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Progress reports

Report by the Secretariat

CONTENTS

A. CONTROL OF HUMAN AFRICAN TRYPANOSOMIASIS

1. Human African trypanosomiasis caused by *Trypanosoma brucei gambiense* is endemic in 24 countries. Between 1997 and 2006 the number of new cases reported to WHO fell by 69%. Of these 24 countries, six (Gambia, Guinea Bissau, Liberia, Niger, Senegal and Sierra Leone) reported no case throughout the whole period. Five countries (Benin, Burkina Faso, Ghana, Mali and Togo) reported sporadic cases. Six countries (Cameroon, Côte d'Ivoire, Equatorial Guinea, Gabon, Guinea and Nigeria) reported an average of fewer than 100 new cases annually. Four countries reported between 100 and 1000 new cases a year (Chad, Central African Republic, Congo and Uganda), and three (Angola, Democratic Republic of the Congo and Sudan) reported an average of more than 1000 new cases a year, or 90% of the total number of cases due to *T. b. gambiense* reported to WHO.

2. In the 13 countries where disease due to *T. b. rhodesiense* is endemic, the number of new cases reported to WHO between 1997 and 2006 fell by 21%.[1] Of these 13 countries, five (Botswana, Burundi, Ethiopia, Namibia and Swaziland) reported no case during the decade, four (Kenya, Mozambique, Rwanda and Zimbabwe) reported sporadic cases (amounting to 2.5% of the total reported number of cases due to *T. b. rhodesiense*), two (Malawi and Zambia) reported an average of fewer than 100 new cases annually (representing 8.7% of the total reported number of cases due to *T. b. rhodesiense*), and two (Uganda and the United Republic of Tanzania) reported between 100 and 1000 new cases annually (88.8% of the total reported number of cases).

3. The situation has dramatically improved since 1997 when deep concerns led the Fiftieth World Health Assembly to adopt resolution WHA50.36 on African trypanosomiasis. In addition to political will (consolidated by the Pan African Tsetse and Trypanosomiasis Eradication Campaign), access to diagnosis and treatment of patients living in areas endemic for trypanosomiasis have been facilitated by the interruption of social upheavals and through capacity building, financial and technical support for outreach activities, and securing the production and distribution of medicines for the treatment of trypanosomiasis free of charge.

4. Unfortunately, with the low number of cases being detected, the priority given to trypanosomiasis has declined. A similar situation occurred 50 years ago when it was believed that the disease had been eliminated. In order to avoid repeating this error, making surveillance and control of trypanosomiasis cost-effective and sustainable is the immediate challenge. Sustainability is feasible only through an integrated approach to surveillance and control activities undertaken within reinforced health systems that are able to face this responsibility. Existing tools, however, make it difficult for health systems to participate in control of the disease. The two main technical impediments are the lack of a sensitive and specific diagnostic test that is inexpensive and easy to perform in field conditions and that could be used at any level of the health system, and the absence of an oral medicine that is cheap, safe and easy to administer, and able to cure both forms of the disease.

5. Until new tools for the control of human African trypanosomiasis become available, the greatest and most immediate challenge is to increase and sustain the current epidemiological trend with existing means. Effective surveillance and control will continue to need appropriate human resources, adequate control activities, effective reporting, maintenance of awareness, and advocacy for a high priority and fund-raising. Research and development must be maintained and priorities directed

[1] Uganda is affected by both forms of the disease and thus appears in both analyses.

towards the goal of sustained elimination of the disease through the provision of adequate tools. WHO will continue to lead in the provision of support to countries and coordinate the work of stakeholders.

E. SMALLPOX ERADICATION: DESTRUCTION OF VARIOLA VIRUS STOCKS

6. The present document reports on the ninth meeting of the WHO Advisory Committee on Variola Virus Research (Geneva, 28 and 29 November 2007) and on the work of the Secretariat. The Advisory Committee was established pursuant to resolution WHA52.10, in which the Health Assembly authorized temporary retention of the remaining stocks of live variola virus, and requested the Director-General to appoint a group of experts to determine what research, if any, must be carried out in order to reach consensus on the timing for the destruction of these virus stocks. In resolution WHA55.15, the Health Assembly authorized the further, temporary, retention of the existing stocks of live virus on the understanding that all approved research would remain outcome-oriented and time-limited, and its accomplishments and outcomes would be periodically reviewed. It also requested the Director-General to report annually to the Health Assembly, through the Executive Board, on progress in the research programme and relevant issues. In resolution WHA60.1, the Health Assembly requested the Director-General to undertake a major review in 2010 of the results of the research undertaken, currently under way, so that the Sixty-fourth World Health Assembly may reach global consensus on the timing of the destruction of existing variola virus stocks.

