# Inclusion body myositis

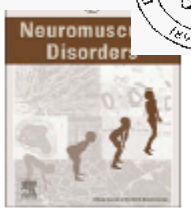
**Prof. Benedikt Schoser**
Friedrich-Baur-Institute
Department of Neurology
Ludwig-Maximilians-University
Munich Germany

Neuromuscular Disorders 20 (2010) 142–147

Contents lists available at ScienceDirect

Neuromuscular Disorders

journal homepage: www.elsevier.com/locate/nmd



Workshop report

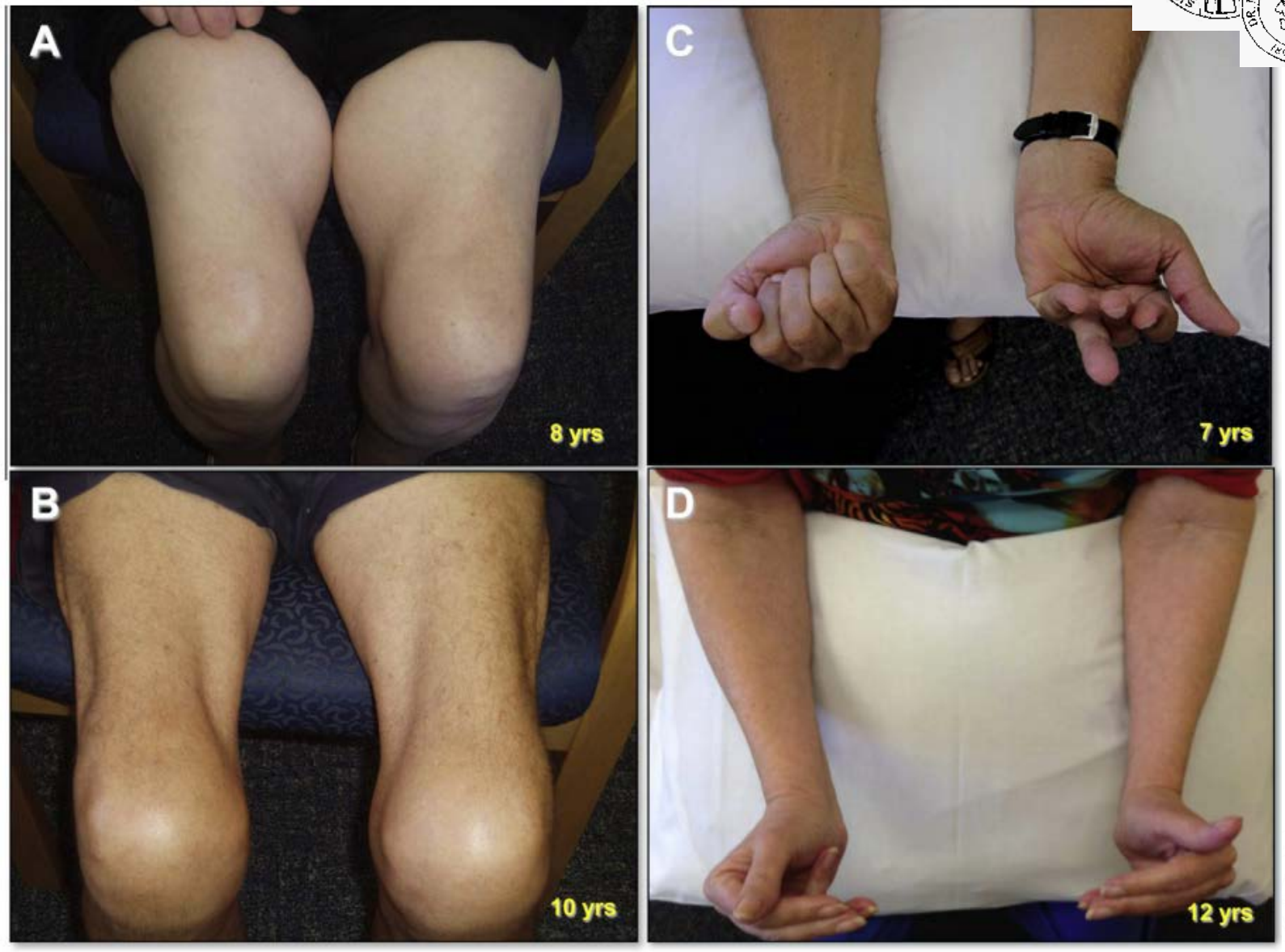
# Inclusion body myositis
## MRC Centre for Neuromuscular Diseases, IBM workshop, London, 13 June 2008

D. Hilton-Jones [a,b], A. Miller [b], M. Parton [b], J. Holton [b], C. Sewry [c], M.G. Hanna [b,*]

[a] Oxford MDC Muscle and Nerve Centre, West Wing, John Radcliffe Hospital, Oxford, UK
[b] MRC Centre for Neuromuscular Disease, UCL Institute of Neurology, Queen Square, London WC1N3BG, UK
[c] MRC Centre for Neuromuscular Disease, UCL Institute of Child Health and Dubowitz Neuromuscular Centre, Great Ormond Street Hospital, London, UK

- Late-onset progressive myopathy
- 80% <50 years
- >60% male
- proximal and distal muscle weakness
- muscle atrophy of quadriceps femoris and finger flexors

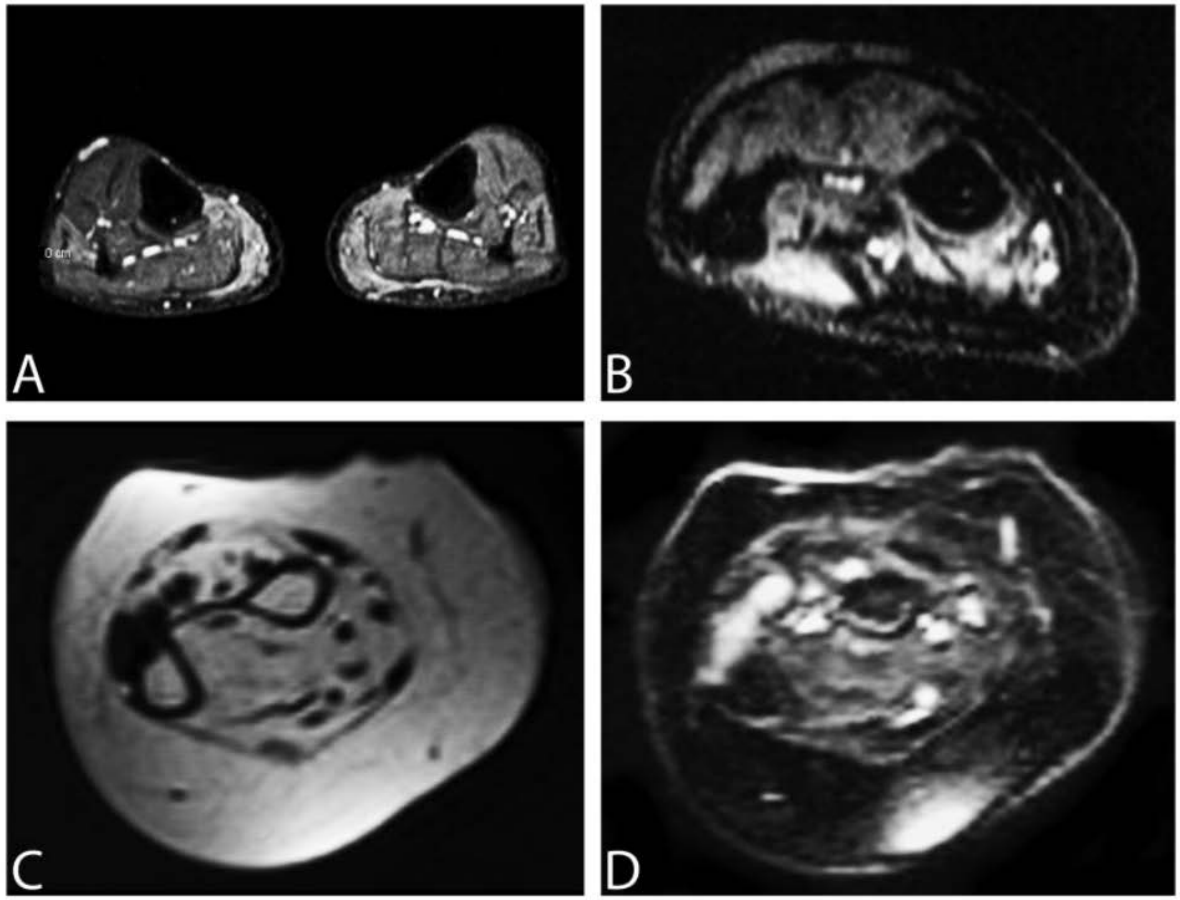
# IBM = progressive disease course




Mastaglia&Needham Journal of Clinical Neuroscience 2015,22:6-13

# MRI imaging sIBM

FIG. 1 Images of inflammation (STIR) of the forearm and legs. Lower legs (**A**), showing inflammation in the medial part of the gastrocnemius muscle. Right forearm (**B**) showing inflammation in the extensor carpi ulnaris (ECU) muscle. Right forearm (**C**; $T_1$-weighted) showing extensive fatty infiltration of all muscles, with sparing of the ECU. An STIR image (**D**) of the same patient shows exclusive inflammation of the ECU.




