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Progress in muscle research through the international congress of neuromuscular diseases (ICNMD): a narrative review

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Abstract

Progress in muscle research has been through different phases over the past decades. Here are reviewed the advances presented at the International Congresses of Neuromuscular Diseases (ICNMD). In the '60 to '80 muscle physiology and interpretations of muscle biopsy were the major focuses, diagnosis of muscle disorders was advanced utilizing histochemical, and ultrastructural techniques, and the focus of first to IVth ICNMD was prevention and Muscle Disorders classification as major issues. After that from '80 to 2000 muscle neuromuscular junction (NMJ) immunology, biochemistry, molecular biology , therapeutic trials, and genetics were the major developments and represented the focus of research in following ICNMD from the Vth to the Xth. From 2000 to 2020 personalized medicine,genotype-phenotype correlation, and the use of DNA/RNA profiling , Imaging was developed and represented substantial signs of progress that were presented in ICNMD XIth to XVIIth. The future is evolving toward a major involvement of the pharmaceutical industry with new drugs and gene-delivered therapy, the use of biomarkers and robotics as well as of artificial intelligence, both for interpreting morphology, DNA, and imaging diagnostic, and such developments will be reflected in research presented in future Congresses.

Key Words: neuromuscular disorders; myology; ICNMD; muscular dystrophy.

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Clinical myology began expanding as a separate discipline in the 1950s creating the need for an international forum for the exchange of information in this field. This focus has been provided by ICNMD congresses, through five decades. This review is based on papers reporting neuromuscular results and abstracts on ICNMDs. Scientific papers were searched from 1970 to February 2023 on the main databases (PubMed, MedLine, Google Scholar). The main categories of inherited neuromuscular diseases are neuropathies (diseases of a peripheral nerve), myopathies, motor neuron diseases, and muscular dystrophies.

Not so long ago, muscular dystrophies were mainly divided into six categories such as Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy, limb-girdle muscular dystrophy (LGMD), distal myopathies, CMDs, facioscapulohumeral muscular dystrophy and myotonic dystrophies.

In the review are included only free and fully available texts written in English, while excluded papers were those concerning pharmacological trials. The temporal interval of 1970– 2023 was selected to include all the information regarding some conditions, i.e. congenital muscular dystrophies (CMDs); while the number of studies on muscular dystrophies has increased in recent decades, consistent reports are still missing for other neuromuscular disoders. We considered the papers on the following neuromuscular disorders: dystrophinopathies, dystroglycanopathies, myotonic dystrophies, facioscapulohumeral dystrophy, limb-girdle muscular dystrophies, congenital myotonias, congenital myopathies, and related terms or abbreviations, identifying different forms of muscular dystrophy. This led to the classification of them in terms of molecular genetic features (genes and functions of the respective proteins affected) rather than clinical symptoms, i.e. clinical pattern of weakness, mode of inheritance, and age of onset.[1] Genetic investigations have expanded our knowledge in muscular dystrophies and now more than 50 forms of neuromuscular disorders have been identified on molecular bases, each one with different clinical features such as. muscle pattern of involvement, variable course different genotype–phenotype correlation. Furthermore, next-generation sequencing (NGS) technology has led to the discovery of novel causative genes and differentiation of novel myopathies.

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The morphological and nosographic era

The first ICNMD Congress in Neuromuscular Diseases took place in Milan on 19-21 May 1969, the Organization Committee included Professor G. Scarlato, M. Aloisi, and N. Canal. The Congress President was G. Gastaldi and Honorary President J. Walton. The meeting was organized after the visit of M. Aloisi to Arden House in New York, through an agreement with MDA Director A.T Milhorat. The Congress although originally planned in Padova was located in Milan and was attended by over 250 scientists, The opening lecture was given by Nobel Price H. Huxley on muscle physiology, and several outstanding international muscle researchers such as Louis P. Rowland, M. Fardeau, V. Dubowitz W.K Engel, A.G. Engel. I. Hausmanowa-Petrusewicz, F. Buchtahl, A. E. H. Emery, G. Serratrice, and D. Gardner-Medwin attended the Milan Meeting. The focus of the congress was on histochemistry, electron microscopy, and diagnostic techniques for muscle disorders. During that Congress, I met William R. Kennedy, and R. Meyers and was offered a position in Minneapolis and Baltimore, that subsequently I took at Mayo Clinic Rochester with A. G. Engel.

After the first ICNMD Congress, a second one took place in Western Australia, Perth on 22-26 November 1971 and was well attended by Italian Myologists (Figure 1).

