

Rheumatic Diseases – a Major Challenge for European Research and Health Care

European Science Foundation Policy Briefing

Contents

- 1 Foreword | Introduction | 2 European state-of-the-art | The European Challenge
3 Recommendations | Specific actions | 4 Expert group on Rheumatic Diseases

Foreword

The World Health Organization recently concluded – at the half way point of the Bone and Joint Decade¹ – that musculoskeletal diseases such as chronic pain syndromes, osteoarthritis, osteoporosis and inflammatory rheumatic diseases are the leading cause of pain and disability in Europe.

In 2005 the European League against Rheumatism (EULAR) and the European Medical Research Councils (EMRC), one of the five scientific units at the European Science Foundation (ESF), established a task force comprised of leading European scientists, in presence of representatives of a patient organisation and a regulatory agency to address science policy issues in the field of rheumatic diseases. The aim was to develop a science policy briefing (SPB) designed to provide policy advice to national and European funding institutions, to the Framework Programmes of the European Commission (EC) as well as to Health Care Systems across Europe.

This policy paper endeavours to evaluate the state-of-the-art, the demand for and potential of research in rheumatic diseases at the European level. Its ambition resides not only in reporting key issues identified in the strategic workshop held on 13-14 December 2005 in epidemiology, basic, translational and public health research but also in achieving a balanced presentation of research priorities streamlined through a consensual Delphi² analysis by the scientific experts.

This paper has been reviewed by EMRC and EULAR and is considered to give a balanced view of research priorities in the field of rheumatic diseases. It will be presented to and further challenged by a broader research community at the annual congress of the European League Against Rheumatism (EULAR) in June 2006 in Amsterdam.

Without pronouncing itself on the priority compared to other domains of research, ESF-EMRC wishes to raise awareness of the need for an acceleration of research in rheumatic diseases. The ESF recommends that the conclusions of this science policy briefing are given serious consideration by all concerned to contribute to reducing the burden of this disease on society.

Bertil Andersson
ESF Chief Executive

Introduction

Approximately 100 million people in Europe suffer from some form of inflammatory or degenerative rheumatic disease³ causing the impact of rheumatic diseases on European societies to be overwhelming for society. Joint diseases account for half of all chronic conditions in persons aged 65 and over.

The quality of life of approximately 7.5% of the European population is severely and permanently reduced by pain and functional impairment caused by rheumatic diseases (Fig. 1).

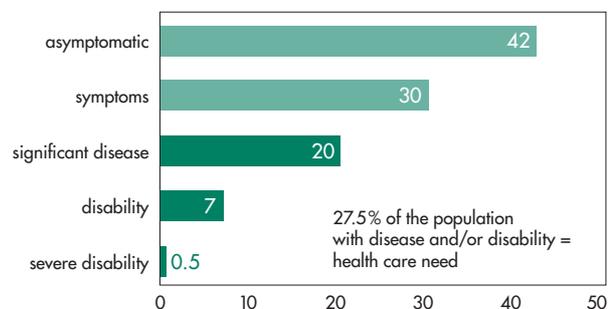


Figure 1. Musculoskeletal diseases in the population
[Badley E.M., Tennant A. Ann Rheum Dis 52:6-13 (1993)]

Immobility and a reduced life expectancy are the most drastic consequences of these, at present, incurable diseases.

In Europe alone, rheumatic diseases impose an economic burden of more than 200 billion euros per year⁴. Indeed, the impact of rheumatic diseases and their social and economic burden will increase dramatically as the European population ages (Fig. 2).

1. "Priority Medicines for Europe and the World – A Public Health Approach to Innovation" commissioned by the Government of the Netherlands, November 2004

2. "Delphi Method" is used to solicit and aggregate expert opinions through three distinguishing characteristics i) iteration with controlled feedback, ii) anonymity, iii) statistical representation of group response (<http://oregonstate.edu/~gordons/research/processes/delphi.htm>)

3. "EULAR. European Action towards better musculoskeletal health. European bone and joint decade strategies project". Published in BJDonline 2005-06-02. www.boneandjointdecade.org

4. The data are extrapolated from national data from the UK and Germany

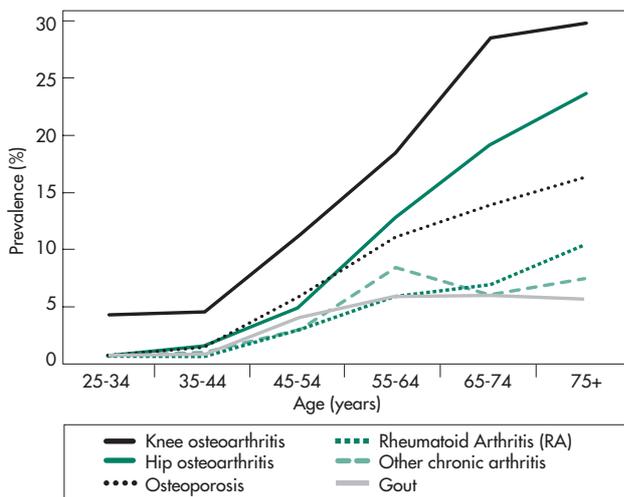


Figure 2. Prevalence of self-reported inflammatory arthritis and osteoarthritis increases with age [Picovet H.S.G., Hazes J.M.W. Ann Rheum Dis 62:644-650 (2003)]

