



GUARD: Groningen Unit for Amyloidosis Research & Development

Opening Symposium
Amyloidosis Center Heidelberg
Saturday 2 May 2009

UMC Groningen - Department of Rheumatology and Clinical Immunology



Amyloid: "starch-like"

Rudolf Virchow (1821 - 1902)

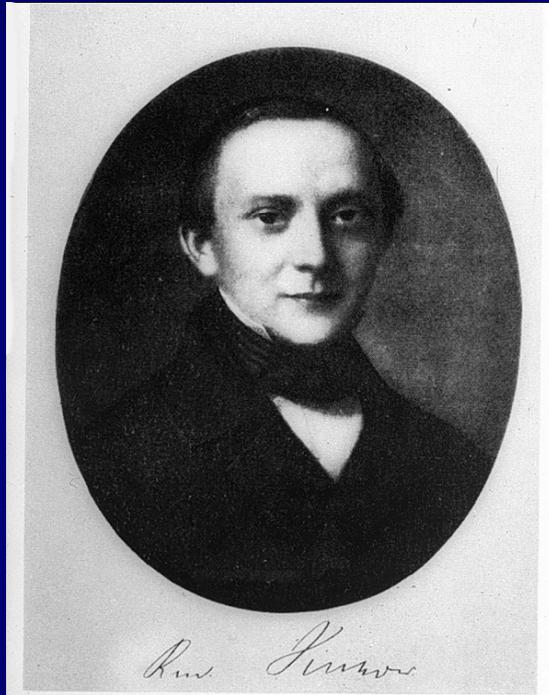
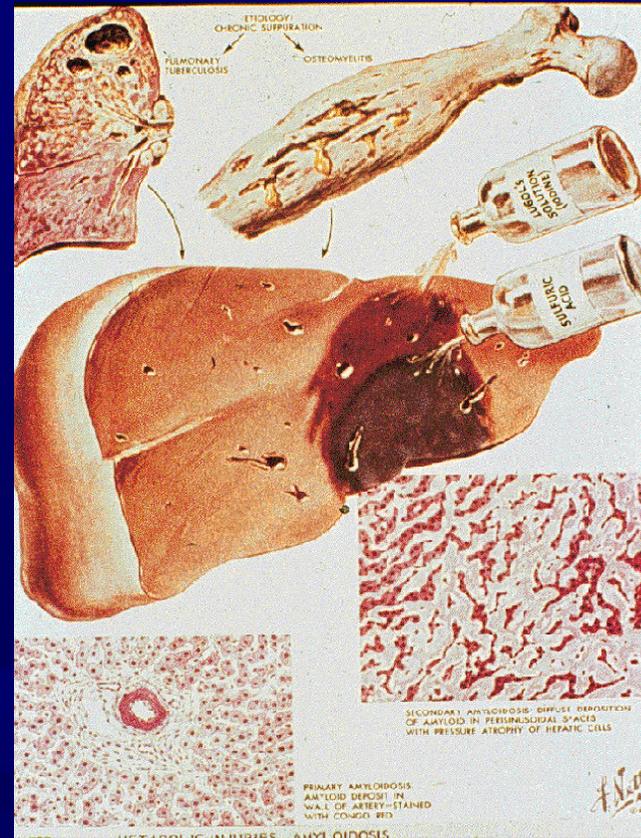


FIGURE 1. Rudolf Virchow (1821-1902) at the age of approximately thirty, when, already world famous, he began to be interested in "amyloid." We could compare Virchow with Columbus, who headed for India and found America. Virchow searched for starch in the human body and discovered an immense field of pathology, the extension, richness and importance of which we have just begun to comprehend.



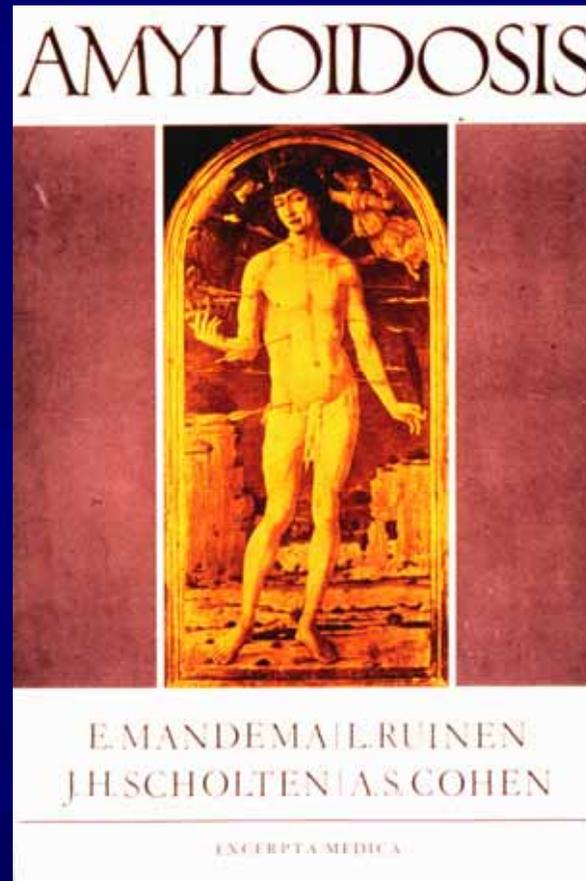
1st International Symposium on Amyloidosis

