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New Vaccines on the Horizon

Jeannette L. Comeau[1,3] · Jocelyn Chan[1] · Kristine K. Macartney[1,2,3]

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Abstract
Purpose of Review Well-established as a powerful tool for preventing disease, vaccines have immeasurably impacted health and disease epidemiology worldwide. In the era of rational vaccine design and ever-evolving technology, vaccine development and delivery is poised to improve the ability to target a range of new diseases and to improve disease prevention, in even the most remote communities worldwide.
Recent Findings New vaccines against influenza, human papillomavirus and meningococcal diseases have focused on targeting an increased number of serotypes and/or improving immunogenicity, while new vaccines against dengue and malaria are closer to being delivered to communities at need. Alternative models of protection, for example, expanded use of maternal vaccination, are also being explored and may prove effective against new diseases, such as respiratory syncytial virus. Further on the horizon are better vaccines against tuberculosis and also new vaccines for HIV, Group B Streptococcus, Group A *Streptococcus*, *Staphylococcus aureus* and cytomegalovirus. Emerging infectious diseases, including ebola and zika virus, present challenges for the traditional bench to bedside timeline of vaccine research, development, and deployment, proving that acceleration of this process is possible.
Summary This review covers new vaccines against the diseases above, and also briefly touches on continued efforts to ensuring life-saving immunisation is provided to all.

Keywords Vaccine · Immunisation · Pediatrics · Infectious Diseases · Vaccine development · Vaccine delivery

Introduction

Vaccines were described in 2007 by the British Medical Journal as one of the great medical milestones in the preceding 160 years [1]. While quantification of their impact is near impossible, a United States Centre for Disease Control (CDC) report based on modelling estimated vaccines prevented 322 million disease episodes in American children between 1994 and 2013 [2]. Although the triumphs of current vaccines are many, challenges in ensuring they are deployed to areas of greatest need and in developing new vaccines remain [3••]. This review aims to update clinicians on new immunisation strategies under development and in early use to prevent childhood diseases. We focus on major pediatric pathogens, and briefly review current strategies in vaccine development, delivery and safety assessment. While it is not possible to focus on all vaccines, we aim to discuss those with the greatest implications for child health around the globe.

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✉ Jeannette L. Comeau
jeannette.comeau@health.nsw.gov.au

[1] National Centre for Immunisation Research and Surveillance (NCIRS), Kids Research Institute, The Children's Hospital at Westmead, Locked Bag 4001, Westmead, NSW 2145, Australia

[2] Discipline of Paediatrics and Child Health, University of Sydney, Sydney, NSW, Australia

[3] The Children's Hospital at Westmead, Sydney, NSW, Australia

New Approaches to Vaccine Development and Deployment

Deploying Vaccines to Areas of Greatest Need

The Global Alliance for Vaccines and Immunisation (GAVI) recently estimated that every year more than 1.5 million children die from vaccine preventable diseases [3••]. In December 2010, global health leaders committed to making the next 10 years the Decade of vaccines (DOV)—to ensure discovery, development, and delivery of life-saving vaccines globally, especially to the poorest countries [4]. The four objectives of the DOV are as follows: intensified research and development for approximately 20 vaccines; advocacy and political will to mobilise donors; increased compliance and shouldering of responsibilities by developing countries; and expanded efforts in communicating the benefits of vaccines. Halfway into this initiative, a number of targeted vaccines (discussed below) have become available, with more progress to come.

Who to Vaccinate?

The target age group for pediatric vaccines has traditionally been young children, however, for certain diseases immunising pregnant women, neonates or adolescents is of increasing interest. Vaccination during pregnancy has been utilised since the 1960s as an effective tool for the prevention of maternal and neonatal tetanus [5]. Active transfer of antibodies (IgG) across the placenta occurs from the second trimester onwards and provides 'passive' immunisation of the infant for up to 6 months against diseases which cause high morbidity and mortality in this time frame. Protection has been shown in multiple studies for influenza vaccine, including in randomised controlled trials in pregnant women in Bangladesh and South Africa (HIV positive and negative) where infants were protected against laboratory-confirmed influenza [6, 7]. Maternal vaccination against pertussis during the early third trimester has also recently been shown to be both efficacious and safe in preventing disease in infants in the first 3 months of life [8–11]. Conducting vaccine clinical trials in pregnant women has been challenging; however, efforts to improve clinical trial and regulatory approval processes are being explored [12, 13]. Factors such as potential blunting of infant immune responses to subsequent routine immunisations and safety of both mother and infant require careful assessment [14].

