

experience suggests that mycophenolate might provide excellent coverage in many cases and have a better profile of side-effects than previously described immune modulating drugs.¹⁰⁻¹² Also, continued pain and disease progression, even with steroid and steroid-sparing treatment, can extend into the mesentery, mediastinum, and even coronary perivascular areas, and newer drugs such as rituximab can be effective in such instances and further our understanding of pathogenesis.¹³ Finally, distinction between idiopathic and secondary forms of retroperitoneal fibrosis will remain a clinical judgment until we have specific pathological or serological markers.

On balance, this contribution by Vaglio and colleagues far outweighs its shortcomings, moving us forward in the elucidation of the pathogenesis of sclerosing diseases such as idiopathic retroperitoneal fibrosis and in definition of optimum treatment. Idiopathic retroperitoneal fibrosis is unusual and demands multidisciplinary attention, but treatment success is satisfying for both patients and practitioners in what was previously a difficult and poorly understood syndrome. Vaglio and colleagues, having already begun other investigations on pathogenesis in idiopathic retroperitoneal fibrosis,² now set the standard for further clinical investigation to define the disease and its treatment.

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The vaccine paradox

The next decade will likely bring astonishing successes in vaccine biology, discovery, and delivery. Justifiable confidence in this proposition led the Bill & Melinda Gates Foundation last year to pledge US\$10 billion to a new Decade of Vaccines. For the world's largest and most influential health foundation, vaccines are the number one priority. The foundation estimates that if vaccine coverage could be scaled up to 90%, the lives of 7.6 million children younger than 5 years could be saved between 2010 and 2019. If a malaria vaccine became available by 2014, this figure could rise by a further 1.1 million.

To address the opportunity the Gates Foundation has identified, we brought together some of the leading scientists working in vaccines today to set out the hopes and possibilities for the coming decade. As we gathered for our first meeting, broad optimism was tempered with caution. One contributor argued that “the present way we work will not sustain the next decade of vaccines”. Another said that despite the manifest successes of today's vaccines, we had to face up to “a relative failure”. We have not created a sustainable environment for new vaccines to thrive.

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This Series on the new decade of vaccines explores why there is an unprecedented opportunity for vaccines, but also why we must choose a different trajectory for this future decade if those opportunities are to be fully realised.

In truth, the global prospects for vaccines seem fragile. Consider recent events. In October, 2009, the UK's *Sunday Express* ran the front-page headline, "Jab 'as deadly as the cancer'". The report referred to the tragic death of a 14-year-old girl who had recently received a vaccine against cervical cancer. The link between the vaccine and her death was quickly proven to be incorrect. But sensational reporting risked inflaming public attitudes about the vaccine's safety. In January, 2010, Thai public health officials faced questions after a woman who received the H1N1 influenza vaccine suffered a miscarriage. Although experts tried to reassure women that the vaccine was safe, authorities were forced to suspend vaccination programmes pending an inquiry. And in March this year, Japanese health officials suspended vaccines against pneumonia and meningitis after the deaths of four children, despite there being no reliable evidence to substantiate public concerns. The traditional response of public health to concerns about vaccine safety is usually to give confident reassurance to the public. This approach often succeeds. But with a more sceptical and questioning media, a more responsive way forward may be, for example, to anticipate public concerns by reporting background rates of possible adverse effects so that, if they do occur, the public (and media) are neither surprised nor alarmed.¹

The challenge faced by the global health community in creating a supportive culture for vaccines is not only one of public confidence. The systems to supply vaccines to where they are most needed—including the capacity of cold chains—are presently inadequate. In addition to logistical difficulties, vaccine production itself is unsustainable. For example, most vaccines funded by the GAVI Alliance are produced in countries outside Africa, despite sub-Saharan Africa accounting for more than half of the world's poorest countries in receipt of those vaccines. There should be stronger efforts to build infrastructure and create the skilled workforce needed to source vaccines from local producers. There are also critical ethical challenges that have so far received little public discussion. For

instance, how should governments allocate limited supplies of vaccine during an epidemic?

One institution that can rightly take credit for mobilising countries and partners to create a new era of opportunity for vaccines is the GAVI Alliance. Founded in 2000, GAVI has accelerated the transfer of technologies from rich to poor countries at unprecedented rates. But GAVI's continued success is not guaranteed. It needs and deserves substantial and sustained financial replenishment. GAVI's foray into health-systems strengthening has been important and valuable (and needs to be developed still further). But it also led to anxieties that GAVI was blurring what should be its central concern—vaccines. A recent and poorly managed change in leadership at GAVI was at least partly precipitated by this feeling of mission drift. Some evidence also exists that vertical health initiatives, such as GAVI, are not without their own complications and adverse effects.² The way the organisation is audited is currently not fully optimal.³ And GAVI needs to be clear about what it should not do. While evaluating its performance should be a stronger part of GAVI's remit, developing its own research agenda would, we believe, be a mistake.⁴ Other organisations are better placed to fund and conduct vaccine-related research.