Groningen

1967

Enno Mandema
Luuk Ruinen

Jan Scholten
Alan Cohen



Participants 1st Symposium

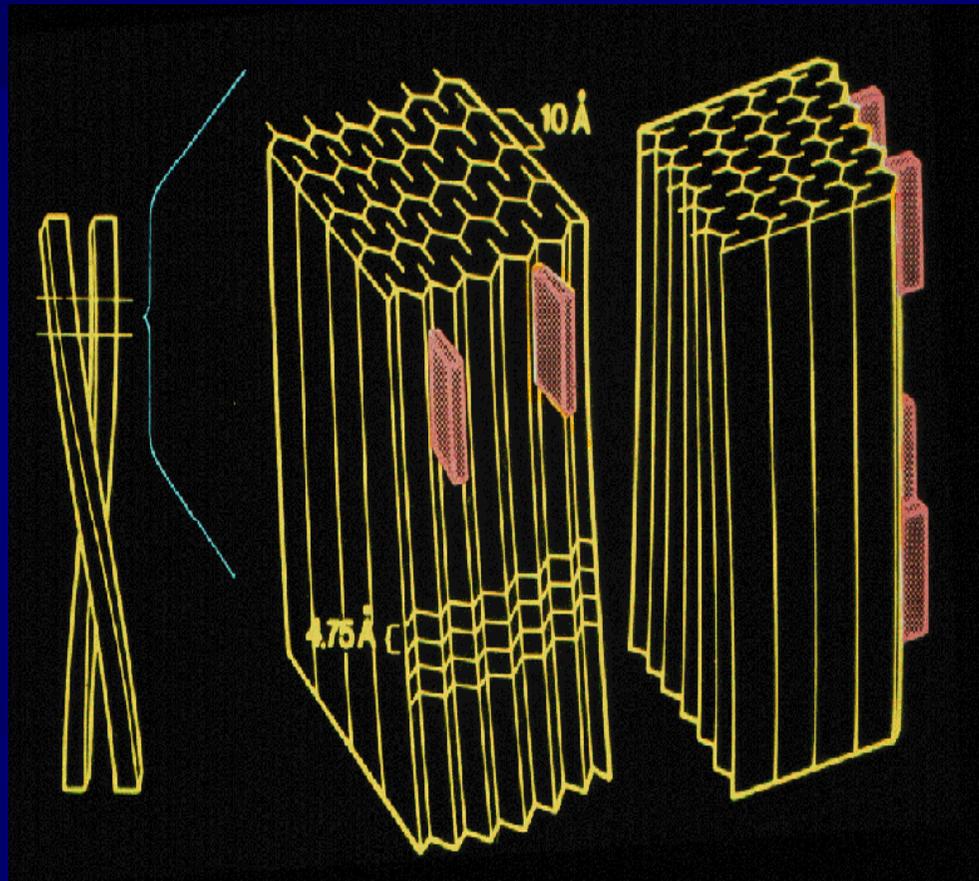


Standing, left to right: Dr. van Bruggen, Dr. Arends, Dr. Molenaar, Dr. Vazquez, Dr. Querido, Dr. Schleyer, Dr. Hoedemacker, Dr. Cohen, Dr. Sorenson, Dr. Arisz, Dr. Pirani, Dr. Benditt, Dr. Calkins, Dr. Gruber, Dr. Gueft, Dr. Janigan, Dr. Nieuwenhuis, Dr. Zschiesche, Dr. Cathcart, Dr. Schmitz-Moormann, Dr. van den Broek, Dr. Glenner, Miss Braam, Dr. Ranløv, Dr. Catchpole, Miss Braaksmā, Dr. Schultz, Miss Zondervan, Mr. Folkerts, Dr. Lehner, Technical Assistant, Dr. Kennedy, Dr. Cessi, Dr. Kark, Technical Assistant, Dr. Pick, Technical Assistant, Dr. Muir, Mrs. Cessi, Mr. Goldberg, Dr. Bywaters, Mr. Smit, Dr. Ben Shaul, Mr. Ferwerda.

Sitting, left to right: Mrs. Lehner, Mrs. Schultz, Mrs. Muckle, Dr. Schwartz, Mrs. Missmahl, Dr. Letterer, Mrs. Ranløv, Dr. Missmahl, Mrs. Janigan, Dr. Andrade, Dr. Ruinen, Dr. Battaglia, Dr. Mandema, Dr. Scholten, Mrs. Christensen, Dr. Muckle, Master Vagn Ewald Christensen, Miss Paola Cessi, Dr. Christensen, Dr. Teilum.



Amyloid: structure of the fibril



San Sebastian looks a bit ill: Secretion of fibrils?



GUARD 1st period: 1968-1988

★ Histology:

- ★ Congo red +/- permanganate
- ★ Immunohistology

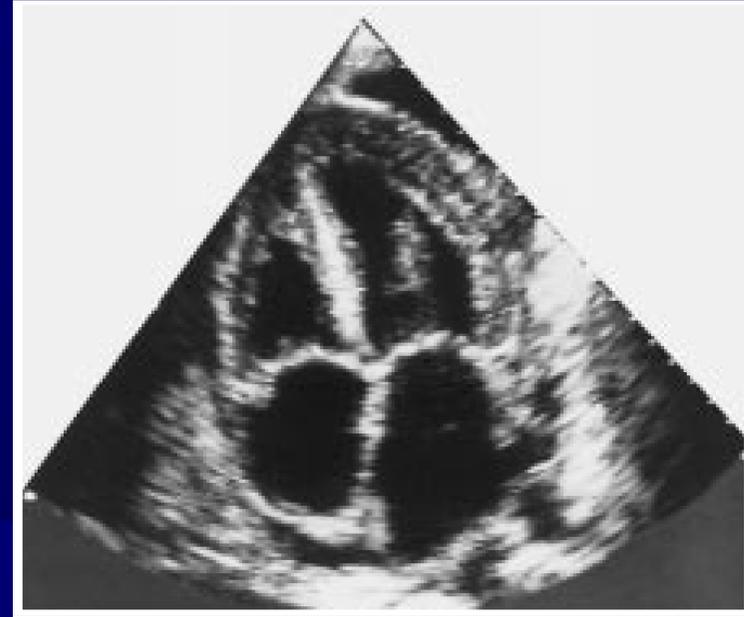
★ Techniques: Echo(cardio)graphy

★ Lab:

- ★ Serum amyloid A protein
 - ★ Immunofix on concentrated urine
 - ★ Immunophenotyping of plasma cells
- ## ★ DMSO treatment for AA amyloidosis
- ## ★ Survival analysis

