



WORLD HEALTH ORGANIZATION

EXECUTIVE BOARD
114th Session
Provisional agenda item 7.1

EB114/13
13 April 2004

Expert committees and study groups¹

Report by the Secretariat

PREVENTION AND MANAGEMENT OF OSTEOPOROSIS

Report of a WHO Scientific Group **Geneva, 7-10 April 2000²**

1. Osteoporosis is a disease characterized by low bone mass and structural deterioration of bone tissue leading to increased susceptibility to fractures, most commonly of the hip, spine and wrist. Hip fractures are considered the greatest burden as they nearly always require admission to hospital, are fatal about 20% of cases, and produce permanent disability in about half the patients. By 2050, the number of hip fractures is expected to increase about three- or four-fold from the estimated 1.7 million in 1990.
2. Bone loss resulting in osteoporosis is primarily a consequence of normal ageing, but can also arise owing to impaired development of peak bone mass or excessive loss during adulthood. As populations age, the number of osteoporotic fractures in elderly people will increase. Additional risk factors, such as urbanization, with the consequent increase in harder surfaces, will also result in greater numbers of fractures.
3. The Scientific Group met to review the nature and consequences of osteoporosis, and strategies for its prevention and management. The report describes normal bone development and the causes of, and risk factors for developing, osteoporosis; the burden of disease, characterized in terms of mortality, morbidity and economic costs; evidence-based methods (both pharmacological and non-pharmacological) for prevention and treatment, and cost-analysis of potential interventions; and development of national policies.

¹ The Regulations for Expert Advisory Panels and Committees provide that the Director-General shall submit to the Executive Board a report of expert committees containing observations on the implications of the expert committee reports and recommendations on the follow-up action to be taken.

² WHO Technical Report Series, No. 921, in press.

Main recommendations

4. The Scientific Group made recommendations for care providers, health administrators and researchers, and the following for the general population:

- maintain a physically active lifestyle with adequate exposure to sunlight – this applies particularly to the elderly in extreme latitudes
- avoid smoking and high intakes of alcohol
- ensure that dietary intake of calcium is that recommended for the country or region concerned
- maintain an appropriate body weight.

Significance for public health policies

5. In many countries, health-care systems tend to focus almost exclusively on acute-onset conditions and diseases caused by trauma or infection. The ability to treat or even diagnose chronic conditions such as osteoporosis is often absent. This state of affairs is understandable and perhaps necessary when one considers that resources are extremely scarce, infectious diseases and trauma often strike persons in their youth or during their most productive years, and treatment for infectious diseases (and to a lesser extent for traumatic injuries) can often be curative with a single-dose low-cost regimen. While this strategy brings benefits, it overlooks chronic diseases and conditions, such as heart disease and cancer, that rank among the top in terms of global mortality and morbidity. Moreover, musculoskeletal conditions and mental health, which are extremely prevalent, tend to attract less attention in all parts of the world because they have low fatality rates.

6. Public health programmes, all of which should promote prevention, need to emphasize two approaches. A strategy for osteoporosis prevention, which fits well with prevention of other noncommunicable diseases, should accentuate proper nutrition (in this case to include adequate intake of calcium, vitamin D and protein), weight-bearing (aerobic) exercise, maintenance of proper body-mass index, abstinence from tobacco use, and avoidance of excessive alcohol use, and should also stress moderate exposure to sunlight. Programmes should also identify those at risk for fractures, on the basis of age, gender, bone mineral density, history of fracture, and lifetime use of agents such as alcohol, tobacco and corticosteroids, and incorporate strategies aimed at such people for preventing falls or lessening their impact. Member States that are currently unprepared to treat osteoporosis should work toward providing better care and prepare for the coming epidemic as their populations age; they will need to train health-care workers, provide better access to bone densitometry (or other reliable methods of diagnosis), find ways of manufacturing or importing treatments decided upon, and create or adopt guidelines for treatment.

