Perspectives on the Future of Bone and Joint Diseases

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ABSTRACT. The diseases of bones, joints, and muscles are common, chronic, and very costly to society. While the impact of these diseases falls across the age spectrum, the worldwide growth in the percentage of elderly in the population makes attention to musculoskeletal disorders and conditions particularly critical. An effective prevention strategy, driven by an understanding of the fundamental biology of bone and connective tissue, can only result from an upshift in the efforts of many sectors — public and private, academic, scientific, and patient-based — with new opportunities for partnerships and collaborative efforts flourishing. The Decade of the Bone and Joint can serve as a catalyst in this effort. The National Institutes of Health (NIH) are pleased to join with other national and international organizations to promote new activities and initiatives during the next decade. The NIH Osteoarthritis Initiative is highlighted as an example of a public-private partnership to develop resources and information on the natural history of the disease process that can drive new clinical intervention studies in osteoarthritis. Hopefully, this initiative and others will pave the way for important, scientifically driven prevention strategies during the next decade. (J Rheumatol 2003;30 Suppl 67:62–64)

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The diseases of bones, joints, and muscles are common, chronic, and very costly to society. While the economic costs of the musculoskeletal diseases are considerable, the psychological and social costs can be devastating to an individual. Although musculoskeletal pain, injury, and dysfunction affect all ages, the elderly are particularly targeted. The growing population of older individuals across the world means an epidemic of chronic bone and joint diseases unless we implement an effective prevention strategy. Such a prevention strategy must be driven by an understanding of the basic pathophysiology of bone and connective tissue, as well as by epidemiological research directed at risk factor identification, and intervention studies to test the effect of strategies to reduce risk. While the toll of particular and very prevalent musculoskeletal diseases such as osteoporosis and osteoarthritis (OA) is in the elderly, it is clear that prevention should begin in childhood.

The mission of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), a part of the National Institutes of Health (NIH), Department of Health and Human Services, is to support research into the causes, treatment, and prevention of arthritis and musculoskeletal and skin diseases. In addition, the Institute supports the training of basic and clinical scientists to carry out this research, and the dissemination of information to the public on research progress in these diseases.

President George W. Bush proclaimed the years 2002-2011 to be the Bone and Joint Decade on March 21, 2002, recognizing the importance of promoting a healthy musculoskeletal structure for all people throughout the world from childhood through adulthood. Many of the institutes and centers at the NIH have research interests in the scientific and medical topics covered by the Bone and Joint Decade. The NIH is pleased to join with many other national and international organizations in endorsing the Decade and developing appropriate activities and initiatives.

Researchers at the NIH as well as those supported by the NIH are studying the influence of genetics, hormones, growth factors, drugs, nutrition, behavior, and physical activity on all aspects of bone and joint function, and are conducting intervention studies to determine the best diagnostic and treatment strategies for the musculoskeletal diseases. President Bush lauded these researchers, stating, "Thanks to the hard work of these dedicated researchers, we have made great progress in understanding and treating musculoskeletal disorders. I commend their efforts and encourage them to pursue diligently further research that will help those suffering from these disorders." The work of the NIH is to facilitate that research through initiatives and support for projects that promise the greatest advances in health.

In the United States, including all orthopedic impairments, fractures and arthritis are the 2 leading causes of activity limitation (Figure 1). Although arthritis and osteoporotic fractures are not leading causes of mortality, these

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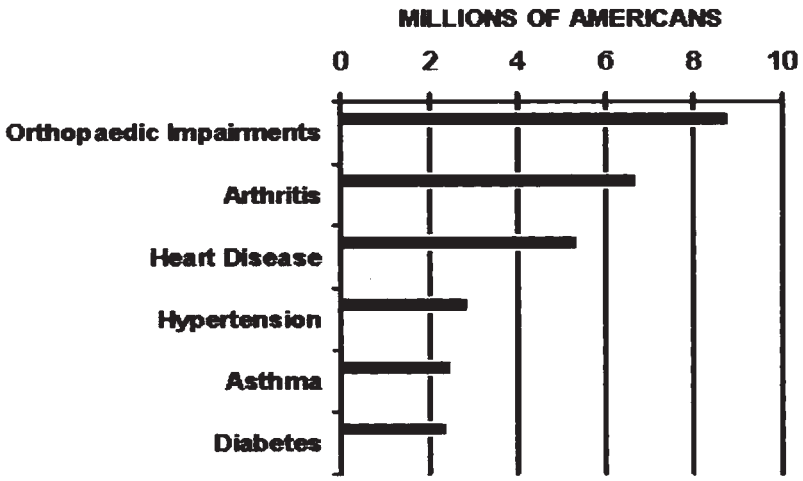

Figure 1. The leading chronic conditions limiting activity[2].

conditions alone account for tremendous pain, disability, and social burden. A hip fracture often spells the end of independent life for older people. The pain and immobility of OA are isolating and can lead to depression. Both bone fractures, due to osteoporosis, and OA can take the life out of living.

The musculoskeletal diseases become even more important as we consider the changing demographics of many of the developed countries. Projections indicate that the percentage of population over age 65 in Japan will increase from 16.1% in 1998 to 22.1% in 2010, while during the same period the population over 65 in the United States will rise from 12.5% to 13.0%[1] (Figure 1). These older individuals will place an increasing burden on the health care system and on their families and communities unless new developments in the prevention and treatment of the musculoskeletal diseases are accelerated. This is certainly one of the driving forces in our urgency to make progress in the next decade to address the degenerative diseases of aging. Of course, as we pursue these goals greater knowledge of musculoskeletal physiology, genetics, and biology will inform and stimulate new insights into congenital and traumatic musculoskeletal disorders and injury.