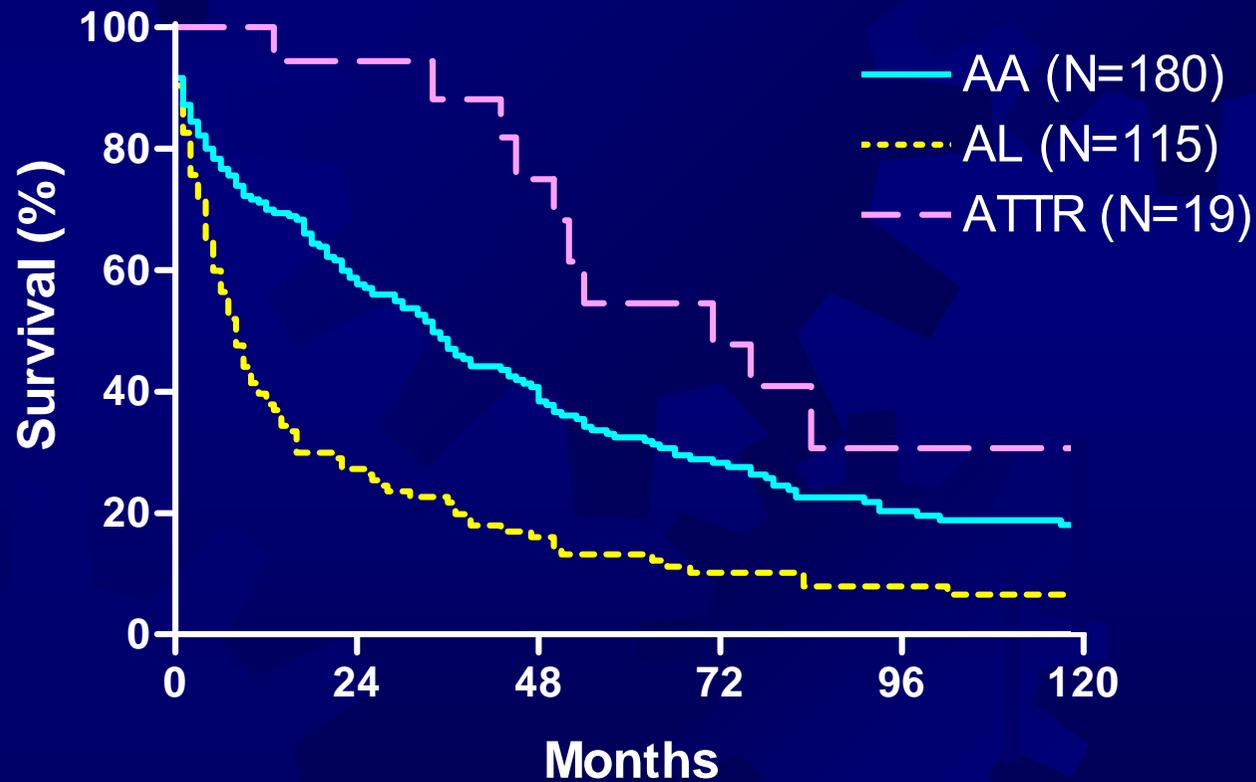


Example of an echocardiogram

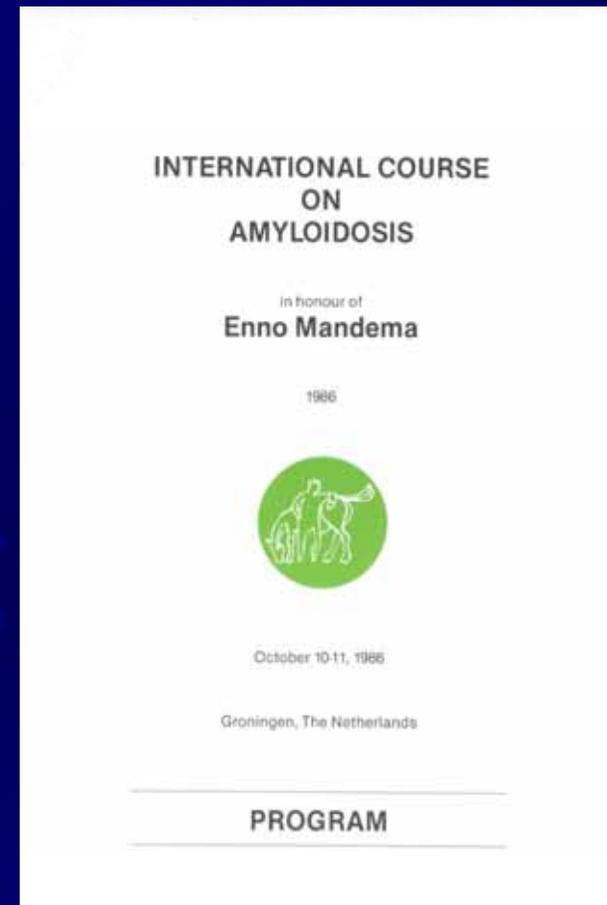
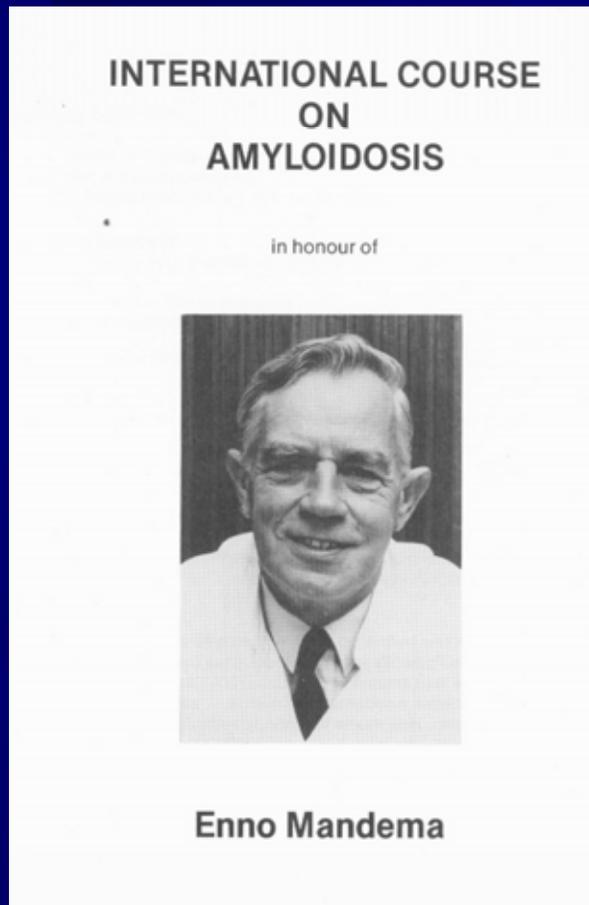