Cox et al. Rheumatology (Oxford). 2011

# IBM: Deep finger flexors

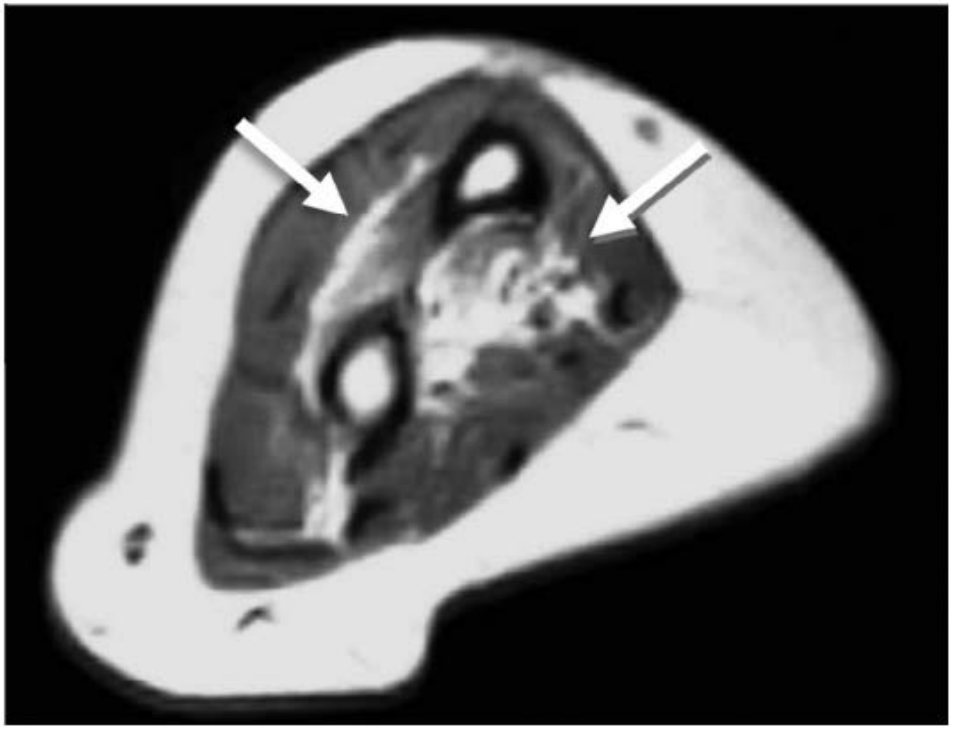
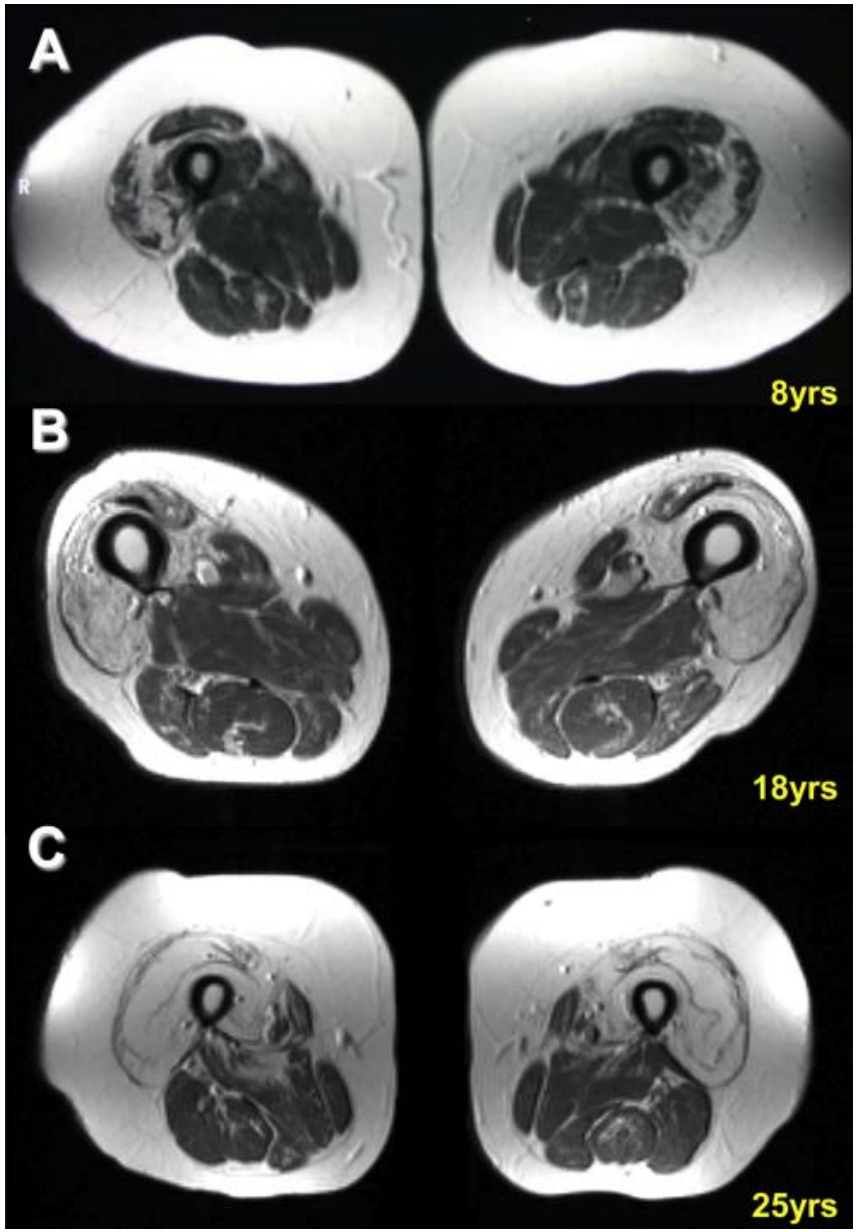


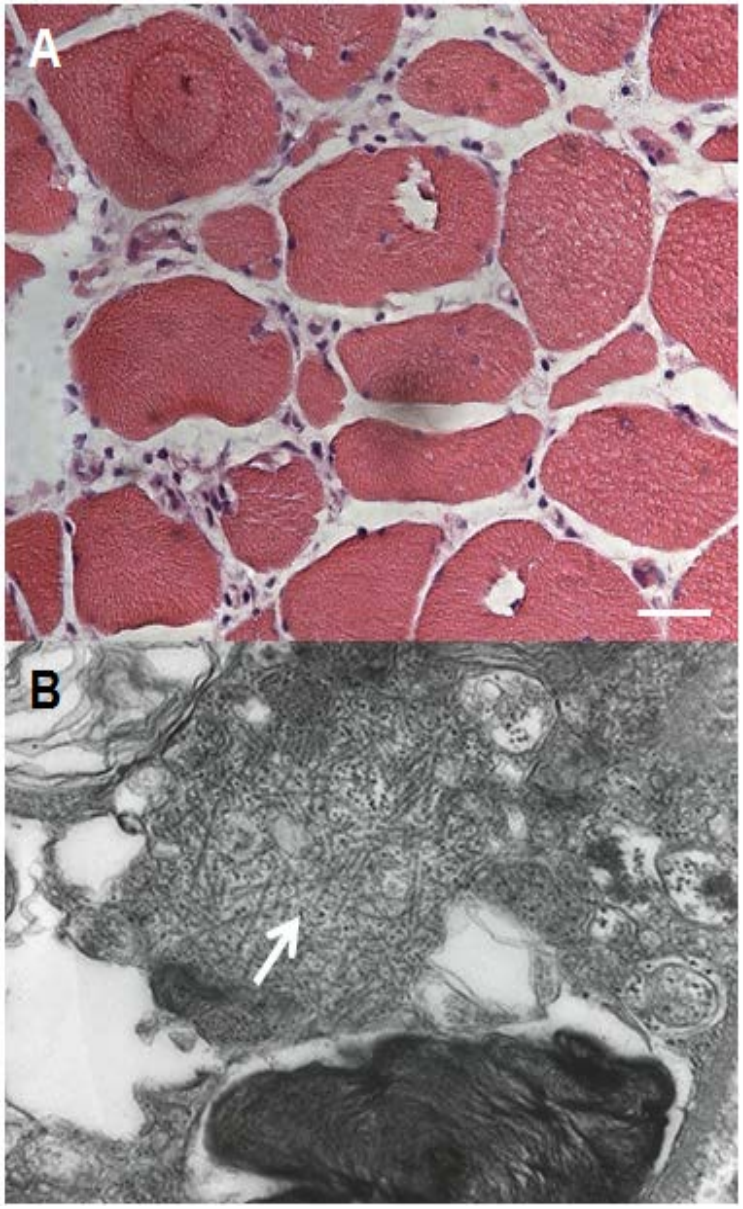
**Fig. 4.** Axial proton-density weighted MRI of the forearm in a patient with longstanding sporadic inclusion body myositis showing signal change in the deep finger flexor muscles (arrows).