The World Health Organization (WHO) reported this year that there will be 2 billion people older than 60 years by 2050. For the first time, there will be more people older than 60 years than people younger than 15 years, and 80% of the older people will be in developing countries[2]. Most people over 60 years of age will have some form of OA and about one-half will have symptoms[3]. The number of osteoporosis related hip fractures worldwide is expected to grow from 1.7 million in 1990 to 6.3 million in 2050[4].

Osteoporosis and osteoporotic fractures do not need to be a consequence of aging and are largely preventable. Remarkable progress has been made in our understanding of the causes, diagnosis, treatment, and prevention of osteoporosis. Many new and exciting scientific opportunities exist to enhance our knowledge about how to build and maintain a healthy skeleton throughout life. A great deal of progress could be made in osteoporosis and fracture prevention in the next decade by putting what is already known about the role of nutrition and physical activity into practice in community based programs. The United States Office of the Surgeon General is planning a Report on Osteoporosis and Bone Health due in the summer of 2004. A large planning conference has been held to discuss the more important areas to cover, and a report of that meeting is available (http://www.hsrnet.com/downloads/BoneHealth/workshop_rpt.htm).

These and other growing health care needs necessitate action by a broad spectrum of public and private agencies and have led to specific goals of the Bone and Joint Decade:

- 25% reduction of expected increase in osteoporotic fractures
- 25% reduction of expected increase in joint destruction in joint diseases
- 25% reduction of expected increase in severely injured people
- 25% reduction of expected increase in indirect health cost for spinal disorders

But how do we get there?

Most of the research supported by the NIH and other funding agencies is fundamental in nature, using cells, animals, and model systems. A key to progress in the musculoskeletal diseases is better understanding of the normal development of bones and joints as well as the pathophysiology of disease and injury. This will help to develop and then implement the important prevention strategies based on clinical studies of the natural history of disease, as well as interventions that are biologically based. It is equally important to recognize that we need to balance

efforts by translating, testing, and validating basic biological discoveries in clinical projects and then bringing them into the realm of health services and community health. We need to study not only what will be effective in diagnosing, preventing, and treating disease but also how to deliver health care to populations at need.

Without these dimensions and without communication from the public and back to the public about the fruits of research, research alone will be a sterile activity. No one sector can accomplish this. Researchers profit with input from the public and disease advocacy groups. Government policy makers also need input not only from scientists but also the public to inform decision-making. Private sector involvement in drug development forms another key element in combating musculoskeletal diseases and injuries.

Partnerships to Foster Progress

A key to reaching the large goals of the Decade is through partnership: the participants and organizers of Decade activities must foster and facilitate new partnerships. The NIH has launched a unique public-private partnership in OA to develop a resource of clinical information, biological samples, and radiologic images, outlining the natural history of the disease. This project is an example of many sectors working together to first identify the most important research needs and then to combine resources and talents to address the needs.

As the US population swells with graying baby boomers, vast numbers of people will suffer from OA. Today, over 35 million people are 65 and older, and more than one-half have radiological evidence of OA in at least one joint. By 2030, 20% of Americans — about 70 million people — will have passed their 65th birthday[1] and will be at risk for OA. Although OA is a major cause of disability and loss of quality of life, at present therapies available to treat it are very limited. Most current treatments are designed only to relieve pain and reduce or prevent the disability caused by bone and cartilage degeneration. Drug therapies target the symptoms but not the cause of this disease. No treatment is known to inhibit the degenerative structural changes that are responsible for the progression of OA. Further, clinical testing of new therapies is complicated by the fact that the disease manifests itself differently in each person.

What we call the Osteoarthritis Initiative (OAI) grew out of a trans-NIH interest in developing surrogate markers as clinical endpoints for use in clinical trials. Clinical endpoint studies are long and expensive and this could limit the testing of many promising avenues of research. Validated biomarkers are the key to decision making for drug development. OA is not unique in lacking the markers that could facilitate shorter, less expensive trials. A pressing need comes from the potential targets that may grow out of the sequencing of the genome.

We have a unique opportunity to make some progress in OA research through a collaborative effort of government, the private sector, and the academic community. In February 2000 a planning meeting, "Osteoarthritis Initiative: A Public/Private Research Collaboration," was attended by over 200 participants from academic institutions, scientific and medical organizations, industry, the US Food and Drug Administration, private foundations, the NIH, and other government agencies. This planning group discussed the needs and opportunities in OA research and began to outline a specific project to address those research needs.

The 7 year project will recruit 5000 men and women aged 50 and above at high risk for developing symptomatic knee OA. When complete, the OAI should provide an unparalleled state of the art database showing both the natural progression of the disease and information on biochemical and structural markers and outcome measures. This database should allow investigators all over the world to conduct research to identify potential new disease targets and develop tools for understanding how to measure clinically meaningful improvements. This will provide for more efficient safety and efficacy assessments in clinical trials, as well as more thorough understanding of the disease and its manifestations in at-risk populations. In addition, the positive, interactive relationships between public and private partners augur well for progress in this disease area. For more information on the OAI, visit http://www.niams.nih.gov/ne/oi/index.htm.

The NIH is committed to the goal of reducing the toll of joint diseases and osteoporosis through research on diagnosis, prevention and treatment, and public information. Although there has been an explosion of basic and clinical research in osteoporosis and OA, as well as other bone and joint diseases, many more fundamental advances in molecular and cellular biology, immunology, genetics, and bioengineering have not yet been applied to these areas. We are optimistic and quite excited by the scientific progress and promise. The payoff we expect from this research investment will be increased years of healthy, pain-free, independent life for people all over the world.

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