In the picture below are recognizable standing from left Prof. Pinelli, Aloisi, Canal, Scarlato, and the Congress organizer Brian Kakulas, in the second raw, are sitting Drs. Nardella, Cornelio, Mondaini and Gentili. The focus of the conference was on biometrics, muscle spindle, myogenesis and muscle regeneration, and the classification of muscular dystrophies, including FSHD, congenital muscular dystrophy, and spinal muscular atrophy. The ICNMD was organized on behalf of the Applied Research Group on Neuromuscular Diseases and had a regular meeting every four years, covering muscle, peripheral nerve, synapse, and anterior horn disorders. The chair of the group rotated and the neurologists leading the World Research Group among others were J. Walton, P.K Thomas, L. P. Rowland, G. Said, and J. England. The third ICNMD Congress took place in Newcastle-upon Tyne in 1974, in the UK, and was organized by Lord Walton, Vice presidents were R. D. Adams and M. Aloisi; the focus was on biochemistry, lipid muscle disorders, and mitochondria. In Newcastle-upon-Tyne, UK there were several attending scientists including G. Serratrice, B. Kakulas, A.T. Milhorat, S. DiMauro, F. Samaha, P. Kark, P. Hudson, T. Munsat, L.P. Rowland and a good number of presentations (420) were delivered. The meeting was supported by the UK Muscular Dystrophy Group, Muscular Dystrophy Association of America, and Canada, EAMDA. There were 39 plenary sessions and 5 round tables covering human muscle diseases and animal models. Scarlato's group presented abstracts on myasthenia and malignant hyperthermia, while prof Oosterhuius presented a series of thymectomised patients in myasthenia gravis without thymoma. Dr. A. G. Engel and F. Jerusalem presented ultrastructural studies in DMD muscle capillaries, Prof. Irena Hausmanowa-Petrusewicz, and Fidzianska's studies on spinal muscular atrophy. There was a tour of participants to the nearby ancient Adrian wall established by the Roman Empire.

The following IV ICNMD Congress took place in Queen Elizabeth Hotel, Montreal Canada in 1978 organized by G. Karpati, A. Aguayo, S. Carpenter, A. Eisen, and others.[2] President was J. Walton and vice-presidents R. D. Adams, M. Aloisi, F. Buchtahl, B. A. Kakulas, S. Refsum, G. Serratrice, A. T. Milhorat, L. P. Rowland and others five Symposia were organized. The first dealt with molecular structure and biophysical aspects of sarcolemma as well chemistry and Chemical Pathology of the sarcolemma. The second dealt with toxic disorders of the nerve. The third was about cell interactions in the Peripheral Nervous System. The fourth dealt with metabolic aspects of Muscle and Nerve. The fifth dealt with Nerve Structure and Function. The sixth dealt with Acetylcholine Receptors and Myasthenia Gravis the seventh with Developmental Disorders of Muscle. There were invited posters, platforms, and poster presentations. The first scales for DMD function were presented by Julaine Florence and Michael Brooke, therefore a complete survey was given of myopathies and neuropathies. Therapy of myasthenia gravis was also presented as well as animal models.

The following Congress was organized by George Serratrice with Claude Desnuelle, Jean Pouget, and others in Marseille.3 Claude attended my laboratory in Padova for several months in the '80 before the Congress. I had the pleasure to meet Valerie Askanas and King Engel in 1982, during the Vth International Congress on Neuromuscular Diseases, organized in Marseille by

Fig 1. *Second ICNMD in Perth,1971. From left Pinelli, Aloisi, Canal, Scarlato Kakulas, below Nardella, Cornelio, Mondaini and Gentili.*

George Serratrice. On that occasion, they received the degree "honoris causa" in Medicine from the Faculty of Marseille and I was impressed by the numerous and outstanding goals they were able to reach during their scientific career. The Congress was particularly lively, the Meeting of a PNS satellite symposium was held on 12 September 1982 at Padova University, Palazzo Centrale del Bò, in the Aula for Medical degrees and Pope Wojtyla gave his benediction, during his visit, and several participants joined up the Congress in Marseille traveling by bus from Padova. The Marseille meeting was attended among others by L. P. Rowland, I. Hausmanowa-Petrusewicz, M. Brooke, J. Florence, S. Di Mauro, J. Morgan-Hughes, D. Stumpf, and T. L. Munsat. The workshop on myasthenia was organized by Angela Vincent, John Newsom-Davis and J. Lindstrom. A workshop on mitochondria and metabolic myopathies was organized by myself with Morgan-Hughes, Di Mauro and Tarui. The focus during that conference was on the beginning of clinical trials and the consequences of biochemical disorders in muscle or antibody-related weakness at the neuromuscular junction. The main progress was therefore a clear view of metabolic myopathies, their treatment, mitochondrial disorders, and myasthenia gravis. A book on Neuromuscular Diseases summarized the highlight of the Congress and was divided into five general sections: "Normal ad diseased muscle," "Normal and diseased nerve," "Muscle and nerve cells in culture," "Neuromuscular junction" and "Therapy and rehabilitation".[3] Emphasis was given to both metabolic myopathies, prevention of DMD, and work with recombinant DNA technology that was anticipating the advent of the molecular era.