Part of the problem GAVI faces is its isolation from other initiatives dedicated to women's and children's health. Ban Ki-moon's 2010 Global Strategy for Women's and Children's Health sets out a comprehensive approach to reaching Millennium Development Goals (MDGs) 4 and 5 for the world's poorest countries. The strategy is broad, inclusive, and ambitious. It commands the support of all health agencies and donors. It has been fashioned through collaboration with countries most threatened by the diseases of poverty that affect women and children. Vaccines are a key part of the Global Strategy. GAVI is given special prominence as a means to bridge financial gaps for funding health programmes. But GAVI itself has been too silent on its contribution to the larger goals of the Global Strategy. It feels a reluctant partner. GAVI needs to position itself as a leading advocate for and contributor to that strategy. It must not be run as an institution divorced from, and without responsibilities to, this larger effort.

The Gates Foundation's notion of a Decade of Vaccines is not merely an advocacy message. It is a joint initiative between WHO, UNICEF, the US National



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Panos

Institute of Allergy and Infectious Diseases, and the Gates Foundation. Launched in December, 2010, it plans to increase coordination across the vaccine community and to create a global vaccine action plan. The focus of the initiative is on delivery and coverage, immunisation systems, equity, and filling the finance gap to achieve these objectives. Country consultations to be completed by the end of this year aim to build commitment to vaccines. A “prioritized delivery action plan” is to be ready by June, 2012. But substantial challenges confront efforts to scale up commitments to vaccines. Many countries have no immunisation technical advisory group to give guidance or leadership on immunisation policies. High prices of new vaccines continue to slow prospects for their delivery. Adverse media reporting can damage vaccination programmes—eg, for *Haemophilus influenzae* type b containing vaccines in several countries. And, like GAVI, in the Decade of Vaccine documents we have seen there is little or no mention of the part this initiative has to play in the Secretary-General’s Global Strategy. The risk is, again, that at country level a new and highly focused vaccine initiative will compete with a broad strategy for achieving the MDGs. The two initiatives need to be linked much more closely, perhaps even integrated.

The Lancet’s Series tries to trace the elements of a plan for vaccines in the 21st century. Vaccines face a strange

paradox. While civil-society movements demand access to new interventions—from antiretrovirals to emergency obstetric care—there is not the same fervour about access to vaccines. The notion, expressed elsewhere in global health, of the right to the highest attainable standard of health is rarely expressed in the field of vaccines. For these attitudes to change, the vaccine community, together with its partners, has an opportunity to rewrite the terms of engagement between vaccines (as part of a larger package of services) and communities threatened with vaccine-preventable diseases. While the past has much to teach us, it is the future of vaccines that must command our priority today.

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A call to action for the new decade of vaccines

No medical intervention has such an unambiguous track record of preventing morbidity and mortality from infectious diseases than that of vaccines.¹ The type of vaccine-preventable diseases ranges from the acute (eg, measles or meningitis) to the chronic (eg, liver and cervical cancers). Further reduction of deaths and disability from infections remains a major challenge. Few would deny that there is a moral imperative to make vaccines widely available on an equitable basis, but governments are frustratingly slow to grasp a different and compelling argument: vaccines create wealth.^{2,3}

This tenet is especially true for the poorest countries, where infectious diseases account for almost half of all deaths.⁴ About 90% of these deaths are caused by six infection-related diseases: diarrhoeal and respiratory

diseases of children, AIDS, tuberculosis, malaria, and measles. But encouraging progress has been made; the availability of rotavirus vaccines against one of the major causes of childhood diarrhoea has great potential.⁵ Pneumonia is the leading cause of child death, and glycoconjugate vaccines against pneumococcal pneumonia—the cause of more than a third of all pneumonia deaths in infants—are now reaching children in the poorest countries.⁶ A highly effective vaccine has substantially affected the burden from measles, although it does not provide protection among infants aged 4–9 months; however, research efforts towards an inhalable measles vaccine⁷ might provide protection for this vulnerable group. It is also hoped that a malaria vaccine will be licensed within the next 3 years or so.

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