Neonates are highly vulnerable to many of the diseases against which vaccines are available, but because of immune immaturity and circulating maternal antibodies vaccine administration shortly after birth is typically not protective [15]. Nonetheless, exploration of the immunogenicity, safety and efficacy of new candidate vaccines given in the first week of life is ongoing [15]. Examples include use of a live-attenuated rotavirus vaccine developed from an immunogenic neonatal strain, RV3 [16] and an acellular pertussis vaccine, shown to be safe and immunogenic in early phase 2 study [17]. The last decade has also seen an increased focus on early adolescence as a vaccine target age group, either for provision of booster doses against diseases such as pertussis, because of waning immunity to acellular pertussis vaccines given in early childhood, or to protect against diseases such as human papillomavirus (HPV). For HPV and hepatitis B vaccines, adolescents have been shown to have a robust immune response to fewer doses of vaccines than young adults.

New Vaccine Technologies

Many current vaccines were developed using 'classical vaccinology' approaches using either killed or live-attenuated pathogens, or modified toxins [3••, 18]. However, rapid progress in virology, genetics, biology, and biotechnology has led to novel vaccine approaches. For example, understanding the role of dendritic cells in presenting antigens to the immune system and the immune response to adjuvants has been critical. Adjuvants are added to vaccine antigens to increase the magnitude of an immune response and increasingly, they can be designed to influence the particular type of immune response elicited [19]. Aluminium-based adjuvants have been used since the 1920s to enhance antibody responses to killed inactivated or subunit vaccines [20]. There are currently over 30 adjuvants that are in use or under evaluation in various vaccines [21], including oil-in-water emulsions (for example AS03 and MF59 in HPV and influenza vaccines, respectively), and a liposome-based adjuvant, AS01, in the recently licensed RTS,S/AS01 malaria vaccine [22].

Alternative vaccine delivery approaches are also being considered. Intradermal, inhaled, nasal or oral administration can be efficacious, but not all vaccines are amenable to these delivery modes. For example, intranasal administration of the live-attenuated influenza vaccine has proven efficacious in children (who are influenza naïve, thus allowing replication of the live-attenuated viruses), but not adults [23]. New technologies include cutaneous microneedle patches with freeze dried antigen coatings that could be used in developing countries where transportation and storage of vaccines are problematic [24, 25], and jet injection [26], a method used in hormone delivery, that may also prove viable for vaccines. Ongoing research and development as well as trials to evaluate efficacy and safety are necessary.

Vaccine Safety and Hesitancy

Over the past 25 years, the number of vaccines on routine childhood immunisation schedules in the United States, Canada, Australia, and Europe has at least doubled. Yet during this time, it has also become evident that public confidence and trust in immunisations is fragile and requires attention [4]. Changing immunisation schedules, conflicting messages in the media and online, and ironically, the success of vaccines in reducing the visibility of serious childhood diseases, have been a threat to vaccine uptake. In some cases, vaccine hesitancy has led to failure to implement new vaccines, caused programs to be suspended, or resulted in low coverage [27]. As one of very few medical interventions that are undertaken in healthy children, ensuring safety and communicating this to parents is paramount.