7. **Update on research proposals submitted to WHO.** The Advisory Committee received a summary of the research proposals approved (12 work programmes) and rejected (12) by its scientific subcommittee. Many of the approved projects are coming to their end, on schedule, and final reports should be submitted. Recently received new proposals will be evaluated according to the revised procedure agreed upon during the Committee's eighth meeting in 2006,[1] whereby there would be a rotation of the membership of the scientific subcommittee. The Committee accepted the new membership of the subcommittee.

8. **Virus strains in the two repositories.**[2] The Committee reviewed data on the variola virus strains and primary isolates held in the two collections and noted no changes. As recommended in previous meetings, these collections had been subject to an annual inventory using a unifying system. The Committee was satisfied that materials in the two collections corresponded to the inventories and were being maintained with appropriate safeguards in place.

9. **Sequence analysis of variola virus DNA.** As previously recommended by the Committee, no further sequencing of genomic DNA was undertaken, with the exception of the sequencing of an Asian strain in the Russian collection, which is currently under way in the Russian collaborating centre in order to complete the coverage of geographical diversity of the viruses.

10. **Clinical manifestations of smallpox.** In response to the Committee's previous recommendation that a review of the archives be undertaken to determine whether there was any correlation between particular variola virus isolates and the severity of clinical manifestations of smallpox, the Committee was presented with the results of an analysis of the records archived at WHO. Most of these reports

[1] Document EB120/39.

[2] Russian State Centre on Virology and Biotechnology, Koltsovo, Novosibirsk Region, Russian Federation and the Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America.

contained little or no clinical information. This investigation therefore yielded no information that would allow linking particular virus isolates to disease characteristics.

11. **Animal models using live variola virus.** The Committee noted that many of the objectives of the work to refine the primate model of human smallpox for testing antiviral compounds had now been achieved but further work may still be needed to make the model more suitable for testing such compounds for gaining licensure.

12. **Antiviral drugs.** The Committee noted recent progress on the development of the antiviral drug, ST-246, which suppresses orthopoxvirus growth in vitro, is active in treating a variety of orthopoxvirus infections in animal models, and appears to be safe and well tolerated in those models. Data on efficacy in different animal models have been submitted to the Food and Drug Administration in the United States of America. The Committee was also informed that these preliminary results with ST-246 were sufficiently positive that small amounts of the drug were being stockpiled by the company producing it for emergency, compassionate use. Work is in progress to determine whether ST-246 can be used in immunocompromised or pregnant individuals.

13. **Vaccines.** The Committee reviewed promising new approaches. A new smallpox vaccine (ACAM 2000) has been licensed for use in one Member State. Work on two third-generation vaccines (MVA and LC16m8) showed that these are safe and less reactogenic, and preliminary data suggest that successful individual vaccination (the take rate) and level of induction of neutralizing antibodies were comparable to those for first- and second-generation vaccines; further studies on both vaccines are in progress. The Committee discussed regulatory issues concerning requirements for licensing third-generation vaccines, highlighting the absence of a satisfactory animal model for testing smallpox vaccines and the lack of knowledge of the correlates of protection against human smallpox. It appeared, however, that an animal model using live variola virus will not be mandatory for licensing a third-generation vaccine by at least two regulatory agencies.

14. **Use of antiviral immunoglobulin, cidofovir and ST-246 in the treatment of eczema vaccinatum.** Treatment of a case of life-threatening eczema vaccinatum was reported. The Committee noted that the use of ST-246 appeared to have been particularly beneficial and was followed by the recovery of the patient. ST-246 should therefore be considered as an early treatment option if safety and efficacy in humans are confirmed by further studies.