The molecular era

On July 6-11,1986 a subsequent meeting was organized by Valerie and King in Los Angeles, honorary President was A. T. Milhorat, and there were Poster presentations, workshops, Meet-the Professor lectures, Plenary sessions on Muscle cells, Schwann Cells, Neuromuscular Junction, Lower Motor Neuron, Genes in Neuromuscular Diseases, a noon time informal session on Planning Therapeutic Trials in Neuromuscular Diseases.[4] During this meeting, there was a shift toward molecular genetics and applied techniques. Kunkel presented the localization of the DMD gene, but still, the missing protein dystrophin was not yet identified. I particularly like to remember that occasion, not only for its high scientific excellence but also for a noontime session on history with the late Shri Mishra; the friendly atmosphere of the Congress was only disturbed by a sudden earthquake, that woke us up in the middle of the night. A practical course on diagnosis and treatment of NMD was done on the last day.

The following ICNMD took place in Munich, organized by Reinhard Rudel and with large participation, both from established and young investigators.[5] Before that a satellite meeting in Venice was organized on 14-15 September 1990,[6] with the title "Muscular Dystrophy Research, from molecular diagnosis toward therapy "and the first results on cell therapy and steroids in DMD were presented. The Munich meeting was particularly large and among other scientists attended by L.P Rowland and E. Hoffman, X-linked muscular dystrophies were extensively covered by K. Bushby and J. Martin. George Padberg communicated the mapping of FSHD to chromosome 4 and Eric Hoffman the various clinical phenotypes of dystrophin defects. The pathobiology of neuromuscular junction defects was reviewed by D. B. Drachman an A. G. Engel for congenital myasthenic syndromes. Coenzyme Q treatment of Progressive External Ophthalmoplegia was presented by C. Desnuelle while Y. Shapira covered treatment with l-carnitine in children with myopathic carnitine deficiency. There was the launch of the new muscle journal "Neuromuscular Disorders" and Brooke, Tomè, Angelini, Fardeau, DiMauro, Davies, Sugita, Jerusalem, Cornelio, Nonaka, Rowland, Dubowitz, Merlini, Emery, Rudel, Brown, Somer, Herrikson, Hausmanowa-Petrusewicz, Walton, van Ommen attended as invited participants member to the Editorial Board of the new Journal. At the end of the Munich meeting, Prof. Reinhold Rudel organized a dinner with wheel-chair dancing.

From Germany, the meeting migrated to Asia and there was a large symposium in Kyoto, Japan organized by Eijiro Satoyoshi, preceded by a satellite meeting in Osaka Sun Palace from 5 to 7 July 1994 (ISGMD) on "Glycolytic and Mitochondrial Defects in Muscle and Nerve"[7] organized by S. Tarui, after which the attendees were transferred to Kyoto by bus, including the late Anita Harding and L. P. Rowland.

The VIII ICNMD meeting was held in Kyoto International Conference Hall from July 10-15 1994, an international Symposium on FSHD was organized on July 10 by H. Sugita and K. Arahata and was attended by G. Padberg, A. E. H. Emery. A total of 9 Satellite Symposia were available during or before the Congress, such as the one in Osaka.

The opening ceremony was at that Conference Hall Garden, there were Breakfast Seminars, Surprise boxes, Plenary lectures by L. Kunkel and A. J. Aguayo, a series of Symposia on Molecular Genetics of DM1, Familial Amiloidotic Polyneuropathy, Prenatal and carrier detection of muscular dystrophy, Pathogenesis and treatment of inflammatory myopathies, Clinical and genetic aspects of mitochondrial myopathies, etc. and a workshop covered Therapeutic trials in DMD by steroid treatment with A. Dubrowski, M. H. Booke, J. R. Mendell, J. Kang, and myself as well as periodic paralysis and channelopathies with L. Ptacek. The meeting was successful, and well attended, and the presenters were well-compensated by local organizers.

Kyoto offered an interesting historical view of many temples as well as the historical town and Nara. Several banquets helped to get familiar with Japanese customs.