In 2011 the World Health Organization (WHO) and partners developed the Global Vaccine Safety Blueprint, a document aimed at ensuring that each country has a mechanism to evaluate and ensure the safety of vaccines [28]. The Global vaccine safety initiative (GVSI) was created to implement the eight Blueprint objectives, which include Adverse events following immunisation (AEFI) detection, vaccine safety communication, and global analysis and response. Within two years of its inception, 50 countries are involved in the GVSI, accounting for approximately 77 % of the world's population [29]. Global coordination of AEFI monitoring, as well as communication between regulatory bodies, allow early detection of adverse events that can prompt investigation. This is essential in the current climate of increasingly complex immunisation schedules. Clinicaltrials.gov is an online resource that enables the public to have access to information on vaccine and many other clinical trials. Maintained by the National Library for Medicine (NLM) at the National Institute for Health (NIH) in the USA, medical trials in human volunteers occurring in 193 countries are recorded. As of May 6, 2016, information on 6016 vaccine trials was recorded, 2159 of which were in pediatrics (children aged 0–17 years); trials recorded on this register by disease are shown in Table 1.

Specific Diseases

Dengue

Dengue virus, a flavivirus spread by the Aedes species of mosquito, infects at least 390 million people per year [30]. It has been estimated that up to 95 % of cases occur in children <15 years of age [31], with varying clinical presentations. There are four dengue serotypes and as only type-specific infection gives lifelong immunity, infection up to four times in possible. In addition, repeat infections present a much higher risk of complications and shock [32]. There is no specific treatment and vector control efforts have been ineffective to date [30].

In 2015, a live recombinant tetravalent chimeric dengue vaccine, with antigens from all four dengue serotypes substituted into a yellow fever vaccine backbone (CYD-TDV) [33], became the first ever licensed dengue vaccine. It was evaluated in two major phase III clinical trials, in Asia among children 2–4 years, and in Latin America in children 9–16 years. The overall vaccine efficacy from these studies was 59.2 % (95 % CI 52.3–65.0) against any of the four serotypes of dengue; however, serotype-specific efficacy for dengue serotype two virus was poor [34]. Immune responses and vaccine efficacy were also greater in children who were flavivirus seropositive (indicating at least one previous infection), suggesting that the vaccine will be most useful in endemic countries [34–36, 37•]. Although modelling studies have demonstrated that even partially efficacious vaccines can lead to significant disease reduction [38], these issues are complex when considering how to deploy the vaccine. The WHO Strategic advisory group of experts (SAGE) on Immunisation is currently developing recommendations for use of CYD-TDV [39], but in the meantime, one endemic country, the Philippines, began mass vaccination in April 2016 [40].

A number of other dengue vaccines are currently in development. DENVax, a mixture of chimeric DENV1, DENV3 and DENV4 antigens on a DENV2 backbone plus a whole live-attenuated DENV2 component [41], is in Phase II studies in Colombia, Puerto Rico, Singapore and Thailand [42, 43]. Other vaccine candidates are tetravalent admixtures of monovalent live-attenuated vaccine strains covering DENV1-4 (TV003 and TV005). First tested individually and then in combination, trials have demonstrated safety and immunogenicity to 6 months [44] with phase II studies currently underway in Thailand and Brazil [45, 46].

Malaria

Despite widespread use of insecticide impregnated bed nets, insecticide spraying, and malaria treatment, morbidity and mortality remain high. In 2015, there were an estimated 438,000 deaths due to malaria, with 70 % occurring in children <5 years of age [47].

The complexities of the parasite lifecycle make vaccine development difficult. Most efforts to date have focused on Plasmodium falciparum, which is responsible for more than 98 % of malaria mortality [48]. In July 2015, the European Medicines Agency, approved the first malaria vaccine, known as RTS,S/AS01 (Mosquirix^{TM}, GSK), for

Table 1 Number of vaccine clinical trials currently registered on clinicaltrials.gov for specified diseases. (Current as of 6 May 2016)

