Auf dem Weg zu einer Impfung gegen Alzheimer?





Prof. Dr. med. Christoph Hock, Öffentlicher Vortrag, PUK, 23.09.2010

Erfolgreiches Altern oder Demenz?



Jeanne Calment 1875 - 1997

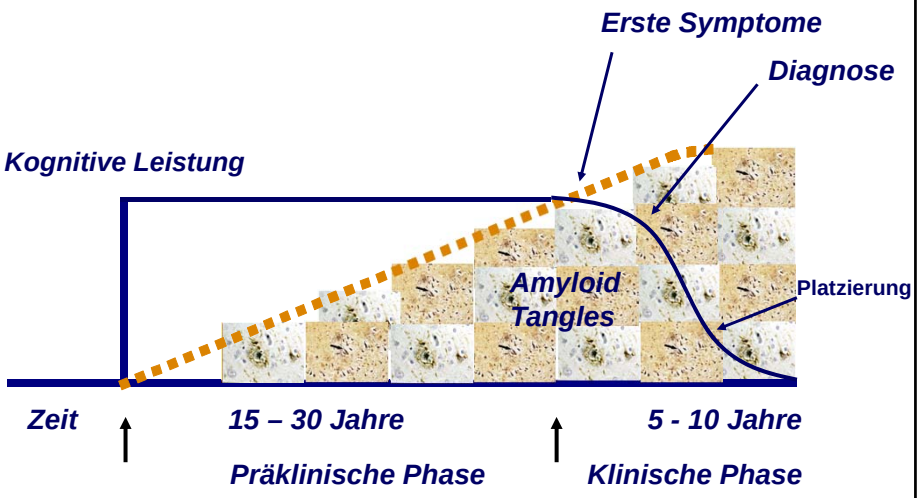
Jeanne Calment starb 1997 in Arles im Alter von 122 Jahren. Sie fing mit 85 J. das Fechten an und fuhr noch als 100-Jährige Fahrrad. Bis zum Alter von 110 J. lebte sie alleine, erst 1985 zog sie in ein Altersheim.



Auguste Deter 1850 - 1906

Auguste Deter starb 1906 im Alter von 55 Jahren an Demenz.

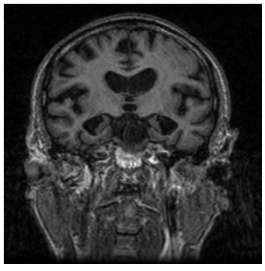
Verlauf der Alzheimer-Krankheit



Klinischer Verlauf und Symptomatik der Alzheimer-Krankheit

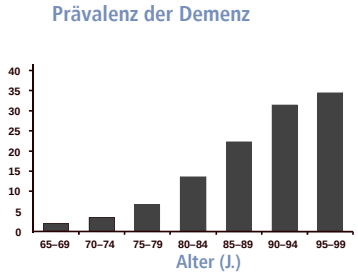
- 3 Stadien zunehmenden Schweregrades
- Progredienter Verlauf bis zum Tod





Die sozioökonomische Dimension der Alzheimer-Krankheit

- Häufigste Hirnerkrankung
- 15 Mio. Patienten weltweit, 4% Wachstum/Jahr
- >20%Prävalenz bei 85-jährigen
- Jährliche Kosten von über $250 Milliarden
- Keine kurativen Behandlungsmöglichkeiten

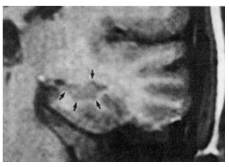


Neuroimaging

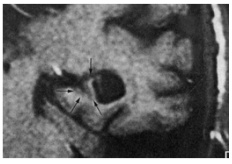
MRI



Normal

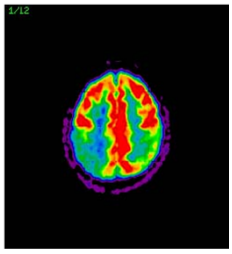


AD

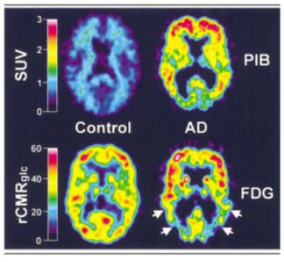


PET

FDG

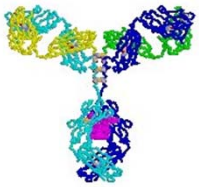


[^{11}C]PIB



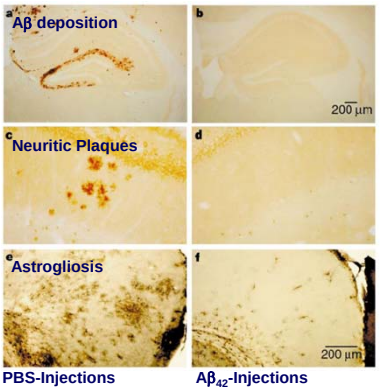
Klunk et al., Ann Neurol 2005

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Jonas Edward Salk (1914 – 1995)
1953 vaccination against polio