15. **Review of research work done by laboratories that have obtained variola virus DNA with WHO's approval.** The Secretariat presented preliminary data on a survey conducted in laboratories known to be engaged in this research. Of the 35 (80%) contacted laboratories that responded to a questionnaire, 24 used variola virus DNA fragments in their research. These activities encompassed studies on diagnostics (52%), host–virus interactions (20%), therapeutics (20%) and vaccines (8%). The Committee considered that WHO should continue to have access to up-to-date information on the use and distribution of variola virus DNA fragments, in order to ensure the confidence of the wider public health community. It recommended that the Secretariat should continue its efforts to maintain an accurate database of research with variola virus DNA fragments distributed with the approval of WHO and to obtain currently-missing information.

16. **Transfer of variola virus DNA.** The Committee recommended that the wording of the current recommendations and guidelines about the transfer of variola virus DNA should not be changed. The major problem identified was one of wider dissemination and communication of the existing recommendations and guidelines. In addition, it was felt that the general principles behind these regulations should be clarified and emphasized. A major concern was the third-party transfer of DNA fragments. The Committee agreed that such transfer requires authorization by WHO and should be

controlled through the material transfer agreements between the distributing and receiving laboratories, with a copy sent to WHO.

17. **Measures to promote wide and equitable access to research outcomes.** The Committee reviewed all the topics mentioned in the Health Assembly's request to the Director-General in resolution WHA60.1 to report on "measures that promote in Member States the widest and most equitable access possible to the outcomes of the research, including antiviral agents, vaccines, and diagnostic tools". Preliminary discussions were held about the availability of antiviral drugs and newer vaccines, but currently these reagents are not yet sufficiently advanced to plan large-scale applications; the Committee will reconsider these items in the future as research progresses. In regard to access to first- and second-generation vaccines, WHO continues to work to enlarge the vaccine supply in its global vaccine bank, and is receiving supplies of second-generation vaccine for the vaccine stockpile held in Switzerland. Should the newer vaccines prove to be both safe and immunogenic, WHO should accept them in the vaccine bank, and Member States producing or purchasing such vaccines should be encouraged to contribute to the stockpile. The Secretariat reported on the updating of the mechanism for release of vaccine from the stockpile in order to take account of the implementation of the International Health Regulations (2005). It also reported on initial steps taken to set up an informal network of laboratories. The plan is to have at least one laboratory, and preferably several, in each WHO region capable of applying orthopox diagnostics in a reliable and efficient manner, including preliminary diagnosis of suspected smallpox using molecular methods on inactivated clinical material. The result would be more rapid access to results on samples from patients for whom the diagnosis was being considered, and the saving of national resources, as shipping costs are high. A tentative list of participating laboratories was presented, but the Committee decided that more consultation was needed to determine which laboratories are interested and qualified to participate. Such a network would require a system to evaluate and maintain reliability of results, and the Secretariat is working with WHO collaborating centres to determine the necessary support.

F. REPRODUCTIVE HEALTH: STRATEGY TO ACCELERATE PROGRESS TOWARDS THE ATTAINMENT OF INTERNATIONAL DEVELOPMENT GOALS AND TARGETS

18. This report updates the one submitted to the Health Assembly in 2006[1] with information on the wide range of activities that Member States and the Secretariat are undertaking in order to implement the strategy endorsed in resolution WHA57.12.

19. The strategy and four policy briefs summarizing key aspects have been widely distributed. An implementation framework,[2] elaborating areas of action and policy and programme recommendations, has been developed in consultation with countries in all regions. In addition, regional workshops have been held to provide further technical assistance to Member States. They brought together policy-makers, programme managers and others to identify bottlenecks, share lessons and define actions for accelerating progress.

20. The assessment tool for monitoring progress in strategy implementation has been updated in line with the framework and distributed among Member States. The strategy and framework are being

[1] Document A59/23.

[2] Document WHO/RHR/06.3.

used to define national sexual and reproductive health strategies; to design road maps to reduce maternal and newborn mortality; to inform strategic planning processes; and to revise policies and set priorities for strengthening health systems.

