Report of the Workgroup on Bacterial Diseases

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Introduction

The Workgroup felt that 14 factors should be considered when discussing the potential feasibility of elimination or eradication of any disease These partially overlap but further expand on the seven issues named in the "Framework for considering candidate conditions." The list comprises the following: disease burden; existence of an effective intervention; surveillance/diagnosis mechanism; commonality of delivery; cost-effectiveness; demonstrated effectiveness of the programme; contribution to overall infrastructure; existence of a delivery infrastructure; barriers; roles of technology; existence of nonhuman hosts; time frame; significance of imported cases; and strategies to be followed.

The results of the pre-Conference survey were discussed. The top 10 conditions identified in the survey, in rank order, were as follows: neonatal tetanus; *Haemophilus influenzae* type b (Hib) infection; leprosy; diphtheria; pertussis; tuberculosis (TB); meningococcal disease; congenital syphilis; trachoma; and syphilis. None of these conditions was considered eradicable in the immediate future, although several were thought to be candidates for national or regional elimination.

Several conditions brought up in the survey were deemed important but not currently amenable to elimination or eradication. Consequently, they were not considered further. For diphtheria and pertussis, it was felt there was an incomplete understanding of the epidemiology of the disease and transmission as well as inadequate surveillance systems. Additionally, there was uncertainty as to whether the available interventions could achieve elimination. Meningococcal disease is an important condition for which effective interventions are under development and, in a few years, it may well be a candidate for elimination. The same can be said for pneumococcal disease, which was not included in the top 10 in the survey but is very important because of its high incidence. Regional elimination of typhoid may be feasible but has not been demonstrated. For each of these conditions, improved control is both feasible and necessary.

Subgroups were formed to discuss neonatal tetanus, Hib, TB (and leprosy), and syphilis (both acquired and congenital, with some consideration of chancroid), and trachoma. In the discussions, a continuum of levels of disease incidence was considered, ranging from the situation in which disease occurs uncontrolled to a level of control which, with additional effort, becomes "very good control". The transition from very good control to elimination is likely to require considerable additional effort, in terms of both programme interventions and surveillance. Elimination is a stage which will take major effort to maintain, which will be more difficult the more common the disease is in other parts of the world and the more transmissible it is. In general, elimination should be viewed as a stepping stone to eradication and considered seriously only when eventual eradication seems possible.

Neonatal tetanus

This is a significant problem, with an estimated 490 000 deaths per year (a global rate of 6.5 per 1000 live births). Actions taken to reduce the occurrence of neonatal tetanus would have other positive impacts on health and health care systems, including decreased neonatal mortality and maternal mortality (from other conditions as well as maternal tetanus). Eradication is clearly not feasible, given the ubiquitous distribution of *Clostridium tetani* spores in the soil. Using the strictest definition, elimination also cannot be guaranteed, although radically improved control is possible and should be a high priority. The WHO "elimination" goal of an incidence of <1 per 1000 live births in every district is attainable. Achievement of this goal will require fuller implementation of a three-pronged strategy: vaccination of women of childbearing age, clean delivery, and application of topical antimicrobials to the umbilical stump. The last-mentioned component is not being sufficiently emphasized at present. Because of the combined nature of the strategies, very close collaboration between the Expanded Programme on Immunization (EPI) and Maternal and Child Health (MCH) programmes will be needed to achieve the goal Since eradication is not feasible and interventions will need to be continued indefinitely, vertical approaches are insufficient; neonatal tetanus control efforts will need to be integrated into developing

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comprehensive care systems. Substantial research needs remain, from ongoing monitoring of immunity levels in girls attaining childbearing age to development of more effective (possibly single-dose) vaccines.

Haemophilus influenzae type b (Hib) infection

In most parts of the world, the burden of Hib infection has been documented and is of comparable severity. However, in some Western Pacific countries (e.g. China, Republic of Korea, Japan) the severity of this burden is not yet clear. Current estimates are that there are 380 000–600 000 deaths per year globally among under-5-year-olds as a result of Hib infections. Although case management is an important strategy to reduce mortality, it does not have a significant impact on transmission; consequently, the primary intervention is vaccination.