Survival in amyloidosis

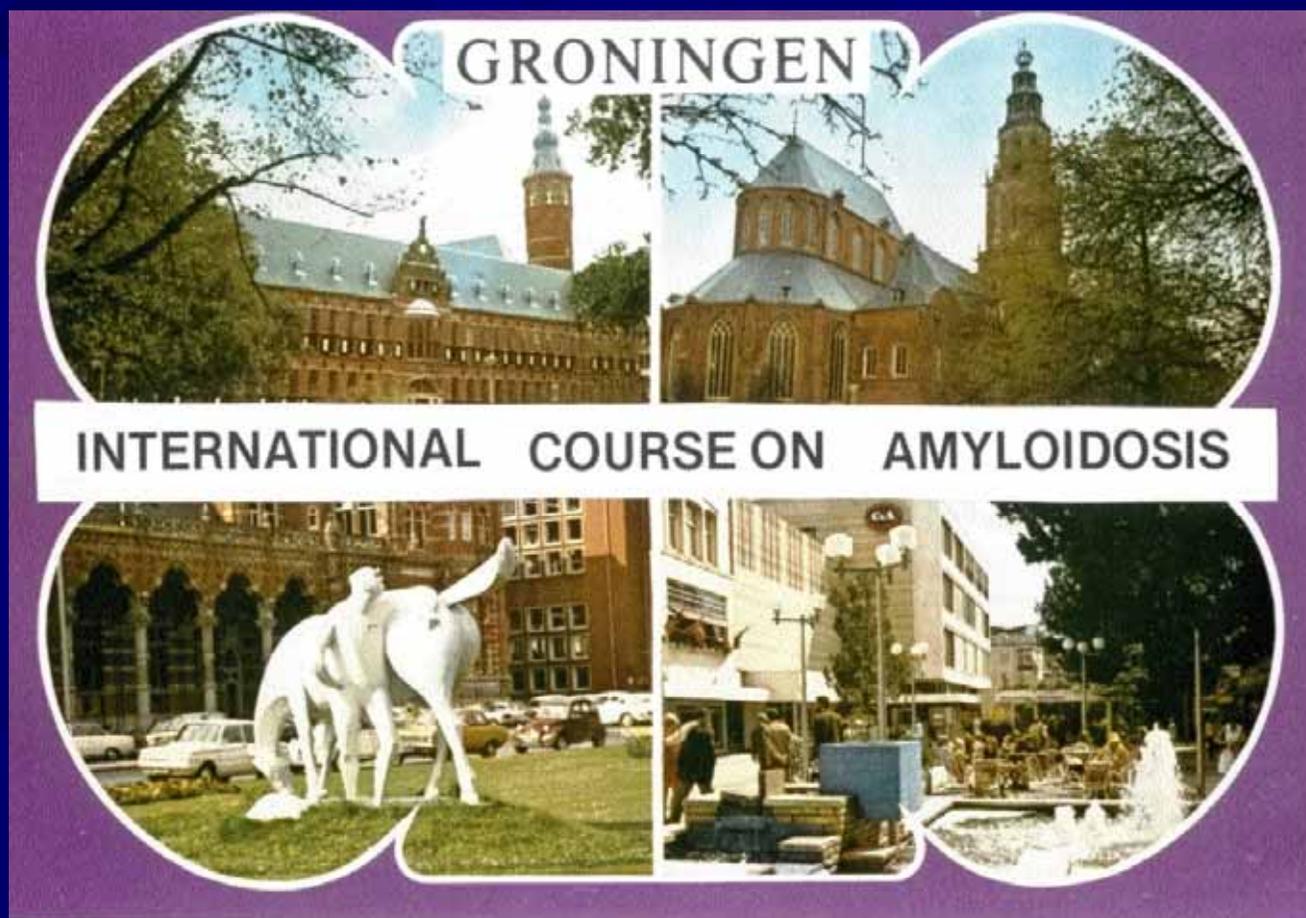
Systemic amyloidosis



1986 International course on amyloidosis



1986 International course on amyloidosis



GUARD 2nd period: 1988-2008

✿ Histology:

- ✿ Fat aspirate Congo red and immunochemistry
- ✿ Fat aspirate quantification

✿ Techniques:

- ✿ SAP scintigraphy and turnover
- ✿ Autonomic neuropathy

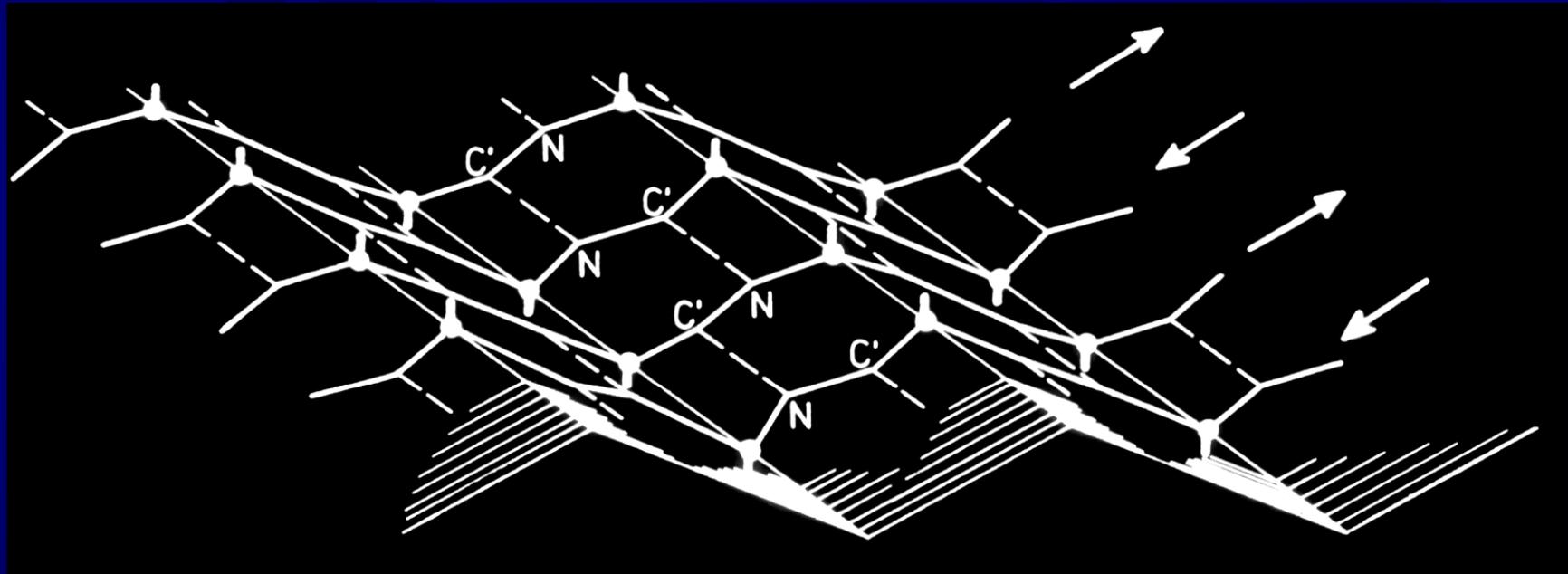
✿ Lab: Free light chains in serum, NT-proBNP

✿ Therapy:

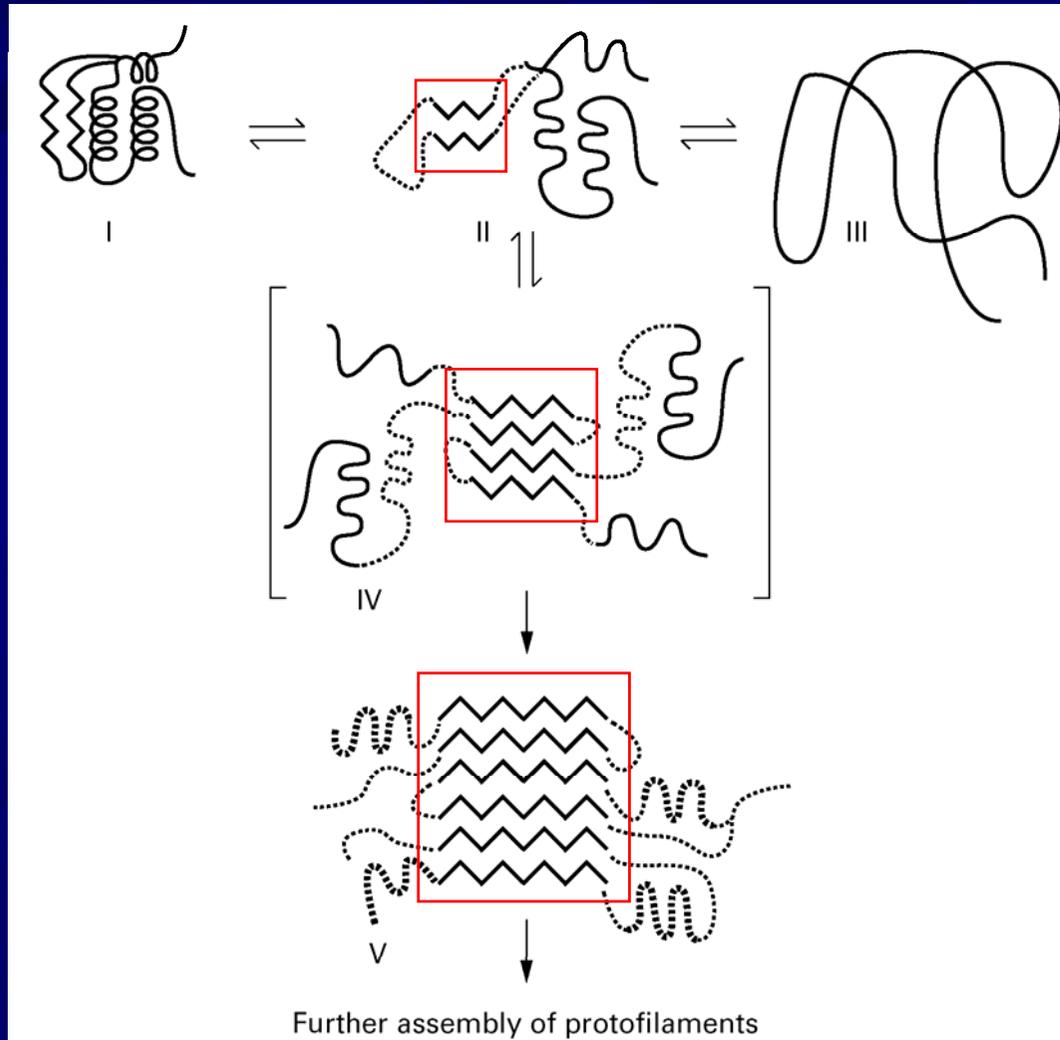
- ✿ AA eprodisate
- ✿ AL Autologous stem cell Tx
- ✿ ATTR liver Tx