For the first time, commercial exhibitions were part of ICNMD and contributed with several booths at its organization, including Allergan, AMCO, Eisai, Carl Zeiss, ENMC, Sandoz, and others. The Congress banquet was held in the ballroom of Miyako Hotel.
On March 26, 1996, the following were elected member of the executive WFN Committee C. Angelini, E. Byrne, F. Cornelio, S. Di Mauro, M. Fardeau, R. C. Griggs, E. Hoffman, J. Kimura, F. Lehman-Horn, J. Newsom-Davis, R. Rudel, H. Sugita. We started planning for the next ICNMD meeting in Adelaide, Australia.
The venue for these Congresses has been selected by the Executive Committee of The re-named Research Group on Neuromuscular Diseases (RGNMD) of the WFN and the Chairman and Secretary of the Group have been involved in their planning. The Group has also been involved in other activities such as the preparation of the classification of neuromuscular diseases. The precise role of RGNMD was defined by P.K.Thomas, as President and L.P.Rowland as secretary, the local organizing committee was financially autonomous, but a Scientific Committee was composed of several members of the RGNMD, and their comments were addressed to the local organizing Committee. Drs Bretag and Byrne described the state of the planning for the 1998 Australian Congress. The two major themes were: i) new concepts in nerve and muscle regeneration; ii) genetic advances.
The following ICNMD was organized in 1998 in Adelaide, Australia, and was well attended, although difficult to reach for young investigators. It was organized by A. Bretag and members of RGNMD with 10 morning and plenary lectures; 10 Symposia, 32 workshops, 5 poster sessions, 40 meet the expert sessions, and 40 lunch sessions, it was scientifically successful, but the economic cost resulted in a major burden for the local organizers and resulted in a financial disaster, with a large deficit. The workshops were on myotonic dystrophy, FSHD, LGMD, ventilation, cell and gene therapy, extracellular matrix and growth factors, general care of DMD, and clinical trials. The LGMD due to dysferlin deficiency was presented by two concurrent groups with R. Brown and K. Bushby as main speakers.
Myotonic Dystrophy, DM1, and DM2 were discussed by K. Ricker and L. Ranum. J. Day and R. Moxley. K. Ricker, at several international presentations, reported later that he does not consider anticipation to be a feature of DM2, that is a well known genetic feature of DM1. Attending the PNS session was E. Nobile-Orazio and several muscle sessions and symposia were followed by G. Siciliano, L. Manca, F. Muntoni, E. Mercuri, J. Florence, and L. Pestronk. W. Bradley covered the complexity of ALS and Franks and George Padberg the FSHD syndrome, while N. Laing and C.Westgren-Pettersen surveyed nemaline myopathies and actinopathies. In Australia, there were also good amusement and the possibility to see natural parks as well the Kangaroo Island with full coverage of local touristic places with the opportunity during the Congress or thereafter for several interesting visits to animal parks and beautiful sceneries of mountains and desert nearby Ayers Rock and to the opportunity to admire the coral reef near Brisbane.
The executive committee of RGNMD met on June 18, 2001, in Earl's Court, London, UK with 12 members in attendance. Plans were made for the election of new officers, Chair, and Secretary to replace Prof. Thomas and Rowland respectively, a subsequent mail ballot of the full executive committee resulted in the election Prof. A. K. Asbury as Chair and Gerard Said as Secretary, both agreed to serve. Planning for the Xth ICNMD was well advanced and the next Meeting of the Executive Committee was scheduled for April 15, 2002, in Denver, Colorado during the meeting of the American Academy of Neurology, and included the presentation preliminary planning of 2006 XI Congress. The bank account showed a year-end balance of 53 £ and no transaction, the cost of the Executive meeting in June 2001 was paid out of pocket.

The era of personalized medicine and neuroimaging

The second meeting in Canada took place on July 7-12, 2002 in beautiful Vancouver, British Columbia. The X ICNMD was held at the West Conference Venue and A. Eisen was President while George Karpati, was Chair of the Organizing Committee.[8] The venue West Conferences Service Ltd acted as Abstract Coordinator and did an excellent job. Our group presented several abstracts on LGMD, dysferlinopathy, familial cases with ataxia, methylmalonic aciduria, and SPECT hypodensity that was accepted in an interactive session. I was also required to Chair the session PLT.1: "Trinucleotide expansion disorders" where Dr. K. Fishbeck was the speaker. Late-breaking news Posters were presented on peripheral neuropathies, dystrophinopathies including deflazacort and prednisone treatment, congenital myopathies, and cell therapy. The congress presented all recent genes developments and their impact on several disorders, including the LGMD group of disorders, where various clinical phenotypes were associated with the same gene defect, and both protein and RNA profiling were studied. CT and MRI muscle imaging were also new techniques to approach neuromuscular disorders utilized by several groups. There was in Vancouver the presence of several international scientists including K. Fishbeck, H. Topaloglu, N. Duprè, M. Shy, J. Vissing, R. Haller, L. Salviati, K. M. Flaningan, N. Barisic, S. Schiaffino, E. Hoffman, Y. Hayashi, J. Florence, A. Pestronk. The ICNMD was organized on various themes as recommended by the World Research Group on Neuromuscular diseases and had therefore to cover all novelties on muscle, peripheral nerve, synapse, and anterior horn disorders. During the X Vancouver meeting several industries held sponsored workshops since antisense oligonucleotides were studied for cases of dystrophin deficiency and AAV rescue of genetic

disorders was started. The field of treatment of diabetic, and inflammatory neuropathies was also promising and supported by workshops, and industry- sponsored symposia. A profitable venue was to familiarize, meet also company-sponsored attendees, and plan future therapeutic developments. At the end of the meeting a dinner banquet with dancing was held.