Results from introduction of Hib vaccine have been dramatic in both industrialized and developing countries. The (unexpected) impact of Hib vaccine in reducing carriers of Hib has raised possibilities of elimination/eradication which were previously not considered. In the USA, United Kingdom, and several other industrialized countries, Hib infections have virtually disappeared (>95% reduction) within 4–7 years after introduction of universal vaccination of infants/young children. The disease appears to have been eliminated in Iceland and Finland. In both Chile and the Gambia dramatic results have been seen, and in the latter country there was also a nearly 25% reduction in the incidence of lobar pneumonia among young children following introduction of vaccination. Whether this finding will be replicated in other countries is currently under study. A major barrier to the wider use of Hib vaccine is its current price: at more than US$ 1 per dose, it may not be cost-effective for introduction in developing countries. Fortunately, it appears that the different formulations of Hib vaccine are interchangeable in terms of safety and efficacy. Important research questions include better estimation of the disease burden (especially in south-east Asia), the need to document changes in carrier rates before and after introduction of vaccine, and the impact of infant vaccination on the reservoir of Hib in older age groups. If the disease burden is such as to justify global use of the vaccines and if vaccination has an impact on carrier rates in adults, eradication might be feasible in the relatively near future.

Tuberculosis

Tuberculosis (TB) is currently the leading infectious cause of death in the world, with 2–3 million deaths each year. A three-pronged strategy has been adopted for control of this disease, including case management, vaccination, and preventive therapy. Case management is currently the essential activity of TB control, and the highest priority is given to providing a short course (3–6 months) of directly observed therapy (DOTS) to infectious cases (those with tubercle bacilli demonstrated on microscopic examination of the sputum), with guaranteed supply of drugs. This strategy has been shown to result in high cure rates and is feasible, even in developing countries. BCG vaccination in infancy prevents a substantial proportion of disseminated tuberculosis in children (e.g. TB meningitis), but has little impact on TB transmission or incidence in adults. Preventive therapy, administered to persons who are infected with TB (i.e. tuberculin-positive) but who have not developed disease, is highly effective in preventing development of the disease and is an important strategy to be introduced once a sufficiently high proportion of diagnosed (i.e. infectious) cases are being effectively treated.

The unfortunate interaction between tuberculosis and HIV infection (in which each exacerbates the other) means that the TB problem will deteriorate further in countries which now suffer most from either TB or HIV (e.g. in sub-Saharan Africa and south-east Asia). In addition, multidrug-resistant TB is an increasing problem in many areas, including the Newly Independent States of the Soviet Union and the Russian Federation. Research needs include development of a more effective vaccine, improvements in preventive therapy, better understanding of latent infections and the existence of a possible animal reservoir, and demonstration that elimination is feasible in a defined geographical area. The US "elimination" target of an incidence of <1 case per million population does not meet the Dahlem criteria. Improvements in TB control depend on (and contribute to) general health infrastructure. A long-term (>70 years) goal of elimination/eradication may help retain focus on these efforts.

Leprosy

There are approximately 500 000 new cases of leprosy each year, occurring in geographically restricted areas; 90% of all cases occur in 15 countries. Current interventions focus on finding cases of leprosy and administering directly observed multidrug therapy for 6–24 months (depending on the type of leprosy)

and on the use of BCG vaccine. An "elimination" goal has been established, with the target being an incidence of <1 case per 10000 population. Neither elimination (using Dahlem definitions) nor eradication is feasible, although there are important opportunities for improved control. Some of the barriers to improved control include insufficient knowledge of the epidemiology, pathogenesis, and transmission of leprosy (including carriage and incubation period) and the difficulty in growing the organism in the laboratory.

Syphilis

Approximately 1 million pregnancies each year are complicated by syphilis. Elimination of congenital syphilis in some geographical areas was considered feasible, but not eradication — more because of weaknesses in the health care delivery system than because of faults with the intervention. The same strategies used to attain control and very good control over congenital syphilis should also be adequate to achieve elimination, but with a considerably higher cost. These strategies are as follows: to examine pregnant women at their first prenatal visit, perform an on-site diagnostic test, treat those who are positive and their partners, and take a systematic approach to reduce adult syphilis through diagnosis and treatment of cases of genital ulcer disease. The antenatal care infrastructure necessary for prevention of congenital syphilis is the same as that necessary for prevention of other perinatal conditions such as neonatal tetanus and iron deficiency anaemia. Improvements to the infrastructure will benefit reproductive health services for women overall.