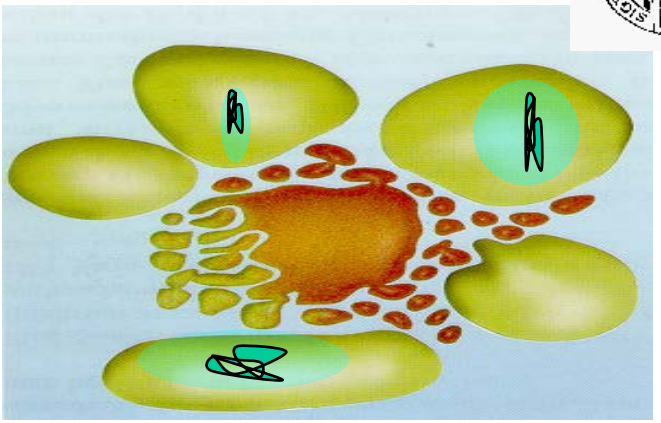
Mastaglia&Needham Journal of Clinical Neuroscience 2015,22:6-13




Mastaglia&Needham Journal of Clinical Neuroscience 2015,22:6-13

# Pathogenesis of sIBM



| | |
|---|---|
| **Diagnostic Muscle biopsy criteria** | Infiltrate variable, endomysial, angulated atrophic fibers, »rimmed vacuoles«, eosinophic inclusions |
| **Immunhistology** | CD8+T-cells<br>protein aggregates in myofibres (amyloid, p62, TDP-43, ubiquitin)<br>Increased cytochrome oxidase-negative |
| **EM** | helical filaments, fibrils<br>autophagic vacuoles |

# Griggs criteria IBM 1995

*Table 1. Proposed Diagnostic Criteria for Inclusion Body Myositis*[a]

I. Characteristic features—inclusion criteria
  A. Clinical features
    1. Duration of illness > 6 months
    2. Age of onset > 30 years old
    3. Muscle weakness
      Must affect proximal and distal muscles of arms and legs *and*
      Patient must exhibit at least one of the following features:
      a. Finger flexor weakness
      b. Wrist flexor > wrist extensor weakness
      c. Quadriceps muscle weakness (= or < grade 4 MRC)
  B. Laboratory features
    1. Serum creatine kinase < 12 times normal
    2. Muscle biopsy
      a. Inflammatory myopathy characterized by mononuclear cell invasion of nonnecrotic muscle fibers
      b. Vacuolated muscle fibers
      c. Either
        (i) Intracellular amyloid deposits (must use fluorescent method of identification before excluding the presence of amyloid) *or*
        (ii) 15–18-nm tubulofilaments by electron microscopy
    3. Electromyography must be consistent with features of an inflammatory myopathy (however, long-duration potentials are commonly observed and do not exclude diagnosis of sporadic inclusion body myositis).
  C. Family history
    Rarely, inclusion body myo*sitis* may be observed in families. This condition is different from hereditary inclusion body myo*pathy* without inflammation. The diagnosis of familial inclusion body myo*sitis* requires specific documentation of the inflammatory component by muscle biopsy in addition to vacuolated muscle fibers, intracellular (within muscle fibers) amyloid, and 15–18-nm tubulofilaments.
II. Associated disorders
  Inclusion body myositis occurs with a variety of other, especially immune-mediated conditions. An associated condition does not preclude a diagnosis of inclusion body myositis if diagnostic criteria (below) are fulfilled.
III. Diagnostic criteria for inclusion body myositis
  A. *Definite* inclusion body myositis
    Patients must exhibit all muscle biopsy features including invasion of nonnecrotic fibers by mononuclear cells, vacuolated muscle fibers, and intracellular (within muscle fibers) amyloid deposits or 15–18-nm tubulofilaments.
    None of the other clinical or laboratory features are mandatory if muscle biopsy features are diagnostic.
  B. *Possible* inclusion body myositis
    If the muscle shows only inflammation (invasion of nonnecrotic muscle fibers by mononuclear cells) *without* other pathological features of inclusion body myositis, *then* a diagnosis of possible inclusion body myositis can be given if the patient exhibits the characteristic clinical (A1,2,3) and laboratory (B1,3) features.

[a]Developed by J. Mendell, R. Barohn, V. Askanas, M. Dalakas, S. DiMauro, A. Engel, G. Karpati, and L. P. Rowland.

# sIBM
# Hilton-Jones Criteria 2008

**Table 1**
Proposed modified IBM diagnostic criteria.

| | | |
|---|---|---|
| Pathologically defined IBM | Conforming to the Griggs criteria [5] – invasion of non-necrotic fibres by mononuclear cells, and rimmed vacuoles, and either intracellular amyloid deposits or 15–18 nm filaments | |
| Clinically defined IBM | Clinical features | Duration weakness > 12 months<br>Age > 35 years<br>Weakness of finger flexion > shoulder abduction *AND* of knee extension > hip flexion |
| | Pathological features | Invasion of non-necrotic fibres by mononuclear cells or rimmed vacuoles or increased MHC-I, but no intracellular amyloid deposits or 15–18 nm filaments |
| Possible IBM | Clinical criteria | Duration weakness> 12 months<br>Age > 35 years<br>Weakness of finger flexion > shoulder abduction *OR* of knee extension > hip flexion |
| | Pathological criteria | Invasion of non-necrotic fibres by mononuclear cells or rimmed vacuoles or increased MHC-I, but no intracellular amyloid deposits or 15–18 nm filaments |

Neuromuscular Disorders 20 (2010) 142–147

doi:10.1093/brain/awr217 Brain 2011: 134; 3167–3175 | 3167

BRAIN
A JOURNAL OF NEUROLOGY

# A 12-year follow-up in sporadic inclusion body myositis: an end stage with major disabilities

Fieke M. Cox,[1] Maarten J. Titulaer,[1] Jacob K. Sont,[2] Axel R. Wintzen,[1] Jan J. G. M. Verschuuren[1] and Umesh A. Badrising[1]

1 Department of Neurology, Leiden University Medical Centre, 2300 RC Leiden, The Netherlands
2 Department of Medical Decision Making, Leiden University Medical Centre, 2300 RC Leiden, The Netherlands

Correspondence to: Fieke M. Cox, MD,
Leiden University Medical Centre,
Department of Neurology,
J3-R166,
PO Box 9600,
2300 RC Leiden, The Netherlands
E-mail: f.cox@lumc.nl

doi:10.1093/brain/awr213 Brain 2011: 134; 3176–3184 | 3176

BRAIN
A JOURNAL OF NEUROLOGY

# Long-term observational study of sporadic inclusion body myositis

Olivier Benveniste,[1,2,3] Marguerite Guiguet,[4] Jane Freebody,[5] Odile Dubourg,[1,6] Waney Squier,[5] Thierry Maisonobe,[6] Tanya Stojkovic,[1] Maria Isabel Leite,[5] Yves Allenbach,[2,3] Serge Herson,[1,2,3] Stefen Brady,[5] Bruno Eymard[1,2] and David Hilton-Jones[5]

1 Assistance Publique – Hôpitaux de Paris, Centre de Référence des Pathologies Neuromusculaires Paris Est, Institut de Myologie, 75013 Paris, France
2 Université Pierre et Marie Curie, 75013 Paris, France
3 Service de Médecine Interne 1, Hôpital Pitié-Salpêtrière, 75013 Paris, France
4 Biostatistique, INSERM – UPMC UMR S 943, 75013 Paris, France
5 Department of Neurology, West Wing, John Radcliffe Hospital, OX3 9DU Oxford, UK
6 Service de Neuropathologie, Hôpital Pitié-Salpêtrière, 75013 Paris, France

Correspondence to: Olivier Benveniste,
Service de Médecine Interne 1,
Groupe Hospitalier Pitié-Salpêtrière,
47-83, boulevard de l'Hôpital,
75651 Paris Cedex 13, France
E-mail: olivier.benveniste@psl.aphp.fr