21. Progress has been reported by countries in each of the five key action areas:

- **strengthening health systems' capacity** – with development of policies to strengthen health systems, and assessment of human resources for health
- **improving information for priority setting** – with establishment of maternal death reviews
- **mobilizing political will** – through global and regional conferences involving policy-makers, e.g. Maputo Plan of Action for achieving universal access to comprehensive sexual and reproductive health in Africa;[1] the Women Deliver Global Conference (London, 18–20 October 2007); initiatives by some Heads of Government and State, e.g. The Global Campaign for the Health Millennium Development Goals (4, 5 and 6); ongoing support to partnerships such as the WHO-hosted Partnership for Maternal, Newborn and Child Health; dissemination of information to media; and civil society outreach programmes
- **creation of supportive legislative and regulatory frameworks** – through legislation on free provision of reproductive health services, and development of national commodity security strategies
- **strengthening monitoring and evaluation** – through incorporation of sexual and reproductive health in monitoring national development plans.

22. Specific areas reported by Member States as requiring further attention include: strengthening human resources and multisectoral collaboration; empowerment of women, families and communities; and improving monitoring and evaluation as well as quality of services.

23. The central aim of the strategy, which echoes that of the International Conference on Population and Development (Cairo, 1994), was reaffirmed at the 2005 World Summit,[2] when Heads of State and Government committed themselves to "achieving universal access to reproductive health by 2015". In October 2006, the United Nations General Assembly[3] took note of the Secretary-General's report in which he recommended the inclusion of four new targets within the Millennium Development Goal framework, including universal access to reproductive health. As a follow up in 2007, the Secretary-General presented to the General Assembly[4] a revised framework integrating into Millennium Development Goal 5 the new target "Achieve, by 2015, universal access to reproductive health", with indicators for measuring progress: contraceptive prevalence rate, adolescent birth rate, antenatal care coverage, and unmet need for family planning. WHO and UNFPA have been collaborating to define

[1] Special Session of the Conference of African Union Ministers of Health, Universal access to comprehensive sexual and reproductive health services in Africa: Maputo Plan of Action for the operationalisation of the continental policy framework for sexual and reproductive health and rights 2007–2010. Maputo, 18–22 September 2006.

[2] United Nations General Assembly resolution 60/1.

[3] Decision 61/504.

[4] Document A/62/1.

and operationalize a broader range of indicators on universal access and supporting countries in their efforts to monitor progress.

24. The subsequent endorsement of the Global strategy for the prevention and control of sexually transmitted infections, 2006–2015[1] has allowed sharper focus on this aspect of sexual and reproductive health, including the need for the elimination of congenital syphilis. Implementation of actions to reach this goal will require sustained efforts and adequate resources for this area, as well as systematic integration of syphilis screening and treatment with antenatal HIV testing.

25. Strengthening linkages between HIV prevention and sexual and reproductive health is an important element of the strategy. The Secretariat has expanded its work in this area, particularly in advocacy, research, policy and programme support. For instance, materials have been developed for Member States on how linkages between sexual and reproductive health and HIV can be incorporated in proposals to the Global Fund to Fight AIDS, Tuberculosis and Malaria.

26. In line with recommendations of the strategy related to monitoring and evaluation, global maternal mortality estimates have been updated by WHO, The World Bank, UNICEF and UNFPA. The new figures estimate 536 000 maternal deaths in 2005, 99% of them in developing countries. In terms of decline in the maternal mortality ratio, progress is uneven: a decline of only 0.1% a year between 1990 and 2005 in sub-Saharan Africa, but greater declines in east Asia, North Africa, south-east Asia and Latin America and the Caribbean, although none of them reached the necessary rate per year (5.5%) for achieving the Millennium Development Goal target of reducing the maternal mortality ratio by three quarters between 1990 and 2015. With regard to abortion, estimates show a decline, particularly in central and eastern Europe, which is attributable to increased contraceptive prevalence rates. However, the prevalence of unsafe abortion shows no improvement: worldwide, the practice causes 68 000 maternal deaths annually.