New therapies targeting the molecules involved in the pathogenesis of chronic inflammatory disease have been developed in recent years. Despite these efforts we are still not able to cure the majority of rheumatic diseases. The therapeutic challenges include chronicity of inflammation, autoimmunity, and regeneration of the inflamed and degenerating musculoskeletal system. Although rheumatic diseases differ in their immunopathology, they share common mechanisms of initiation and perpetuation. Moreover, there is a considerable translational potential for the understanding of other diseases involving the immune system, e.g. autoimmune disease, allergy and infection.

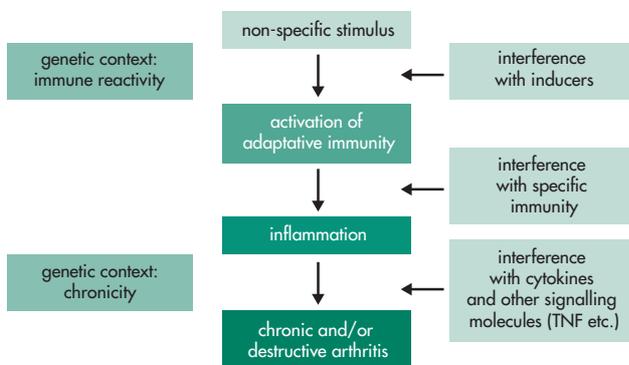


Figure 3. Challenges in basic and translational research [Klareskog L., Radbruch A. (2006)]

The diversity of rheumatic diseases, the multiplicity of tissues involved, i.e. bone, cartilage, joints, kidney, skin, blood vessels, and the multidisciplinary approach required to understand the molecular basis of these diseases, call for a pan-European effort to accelerate the development of concepts of curative therapies and to translate them into clinical application.

Multidisciplinary research is required to understand the interaction of genetic, environmental and lifestyle causes of the onset and progression of rheumatic diseases and to develop better strategies for prevention and treatment.

This policy briefing is the result of an intensive discussion among European experts with epidemiological, basic, translational and clinical perspectives of the field, aiming at the promotion of concerted research on all of these aspects of rheumatic diseases.

European state-of-the-art

Research in Europe has contributed significantly to our current understanding of rheumatic diseases.

Europe was at the forefront of developing effective therapies against rheumatic diseases through pioneering treatment with biological agents that block tumor necrosis factor alpha (TNF- α).

Basic research reflects the European strength in molecular and cell biology. The integration of basic, translational and clinical research as well as epidemiology is being developed to various degrees at the national level. While the annual European rheumatology congress is the largest meeting of its kind in the world, integrated research at the European level is hampered by the lack of funding for translational research. There is also a lack of funding in paediatric rheumatology. Clinical trials involving large patient cohorts are driven by industry and performed at the European level. However, epidemiologic research which focuses on the complex aetiology and the burden of illness, as well as evaluative health care research, is restricted to the national level.

The European Challenge

The development of research on rheumatic diseases in Europe should aim, in a three-dimensional fashion, at the:

- Integration of successful national research efforts into a pan-European research strategy,
- Integration of basic, clinical and health care research for a fast translation of new concepts, and
- Integration of competence in developmental and molecular biology, genetics, immunology and systems biology.

Start-up funding at the European level is required to network scientific experts from academia and industry, integrated projects, bio-banking and the scientific community at large. The goal of research should be to achieve a better understanding of the initiation and pathogenesis of rheumatic diseases, their unifying and disease-specific principles. This understanding should develop into strategies to prevent the incidence and aggravation of rheumatic diseases by defined changes in the lifestyle and environment of the European population. Individuals at risk because of lifestyle, environment and genetic predisposition could be informed for their own benefit. A basic understanding of rheumatic diseases will also allow the development of curative therapies that target the chronicity of such diseases, stop inflammation and degeneration, and initiate the regeneration of specific tissues. Special emphasis should be given to paediatric rheumatology, and the consequences of these diseases for later life. Patient empowerment is a general challenge for basic and clinical research and should be addressed at the European level. National and European patient organisations should be integrated in research and science policy as well as decision making.

Recommendations

1. To promote a pan-European research effort for a better understanding of the molecular and cellular basis of chronicity in rheumatic diseases for the development of curative and preventative strategies. This would include the development and analysis of (genetic) animal models, biological samples from patients, defining relevant genes, pathological pathways and novel therapeutic targets, and the establishment of pre-clinical validation of candidate therapeutics.