Schenk et al., Nature 1999

PBS-Injections $A\beta_{42}$-Injections

Transgenic mouse models for Alzheimer's disease





Normal

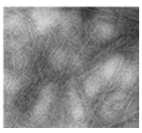


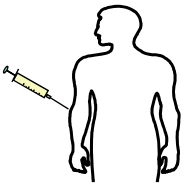
Impairment

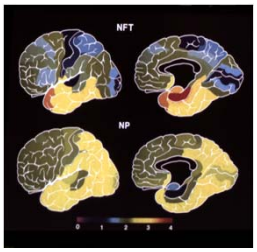


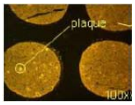
Aktive Immunisierung

vaccination against therapeutic target





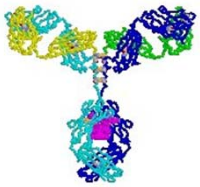




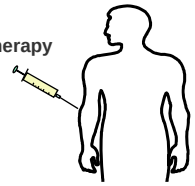
BBB

polyclonal B-cell response

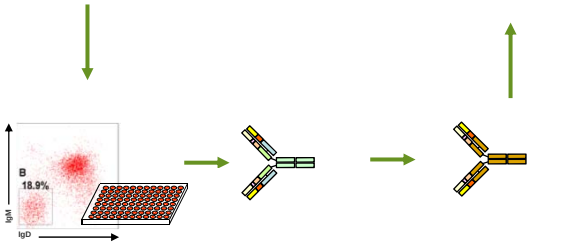
Passive Immunisierung







- **Murine (hybridoma)**
- **Chimeric (murine variable regions/human constant regions, 65% human)**
- **Humanised (grafting murine hypervariable amino acid domains into human antibodies; 95% human)**
- **„Human“ (tg Ig mice, phage display libraries)**



cloning and expression “humanization”

Immuntherapien in der klinischen Entwicklung – Passive Immunisierung

Antibody	Company	Phase	Epitope	Patients / trials	Duration / dosing	estimated completion
Bapineuzumab	Pfizer/JANSSEN	Phase III	Aβ N-term	>6000 / 9 trials ApoEε4 +/-	78 w - 2.5 yr 0.15-1 mg/kg q13w	April 2011 June 2012 February 2014
Solanezumab	Eli Lilly	Phase III	Aβ mid domain	2000 / 2 trials	80 w 400 mg q4w	September 2012
Gammaguard 10%	Baxter	Phase III	polyclonal IgG	360	70 w 200-400mg/kg q2w	July 2011
Bapineuzumab	Pfizer/JANSSEN	Phase II	Aβ N-terminus	240 / 2 trials	6-12 m 5-20 mg 1qw SC	March 2010 / November 2011
PF04360365	Pfizer	Phase II	Aβ C-terminus	175	18m 0.1-8.5mg/kg q60d	November 2011
Octagam 10%	Octapharma	Phase II	polyclonal IgG	56	24 w 0.1-0.8g/kg q2/4w	September 2009
PF04360365	Pfizer	Phase II brain amyloid	Aβ C-terminus	36	1 yr 7.5-10mg/kg q30/90d	June 2011
PF04360365	Pfizer	Phase I CSF Aβ clearance	Aβ C-terminus	18	36 h 10mg/kg single dose	January 2011
GSK933776A	GlaxoSmithKline	Phase I	Aβ	122	52w	August 2010
MABT5102A	Genentech	Phase I	Aβ conformational	72 / 2 trials	single and multiple dose; SC, IV	May 2010
Gantenerumab	Roche	Phase I	combined Aβ N-term + mid	60	3-12 m	May 2009

NIH ClinicalTrials.gov

Immuntherapien in der klinischen Entwicklung – Aktive Immunisierung

Vaccine	Company	Phase	Epitope	Patients / trials	Duration / dosing	estimated completion
ACC-001	Pfizer/JANSSEN	Phase II	Aβ N-term conj. +/- QS-21	580 / 6 trials	24 m 3-30ug +/- QS-21 d1, m1,3,6,12	November 2011 - July 2014
CAD106	Novartis	Phase II	Aβ N-term-Qβ	57 / 2 trials	repeated SC	January 2010 April 2012
V950	Merck	Phase I	Aβ N-term +/-iscromatrix	124	4 yr 0.5-94ug +/- iscromatrix	October 2014
AD01	GlaxoSmithKline	Phase Ib	Aβ N-term mimetic	24	1yr + 1yr follow-up 4xSC q4w	November 2009
AD02	GlaxoSmithKline	Phase Ib	Aβ N-term mimetic	24	1yr 1 1yr follow-up 4xSC q4w	April 2010
UB311	United Biomedical	Phase I	Aβ1-14UBITh	18	28-30 w 3 doses 0,4,12 w	December 2010

NIH ClinicalTrials.gov

Kontakt





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