PO, Moström U (1978) Computerized tomography in severe methanol intoxication. Br Med J 2:929–930
3. Aquilonius SM, Bergström K, Enoksson P, Hedstrand U, Lundberg PO, Moström U, Olsson Y (1980) Cerebral computed tomography in methanol intoxication. J Comput Assist Tomogr 4:425–428
4. Arena JM (1979) Poisoning, 4th Edn. Charles C. Thomas, Springfield, Ill, p 236
5. Braico KT, Humbert JR, Terplan K, Lehotay JM (1979) Laetrile intoxication. Report of a fatal case. N Engl J Med 300:238–240
6. Brierley JJB (1975) A comparison between the effects of profound hypotension, hypoxia and cyanide on the brain of M. Mulatta in primate models of neurological disorders. Meldrum BS (ed) Raven Press, New York
7. Brierley JB (1976) Cerebral hypoxia. In: Blackwood W, Corsellis JAN (eds) Greenfields neuropathology. Histotoxic hypoxia, cyanide. Edward Arnold Publ. LTD, Baltimore and London
8. Brown KS, Rosinette RR (1967) No simple pattern of inheritance in ability to smell solutions of cyanide. Nature (Lond) 215:406–408
9. Canavan MM, Cobb S, Drinker CK (1934) Chronic manganese poisoning: report of a case with autopsy. Arch Neurol Psychiatr 32:501–512

10. Denny-Brown D (1966) The cerebral control of movement. The Sherrington Lectures VIII. Liverpool Univ. Press, Liverpool
11. Denny-Brown D, Yanagisawa N (1976) The role of the basal ganglia in the initiation of movement. In: Yahr D (ed) The basal ganglia. Raven Press, New York, pp 115–149
12. Destee A, Courteville V, Devos PH, Besson P, Warot P (1985) Computing tomography and acute carbon monoxide poisoning. J Neurol Neurosurg Psychiatr 48:281–282
13. Edelmann F (1921) Ein Beitrag zur Vergiftung mit gasförmiger Blausäure, insbesondere zu den dabei auftretenden Gehirnveränderungen. Dtsch Z Nervenheilkd 72: 259–287
14. Editorial (1949) J Am Med Assoc 140:541
15. Finelli PF (1981) Case report changes in the basal ganglia following cyanide poisoning. J Comput Assist Tomogr 5: 755–756
16. Funata N, Song S-Y, Okeda R, Funata M, Higashino F (1984) A study of experimental cyanide encephalopathy in the acute phase-physiological and neuropathological correlation. Acta Neuropathol 107:64–99
17. Geldmacher V, Mallinckrodt M (1975) Forensische Toxikologie. In: Mueller B (Hrsg) Gerichtliche Medizin, Bd 2. Springer, Berlin Heidelberg New York, pp 856–862
18. Haymaker W, Ginzler AM, Ferguson RL (1952) Residual neuropathological effects of cyanide poisoning: a study of the central nervous system of 23 dogs exposed to cyanide compounds. Milit Surg 111:231–246
19. Hurst EW (1940) Experimental demyelination of the central nervous system. I. The encephalopathy by potassium cyanide. Aust J Exp Biol Med Sci 18:201–223
20. Hurst EW (1942) Experimental demyelination of the central nervous system III. Poisoning with potassium cyanide, sodium azide, hydroxylamine, narcotics, carbon monoxide etc. with some consideration of bilateral necrosis occurring in the basal ganglia. Aust J Exp Biol Med Sci 20:297–312
21. Ikeda T, Kondo T, Mogami H, Miura T, Mitomo M, Shimazaki S, Sugimoto T (1978) Computerized tomography in cases of acute carbon monoxide poisoning. Med J Osake Univ 29:253–262
22. Jacobs K (1984) Erfahrungsbericht über Anwendung von 4-DMAP bei einer schweren Blausäure-Vergiftung. Konsequenzen für die Praxis. Zentralbl Arbeitsmed 34:274–277
