**ALS, Amyotrophe Lateralsklerose, amyotrophic lateral sclerosis, Myatrophische Lateralsklerose, Lou-Gehring Syndrom, Motor neuron disease, Charcot Krankheit.**

Die **Amyotrophe Lateralsklerose** (**ALS**) ist eine degenerative Erkrankung des motorischen Nervensystems. **Ursachen der ALS** http://www.als-charite.de/home/ursachen/

**Bildgebende Verfahren: Elektromyografie** (EMG, Messung der elektrischen Muskelaktivität) und die Messung der **Nervenleitgeschwindigkeit** (ENG, Elektroneurografie).
Zum Ausschluss anderer neurologischer Erkrankungen: **Magnet-Resonanz-Tomografie** (MRT), **Blut-Untersuchungen, Hirnwasser-Untersuchung** (Liquorpunktion).

**Für die Therapie:** Abgrenzung z.B.: zu **Parkinson (Schüttellähmung), Multipler Sklerose (MS),** zu **Unterformen der ALS** (sporadisch, familiär, endemisch)**, progressive spinale muskuläre Atrophie** oder der **Neuro-Borreliose.**

**Amyotrophic lateral sclerosis (ALS)** is a degenerative disease of the motor nervous system. **Causes of the ALS** http://www.als-charite.de/home/ursachen/

**Electromyography** (EMG, measurement of electrical muscle activity) and the measurement of **nervous conduction velocity** (ENG, Electoneurography).
To the exclusion of other neurological diseases: **magnetic resonance tomography** (MRT), **blood tests, brain water examination** (cerebrospinal fluid).

**For the therapy:** delimitation, eg: **Parkinson's disease, multiple sclerosis (MS), subforms of ALS** (sporadic, familial, endemic), progressive spinal cord muscular atrophy or **neuro-borreliosis**.

**Immunology**
Cashman NR (1985), Jeong SY (2009), Mitchell J (2010), Deng HX (2011)

**Bacteria**
Waisbren BA (1987), Fredrikson S (1988), ElAlaouli F (1990), Halperin JJ (1990), Hänsel Y (1946, 1995), Miller AI (2017)

**Mycoses, fungi**
Alonso R (2017)

**Toxins**
Watts DL (1988), Yasui M (1993), Zecca L (2004), Wang Q (2011), Rouault TA (2013), Veyrat-Durebex C (2014)

**Charcot**, J. M. (**1874**) **De la sclérose latérale amyotrophique**. Le Progrès médical, series 1, 2 : 325-327, 341-342, 453-455.

Gawel M, Zaiwalla Z, Rose FC. (1983) Antecedent events in motor neuron disease. J Neurol Neurosurg Psychiatry. 46(11), 1041-3.

Salazar AM, Masters CL, Gajdusek DC, Gibbs CJ Jr (1983) **Syndromes of amyotrophic lateral sclerosis and dementia: relation to transmissible Creutzfeldt-Jakob disease.** Ann Neurol. 14(1), 17-26. https://www.ncbi.nlm.nih.gov/pubmed/6351721
**« The findings suggest that most cases of dementia associated with early amyotrophy are more closely related to classic amyotrophic lateral sclerosis than to transmissible Creutzfeldt-Jakob disease and do not deserve the label of "amyotrophic Creutzfeldt-Jakob disease «**

Cashman NR, Gurney ME, Antel JP. (1985) Immunology of amyotrophic lateral sclerosis. Springer Semin Immunopathol. 8(1-2), 141-52. Review.

Waisbren BA, Cashman N, Schell RF, Johnson R. (1987) **Borrelia burgdorferi antibodies and amyotrophic lateral sclerosis.** Lancet. 2(8554), 332-3.

Fredrikson S, Link H. (1988) **CNS-borreliosis selectively affecting central motor neurons**. Acta Neurol Scand 78, 181-184 [Medline].