Implications for WHO's programmes

7. There are still few epidemiological data on osteoporosis and osteoporotic fractures in much of the world. As diet, genetics, and geographical location affect the disease and thus fracture rates, WHO should work with surveillance groups to facilitate the collection of such data. A first step would be to produce uniform guidelines on data collection. WHO should further the process by maintaining databases of research scientists, monitoring studies in progress, and maintaining a central repository for data on incidence and prevalence of osteoporosis and other musculoskeletal conditions.

8. Lightening the burden of osteoporosis will require a more robust plan and the creation of a global strategy for prevention and control, in a cross-organizational initiative.

RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE

Report of a WHO Expert Consultation Geneva, 29 October – 1 November 2001¹

9. An Expert Consultation on Rheumatic Fever and Rheumatic Heart Disease was held to update a previous report on the subject.²

10. WHO has long been concerned with rheumatic fever, a nonsuppurative condition following group A streptococcal infections. Sentinel studies conducted under its auspices during the past four decades clearly documented that the control of the preceding infections and their sequelae is cost-effective and that appropriate public health control programmes and optimal medical care reduce the burden of disease. Despite the existence of such strategies, however, these diseases remain significant public health problems, particularly in developing countries. The most devastating effects are on children and young adults in their most productive years. Available data suggest that the incidence of group A streptococcal pharyngitis and other infections and the prevalence of asymptomatic carriers have remained unchanged in both developed and developing countries.

11. The control of rheumatic fever and rheumatic heart disease in developing countries has been largely ineffective, because of poverty and its associated conditions such as substandard nutrition, overcrowding and inadequate housing. Weak infrastructure and limited resources for health care also contribute to the poor status of control. Although progress has been made in the understanding of the pathogenesis underlying the epidemiology and the development of these nonsuppurative complications, the precise pathogenic mechanism(s) are not identified or understood.

Main recommendation

12. The experts at the consultation recommended modifications to the diagnostic criteria for rheumatic fever and rheumatic heart disease based on both new information and the need to offer physicians and public health authorities practical guidelines for prevention, diagnosis and management.

Significance for public health policies

13. Surveillance of acute rheumatic fever and rheumatic heart disease needs to be incorporated into national statistical reporting to provide information on the epidemiological trends of the disease. Clinical microbiology laboratories play an essential role in rheumatic fever control programmes, by facilitating the identification of group A streptococcal infections and providing information on the streptococcal types causing the disease. As national and regional streptococcal reference laboratories are lacking in many parts of the world, attention needs to be given to establishing such laboratories and assuring quality control.

¹ WHO Technical Report Series, No. 923, 2004.

² WHO Technical Report Series, No. 764, 1988.

14. Primary prevention of rheumatic fever consists of the effective treatment of group A beta-haemolytic streptococcal pharyngitis. While it is not always feasible to implement broad-based primary prevention programmes in most developing countries, a provision for the prompt diagnosis and effective therapy of streptococcal pharyngitis should be integrated into existing health-care facilities.

15. Secondary prevention of rheumatic fever consists of regular administration of antibiotics (usually benzathine penicillin G given intramuscularly) to patients with a previous history of rheumatic fever and/or rheumatic heart disease in order to prevent group A streptococcal pharyngitis and recurrence of acute rheumatic fever. Establishment of registries of known patients, in order to monitor secondary prophylaxis programmes, has proven effective in reducing morbidity and mortality.

16. The establishment of a national prevention programme for rheumatic fever is essential in countries where that and rheumatic heart disease remain significant health problems. It is important to include such programmes in national health development plans, and to implement them through the existing national infrastructure of ministries of health and education without requiring a new administrative framework or health-care delivery infrastructure.