**Table 1** Comparison of the main results of the Dutch and French–British sporadic IBM studies

| | Dutch study (Cox *et al.*, 2011) | French/British study (Benveniste *et al.*, 2011) |
|---|---|---|
| Number of patients | 64 total<br>46 deceased<br>15 surviving patients had a second evaluation | 136 total<br>25 deceased |
| Design and methods | Prospective/cross-sectional: 15 surviving patients<br>Retrospective (information obtained from records and/or treating physicians): all others | Cross-sectional (*ad hoc* visit in clinic): 71 patients<br>Retrospective (phone interview or medical records): 65 patients |
| Diagnostic criteria | Verschuuren *et al.* (1997); see Table 2 | Hilton-Jones *et al.* (2010) (based on Griggs *et al.*, 1995); see Table 3 |
| Distribution of patients across diagnostic categories | Definite sporadic IBM: 58/64 (91%)<br>Probable sporadic IBM: 6/64 (9%) | Pathologically defined sporadic IBM (Hilton-Jones *et al.*, 2010) and definite sporadic IBM (Griggs *et al.*, 1995): 40/136 (29.4%)<br>Clinically defined sporadic IBM (Hilton-Jones *et al.*, 2010) and possible sporadic IBM (Griggs *et al.*, 1995): 45/136 (33.1%)<br>Clinically defined sporadic IBM (Hilton-Jones *et al.*, 2010) with endomysial inflammation, but without invaded fibres: 51/136 (37.5%) |
| Percentage of patients with biopsy findings of | | |
| Invaded fibres | 100 | 62.5 |
| Rimmed vacuoles | 100 | 74 |
| Gender ratio male/female *n* (%) | 43/64 (67.2) | 78/136 (57.4) |
| Median duration of follow-up (years) | 12 | 8.6 (O. Benveniste, personal communication) |
| Age of onset (years) (mean ± SD or median) | 57 ± 9 | 61 |
| Time to wheel-chair (years) (mean ± SD or median) | 16 ± 4 | 14 |
| Mean decline of muscle strength per year (test/score, mean ± SD) | 3.5 ± 1.6% (manual muscle testing)<br>5.4 ± 3.5% (quantitative muscle testing) | ~4% (IWCI; estimated from Fig. 1, Benveniste *et al.*, 2011) |
| Life expectancy (years) | 81 (normal) | Normal |
| Dysphagia (%) | 12/15 (80) of surviving patients | 62/136 (45.6) of entire cohort |
| Number of patients treated with immunosuppressive agent at any time (%) | 21/64 (33) of patients received methotrexate during 48 weeks as part of a controlled trial (F. Cox, personal communication)<br>3/15 (20) of surviving patients used corticosteroids over a longer period of time; 6/15 (40) had received methotrexate during the trial (F. Cox, personal communication) | 71/136 (52) were treated with any immunosuppressive therapy |

doi:10.1093/brain/awr217 Brain 2011: 134; 3167–3175 | 3167

BRAIN
A JOURNAL OF NEUROLOGY

# A 12-year follow-up in sporadic inclusion body myositis: an end stage with major disabilities

Fieke M. Cox,[1] Maarten J. Titulaer,[1] Jacob K. Sont,[2] Axel R. Wintzen,[1] Jan J. G. M. Verschuuren[1] and Umesh A. Badrising[1]

**Table 1** Characteristics of patients

| | Complete cohort | Deceased patients | Surviving patients | *P*-value† |
|---|---|---|---|---|
| Number of patients | 64 | 46 | 15 | |
| Male | 43 | 31 | 11 | 0.76 |
| Female | 21 | 15 | 4 | |
| Age at first visit (years) | 68 ± 9 | 71 ± 8 | 60 ± 8 | <0.001* |
| Male | 66 ± 8 | 68 ± 8 | 60 ± 8 | |
| Female | 72 ± 10 | 75 ± 8 | 60 ± 9 | |
| Age at second visit (years) | – | – | 73 ± 8 | – |
| Male | – | – | 73 ± 8 | |
| Female | – | – | 73 ± 8 | |
| Age at onset (years) | 57 ± 9 | 58 ± 9 | 52 ± 9 | 0.03* |
| Symptom duration at first visit (years) | 11 (5–15) | 11 (6–16) | 7 (4–11) | 0.06 |
| Symptom duration at second visit (years) | – | – | 20 ± 5 | – |
| sCK levels at first visit (U/l) | | | | |
| Male | 501 (254–717) | 443 (259–658) | 581 (207–1310) | 0.37 |
| Female | 246 (173–466) | 233 (175–454) | 461 (178–771) | 0.31 |
| sCK levels at second visit (U/l) | | | | |
| Male | – | – | 228 (106–512) | – |
| Female | – | – | 151 (41–317) | – |
| HLA positive (%) | | | | |
| B8 | 56 | 48 | 80 | 0.100 |
| DR3 | 64 | 61 | 73 | 1.000 |
| DR53 | 6 | 2 | 20 | 0.081 |
| First weakness (%) | | | | |
| Quadriceps | 63 | 59 | 80 | 0.247 |
| Finger flexors | 14 | 19 | 13 | |
| Pharyngeal muscles | 9 | 11 | 7 | |
| Other | 14 | 11 | 0 | |
| Manual muscle testing first visit | 265 (237–285) | 257 (223–277) | 285 (266–298) | <0.001* |
| Quantitative muscle testing first visit | 2407 ± 887 | 2215 ± 817 | 2996 ± 913 | 0.003* |
| Functional grading scales first visit | | | | |
| Barthel | 19 (17–20) | 18 (16–20) | 20 (19–20) | 0.013* |
| Rivermead | 13 (9–14) | 12 (9–13) | 13 (12–14) | 0.023* |
| Brooke's | 6 (5–8) | 7 (5–8) | 4 (4–6) | 0.001* |

Numbers in brackets represent the interquartile range.

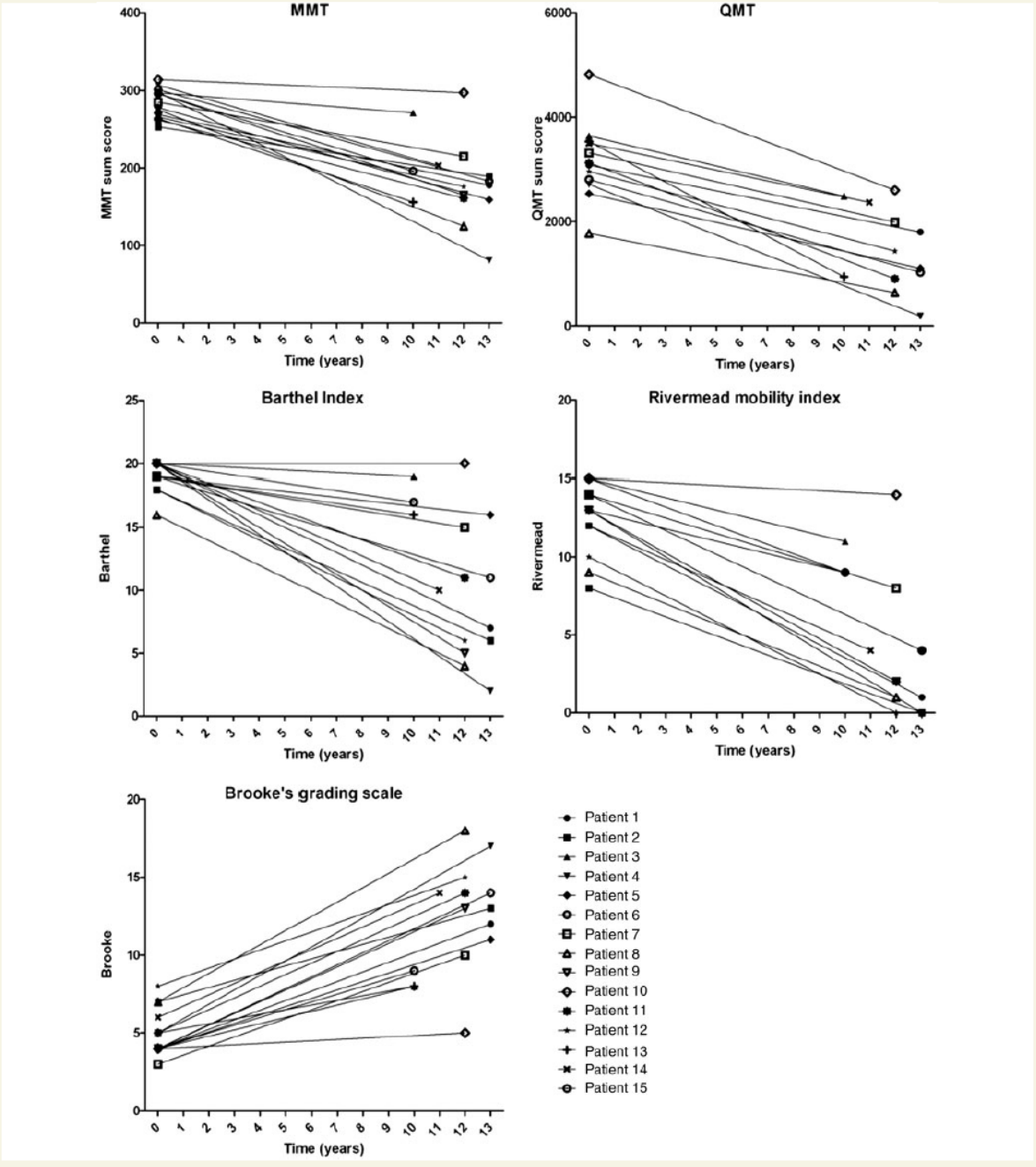



**Figure 1** Sum scores of manual muscle testing (MMT) and quantitative muscle testing (QMT) and functional grading scales (Barthel index, Rivermead mobility index, Brooke's functional grading scale) for the surviving patients at baseline and follow-up. All figures show a decline in strength and function in time. QMT was not performed in one patient at baseline and in 2 patients at follow-up.