Amyloid: β -pleated structure



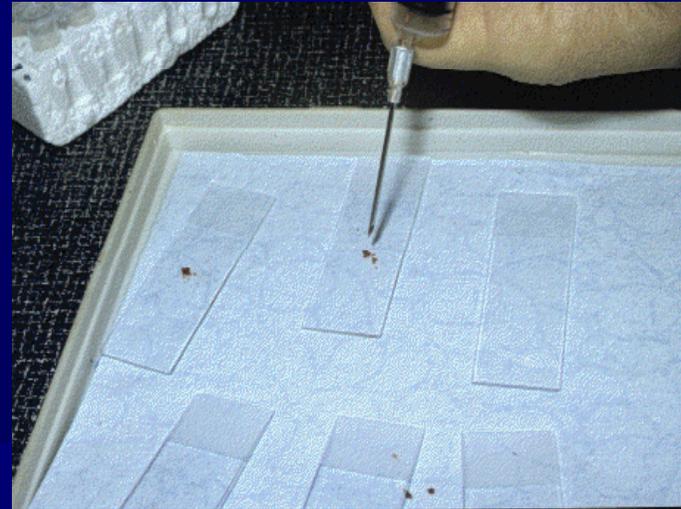
Amyloid: β -pleated structure



Gillmore, Thorax 1999



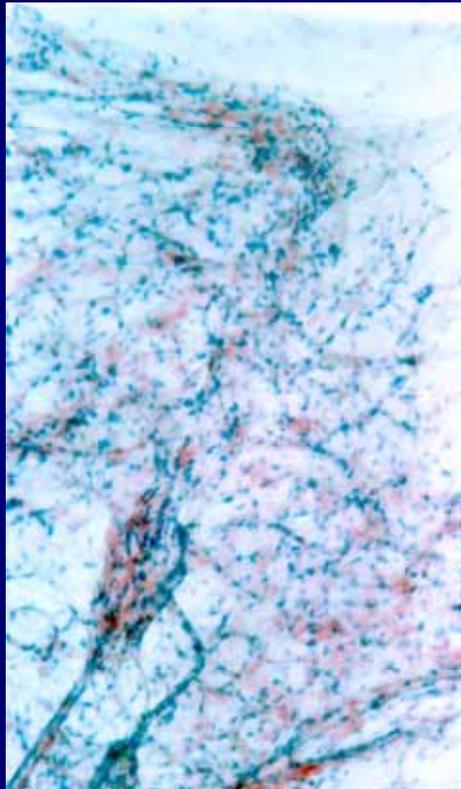
Fat aspiration procedure



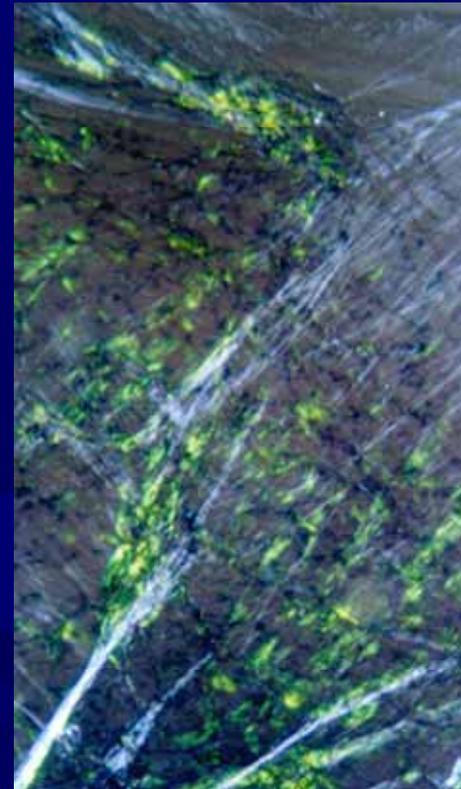
Simple technique



Congo red stained fat tissue



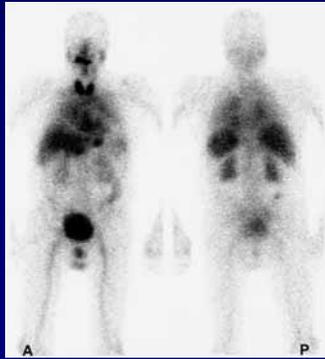
Normal light



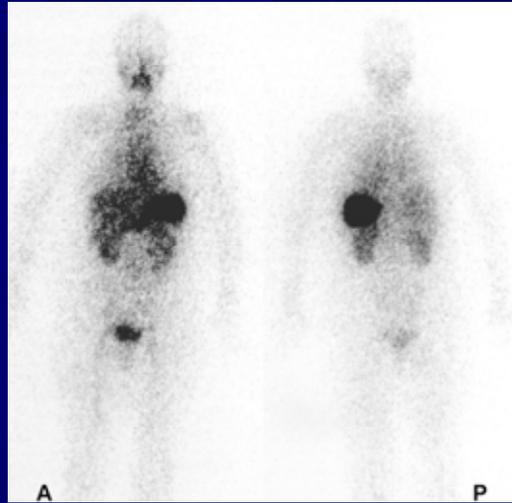
Polarised light



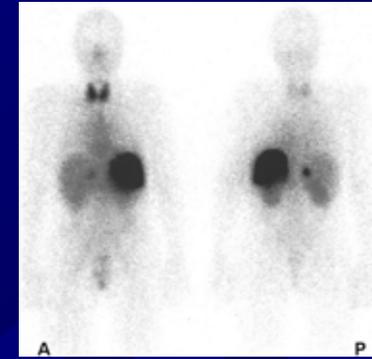
Patterns of tracer localisation: AA



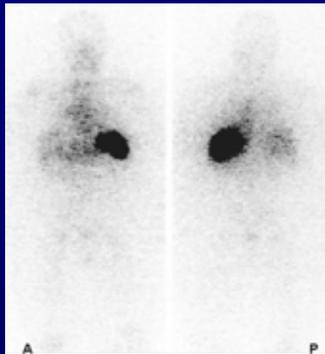
Kidney 3%



Kidney and spleen 35%

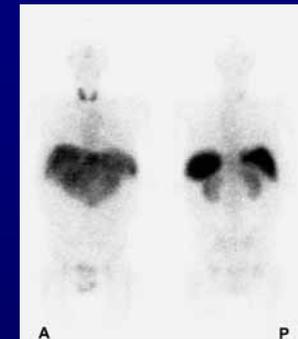


Kidney, spleen, and adrenal glands 20%



Spleen 23%

5 patterns related to spleen and kidney



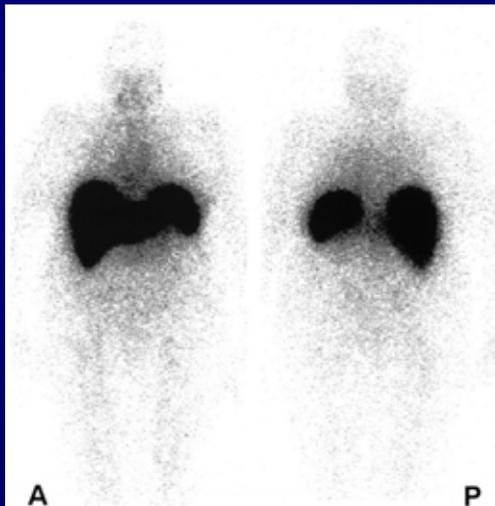
Kidney, spleen, and liver 8%



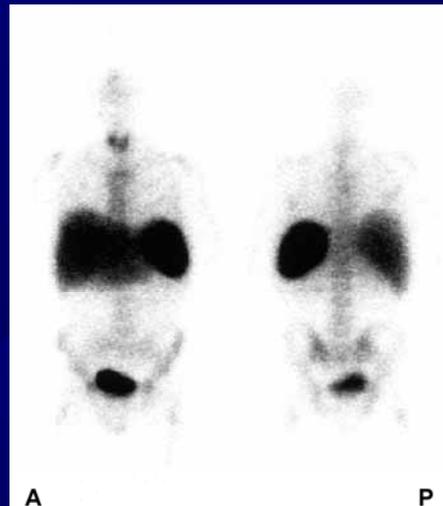
Patterns of tracer localisation: AL

Very **diverse** patterns of uptake

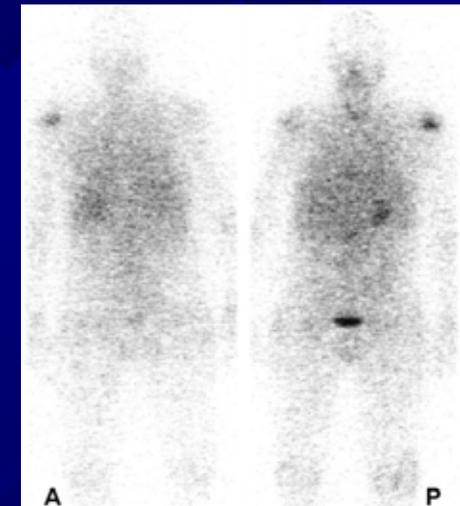
★ AA-type alike 38%; others such as:



Spleen and liver 20%



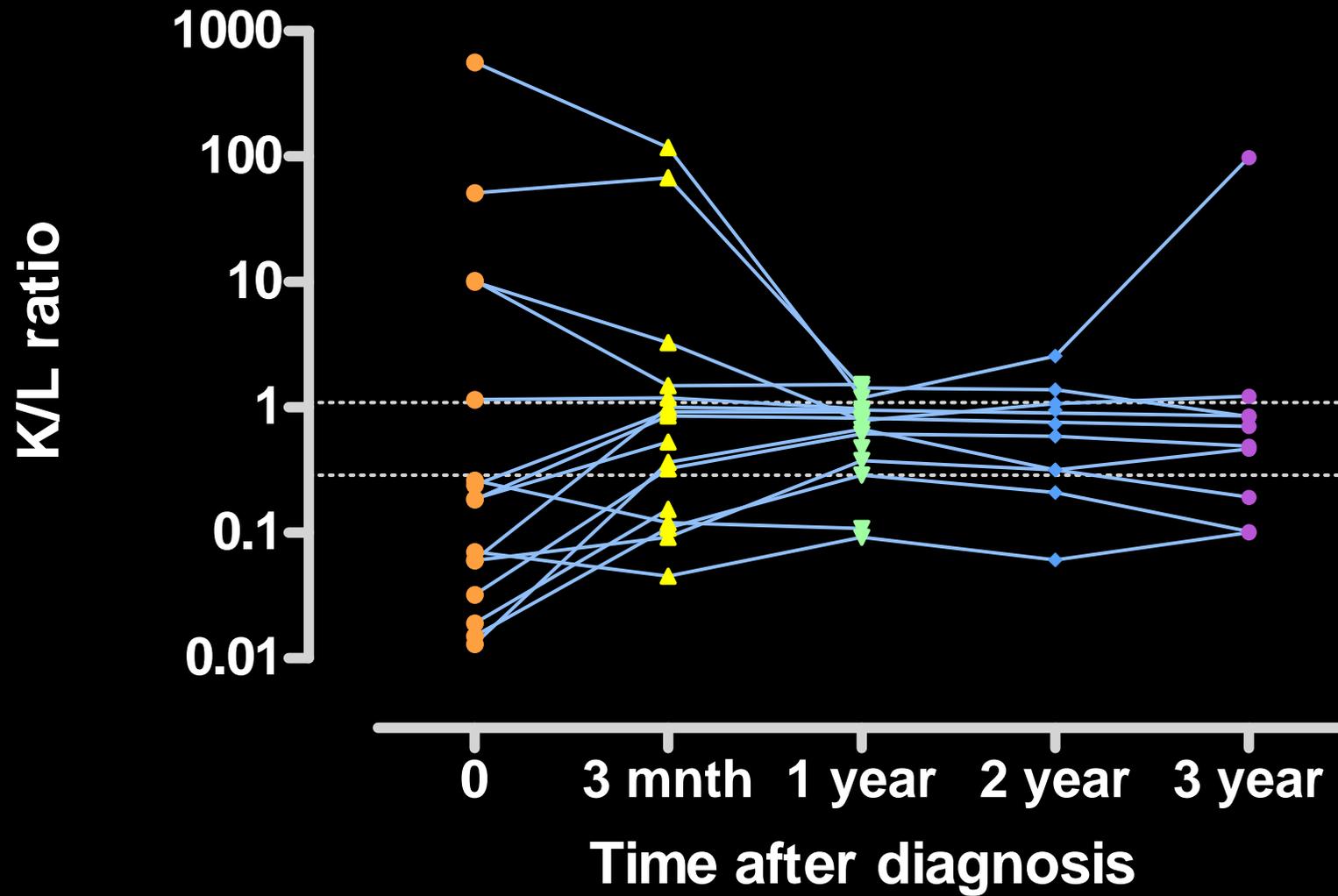
Spleen, liver, and
bone marrow 10%



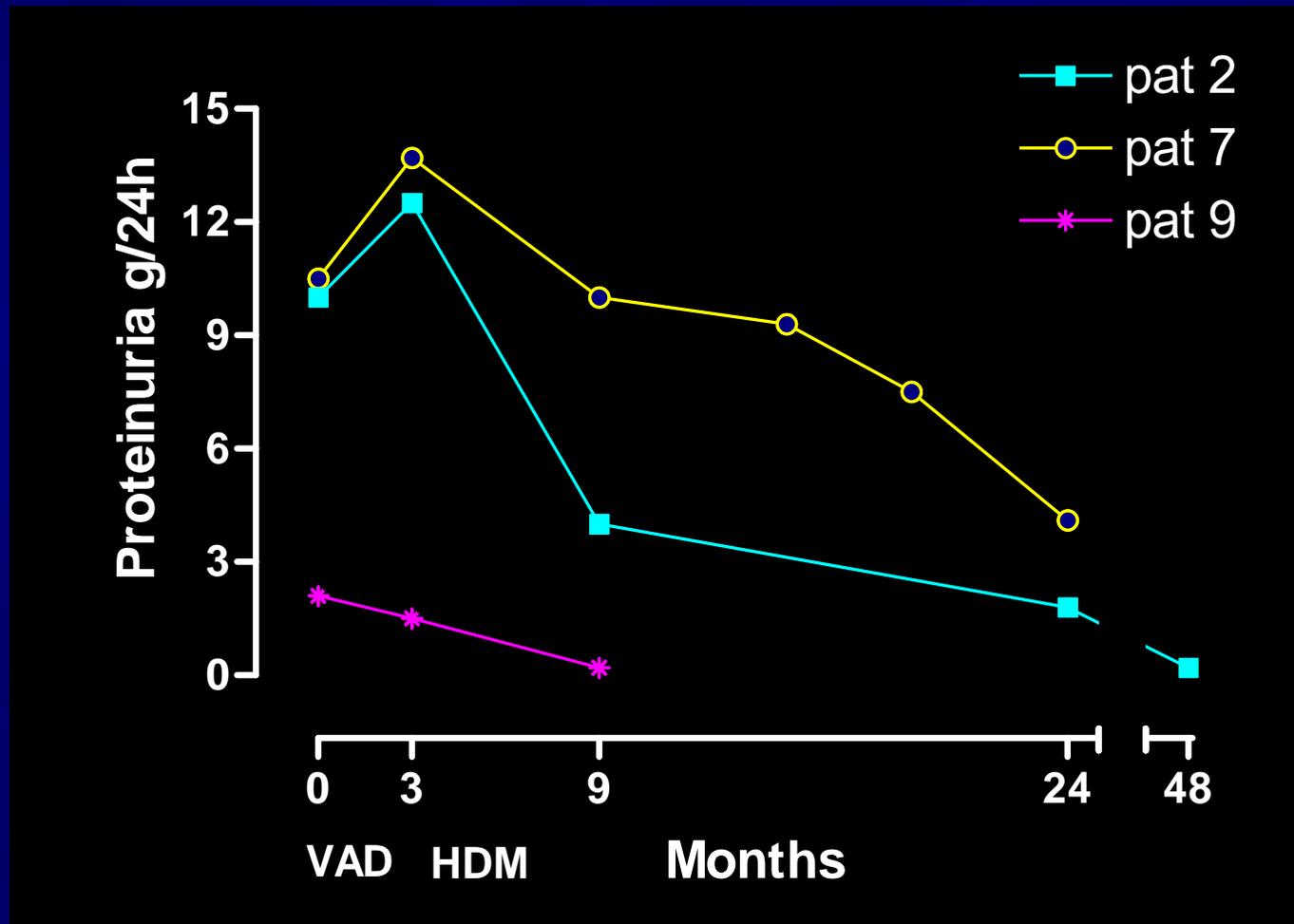
Joints only 8%



K/L ratio



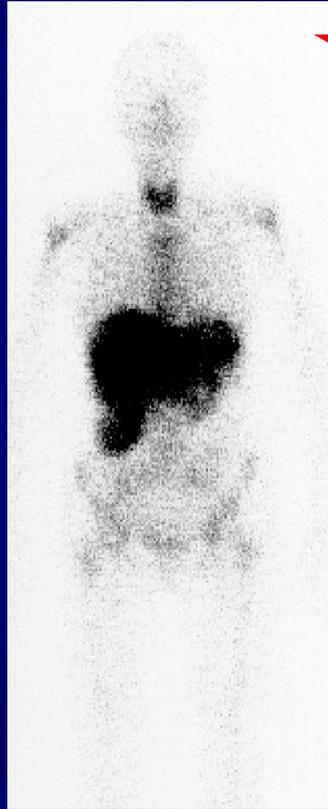
AL amyloidosis: effect of chemotherapy on proteinuria