Implications for the Organization's programmes

17. Well planned and broad studies are required to gather epidemiological data on group A streptococcal infections, rheumatic fever and rheumatic heart disease. The network of national and regional streptococcal reference laboratories needs to be expanded for confirmation of group A streptococcal infections, bacterial identification and ensuring quality control of diagnostic tests. Operational research needs to be done to evaluate the feasibility of implementing primary and secondary prevention programmes and their integration into existing national health infrastructure and school health programmes. Such integration can result in more effective use of often-limited financial and human resources for providing preventive measures for individuals and populations. Technical assistance needs to be provided to Member States to strengthen capacity for primary and secondary prophylaxis of rheumatic fever and rheumatic heart disease, particularly in primary health care. Steps need to be taken to ensure the quality, accessibility and availability of long-acting penicillin preparations for secondary prophylaxis programmes. Basic research studies are also needed for further elucidation of the pathogenetic mechanisms underlying the sequelae.

WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Fifty-second report

Geneva, 26-30 November 2001¹

18. The Expert Committee on Biological Standardization reviews developments in the field of biological substances used in human medicine, which include vaccines, plasma products and biological therapeutics. It coordinates activities leading to the adoption of recommendations for assuring their quality, safety and efficacy and to the establishment of international reference materials.

¹ WHO Technical Report Series, No. 924, in press.

Main recommendations

19. The use of international reference materials for designating the activity of biological substances used in prophylaxis or therapy, or for ensuring the reliability of quality control or diagnostic procedures, allows comparability of data worldwide. Based on the results of international collaborative laboratory studies, the Expert Committee established 13 new or replacement international reference materials. Additionally, several international reference materials no longer required were disestablished. An up-to-date list of WHO International Standards and Reference Materials is available on the Internet.

20. The Expert Committee adopted new guidelines on regulatory expectations for the clinical evaluation of vaccines; recommendations for the production and quality control of group C meningococcal conjugate vaccines; guidelines for the production and control of inactivated oral cholera vaccines; and guidelines on the viral inactivation and removal procedures intended to assure the safety of human blood plasma products.

21. The Expert Committee made recommendations on the standardization and control of antivenoms. This topic had not been reviewed since 1979 and WHO's renewed activity had attracted considerable worldwide interest. The Committee recommended the development of a new guidance document on the production and quality control of antivenoms that took account of the progress in the production and quality control of biologicals in recent years.

22. The Expert Committee was informed of the considerable activity worldwide in the field of gene therapy, with many clinical evaluations of products already at different stages in several countries. These included products for treating a range of genetic diseases, cancer, diabetes, rheumatoid arthritis and high blood pressure. The Committee recommended that WHO should monitor progress in this rapidly changing field and consider developing guidelines for gene-therapy products.

Significance for public health policies

23. Recommendations published by WHO provide guidance for national regulatory authorities and manufacturers on production, quality control and associated safety and regulatory issues. These serve as the basis for national regulations. WHO's International Standards are used to calibrate regional, national or manufacturers' standards and often form the basis for licensing, routine lot release and clinical dosing worldwide.

24. The "Guidelines on clinical evaluation of vaccines: regulatory expectations" outline the data that should be obtained during the different stages of vaccine development in order to support a marketing approval. The document was prepared in response to requests from national regulatory authorities for assistance in the evaluation of clinical trials, both during the clinical development of a new vaccine and during the regulatory review of dossiers submitted in support of applications for marketing authorizations. The guidelines provide the basis for protection of individual patient safety and also to safeguard the public health.

25. Human blood is the source of a wide range of medicinal products used for the treatment and prevention of a variety of often life-threatening injuries or diseases. Despite measures such as donor selection and testing of donations and plasma pools, transmission of blood-borne viruses by plasma and purified plasma products is still considered to constitute a risk to patients. Over the past 15-20 years, the transmission of the principal viral pathogens historically associated with these products – hepatitis B virus, hepatitis C virus and human immunodeficiency virus – has been greatly

reduced or eliminated in many areas of the world, as a consequence of more sensitive methods used to screen donated blood and plasma pools and the introduction of manufacturing practices that to a significant extent kill and remove the viruses. Several such procedures have proven to be robust and contribute substantially to the safety of blood and blood products. Thus, viral inactivation methods should be applied to all blood protein solutions. The new WHO guidelines summarize current experience with well recognized methods and will help to set expectations, to serve as a guide to speed implementation, and to ensure that implementation is appropriate.