23. Jaeckle RS, Nasrallah HA (1985) Major depression and carbon monoxide-induced parkinsonism: diagnosis, computerized axial tomography, and response to L-DOPA. J Nerv Ment Dis 173:503–508
24. Kim KS, Weiberg PE, Suh JH, Ho SU (1980) Acute carbon monoxide poisoning. Computed tomography of the brain. Am J Neuroradiol 1:399–402
25. Kim YH, Foo M, Terry RD (1982) Cyanide encephalopathy following therapy with sodium nitroprusside. Arch Pathol Lab Med 106:392–393
26. Klawans HL, Stein RW, Tanner CM, Goetz CG (1982) A pure Parkinsonian syndrome following acute carbon monoxide poisoning. Arch Neurol 39:302–304
27. Kobayashi K, Isaki K, Fukutani Y, Kurachi M, Eboshida A, Matsubara R, Yamaguchi N (1984) CT-Findings of the interval form of carbon monoxide poisoning compared with neuropathological findings. Eur Neurol 23:34–43
28. Lasch EE, El Shawa R (1981) Multiple cases of cyanide poisoning by apricot kernels in children from gaza. Pediatrics 68:5–8
29. McLean DR, Jacobs H, Miekle BW (1980) Methanol poisoning. A clinical and pathological study. Ann Neurol 8:161–167
30. Meyer A (1933) Experimentelle Vergiftungsstudien. III. Über Gehirnveränderungen bei experimenteller Blausäurevergiftung. Z Ges Neurol Psychiatr 143:333–348
31. Miura T (1979) CT-Findings in acute carbon monoxide intoxication. Rinsho Hoshasan 24:1281–1285
32. Moeschlin S (1972) Klinik und Therapie der Vergiftungen, 5. Aufl. Thieme, Stuttgart
33. Moeschlin S (1980) Klinik und Therapie der Vergiftungen, 6. Aufl. Thieme, Stuttgart, pp 252–256
34. Nardizzi LR (1979) Computerized tomographic correlates of carbon monoxide poisoning. Arch Neurol 36:38–39
35. Nightmare in Jonestown. Time, Dec 4, 1978, 112:23, 16–21
36. Pentschew A (1958) Blausäurevergiftung. In: Lubarsch VO, Henke F, Rössle R (Hrsg) Handbuch der speziellen Pathologischen Anatomie und Histologie, Bd XIII: Nervensystem, 2. Teil, Bandteil B. Springer, Berlin Göttingen Heidelberg, pp 2149–2156
37. Quadbeck G, Ule G (1983) Die toxischen Stoffgruppen. II. Zyanwasserstoff und Zyanide. In: Berlet H, Noetzel N, Quadbeck G, Scholz W, Schmitt HP, Ule G, Ule VG (eds) Pathologie des Nervensystems II. Springer, Berlin Heidelberg New York, pp 291–299
38. Ringel SP, Klawans HL (1972) Carbon monoxide-induced Parkinsonism. J Neurol Sci 16:245–251
39. Rosenthal-Deussen E: Zit. nach Pentschew A
40. Sawada Y, Takahashi M, Ohashi N (1980) Computerized tomography as an indication of long-term outcome after acute carbon monoxide poisoning. Lancet I:783–784
41. Sawada Y, Sakamoto T, Nishide K (1983) Correlation of pathological findings with computed tomographic findings after acute carbon monoxide poisoning. N Engl J Med 308: 1296
42. Schwab RS, England AC (1968) Parkinson syndrome due to various specific causes. In: Vinken PJ, Bruyn GW (eds) Handbook of clinical neurology, vol 6. North-Holland, Amsterdam, p 242
43. Schmorl G (1920) Gehirn bei Blausäurevergiftung. Münch Med Wochenschr 67:913
44. Thienes CM, Haley TJ (1972) Clinical toxicology. 5th edn. Lea & Febiger, Philadelphia, p 203
45. Uitti RJ, Rajput AH, Ashenhurst EM, Rozdilsky B (1985) Cyanide-induced parkinsonism: a clinico-pathologic report. Neurology 35:921–925
46. Ule G, Pribilla O (1962) Hirnveränderungen nach Cyankalivergiftung mit protrahiertem (intervallären) klinischen Verlauf. Acta Neuropathol (Berlin) 1:406–410
47. Weger N (1968) Aminophenole als Blausäureantidot. Arch Toxikol 24:49–50

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