The following meeting was planned in Turkey in 2006. There were relevant workshops, lectures, and posters, and the participants were taken on a boat trip on Bosphorus. There was good attendance in 2006, in Istanbul, Turkey, the Congress hall was nearby Taxim Square for the full X1th International Congress on Neuromuscular Diseases, which was organized by Piraye Serdaroglu and Haluk Topaloglu with great success. Before the ICNMD Meeting a Symposium Muscular Dystrophy Research on 30 June 2006 was organized in Archivio Antico, Bò Central University Palace in Padova with the attendance of J. Florence, S. Di Mauro, M. Zeviani, M. Carelli, A. Picchiecchio, a second day was done in Aula Nievo. The participants at XIth ICNMD that was held from 2 to 7 July in Istambul included T. Voit, S. Iannaccone, F. Deymeer, A. G. Engel, L. P. Rowland, R. Finkel, K. Fishbeck, A. Pestronk, J. Florence, J. Newsom-Davis, J. Wokke. We had the opportunity to visit Istambul's several Mosques, including the Blue Mosque, Aya Sofia Museum, and Topkapi Palace.

The Executive Committee for the Research Group of NMD met on 4 July 2006 in Sultan room 1 under the Presidency of G. Said There were proposals to host the next ICNMD from India by Chopra and from Italy from Naples group. During this meeting, we had the opportunity to discuss with Valerie and King the proposal to host Naples in 2010 at the XII ICNMD Congress. They were very active in convincing most of the members of the World Federation of Neurology to elect Naples with a vote of 17 to 7 as hosting city and Giovanni Nigro as President of the Congress (Figure 2), it was then decided to charge Valerie as President of the Scientific Committee. She accepted with enthusiasm showing her great quality of being "hard-working" and an expert of the state of the art in all scientific aspects of muscle diseases. In 2009, Nicosia, Cyprus, where it was held the IX Congress of the Mediterranean Society of Myology, during the congress there was a very important meeting of the Scientific Committee of XII ICNMD which participated, among others, L. Middleton, L. Comi, L. Politano, K. Engel, and V. Askanas.

On 15-16 July MDR 2010 on "New Diagnostic and therapeutic challenges in muscle disorders" was held in Archivio Antico and Aula Nievo Palazzo del Bò, Padova University, scientists participants were P. Laforet, B. Schoser, M. Walker, J. Florence, S. Sacconi, L. Salviati, G. Siciliano, and others, the dinner was at Osteria dei Fabbri. On the next day, we left for Naples. During the successful Naples meeting that was patronaged not only by WFN but also by G. Conte Academy, Italian Ministry of Health, AFM, UILDM, Regione Campania, and Genzyme-Sanofi company after the opening at the Royal Palace Theatre we moved to Centro Congressi Federico II, nearby Monte S. Angelo. The inauguration was chaired by Lord Walton, while in Centro Congressi, the whole meeting took place; there were Meet-the-Professor lectures, Plenary lectures, teaching courses, and a successful small symposium dealing with the natural history of dysferlinopathy was organized by Z. Argov on behalf of Jain Foundation and during the plenary lectures a presentation of the first data on ERT therapy for glycogenosis type II was done.[9] During the following days after the teaching courses, there were posters, simultaneous symposia, and platform presentations on various new subjects including veterinary medicine, cardiomyopathies, and novel therapeutic targets at the neuromuscular junction. The Congress took place at the Second University Federico II of Naples. Here the only major hurdle was a wave of heat throughout the meeting since only a blue and red hall were efficiently air-conditioned. However, lunch was provided during

Fig 2. *Istambul, Turkey, 2006. From left Lucia Comi, Serenella Papparella, Valerie Askanas, Orlando Paciello, Gio- vanni Nigro, and Corrado Angelini celebrate the nomination for the next ICNMD in Naples.*