# sIBM

- Brookes-Score best to monitor the follow-up

All types of immunosupression therapy (IVIG, steroids, MTX) without evidence of a better long-term outcome

doi:10.1093/brain/awr217 Brain 2011: 134; 3167–3175 | 3167

BRAIN
A JOURNAL OF NEUROLOGY

# A 12-year follow-up in sporadic inclusion body myositis: an end stage with major disabilities

Fieke M. Cox,[1] Maarten J. Titulaer,[1] Jacob K. Sont,[2] Axel R. Wintzen,[1] Jan J. G. M. Verschuuren[1] and Umesh A. Badrising[1]

Table 2 Causes of death in the Dutch population in the age category 80–85 years and the sporadic IBM cohort

| | Dutch population age category 80–84 years (%) | Patients with sporadic IBM (%) | *P*-value | Corrected *P*-value† |
|---|---|---|---|---|
| Infectious diseases | 1.4 | 2.2 | 0.66 | NS |
| Neoplasms | 23.8 | 4.3 | 0.002 | 0.03* |
| Diseases of blood/blood-forming organs | 0.4 | 0 | 0.67 | NS |
| Endocrine/metabolic diseases | 3.6 | 0 | 0.19 | NS |
| Mental and behavioural disorders | 5.6 | 0 | 0.10 | NS |
| Diseases of the nervous system | 2.8 | 2.2 | 0.80 | NS |
| Diseases of the circulatory system (myocardial infarction) | 37.7 (7.8) | 19.6 (4.3) | 0.01 | 0.16 |
| Diseases of the respiratory system (pneumonia) | 11.5 (4.4) | 41.3 (28.3) | 0.0001* | 0.001* |
| Diseases of the digestive system | 4.2 | 0 | 0.16 | NS |
| Diseases of the skin | 0.3 | 0 | 0.71 | NS |
| Diseases of the bone/connective tissue | 0.7 | 0 | 0.57 | NS |
| Diseases of the genitourinary system | 2.8 | 0 | 0.25 | NS |
| Cachexia | 0.1 | 6.5 | 0.0001* | 0.001* |
| External causes of injury and poisoning | 2.1 | 6.5 | 0.04 | 0.51 |
| Other/uncertain | 3.0 | 17.4 | | |

†Corrected *P*-value is calculated with a Bonferroni correction of 14. *Significant value.

- normal life expectancy
- 13% with active dying help

**Table 2 Characteristics of 136 patients diagnosed with sporadic IBM between 1990 and 2008 in two European clinical centres**

| Variable | Result |
|---|---|
| Gender, male ($n = 136$) | 78 (57.3) |
| Age at first symptoms, years ($n = 136$) | 61 (55–69) |
| First symptoms ($n = 136$) | |
| Muscle weakness only | 119 (87.5) |
| Swallowing troubles only | 6 (4.4) |
| Muscle weakness and swallowing troubles | 11 (8.1) |
| Previous diagnosis ($n = 136$) | |
| None | 94 (69.1) |
| Polymyositis | 23 (16.9) |
| Amyotrophic lateral sclerosis | 3 (2.2) |
| Dystrophy | 4 (2.9) |
| Other | 12 (8.8) |
| Delay between first symptoms and diagnosis, months ($n = 136$) | 59 (29–95) |
| Status at the last visit | |
| Duration since diagnosis, months ($n = 136$) | 31 (5–75) |
| Age, years ($n = 136$) | 72.5 (65–77) |
| Muscle weakness ($n = 136$) | 136 (100) |
| Severe proximal weakness[a] ($n = 134$) | 64 (48) |
| Severe distal weakness[a] ($n = 133$) | 53 (40) |
| Swallowing difficulties ($n = 136$) | 62 (45.6) |
| Creatine kinase, IU/l ($n = 87$) | 267 (135–621) |
| Grip test, kgN ($n = 76$) | 13 (10–17) |
| Walton ($n = 113$) | 5 (3–6) |
| RMI ($n = 88$) | 10 (7–12) |
| IWCI ($n = 71$) | 55 (35–70) |
| Current handicap for walking ($n = 136$) | |
| None | 33 (24.3) |
| One, two canes or rollator | 52 (38.2) |
| Wheelchair | 51 (37.5) |

Data are median (IQR) or *n* (%).
a Severe muscle weakness defined by MRC < 3/5.
RMI = Rivermead Mobility Index.

doi:10.1093/brain/awr213 Brain 2011: 134; 3176–3184 | 3176
BRAIN
A JOURNAL OF NEUROLOGY

# Long-term observational study of sporadic inclusion body myositis

Olivier Benveniste,[1,2,3] Marguerite Guiguet,[4] Jane Freebody,[5] Odile Dubourg,[1,6] Waney Squier,[5] Thierry Maisonobe,[6] Tanya Stojkovic,[1] Maria Isabel Leite,[5] Yves Allenbach,[2,3] Serge Herson,[1,2,3] Stefen Brady,[5] Bruno Eymard[1,2] and David Hilton-Jones[5]

**Table 4 Description of treatment received by 71 patients with sporadic IBM**

| Variable | Result |
|---|---|
| Delay between first symptoms and first treatment, years ($n = 70$) | 3.7 (1.7–6.6) |
| Corticosteroids (prednisone) | 65 (91.5) |
| Duration of treatment, months ($n = 63$)[a] | 37.1 (8.3–93.0) |
| Intravenous immunoglobulins | 40 (56.3) |
| Duration of treatment, months ($n = 39$)[a] | 9.7 (2.5–70.1) |
| Azathioprine | 19 (26.8) |
| Duration of treatment, months ($n = 17$)[a] | 25.5 (5.2–50.3) |
| Methotrexate | 23 (32.4) |
| Duration of treatment, months ($n = 21$)[a] | 11.0 (7.2–27.9) |
| Cyclophosphamide | 2 (2.8) |
| Combination of treatment[b] | |
| Corticosteroids only | 19 (26.8) |
| Corticosteroids and other drugs | 46 (64.8) |
| Other drugs only | 6 (8.4) |
| Duration of treatment, months ($n = 69$)[c] | 40.8 (13.0–89.2) |

Data are median (IQR) or *n* (%).
a Duration between initiation and either the date of last prescription or the date of last visit.
b All drugs received whatever the timing of prescription.
c Duration between initiation of first treatment and either the date of last prescription of any treatment or the date of last visit.

doi:10.1093/brain/awr213 Brain 2011: 134; 3176–3184 | 3176

BRAIN
A JOURNAL OF NEUROLOGY

# Long-term observational study of sporadic inclusion body myositis

Olivier Benveniste,[1,2,3] Marguerite Guiguet,[4] Jane Freebody,[5] Odile Dubourg,[1,6] Waney Squier,[5] Thierry Maisonobe,[6] Tanya Stojkovic,[1] Maria Isabel Leite,[5] Yves Allenbach,[2,3] Serge Herson,[1,2,3] Stefen Brady,[5] Bruno Eymard[1,2] and David Hilton-Jones[5]

Table 3 Comparison of patients with definite IBM or possible IBM by Griggs' criteria, or clinically defined IBM according to Hilton-Jones' criteria

| Characteristics of patients | Definite IBM ($n = 40$) | Possible IBM ($n = 45$) | Clinically defined IBM ($n = 51$) | P |
|---|---|---|---|---|
| Gender, male ($n = 136$) | 27 (67.5) | 23 (51.1) | 28 (54.9) | 0.28 |
| Age at first symptoms, years ($n = 136$) | 62.5 (54–72) | 63 (56–69) | 59 (55–68) | 0.42 |
| First symptoms ($n = 136$) | | | | |
| Muscle weakness and swallowing difficulties | 4 (10.0) | 4 (8.9) | 3 (5.9) | 0.85 |
| Muscle weakness only | 35 (87.5) | 38 (84.4) | 46 (90.2) | |
| Swallowing troubles only | 1 (2.5) | 3 (6.7) | 2 (3.9) | |
| Previous diagnosis ($n = 136$) | | | | |
| None | 26 (65.0) | 32 (71.1) | 36 (70.6) | 0.50 |
| Polymyositis | 10 (25.0) | 5 (11.1) | 8 (15.7) | |
| Other | 4 (10.0) | 8 (17.8) | 7 (13.7) | |
| Delay between first symptoms and sporadic IBM diagnosis, months ($n = 136$) | 49 (25–82) | 64 (38–99) | 56 (27–111) | 0.45 |
| Status at the last visit | | | | |
| Time since sporadic IBM diagnosis, months ($n = 136$) | 20 (1–86) | 25 (6–69) | 42 (14–66) | 0.28 |
| Age, years ($n = 136$) | 74 (65–79) | 74 (66–78) | 71 (64–76) | 0.48 |
| Muscle weakness ($n = 136$) | 40 (100) | 45 (100) | 51 (100) | 1.0 |
| Severe proximal weakness[a] ($n = 136$) | 20 (50.0) | 21 (46.7) | 23 (45.1) | 0.89 |
| Severe distal weakness[a] ($n = 136$) | 14 (35.0) | 14 (31.1) | 25 (49.0) | 0.16 |
| Swallowing troubles ($n = 136$) | 14 (35.0) | 25 (55.6) | 23 (45.1) | 0.17 |
| Creatine kinase, IU/l ($n = 87$) | 272 (93–649) | 229.5 (135–406) | 359.5 (183.5–738) | 0.31 |
| Grip strength, kgN ($n = 76$) | 12.6 (16.7–15.0) | 14.8 (10.4–22.4) | 13.9 (10.0–16.0) | 0.26 |
| Walton ($n = 113$) | 6 (3–6) | 5 (3–6) | 4 (3–6) | 0.11 |
| RMI ($n = 88$) | 9.5 (3–11) | 10 (8–12) | 10 (7–12) | 0.37 |
| IWCI ($n = 71$) | 50 (40–65) | 62.5 (35–75) | 50 (35–67.5) | 0.61 |
| Current handicap for walking ($n = 136$) | | | | |
| None | 7 (17.5) | 11 (24.5) | 15 (29.4) | 0.79 |
| One or two canes | 17 (42.5) | 17 (37.8) | 18 (35.3) | |
| Wheelchair | 16 (40.0) | 17 (37.8) | 18 (35.3) | |