Watts DL (1988) **The Nutritional Relationships of Iron**. Journal of Orthomolecular Medicine 3(3**)** http://www.traceelements.com/Docs/The%20Nutritional%20Relationships%20of%20Iron.pdf

ElAlaouli F, Medejel A, AlZemmouri K, Yahyaoui M, Chkili T. (1990) **Syphilitic lateral amyotrophic sclerosis**. A study of 5 cases. Rev Neurol 146, 41-44 [Medline].

Halperin JJ, Kaplan GP, Brazinsky S, Tsai TF, Cheng T, Ironside A, Wu P, Delfiner J, Golightly M, Brown RH, et al. (1990) **Immunologic reactivity against Borrelia burgdorferi in patients with motor neuron disease.** Arch Neurol. 47(5), 586-94.http://www.ncbi.nlm.nih.gov/pubmed/2334308
**„There appears to be a statistically significant association between ALS and immunoreactivity to B burgdorferi, at least among men living in hyperendemic areas.“**

Yasui M, Ota K, Garruto RM et al. (1993) **Concentrations of zinc and iron in the brains of Guamanian patients with amyotrophic lateral sclerosis and parkinsonism-dementia.** Neurotoxicology. 14(4), 445-50. http://www.ncbi.nlm.nih.gov/pubmed/8164889

Oba H, Araki T, Ohtomo K, Monzawa S, Uchiyama G, Koizumi K, Nogata Y, Kachi K, Shiozawa Z, Kobayashi M. (1993) **Amyotrophic lateral sclerosis: T2 shortening in motor cortex at MR imaging.** Radiology. 189(3), 843-6. PubMed. https://www.ncbi.nlm.nih.gov/pubmed/8234713

Carelli V, Liguori R, Cordivari C, Bianchedi G, Montagna P**.** (1994) **Ceftriaxone is ineffective in ALS**. Ital J Neurol Sci. 15(1), 66.

Imon Y, Yamaguchi S, Yamamura Y, Tsuji S, Kajima T, Ito K, Nakamura S. (1995) Low intensity areas observed on T2-weighted magnetic resonance imaging of the cerebral cortex in various neurological diseases. J Neurol Sci. 134 Suppl:27-32. PubMed.

Hänsel Y, Ackerl M, Stanek G (1946, 1995) **ALS-like sequelae in chronic neuroborreliosis.**. Wiener medizinische Wochenschrift 145(7-8), 186–8 Abstract URL BibTeX4

Halperin J, Logigian E, Finkel M, Pearl R. (1996) Practice parameters for the diagnosis of patients with nervous system Lyme borreliosis (Lyme disease). Neurology. 46, 619_27.

Desai J, Sharief M, Swash M. (1998) **Riluzole has no acute effect on motor unit parameters in ALS**. J Neurol Sci. 160 Suppl 1, S69-72.

Plato CC, Galasko D, Garruto RM, Plato M, Gamst A, Craig UK, et al. (2002) ALS and PDC of Guam: forty-year follow-up. Neurology. 58(5), 765-73.

Zhu S, Stavrovskaya IG, Drozda M, Kim BYS, Ona V, Li M, Sarang S, Liu AS, Hartley DM, Wu DC, Gullans S, Ferrante RJ, Przedborski S, Kristal BS, Friedlander RM. (2002) **Minocycline inhibits cytochrome c release and delays progression of amyotrophic lateral sclerosis in mice.** Nature, 417(688), 74-78. http://www.ncbi.nlm.nih.gov/pubmed/11986668
**„Here we report that minocycline delays disease onset and extends survival in ALS mice. Given the broad efficacy of minocycline, understanding its mechanisms of action is of great importance. We find that minocycline inhibits mitochondrial permeability-transition-mediated cytochrome c release. Minocycline-**

**mediated inhibition of cytochrome c release is demonstrated in vivo, in cells, and in isolated mitochondria. Understanding the mechanism of action of minocycline will assist in the development and testing of more powerful and effective analogues. Because of the safety record of minocycline, and its ability to penetrate the blood-brain barrier, this drug may be a novel therapy for ALS."**

Dupuis L, Gonzalez de Aguilar JL, Oudart H, de Tapia M, Barbeito L, Loeffler JP. (2004) **Mitochondria in amyotrophic lateral sclerosis: a trigger and a target**. Neurodegener Dis. 1(6), 245-54. PubMed. http://www.ncbi.nlm.nih.gov/pubmed/16908975