Elimination cannot be achieved strictly through approaches to pregnant women, but also requires activities to prevent and control acquired syphilis in adults. Syndromic approaches to management of genital ulcer disease (primarily syphilis and chancroid) can also have a significant impact on decreasing the transmission of HIV. A goal of "elimination" from the Region of the Americas, which does not meet the Dahlem definition has been established by the Pan American Health Organization. True elimination in the Americas was felt feasible in the next 5–10 years. Elimination of adult syphilis was not considered programmatically feasible at present, although substantial improvements in surveillance and control are both feasible and necessary It is possible that mass therapy in high prevalence areas could be quite effective in improving control, as it was with yaws. Research needs include development of less invasive diagnostic techniques, effective single-dose oral therapies and vaccines, as well as operational research.

Although elimination of chancroid might be biologically feasible, it does not seem programmatically attainable at present. Factors favouring the potential for elimination include availability of effective oral therapy: clinically apparent, symptomatic disease; a relatively short period of transmissibility; and a high concentration of disease in core transmission groups. Pilot efforts to eliminate chancroid could be undertaken as part of the genital ulcer disease component of congenital syphilis elimination.

Trachoma

Trachoma is the leading preventable cause of blindness worldwide, with an estimated 5.9 million persons blind or at immediate risk because of trichiasis. Trachoma accounts for nearly one-sixth of the global burden of blindness; women are affected disproportionately. Genital strains of *Chlamydia trachomatis* do not infect the eye. Effective interventions have been demonstrated in developing countries to have a major impact on blindness due to trachoma using the "SAFE" strategy — Surgery to correct lid deformity and prevent blindness, Antibiotics for acute infections and community control, Facial hygiene, and Environmental change, including improved access to water and sanitation, and health education.

An "elimination" target of 2020 has been established by an international alliance but does not meet the Dahlem definition. Elimination of blindness due to trachoma is considered feasible; eradication of trachoma is not. Research needs include validation of rapid community assessment techniques, identification of barriers to the acceptance of the preventive surgical procedure, operational research on the effectiveness of annual treatment cycles, and cost–benefit and cost-effectiveness studies.

Conclusions and recommendation

- Each of the above conditions has a significant disease burden, most notably in developing countries.
- Each of these conditions has an effective intervention with at least some existing infrastructure to deliver it, but many of the interventions are not optimal.
- Each condition is poorly controlled globally.

- Each condition has surveillance techniques available, although they may not be in place in all areas.
- None of these conditions is a candidate for eradication in the next 10–15 years with current interventions. Hib infection and congenital syphilis are currently candidates for regional (but not global) elimination. The long-term vision for Hib infection and tuberculosis is eradication (for TB, this would require decades); for congenital syphilis and trachoma the long-term vision is regional elimination.
- Effective control or elimination of most of these conditions requires a combination of strategies, rather than a single strategy such as vaccination.
- Improved control or elimination of each of the conditions is closely related to existing health care delivery systems, rather than a vertical approach. However, it is important that health workers be identified and made responsible for achieving the goals, even though they have many other responsibilities (the concept of "designated" but not "dedicated" personnel).
- Public education and social mobilization are important factors in improved control or elimination/eradication for each of these conditions.
- Behavioural modification is an important factor for the control of most of these conditions.
- There are many research needs for each of the conditions which must be addressed before eradication could be attempted. These range from the need for improved understanding of the epidemiology of disease to developing improved interventions and improved strategies to deliver interventions.
- Elimination is expensive, both in the extra effort needed to achieve zero incidence and in the surveillance system needed to document zero incidence.
- Unless elimination is a step on the road to eradication, very good control may be a more appropriate goal This would potentially allow broader use of the additional resources which may be required for elimination.
- Public health institutions have been imprecise in their use of the term "elimination", often using it to indicate very good control (e.g. "elimination as a public health problem"). Several incidence goals have been set and labelled as elimination goals which do not meet the definitions agreed at the Dahlem Workshop. Efforts should be made to use this term precisely. None the less, it is important to set specific targets for control activities ("control with a goal"), which could encompass some of the targets currently labelled as "elimination" (e.g. global goal for neonatal tetanus, U S. goal for tuberculosis).

Given all these factors, the Workgroup recommends that, while actively pursuing the research needed to improve our understanding of these diseases and our interventions for dealing with them, the global community should take aggressive action to improve global control of neonatal tetanus, *Haemophilus influenzae* type b infection, tuberculosis, leprosy, congenital syphilis, and trachoma.

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