G. INFANT AND YOUNG CHILD NUTRITION: BIENNIAL PROGRESS REPORT

27. Malnutrition is responsible, directly or indirectly, for about half of the world's annual deaths among children under five. There are 178 million stunted children under five years old in the world, 90% of whom live in high-burden countries. A major intervention to rectify this situation is to improve infant and young child feeding practices.[2] Current data indicate that only about a third of children in the high-burden countries are exclusively breastfed for six months and for less than half breastfeeding is initiated within the first hour of life;[3] this state of affairs is far from the global infant and young child feeding recommendation.[4]

28. WHO continues to promote infant and young child feeding as essential for achieving the Millennium Development Goals, in particular, those relating to the eradication of extreme poverty and hunger and to the reduction of child mortality. In line with the Global Strategy for Infant and Young

[1] Document WHA59/2006/REC/1, Annex 2.

[2] Global strategy for infant and young child feeding, document WHA55/2002/REC/1, Annex 2.

[3] WHO global database on infant and young child feeding, updated 5 December 2007.

[4] Exclusive breastfeeding for the first six months of life, with nutritionally adequate and safe complementary feeding through introduction of safe and adequate amounts of indigenous and local foods while breastfeeding continues up to the age of two years or beyond.

Child Feeding, the Secretariat's approach is two-fold: to develop guidelines and tools for achieving the Strategy's operational targets, and subsequently help to ensure that they are used through national capacity building; and to provide support for research and disseminate its findings. A joint WHO/UNICEF planning guide has been issued in 2007 to assist countries in translating the Strategy into national action plans.

29. Amid extensive media coverage, WHO launched the Child Growth Standards in April 2006, along with tools for ensuring implementation. Many countries have either since implemented or officially adopted the Standards. Their use is prompting significant changes towards best practices, as countries standardize their guidelines for assessing child growth, and revitalize their programmes for promoting child growth. The Secretariat has also scaled up its activities for creating a network of trainers for growth assessment.

30. With UNICEF, WHO in 2006 published an integrated course on counselling for infant and young child feeding. The aim is to increase the number of health workers skilled in counselling on breastfeeding, complementary feeding, and feeding infants with HIV. Also with UNICEF, WHO has published an updated version of baby-friendly hospital initiative materials, in 2007. WHO finished a technical review of evidence on the optimal feeding of low-birth-weight infants in 2006, and has completed a systematic review, from observational and randomized studies, of the long-term effects of breastfeeding in 2007. Currently, the Organization is developing techniques to design food-based dietary guidelines based on mathematical modelling with linear programming.

31. At a consultation (Washington, DC, 6–8 November 2007) WHO and partners reviewed the evidence and agreed on a set of indicators for assessing feeding practices for infants and young children. These indicators will be incorporated into the WHO's Global Data Bank on Infant and Young Child Feeding.

32. Several countries took steps to give further effect to the International Code of Marketing of Breast-milk Substitutes, including strengthening capacity for implementation and monitoring, and adopting or reforming legislation and regulations. The Western Pacific Regional Office held a WHO/UNICEF consultation with experts from 18 countries (Manila, 20–22 June 2007) to review the status of the Code's implementation and to identify steps for raising the rate of implementation. Training on implementation and monitoring of the Code was conducted for eastern and southern African countries.

33. In October 2006, on behalf of the Interagency Task Team on Prevention of HIV Infections in Pregnant Women, Mothers and their Infants, WHO held a technical consultation in Geneva on HIV and infant feeding in order to review new evidence and the most recent experience in this area, and to clarify and refine existing recommendations. The consultation endorsed the general principles underpinning earlier recommendations, and issued a consensus statement on feeding options in the context of HIV.

34. In order to identify and prevent early cases of malnutrition, WHO is strengthening the integrated approach to improving management of severe malnutrition among children through an innovative approach that integrates community-based management with facility-based management. It is also developing operational guidance for emergency relief staff and programme managers.

35. The guidelines on indicators for iodine deficiency disorders, developed by WHO, UNICEF and the International Council for the Control of Iodine Deficiency Disorders were updated, and a joint statement with WFP and UNICEF on preventing and controlling micronutrient deficiencies was

issued. The Secretariat has produced a draft strategy for advocacy, communication and community engagement on nutrition.

36. With its partners, WHO began an analysis of readiness to act in nutrition, funded by the Bill & Melinda Gates Foundation. The analysis is assessing gaps and constraints, and identifying opportunities for action to reduce maternal and child undernutrition in the 36 countries that are home to 90% of the world's stunted children.

ACTION BY THE EXECUTIVE BOARD

37. The Board is invited to note these reports.

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