Zecca L, Youdim MB, Riederer P, Connor JR, Crichton RR. (2004) **Iron, brain ageing and neurodegenerative disorders.** Nat Rev Neurosci. 5(11), 863-73. PubMed. http://www.ncbi.nlm.nih.gov/pubmed/15496864
**"By studying the accumulation and cellular distribution of iron during ageing, we should be able to increase our understanding of these neurodegenerative disorders and develop new therapeutic strategies."**

Nagai M, Re DB, Nagata T, Chalazonitis A, Jessel TJ, Wichterle H, Przedborski S. (2007) Astrocytes expressing ALS-linked mutated SOD1 release factors selectively toxic to motor neurons. Nature Neuroscience, 10(5), 615-622.

Harvey WT, Martz D. (2007) **Motor neuron disease recovery associated with IV ceftriaxone and anti-Babesia therapy**. Acta Neurol Scand. 115, 129_31.

Di Giorgio FP, Carrasco M, Siao M, Maniatis T, Eggan K. (2007) An embryonic stem cell based model for ALS: Non-cell autonomous affects of glial cells on motor neurons. Nature Neuroscience, 10(5), 608-614.

Sorenson EJ, Windbank AJ, Madrekar JN, Bamlet WR, Appel SH, Armon C, et. al. (2008) Subcutaneous IGF-1 is not beneficial in 2-year ALS trial. Neurology 71(22), 1770_1775.

Mitka M. (2008) Chelation therapy trials halted. JAMA 300(19), 2236. PubMed.

Jeong SY, Rathore KI, Katrin Schulz K (2009) **Dysregulation of Iron Homeostasis in the CNS Contributes to Disease Progression in a Mouse Model of Amyotrophic Lateral Sclerosis.** The Journal of Neuroscience, 29(3), 610-619; doi: 10.1523/JNEUROSCI.5443-08.2009 http://www.jneurosci.org/content/29/3/610.short
**„These data suggest that iron chelator therapy might be useful for the treatment of ALS."**

Bedlack RS, Hardiman O. (2009) ALS Untangled (ALSU): A scientific approach to off-label treatment options for people with ALS using tweets and twitters. ALS. 10, 1290130.

Qureshi M, Bedlack RS, Cudkowicz ME. (2009) **Lyme disease serology in amyotrophic lateral sclerosis.** Muscle Nerve. 40(4), 626-8. doi: 10.1002/mus.21438. Abstract URL, DOI BibTeX http://www.ncbi.nlm.nih.gov/pubmed/19697382
**„Lyme disease was rare in 414 patients with ALS and is not likely to be causative."**

Willams AH et al. (2009) MicroRNA-206 Delays ALS Progression and Promotes Regeneration of Neuromuscular Synapses in Mice. Science, 326, 1549-1554.

Mitchell J, Paul P, Chen HJ et al. (2010) **Familial amyotrophic lateral sclerosis is associated with a mutation in D-amino acid oxidase.** In: Proc. Natl. Acad. Sci. U.S.A. 107(16), 7556–7561, doi:10.1073/pnas.0914128107, PMID 20368421, PMC 2867752 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2867752/
**„DAO [mutation in the D-amino acid oxidase gene (R199W DAO)] controls the level of D-serine, which accumulates in the spinal cord in cases of sporadic ALS and in a mouse model of ALS, indicating that this abnormality may represent a fundamental component of ALS pathogenesis."**

Süssmuth SD, Sperfeld AD, Hinz A et al. (2010) CSF glial markers correlate with survival in amyotrophic lateral sclerosis. Neurology. 74(12), 982-7. doi: 10.1212/WNL.0b013e3181d5dc3b. http://www.ncbi.nlm.nih.gov/pubmed/20308682

Raphael B Stricker and Lorraine Johnson. (2011) **Lyme disease: the next decade.** Infection and drug resistance 4, 1–9, Abstract URL, DOI BibTeX