Data are *n* (%) or median (IQR).
a Severe muscle weakness defined by MRC < 3/5.
RMI = Rivermead Mobility Index.

doi:10.1093/brain/awr213 Brain 2011: 134; 3176–3184 | 3176

BRAIN
A JOURNAL OF NEUROLOGY

# Long-term observational study of sporadic inclusion body myositis

Olivier Benveniste,[1,2,3] Marguerite Guiguet,[4] Jane Freebody,[5] Odile Dubourg,[1,6] Waney Squier,[5] Thierry Maisonobe,[6] Tanya Stojkovic,[1] Maria Isabel Leite,[5] Yves Allenbach,[2,3] Serge Herson,[1,2,3] Stefen Brady,[5] Bruno Eymard[1,2] and David Hilton-Jones[5]

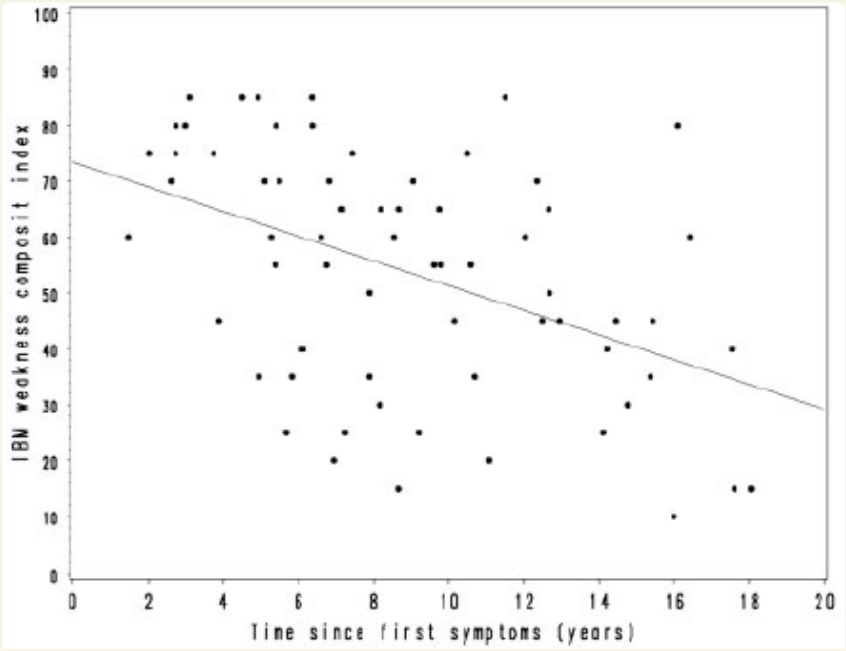



**Figure 1** Relationship between IWCI measured at the last visit and disease duration (years) since the first symptoms.

**Table 1** Sporadic IWCI

| Measured parameters | |
|---|---|
| Arms outstretched forwards (s) | |
| 150 | 15 |
| 100 | 10 |
| 50 | 5 |
| <50 | 0 |
| Legs held outstretched at 45° supine (s) | |
| 75 | 15 |
| 50 | 10 |
| 25 | 5 |
| <25 | 0 |
| Neck flexors, lying in bed | |
| Against resistance | 10 |
| Without resistance | 5 |
| Impossible | 0 |
| From lying in bed to standing | |
| Without support | 10 |
| With support | 5 |
| Impossible | 0 |
| Walk | |
| Normal | 10 |
| With cane(s) or walker | 5 |
| Impossible (wheelchair) | 0 |
| From sitting position in a chair to standing | |
| Without support | 10 |
| With support | 5 |
| Impossible | 0 |
| Force of finger flexors | |
| MRC = 5 | 10 |
| MRC = 3 or 4 | 5 |
| MRC = 0, 1 or 2 | 0 |
| Force of the quadriceps | |
| Normal (MRC = 5/5) | 10 |
| Decreased (MRC = 3 or 4) | 5 |
| Weak (MRC = 0, 1 or 2) | 0 |
| Swallowing | |
| Normal | 10 |
| Moderate or intermittent difficulties | 5 |
| Severe or permanent difficulties | 0 |
| Total | /100 |

- IBM Weakness Composite index (IWCI)

# sIBM

# Summary

# Dutch/FRENCH/UK studies 2011

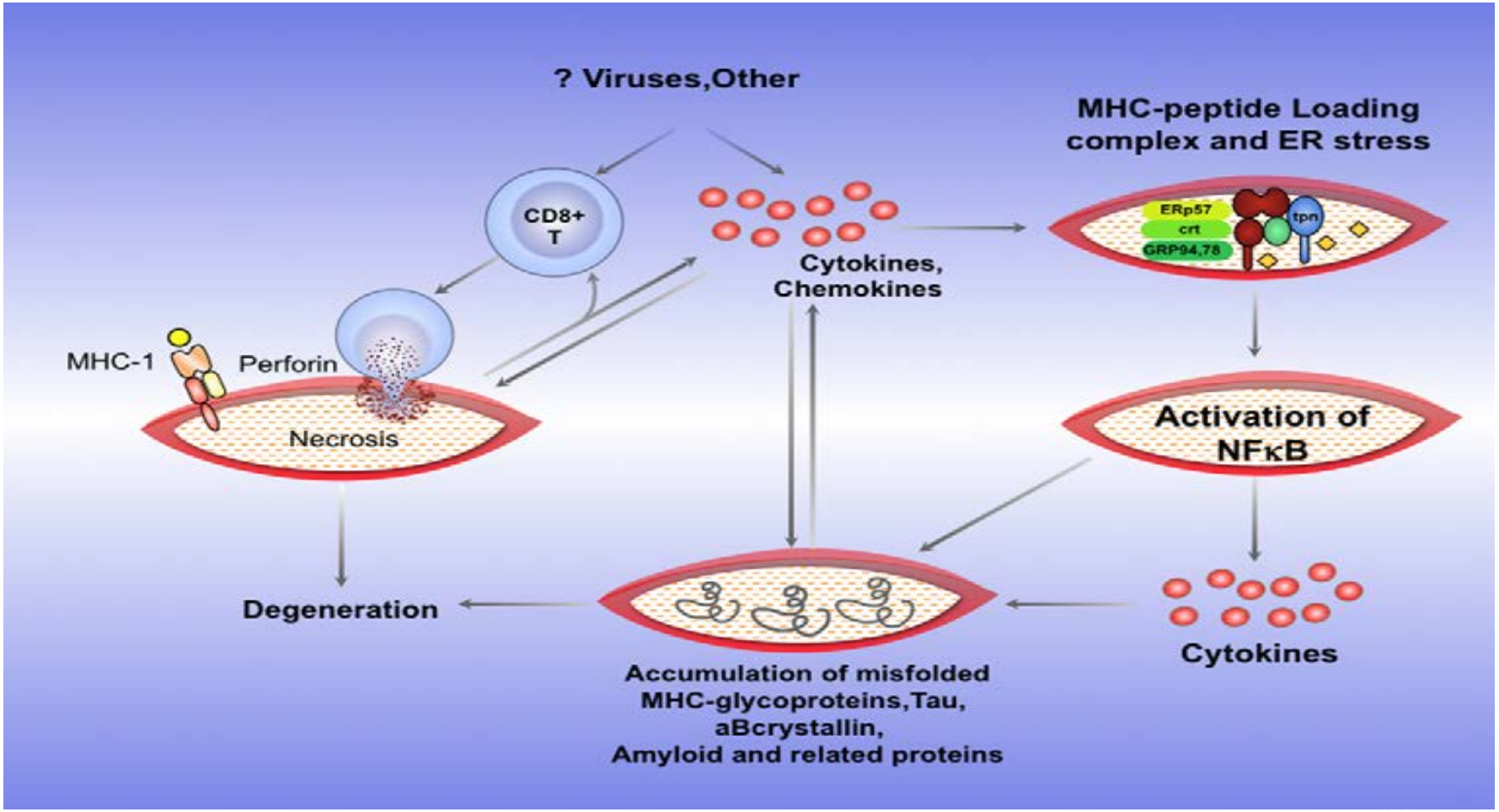
- Longterm outcome independent of any therapy
- About 5% strength decline per year
- Life expectancy normal
- Qualitiy of life massively reduced
- Time to wheelchair median 14 years