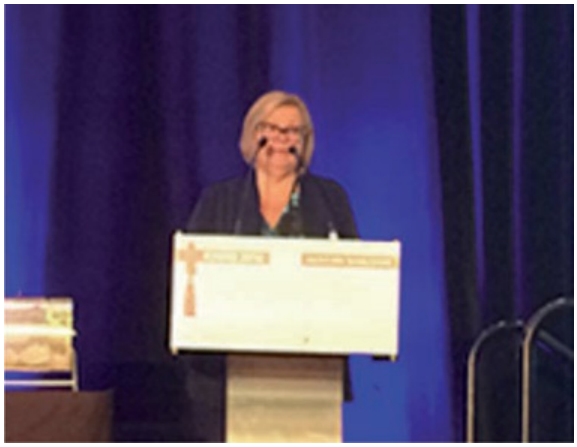

Fig 3. *Prof. Vera Bril, Toronto, president of the XIV ICNMD Congress.*

Congress in the area. Several international scientists attended the XIIth ICNMD including A. Vincent, B. Kakulas, S. Appel, M. Roberts,W. K. Engel, and H. Lochmuller, S. DiMauro, G. Novelli, A. E. H. Emery, M. Hanna, R. Baloh, I. Tein, D. Duboc, M. Hirano, A. Oldfors, J. Pumyrat, P. J. Shaw, R. Griggs, D. Shelton, L. Gou. On 18 July 2010, the WFN Research Group on Neuromuscular Diseases met to discuss the organization of the XIII ICNMD, which was assigned to C. Desnuelle. There was some preliminary discussion with G. Said and Z. Argov since alternatives such as Montreal were proposed by J. England and B. Griggs, but the vote was 9 to 5 in favor of Nice. In Naples, we had the opportunity to appreciate several lunches and dinners outside of Congress with excellent food and company. A satellite Meeting dedicated to R. T. Edwards was held subsequently in Pisa on "Fatigue in Neuromuscular Disorders" organized by G. Siciliano and attended by R. Haller, J. Vissing, M. Zeviani, F. Mastaglia myself and numerous scientists as well as local scholars.

The XII ICNMD meeting took place in Acropolis Palace in Nice on 6-12 July with over 1400 participants. The inauguration was done on the terrasse of the Acropolis. The organizers received several proposals and suggestions; on that occasion, I particularly appreciated Claude's ability to understand and solve problems. There were posters, Meet-the-Professor lectures, workshops, teaching courses, and plenary sessions, and were all of great interest. A teaching course held by myself and V. Nigro on "What about the classification of LGMD" put the basis for the further reclassification of LGMD at ENMC center in the following years. An outstanding speaker was K. Campbell from Iowa (USA) who reviewed the muscular dystrophies due to components of the dystroglycan complex.[9] Attending the meeting were J. Vissing, A. G. Engel, E. Feldman, P. Laforet, N. Lewy, W. Grisold, J. J. Vilchez, and H. Lochmuller. An opening cocktail and presidential Party were also given at Chagall Museum on 7 July, the Gala dinner was held at Negresco on the evening of 8 July, as Vice- President of the Congress. I delivered a speech after Michel Fardeau on the evolution of science at ICNMD, describing also the Nice history. At that dinner were present G. Serratrice, A. G. Engel, M. Dalakas, K. Claeys, M. Zeviani, S. Ravaglia, A. Toscano, and V. Mirabella. The Congress full report and Abstracts were hosted by a Supplement of the new Journal of Neuromuscular Diseases.[10] The final goodbye dinner was at Hotel Ascar La Scala with a beautiful night view of Nice.

After that the ICNMD meeting was organized every two years, the XIV ICNMD took place on 5-8 July 2016 at Sheraton Center Toronto organized by V. Bril, attending 750 delegates. Vera Bril, MD (Figure 3), organized the Congress on behalf of the World Federation of Neurology (WFN) neuromuscular research group. This ICNMD Congress covered the broad spectrum of neuromuscular diseases and aimed to fill the gap between new developments in research, in particular genetics and immunology, and patient assessment and care. The aim was to include the spectrum of neuromuscular diseases and focus on practical issues and emerging therapies. The plenary session topics focused on new genetic avenues in muscle disease, new treatment strategies in neuromuscular disease, treatment of inflammatory neuropathies, therapy in muscle disease, motor neuron disease, advances in myasthenia, and late-breaking news on the neuromuscular complications of Zika infections. The scientific sessions were preceded by a rich selection of teaching courses, also with a wide variety of topics, such as motor neuron diseases, neuropathies,

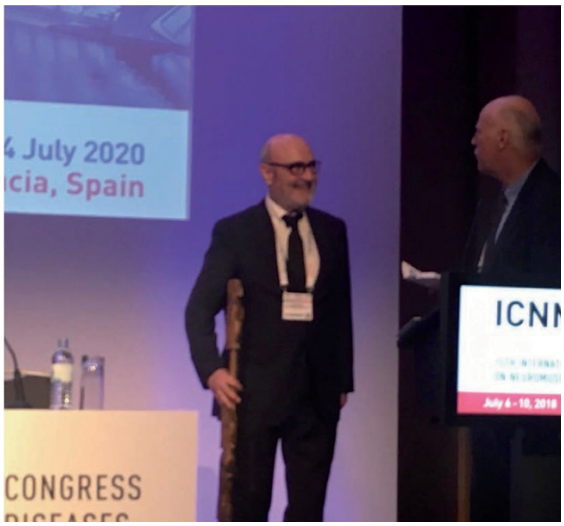

Fig 4. *Wien 2018. J.J. Vilchez receives Canada's 2014 tomahawk from Wolfgang Grisold for the next ICNMD.*