Halperin JJ (2011) **Nervous system lyme disease: is there a controversy?** Seminars in neurology 31(3), 317–24. Abstract URL, DOI BibTeX

Wang Q, Zhang X, Chen S, Zhang X et al. (2011) **Prevention of motor neuron degeneration by novel iron chelators in SOD1(G93A) transgenic mice of amyotrophic lateral sclerosis.** Neurodegener Dis. 8(5), 310-21. doi: 10.1159/000323469. http://www.ncbi.nlm.nih.gov/pubmed/21346313
**CONCLUSIONS: These results provide evidence that iron is involved in the pathogenesis of ALS and iron chelation therapy may have the potential for the prevention and treatment of ALS.**

Rouault TA (2013) **Iron metabolism in the CNS: implications for neurodegenerative diseases.** Nature Reviews Neuroscience 14, 551–564 doi:10.1038/nrn3453
https://www.nature.com/articles/nrn3453

Deng HX, Chen W et al. (2011) **Mutations in UBQLN2 cause dominant X-linked juvenile and adult-onset ALS and ALS/dementia**. In: Nature. doi:10.1038/nature10353
**„Here we show that mutations in UBQLN2, which encodes the ubiquitin-like protein ubiquilin 2, cause dominantly inherited, chromosome-X-linked ALS and ALS/dementia. We describe novel ubiquilin 2 pathology in the spinal cords of ALS cases and in the brains of ALS/dementia cases with or without UBQLN2 mutations. Ubiquilin 2 is a member of the ubiquilin family, which regulates the degradation of ubiquitinated proteins. Functional analysis showed that mutations in UBQLN2 lead to an impairment of protein degradation. Therefore, our findings link abnormalities in ubiquilin 2 to defects in the protein degradation pathway, abnormal protein aggregation and neurodegeneration, indicating a common pathogenic mechanism that can be exploited for therapeutic intervention.“**

**Dr David Martz - 2011 IDA Research Award** https://www.youtube.com/watch?v=UY9FdULDV6M

Veyrat-Durebex C, Corcia P, Mucha A (2014) Research Article. **Iron Metabolism Disturbance in a French Cohort of ALS Patients.** BioMed Research International. Volume 2014 (2014), Article ID 485723, 6 pages. http://dx.doi.org/10.1155/2014/485723 http://www.hindawi.com/journals/bmri/2014/485723/
**„Conclusion. This is the first study showing a higher concentration of serum iron in ALS patients, strengthening the involvement of a deregulation of iron metabolism in ALS“.**

Ahmet Z Burakgazi AZ (2014) **Lyme Disease -Induced Polyradiculopathy Mimicking Amyotrophic Lateral Sclerosis.**. The International journal of neuroscience. Abstract URL, DOI BibTeX

NIH **Amyotrophic Lateral Sclerosis (ALS) Publications** (2014)
http://www.ninds.nih.gov/disorders/amyotrophiclateralsclerosis/pubs_ALS.htm

**MMWR** (2014) Prevalence of Amyotrophic Lateral Sclerosis — United States, 2010–2011. Surveillance Summaries / Vol. 63 / No. 7 ISSN: 1546-0738
http://www.cdc.gov/mmwr/pdf/ss/ss6307.pdf

Chio A, Calvo A, Dossena M, Ghiglione P, Mutani R, Mora G (2009) **ALS in Italian professional soccer players: the risk is still present and could be soccer-specific.** Amyotroph Lateral Scler. 10(4):205-9. doi: 10.1080/17482960902721634.
https://www.ncbi.nlm.nih.gov/pubmed/19267274
**« The absence of ALS cases in professional road cyclists and basketball players indicates that ALS is not related to physical activity per se. »**

Alonso R, Pisa D, Fernández-Fernández AM (2017) **Fungal infection in neural tissue of patients with amyotrophic lateral sclerosis.** Neurobiol Dis. 108, 249-260. doi: 10.1016/j.nbd.2017.09.001. Epub 2017 Sep 6. https://www.ncbi.nlm.nih.gov/pubmed/28888971
**„Overall, our present observations provide strong evidence for mixed fungal infections in ALS patients. The exact mixed infection varies from patient to patient consistent with the different evolution and severity of symptoms in each ALS patient.“**