2. To promote coordinated European studies and trials in order to evaluate the incidence and outcome of rheumatic diseases and the development of prevention strategies and also to evaluate different therapeutic strategies for adults and children, including health economy aspects, research on the relevance of non-genetic risk factors (e.g. smoking, obesity, social status).

3. To establish a pan-European network developing basic strategies for cell therapies of rheumatic diseases, especially immune ablation of pathogenic cells, reinstallation of tolerance and regeneration of degenerated or inflamed tissues.

4. To promote a pan-European research effort towards a better understanding of the molecular and cellular pathology of osteoarthritis and osteoporosis.

5. To set up a Scientific Advisory Group (SAG) for rheumatic diseases at the European Medicines Agency (EMA) with members from academia (i.e. basic, translational, clinical and epidemiological research) and patient organisations.

Specific actions

To achieve implementation of the recommendations stated in this ESF Science Policy Briefing, funding of research on rheumatic diseases should be prioritised at the national and European levels. Within the EC Framework Programmes, **rheumatic diseases must be acknowledged as major diseases.**

Basic research should aim to develop better animal models for rheumatic diseases, reflecting the heterogeneity of human diseases – its chronicity and genetic and aetiopathogenic variability. This will require a major investment in basic molecular and cellular research on human rheumatic disease, from the bedside to the bench. The translation of basic research concepts into strategies for curative therapies, e.g. cell-therapy, requires a pan-European study network for pre-clinical testing with small, defined cohorts of patients representing distinct rheumatologic entities.

The promotion of large, independent European clinical trials as well as coordinated pan-European research in epidemiology, to answer urgent questions pertaining to prevention and control of the diseases, should be facilitated by creating an appropriate platform. An independent evaluation of therapeutic efficacy and its impact on the quality of health care and the health economy can only be undertaken if appropriate funding from the EC and the pharmaceutical industry can be secured.

Special emphasis should be given to the understanding of degenerative rheumatic diseases, in particular osteoarthritis, with the aim of focusing on underlying pathogenetic processes, to stop the degeneration and initiate regeneration of the damaged tissue.

The Expert group recommends setting up an EMA Scientific Advisory Group (SAG) for rheumatic diseases to maintain continued independent expertise in the European Medicines Agency. On request of the Committee for Medicinal Products for Human Use (CHMP), the SAG would be asked to answer specific questions during the evaluation process of new products when additional advice is needed.



European Science Foundation

1 quai Lezay-Marnésia, BP 90015
67080 Strasbourg cedex, France
Tel: +33 (0)3 88 76 71 00
Fax: +33 (0)3 88 37 05 32
www.esf.org

Expert group on Rheumatic Diseases

Chairs:

Maxime Dougados, Groupe Hospitalier Cochin – Paris (France)
Andreas Radbruch, DRFZ – Berlin (Germany)

Basic and Translational Research:

Francis Berenbaum, Université Paris 6 – Paris (France)
Andrew Cope, Kennedy Institute of Rheumatology – London (United Kingdom)
François Cornelis, ECRAF – Evry Genopole (France)
Steffen Gay, Universitäts Spital Zürich – Zürich (Switzerland)
Rikard Holmdahl, Medical Inflammation Research – Lund (Sweden)
George Kollias, BSRC Alexander Fleming – Varkiza (Greece)
Jutta Steinkötter, Competence Network Rheumatology – Berlin (Germany)

Clinical and Epidemiological Research:

Ferdinand C. Breedveld, University Medical Centre St Radboud – Leiden (Netherlands)
Paul Emery, Leeds General Infirmary – Leeds (United Kingdom)
Johanna Mieke Hazes, Erasmus Medical Centre - Rotterdam (Netherlands)
Joachim R. Kalden, Universität Erlangen – Erlangen (Germany)
Lars Klareskog, Karolinska Institutet – Stockholm (Sweden)
Wietse Kuis, University Medical Centre of Utrecht – Utrecht (Netherlands)
Tore K. Kvien, Diakonhjemmet Hospital – Oslo (Norway)
Josef Smolen, Klinik für innere Medizin III – Vienna (Austria)
Cornelia Rufenach, Competence Network Rheumatology – Berlin (Germany)
Jeremy Saklatvala, Kennedy Institute of Rheumatology – London (United Kingdom)
Angela Zink, DRFZ – Berlin (Germany)

Observers

European Medicines Agency:

Eberhard Blind, EMEA – London (United Kingdom)

Patient Organisation:

Robert Johnstone, PARE – Skelmersdale (United Kingdom)

ESF Standing Committee – European Medical Research Councils (EMRC) Chair:

Clemens Sorg, Innsbruck Medical University, Innsbruck (Austria)

ESF-EMRC Staff:

Carole Moquin-Pathey, Head of Unit
Thomas Bruhn, Science Officer
Nathalie Geyer, Administrative Assistant

The European Science Foundation is the European association of 78 national research organisations in 30 countries, devoted to scientific research.

The ESF provides a common platform for its Member Organisations in order to:

- Advance European Research;
- Explore new directions for research at the European level.