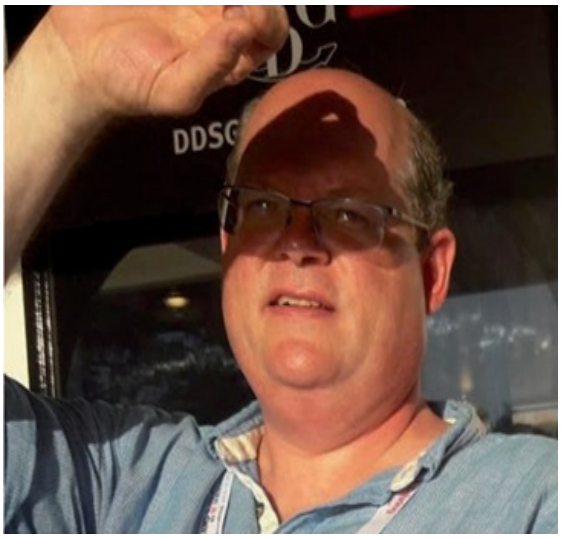

Fig 5. *P. James Dyck Chair of WFN NMDG, during a boat trip in Wien.*

Table 1. ICNMD meetings endorsed by the World Federation of Neurology (WFN) Neuromuscular Disease Research Group.

ICNMD I	Milan	G. Scarlato, M. Aloisi ,N. Canal	1969
ICNMD II	Perth	B. Kakulas	1971
ICNMD III	Newcastle upon-Tyne	Lord J. Walton	1974
ICNMD IV	Montreal	G. Karpati, A. Aguayo	1978
ICNMD V	Marseille	G. Serratrice	1982
ICNMD VI	Los Angeles	V. Askanas, King Engel	1986
ICNMD VII	Munich	R. Rudel	1990
ICNMD VIII	Kyoto	H. Sugita	1994
ICNMD IX	Adelaide	A. Breitag	1998
ICNMD X	Vancouver	G. Karpati, A. Eisen	2002
ICNMD XI	Istanbul	P. Serdaroglu, H. Topaloglu	2006
ICNMD XII	Naples	G. Nigro	2010
ICNMD XIII	Nice	C. Desnuelle	2014
ICNMD XIV	Toronto	V. Bril	2016
ICNMD XV	Wien	W. Grisold	2018
ICNMD XVI	Valencia (virtual)	J.J. Vilchez	2020
ICNMD XVII	Bruxelles	G. Remiche	2022
ICNMD XVIII	Perth	S. Koks	2024

neuromuscular transmission disorders, and muscle diseases. In Toronto, there were successful presentations on Myasthenia Gravis treatment by J. F. Howard,[11] several scientists attending and among the clinicians that participated to that Congress there were: S. Ianaccone, W. Grisold, J. Leger, J. Kissel, A. Amato. R. Bahron dealt with Investigator-Initiated Clinical Trials, and R. Haller and J. Vissing with exercise therapy in mitochondrial and metabolic myopathies respectively; on that occasion Wolfgang Grisold received the next assignation to organize the XV ICNMD meeting in Wien.

The XV Congress was hosted from July 6 to 10 1918 at Hilton Hotel in Wien with a record presence of 1500 participants. There was a boat trip for Faculty members, family, and friends on the Danube and a lively inauguration with Bavarian alpine music and dancing of the Congress, that in five days covered both teaching courses and several Overarching Sessions on various features of neuromuscular disorders, including the disorders with brain and muscle dysfunction.[12,13] A symposium on LGMD was chaired by myself with the participation of V. Nigro, K. Claeys, and A. Urtizberea. Myasthenia Gravis history was presented by R. Bahron, and GBS syndrome treatment was updated and analyzed. The Agenda included the presence of breakfast seminars, and satellite Symposia either from the pharmaceutical industry and ENMC or other commercial-oriented Companies, such as Alexion, Biogen, Sarepta, etc. In that meeting Dr. Vilchez received the designation for the XVI symposium (Figure 4), While W. Grisold was designated as a Co-Chair; the XVI ICNMD due to the COVID-19 pandemic was organized only virtually and eventually shifted to 2021. In 2022 the XVII ICNMD was again organized in the presence of G. Remiche, with over 1500 participants in Bruxelles, there were Overarching sessions, Teaching courses, and Workshops, Hand-On-Corses The host institution was Brussels' Convention Centre that is situated in the historical and cultural heart of the capital, next to the European headquarters and embedded in a neighborhood consortium dedicated to Meeting Industry activities including 10.000 quality hotel rooms, Brussels International train station,[11]