- ➔ **Elektrolyte und Spurenelemente** http://www.xerlebnishaft.de/elektro_spur_ph.pdf
- ➔ **Wasserstoffionenkonzentration, PH-Wert** http://www.kabilahsystems.de/ph.pdf

- ➔ **Mitochondrien Dysfunktion etc.** http://www.xerlebnishaft.de/mitochondrien.pdf, **Mitochondrien Therapie** http://www.kabilahsystems.de/q10_und_l.pdf
- ➔ **Zytoskelett-Krankheiten** http://www.xerlebnishaft.de/zytoskelett.pdf
- ➔ **Fettsäuren (Zellmembran)** http://www.kabilahsystems.de/ungesaettfetts.pdf
- ➔ **Biogene Amine und Peptide** http://www.kabilahsystems.de/biogeneamineundpeptide.pdf
- ➔ **Zytokine, zelluläre Abwehr** http://www.xerlebnishaft.de/kommentinhalt_zell.pdf

- ➔ **Antimikrobiose** http://www.kabilahsystems.de/antibiosetherapieplan.pdf
- ➔ **Begleit-Therapien** http://www.kabilahsystems.de/kommentmedbegleittherapie.pdf
- ➔ **Antibiotikatherapie Spektrum** www.kabilahsystems.de/therap_01_basis.pdf

Vaulont S, Lou DQ, Viatte L, Kahn A (2005) **Of mice and men: the iron age.** J. Clin. Invest. 115(8), 2079–2082, doi:10.1172/JCI25642, PMID 16075054, PMC 1180554
https://www.ncbi.nlm.nih.gov/pubmed/16075054
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1180554/

**Eisen-Toxizitaet sei bei ca. 30% der ALS – Patienten nachweisbar;**
**Iron toxicity is seen at about 30% of ALS – patients;**

**Diagnostik: Klinik, Ferritin, Transferrin, Serumeisen.**
**Diagnose: Clinic, Ferritine, Transferrin, Serum iron.**

**Therapie: Aderlass, Chelattherapie mit Deferasirox** (oral, einmal täglich)
**Therapy: Bloodletting, chelation with deferasirox** (orally once daily) oder/or
Deferipron (cave Neutropenie oder Agranulozytose), oder Deferoxamin als Infusion

**„Sehr aufwändig für die Erkrankten: So müssen diese in der Regel an fünf bis sieben Tagen pro Woche eine acht- bis zwölfstündige Infusion in das Unterhautfettgewebe erhalten. Da die Eisenchelat-Therapie über viele Jahre verläuft, war die Therapietreue in der Vergangenheit häufig entsprechend schlecht - zum Teil mit ernsthaften gesundheitlichen Folgen“.**
**"Very consuming for the patients: these must usually five to seven days per week an eight- to twelve-hour infusion received in the subcutaneous fatty tissue. Since the iron chelate Therapy extends over many years, treatment adherence was often in the past correspondingly poor - some with serious health consequences."**

Dexter DT, Carayon A, Javoy-Agid F et al. (1991) **Alterations in the levels of iron, ferritin and other trace metals in Parkinson´s disease and other neurodegenerative diseases affecting the basal ganglia**. Brain 114, 1935-75

Mastroberardino PG, Hoffman EK, Horowitz MP et al. (2009) **A novel transferrin/TfR2-mediated mitochondrial iron transport system is disrupted in Parkinson's disease.** Neurobiol. Dis. 34(3), 417–431, doi:10.1016/j.nbd.2009.02.009, PMID 19250966, PMC 2784936
https://www.ncbi.nlm.nih.gov/pubmed/19250966

- ➔ **Parkinson, Alzheimer** http://www.erlebnishaft.de/alzheimerspirochaetosis.pdf

- ➔ Miller Al (2017) **Lyme Disease.** https://www.youtube.com/watch?v=Fr61GV8JCYQ

Bernt - Dieter Huismans Letzte Revision Februar 2018 www.Huismans.click 
Back to top: http://www.xerlebnishaft.de/als.pdf