# Pathogenesis of sIBM

**Primary degenerative, secondary inflammatoric?**

**vs.**

**Primary inflammatoric, secondary degenerative?**




Dalakas MC Ann of Neurology 2008

# Diagnostic algorithm sIBM

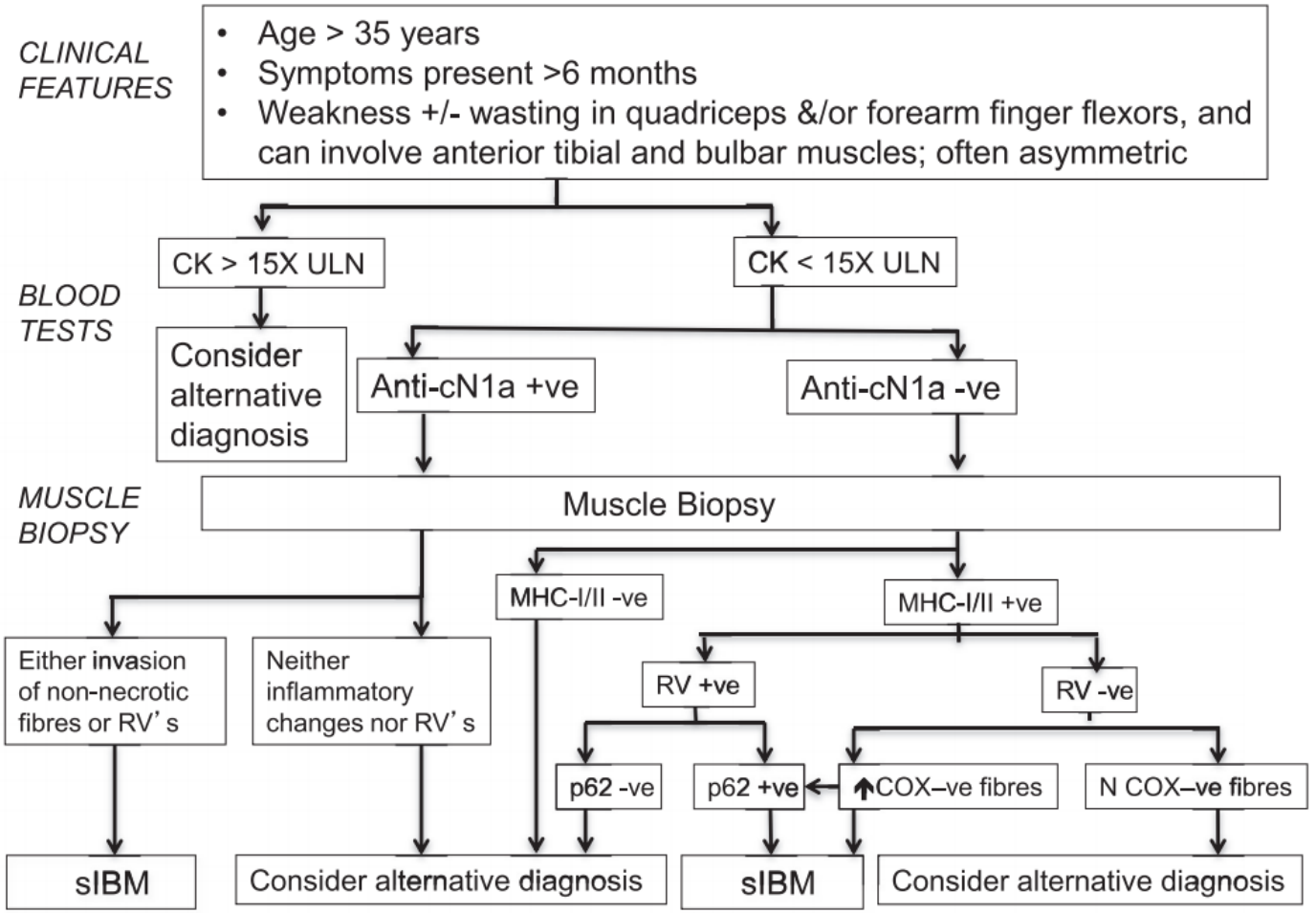


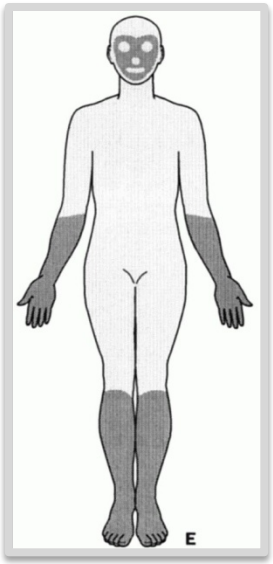

**Fig. 7.** Proposed diagnostic algorithm for sporadic inclusion body myositis. Anti-cN1a Ab = antibody to cytosolic 5′-nucleotidase, CK = serum creatine kinase level, COX = cytochrome oxidase, MHC = major histocompatibility complex, N = normal numbers, RV = rimmed vacuoles, sIBM = sporadic inclusion body myositis, ULN = upper limit of normal, –ve = negative, +ve = positive. Derived in part from Brady et al. [56].