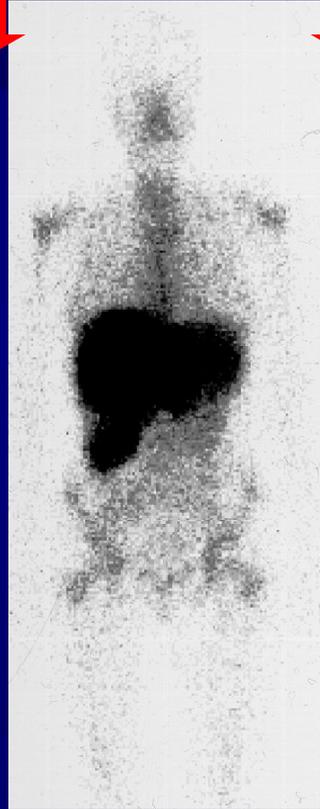
AL: effect of chemotherapy

3 x VAD

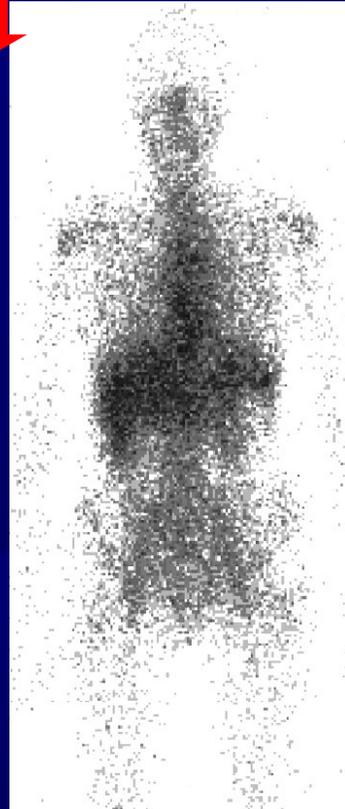
HDM + ASCT



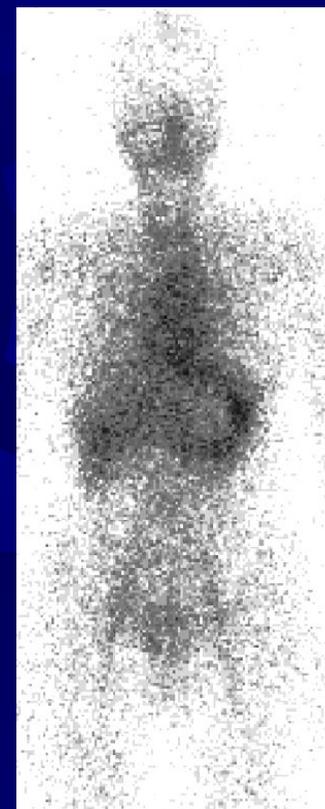
Start



4 months



1 year



2 years



3 years

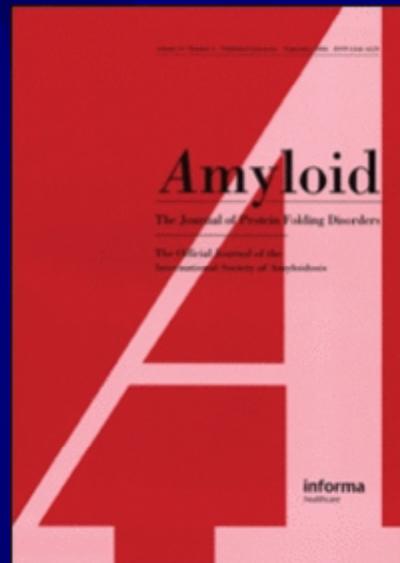


Developments 1967 - 2009

- Amyloid structure and pathogenesis
- Detection of amyloid
- Diagnosis of systemic disease
- Exact classification and detection of underlying process
- Thoughtful clinical evaluation of amyloidosis
- Therapy directed against precursor production
- Systematic monitoring of organ disease and precursor production during follow-up



1994: Amyloid Journal



Editor in Chief : Alan Cohen



2004: International Society of Amyloidosis



2006: EURAMY consortium



Systemic Amyloidoses in Europe
EU founded project



1st EURAMY meeting in
Uppsala 14-15 December 2006

UMC Groningen - Department of Rheumatology and Clinical Immunology



EURAMY: meetings

1. Uppsala, 13-15 December 2006: **Start**
2. Rome, 20-22 September 2007
3. Berlin, 15-16 February 2008
4. Paris, 13-14th May 2008: **Midterm**
5. Porto, 17-18 October 2008
6. Amsterdam, 3-4 April 2009
7. Uppsala, 22-23 October 2009: **End**



Groningen: Current focus

- Basic research
 - Proteomics of fat tissue
 - Amyloidogenesis in vitro studies
- National collaboration
- European collaboration
 - Continuation of the EURAMY consortium
 - European Network of amyloid centres of excellence for:
 - Laboratory and histological diagnosis
 - Basic research on amyloidogenesis
 - Translational research
 - Therapy protocols and phase I and II trials
- International collaboration in randomised clinical trails for AL, ATTR, and AA



Current Groningen group



UMC Groningen - Department of Rheumatology and Clinical Immunology



European collaboration has not always been smooth and easy ...



But it is certainly possible!



Sjögren's Syndrome and Localized Nodular Cutaneous Amyloidosis

Coincidence or a Distinct Clinical Entity?

Jiska M. Meijer,¹ Stefan O. Schonland,² Giovanni Palladini,³ Giampaolo Merlini,³
Ute Hegenbart,² Olga Ciocca,³ Vittorio Perfetti,³ Martha K. Leijmsma,¹
Hendrika Bootsma,¹ and Bouke P. C. Hazenberg¹



Good luck Heidelberg!



Groningen



Heidelberg