museums, antique shops, avant-garde boutiques, and parks, the Congress Square was relatively simple to reach. During Bruxelles ICNMD a workshop on biomarkers was organized by myself, H Lochmuller and M. Otto. A first workshop was held on the first day of Congress on brain involvement in myopathies with the participation of Prof. L. Bello on DMD and myopathies with glycoprotein defects, T. Klopstock on mitochondrial encephalomyopathies and myself on brain involvement in DM1 and DM2. Given the pandemic, a great emphasis was given to digital outcomes with two workshops one organized by Gabriele Siciliano, and another by myself on telemedicine, home infusion, and quick outcomes scales with G. Sicilano, T. Tuong, on the last day of Congress.[14] Prof. G. Remiche delivered prices for best conferences, which were attributed to M. Shy, and prices for posters. A. Evoli in plenary sessions covered myasthenia gravis treatment and David Beeson's congenital myasthenic syndromes. Servais and Maggie Walker the treatment of infantile and adult cases of spinal muscular atrophy. The Presidency of the World Neuromuscular Group rotated from Dr. England to Dr. Dyck (Figure 5) and the next 2024 meeting will again convene in Perth, Australia, in October 2024 (Table 1). The future meeting was discussed during a meeting of the executive of RGNMD, at Bruxelles Convention Center.

Future developments

As planned at present the ICNMD International Congress on Neuromuscular Diseases is organized on behalf of the Research Specialty Group on Neuromuscular Diseases (RGNMD) of the World Federation of Neurology (WFN). Since 2014, the Congress has taken place in a two-year cycle and covers the whole field of nerve and muscle disorders, genetic and acquired. There have been substantial progresses over the 50 years ICNMD has taken place in different countries since from the preliminary techniques covering histochemistry and morphology in muscle biopsies, the interest has shifted toward molecular biology and biochemistry, DNA, RNA, and protein expression are used nowadays with imaging to identify and use in the follow-up of neuromuscular disorders. Basic research has remained an important field, but clinical trials and MRI imaging appear nowadays always more prominent. Another major change is the use of novel therapies both in muscle, such as antisense oligonucleotides, monoclonal antibodies, and various forms of immuno-therapies that have changed the treatment of several immune-related neuropathies, as well as myasthenia gravis. The use of artificial intelligence, robotics, and new technological gadgets for clinical trial monitoring is in full development and will be more and more represented in the future of ICNMD. The price to pay for such advances is the presence of several commercial symposia promoted by the pharmaceutical industry, that have complemented the traditional scientific sessions and workshop presentations. Another field of great advancement has been the one on gene-delivered therapies, with major advancement in the field of both spinal muscular atrophy, myasthenia gravis, and metabolic myopathies with change in the natural history of such disorders, now extending from glycogen storage disorders to myotubular myopathies, etc. The advent of new drugs has increased the interest in neuromuscular disorders, which are evolving from a neglected field of diagnosis toward the more popular clinical practice of treatment. Similarly, the use of ventilation and cardio-protective drugs have extended the life of neuromuscular patients and will be in the future readily available to an increased number of muscle disease cases. The future aim of the ICNMD Congresses is to offer attendees an updated view of neuromuscular disorders and create networking opportunities to increase international experience and collaboration. The scientific and program committee are invited from all the continents around the world to enable this wide spectrum of clinical and basic science interaction.

Conclusions

The ICNMD Congresses aim to offer to attendees an updated view on neuromuscular disorders and those networking opportunities that increase their international experience and collaborations. The scientific and program committee are invited from all continents around the world to enable this wide spectrum of events and well balance the clinical and basic reports mixture in this growing field. The progress in neuromuscular research has been documented following the Congresses and Meetings International Congress of Neuromuscular Diseases ICNMD organized on behalf of the WFN Neuromuscular Specialty Group, that now is preparing the congress of Perth. All topics of neuromuscular diseases will be covered, but it seems likely that the large number of participants that were reached at the ICNMD 2018 in Vienna might be difficult to reach, beacause of the location.

The WFN tries also to have session on neuromuscular issues in low-income parts of the world, under the Chair of P. J. Dyck and Wolfgang Grisold. The next ICNMD congress will be in Perth in 2024, and a call for the ICNMD subjects and abstracts is on the way. Thousands of the world's brightest muscle scientists are set to gather in Perth in 2024,when the ICNMD returns for the first time after fifty years.

This review documents the changes in the field that occurred in these five decades. The ICNMD is one of the leading global conferences, in neuromuscular diseases, it will attract delegates from around the World, following the ground-breaking research by western Australian emeritus Byron Kakulas, who showed that degenerated muscle could regenerate in quokkas, similarly to what happens in avitaminosis E in rabbit.[15]

List of acronyms

ICNMD - International Congress Neuromuscular Diseases - NGS Next Generation Sequencing
CMD - Congenital Muscular Dystrophy

LGMD - Limb-Girdle Muscular Dystrophy 3

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