Implications for the Organization's programmes

26. The Expert Committee provides up-to-date recommendations on the quality, safety and potency of biological substances used in human medicine and ensures the availability of necessary international reference materials. Its work enables WHO to fulfil its constitutional responsibilities in this area.

27. The Committee's observations, conclusions and recommendations have significant implications for several of WHO's activities. In particular, they provide timely recommendations and reference preparations for assuring the quality, safety and efficacy of vaccines, and reference materials for standardizing essential diagnostic assays for the detection of virological contaminants in plasma products. The global norms and standards defined by the Committee provide the basis for assessing the acceptability of vaccines for purchase by international agencies, such as UNICEF and WHO.

28. Continuing concerns about the quality and safety of plasma-derived medicinal products have resulted in urgent requests from Member States for support and advice from WHO. Moreover, resolution WHA50.20 on the "Quality of biological products moving in international commerce", requests the Director-General to extend the assistance offered to Member States to develop and to strengthen their national regulatory authorities and control laboratories so as to increase competence in the area, and to extend efforts to upgrade the quality and safety of all biological products worldwide. The development of the guidelines on viral inactivation is a part of this process.

THE SELECTION AND USE OF ESSENTIAL MEDICINES

Report of the WHO Expert Committee (including the 13th Model List of Essential Medicines)

Geneva, 31 March – 3 April 2003¹

29. The Expert Committee met for the second time under the new procedures established in 2002. The agenda and all applications for additions, changes and deletions had been posted on the WHO web site four months before the meeting. All submissions were reviewed by WHO or members of the Expert Committee; these reviews were also posted before the meeting on the web site. The meeting began with an open session on the first day, in which stakeholders provided additional information and commented on various issues.

¹ WHO Technical Report Series, No. 920, 2004.

Main recommendations

30. With regard to procedures, the Committee recommended changes in the definitions of the core and complementary lists, and in the use of the square box symbol indicating similar clinical performance within a pharmacological class. The Committee reviewed and reclassified all medicines on the Model List in line with the new definitions.

31. The Committee recommended that amodiaquine, azithromycin and levonorgestrel should be added to the Model List; that the applications for the addition of paediatric ibuprofen, porcine insulin suspension (insulin semilente), miconazole nitrate buccal tablets, misoprostol and valaciclovir to the List should be rejected; that 15 medicines should be deleted from the List; that the formula of oral rehydration salts and the dosage form of streptokinase should be changed; that 15 medicines should be moved from the core to the complementary list, and six from the complementary to the core list; that the square box symbol should be removed from 32 items; and that 33 items should be listed for review and possible deletion at the next meeting.

Significance for public health policies

32. The consequence of the review of the core and complementary lists and the definition of the square box symbol is that the Model List is now much more consistent in its advice. For the first time, medicines with similar clinical performance within a pharmacological class are identified and listed in the WHO Model Formulary and the Web-based WHO Essential Medicines Library.

33. The deletion of many obsolete items and the systematic review of certain therapeutic sections has increased the practical value of the Model List as an up-to-date public health tool. Work continues on further increasing consistency between medicines in WHO clinical guidelines and those listed in the Model List. The inclusion of the Model List in the WHO Essential Medicines Library with the WHO Model Formulary greatly expands the amount and level of independent drug information available to national and institutional medicine and therapeutic committees.

Implications for the Organization's programmes

34. The drive for consistency between the Model List and WHO's clinical guidelines underlines the importance of ensuring coordination within WHO, and further accentuates the need for a systematic evidence-based approach to developing and updating WHO clinical guidelines.

= = =