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FOREWORD

Vaccines at the turn of the 21st century: a new era for immunization in public health

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Since Edward Jenner's discovery of the basic concept of vaccination in 1796, vaccines have become a critical component of our armamentarium for preventing a broad spectrum of infectious diseases. Vaccination now sits at center stage in our ability to impact public health on a global scale, and, aside from sanitation and clean water, represents one of the easiest and most cost-effective means to control infectious diseases and improve people's standards of life.

The beneficial impact of vaccination extends beyond protection of the individual – also it gives rise to "herd immunity," an effect whereby vaccination of a large proportion of the population hinders the transmission of an infectious agent and thereby protects the entire population, even those not vaccinated.[1] Indeed, this effect has led to some remarkable results, including eradication of smallpox and virtual disappearance of diphtheria, tetanus, and paralytic poliomyelitis.[1] However, it is clear that much remains to be accomplished to close the global vaccination gap[2] and to reduce the annual toll of approximately 3 million children dying from vaccine-preventable diseases.[3]

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As the science of vaccinology enters its third millennium, it is appropriate to reflect on some of the current key trends in the global vaccine scene. Advances in molecular biology have led to monumental leaps in vaccine development,[4] and, in this regard, several new scientific capabilities are particularly noteworthy: reassortment technology, virus-like particles (VLPs), and recombinant subunit vaccines. Reassortment technology is especially useful for developing vaccines against organisms that exist as multiple different subtypes, usually with segmented genomes (e.g., rotaviruses).[5] The process involves substituting gene sequences from human into animal viruses to generate reassorted progeny strains that are nonvirulent to humans, but nevertheless elicit a protective immune response to multiple strains. Another remarkable advance has been the application of recombinant DNA technology to create novel VLPs. This technology has been applied for the first time to develop human papillomavirus (HPV) vaccines devoid of the entire HPV genome, thereby avoiding the potential exposure of people to viral oncogenes.[6,7] These VLPs elicit high-titers of virus neutralizing antibodies and other protective HPV-specific immune responses.[6,8]

We also are witnessing a paradigm shift in the clinical evaluation of vaccines. The introduction of more stringent national and international regulatory requirements for the clinical characterization of vaccines, together with greater emphasis on vaccine safety, has ushered in the era of the mega trial (more than 70,000 infants were enrolled in a recent rotavirus vaccine trial).[9] These trials enroll many tens of thousands of subjects and also sometimes employ surrogate endpoints (e.g., CIN 2/3 as a surrogate endpoint for cervical cancer in HPV vaccine trials). In addition, studies are now more frequently conducted in a much

broader spectrum of individuals. In the past, immunization has traditionally focused on infants and young children, but it is now clear that other target populations might benefit from certain vaccines, including adolescents and young adults, the elderly and, immunocompromised patients.[4] Clinical evaluation is also taking place of vaccines directed toward infectious agents that could potentially be used in bioterrorist attacks (e.g., anthrax and vaccinia).[4]

The renewed global interest in vaccines in recent years is evidenced by the formation of GAVI Alliance (formerly known as the Global Alliance for Vaccines and Immunization) in 2000.[3] The GAVI Alliance is a collaborative venture between public and private sectors with the goal of bringing the benefits of immunization to children who are in the greatest need. The cornerstone of the GAVI Alliance's mission is the belief that all children — no matter where they live — deserve a healthy start. Working through the GAVI Alliance, the International Finance Facility for Immunization (IFFIm[10]) and other new funding mechanisms are accelerating the availability of funds for health and immunization programs to many of the world's poorest countries. The increased global demand for vaccines has resulted in a substantially enlarged manufacturing base that now includes production capabilities in mid-developed countries such as India and China.

Despite the remarkable achievements in vaccine research and development, and a renewed interest in the global public health benefits of vaccination, a number of major roadblocks remain. Foremost is the existence of a narrow base for discovery and development of new vaccines, a situation linked, in part, to the enormous costs associated with research, development, manufacture, and launch of new vaccines. These costs are so large ($400 to 800 million per vaccine[1]) that only the largest international pharmaceutical companies can shoulder the burden. Since economic principles dictate that companies price their products according to the level of investment made, this has led to the unevenness of deployment of vaccines between the developed and developing world. This disparity is being addressed immediately. Some partial solutions include: differential pricing of vaccines; highlighting that local costs of vaccines can be more than offset by long-term national healthcare savings; and by promoting and supporting public-private partnerships that purchase and distribute vaccines to poorer nations.

In addition to GAVI Alliance, World Health Organization and UNICEF, other global and national champions for immunization are urgently needed to take a strong stand on the need to realize the full potential of vaccines to relieve human misery. One of their key goals should be to counter the anti-vaccination campaigns that seriously impede immunization efforts in both developed and developing countries. Another goal must be to improve the infrastructure for vaccination programs, especially in developing countries. While an adequate infrastructure will invariably be complex and costly, it is crucial for ensuring the optimal delivery of vaccines, preventing vaccine shortages, conducting outreach and education programs, maintaining coverage rates, and addressing control of outbreaks.

While many problems remain in terms of vaccine production, regulation, distribution, and funding, it is clear that exciting new research and discovery tools are now available, and that these are likely to lead to introduction of new vaccines to prevent more human disease. The purpose of this supplement is to highlight four new vaccines — quadrivalent HPV (types 6, 11, 16, 18) vaccine, pentavalent human-bovine reassortant rotavirus vaccine, herpes zoster vaccine, and pediatric quadrivalent vaccine for measles, mumps, rubella, and varicella — that have arisen, in part, from the creative application of some of these powerful new techniques.

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Conflict of Interest statement

No competing interest declared.

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