Mastaglia&Needham Journal of Clinical Neuroscience 2015,22:6-13

# Differential diagnoses

# Differential diagnosis
# Distal weakness

Distal weakness



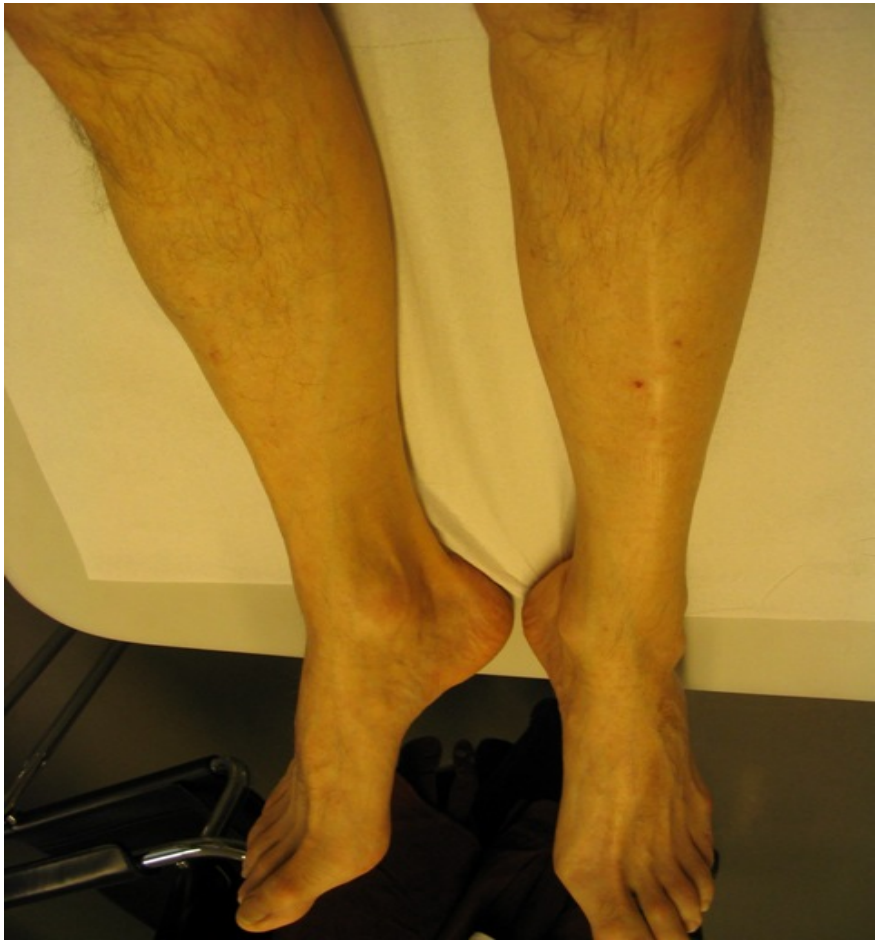
IBM

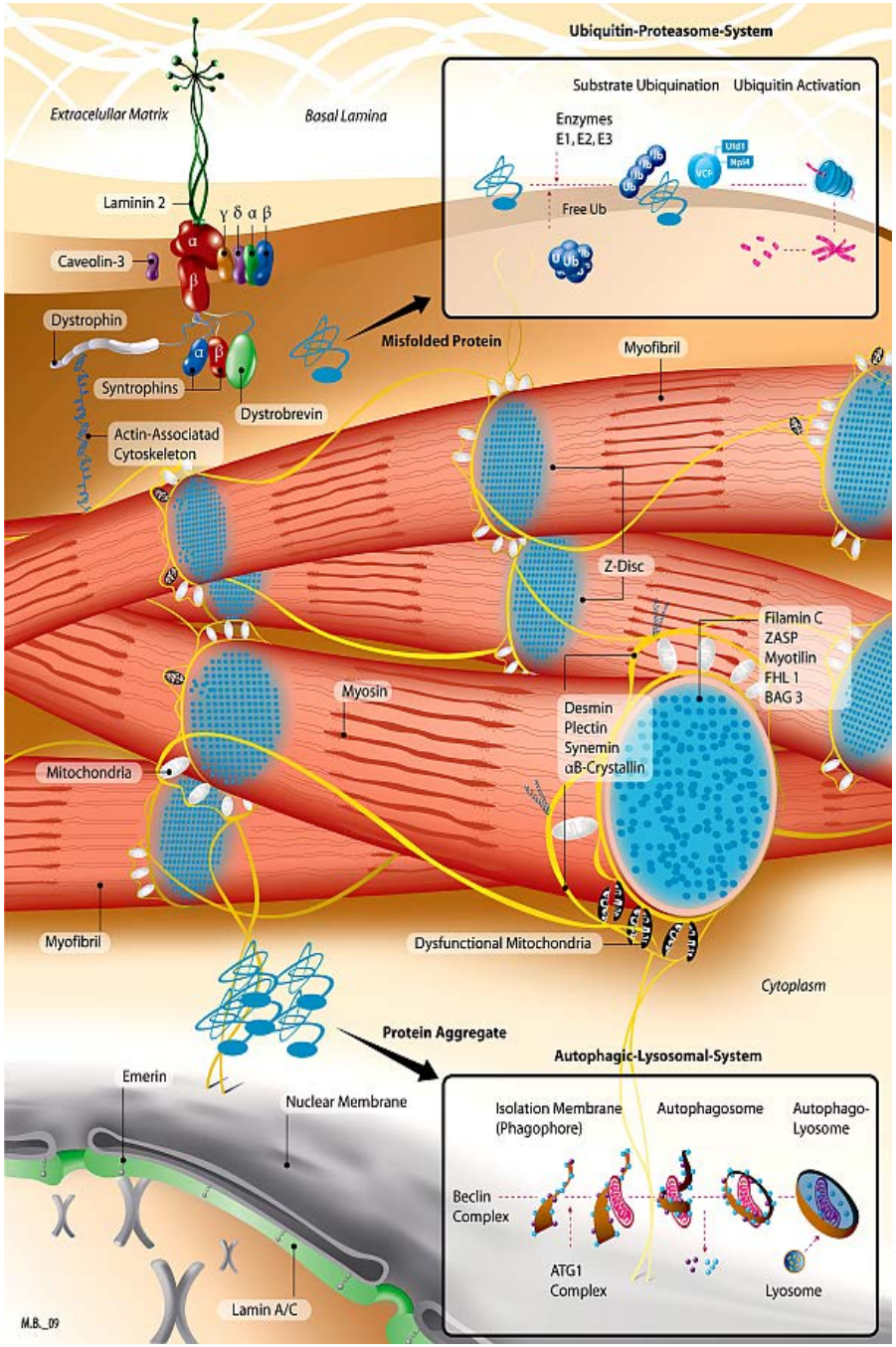
Myotonic dystrophy type 1
Metabolic myopathiens (GSD3)

Distal LGMDs
LGMD 1C, 2A, 2B, 2I, 2J
Myofibrillar myopathies

DD neurogenic neuropathies

# Myofibrillar Myopathies






Schröder&Schoser Brain pathology 2009

# Clinical differential diagnosis Myofibrillar Myopathies Distal myopathies

| Disease | Muscle weakness | Heart | Lung | CK levels | Extramusuclar |
|---|---|---|---|---|---|
| Desminopathy | distal>proximal | DCM, CB | insufficiency | n-5x | |
| aBCopathy | proximal>distal | DCM, CB | | n-7x | catarcats |
| Filaminopathy | proximal>distal | DCM, CB | insuffiency | n-8x | neuropathy |
| Myotilinopathy | proximal>distal | DCM | insuffiency | n-5x | neuropathy, contractures |
| Bag3opathy | proximal | DCM | insuffiency | n-15x | ridid-spine, scoliosis, contractures |
| FHL1opathy | distal=proximal, axial hypertrophy, scapuloperoneal | CB | insuffiency | n-10x | rigid-spine, scoliosis, contractures |
| ZASPoppthy | distal>proximal | DCM, CB | | n-10x | neuropathy |
| Plectionpathy | distal>proximal | | | n-10x | epidermolysis bulosa simplex |
| Titinopathy | distal>proximal | DCM | insuffiency | n-10x | |
| Matrin3opathy | distal>proximal, axial | | insuffiency | n-7x | |

DCM = dilative cardiomyopathy; CB = conduction block

**Modified from Schoser Aktuelle Neurolie 2009**

LMU KLINIKUM DER UNIVERSITÄT MÜNCHEN
FRIEDRICH-BAUR-INSTITUT
AN DER NEUROLOGISCHEN KLINIK UND POLIKLINIK

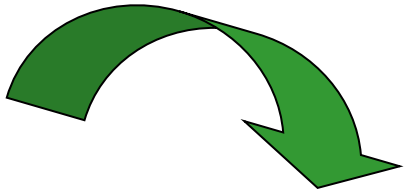
# Treatment options in myositis

**Prof. Benedikt Schoser**
Friedrich-Baur-Institute
Department of Neurology
Ludwig-Maximilians-University
Munich, Germany

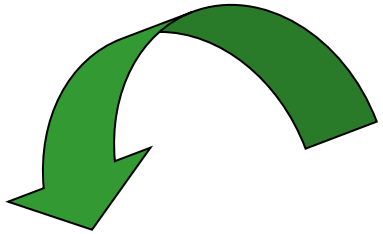
ean the home of neurology

# Classic treatment of Myositis

**1.Option**
**Corticosteroids (pulse or add on azathioprine**
**CD-20 antibody**



**2.Option**
**MTX**
**ivIG**



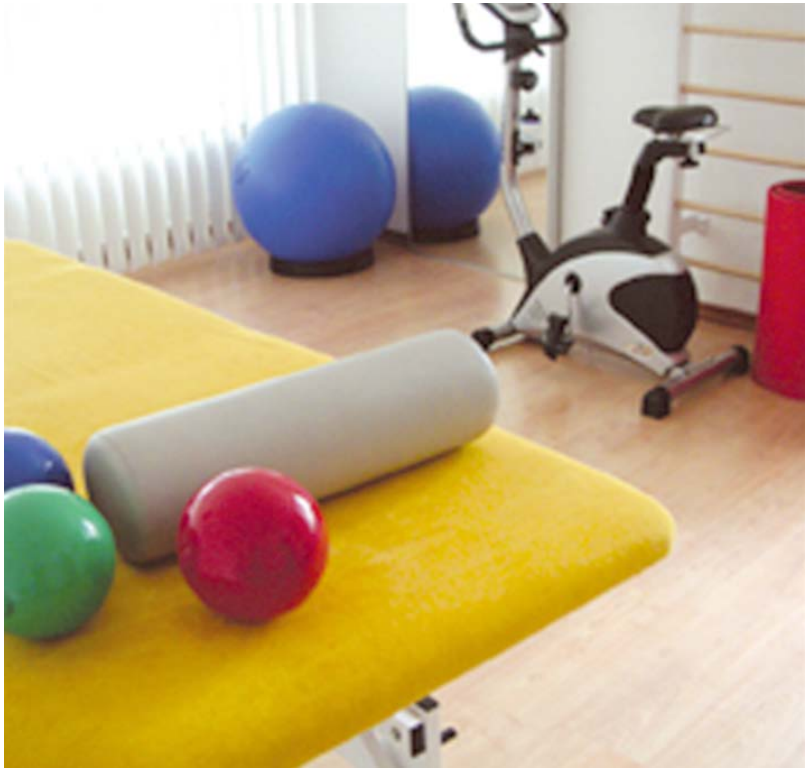
**3.Option**
**cyclosporine**
**mycofenolat mofetil**
**cyclophosphamide**

# Non-drug treatment of Myositis

## Physiotherapy

Stabilisation of motor function
Strength improvemennt in
non-atrophic muscles

(Spector et al., 1997)



## Ocupational therapy

Prophylaxis of contractures
Stabilization of hand function in IBM

## Training

Alexanderson H, Lundberg IE et. al., Arthritis Rheum 2007;57:768-777

Chung YL, Alexanderson H et. al., Arthritis Rheum. 2007;57:694-702.

# Alternative novel therapeutical option in Myositis

**Intracellular signal pathways**

- Anti-CD52 (Alemtuzumab)
- Calcineurin-Inhibitors (Tacrolimus and Ciclosporin)
- TOR-Kinase via FK-506-binding-protein (Rapamycin)
- Inhibition of Purinbiosynthesis (Mycophenolat mofetil)

**B-Cell and autoantibodies**

- Rituximab
- IVIG

**Cytokine/Chemokine/Adhasionsmolecules**

- TNFalpha inhibitor (Etanercept - IBM, Infliximab)?
- Beta-Interferone – IBM?
- IVIG

**Complement inhibitor**

- IVIG
- Anti-C5 /Eculizumab - dermatomyositis?

**T-cell transmigration-inhibitor**

- Natalizumab – IBM??
- IVIG