Disease	N Trials		Phase III & IV		Completed with results		Completed with results phase III & IV		Vaccine currently available
	All	Peds	All	Peds	All	Peds	All	Peds	
All vaccine clinical trials	6061	2159	1815	1042	976	490	524	326	–
CMV	36	4	5	0	1	0	0	0	No
Dengue virus	83	27	8	7	2	1	0	0	Yes
Ebola virus	45	5	6	2	0	0	0	0	No
GAS	18	2	0	0	4	0	0	0	No
GBS	15	0	0	0	4	0	0	0	No
HIV[†]	576	113	72	20	43	14	5	3	No
HPV	233	134	99	68	74	46	48	31	Yes
Influenza	1366	491	589	274	318	135	187	94	Yes
Malaria	172	53	12	12	7	7	0	0	No
Meningococcus	91	80	53	48	32	30	15	13	Yes
Rotavirus	127	120	58	58	32	31	22	22	Yes
RSV	38	15	3	1	3	3	0	0	No*
Staphylococcus aureus	24	0	8	0	5	0	0	0	No
Tuberculosis	96	22	8	2	5	2	0	0	Yes (BCG)
Zika virus	0	0	0	0	0	0	0	0	No

* Passive immunisation via monoclonal antibody infusion (Palivizumab)

[†] Includes clinical trials of HIV vaccines and other vaccines in HIV-infected population

CMV Cytomegalovirus, *GAS* Group A Streptococcus, *GBS* Group B Streptococcus, *HIV* Human immunodeficiency virus, *HPV* Human papillomavirus, *RSV* Respiratory syncytial virus, *BCG* Bacillus Calmette-Guérin

use outside of Europe. The vaccine was developed in partnership between GSK and the PATH Malaria vaccine initiative, with support from the Bill and Melinda Gates Foundation, representing an innovative new funding model and public–private partnership. It is a recombinant vaccine, where a sporozoite protein is fused with HBsAg inducing a specific immune response to prevent blood stage infection. Phase III studies using a three dose schedule and a 4th booster dose were conducted in seven African countries [49]. Efficacy against malaria 14 months after vaccination was 50.4 % (95 % CI 45.8–54.6) in children immunised at 5–17 months, but lower in infants immunised at 6-12 weeks of age (30.1 % [95 % CI 23.6–36.1]). Efficacy waned thereafter and an increased risk of severe malaria among vaccinated children occurred in the last 27 months of the study. This suggests the need for a 4-dose schedule starting from 5–6 months of age. Given the complexities involved, WHO recommended pilot implementation in 3-5 subnational sub-Saharan areas before considering wider country level introduction [50]. Other vaccines being trialled include three promising candidates using whole sporozoites [51–53] and a heterologous 'prime boost' strategy [54, 55]. Interesting "transmission-blocking" vaccines target sexual erythrocytic and early mosquito stage antigens, as the parasite passes from human host to mosquito and aim to reduce burden of disease by reducing transmission [56, 57].

Tuberculosis and Human Immunodeficiency Virus (HIV) Vaccines

Tuberculosis (TB) remains a significant cause of child morbidity and mortality worldwide, with an estimated 140 000 deaths in children worldwide in 2014 [58]. The emergence of drug resistant *Mycobacterium tuberculosis* strains and prevalence of HIV co-infection has further complicated management [59]. The live-attenuated bacillus calmette-guérin (BCG) vaccine is the only licensed TB vaccine and has some effectiveness at preventing miliary and meningeal TB in children [60, 61]. However, BCG has limited effectiveness in older children and adults, and against pulmonary TB, and carries a small risk of severe complications including disseminated BCG infection [62], which outweighs potential benefits in countries with low TB prevalence [63]. Recently supply has been threatened by a global shortage [64]. A limited understanding of the specific human immune response to *M. tuberculosis* infection and a lack of immunological correlates of

protection that can predict vaccine efficacy in humans with certainty remain challenges in vaccine development [65].

TB vaccine candidates in development (approximately 13) are broadly aimed either at replacing BCG or boosting the immune response in already infected persons, and include whole cell derived, viral vectored or adjuvanted protein subunit vaccines. For example, in South Africa, one recombinant BCG vaccine candidate (VPM1002) has been evaluated through a phase II study in newborn children with results awaited [66], and a candidate live-attenuated mycobacterium tuberculosis vaccine is entering into a phase 1b trial of safety and immunogenicity in healthy neonates [67].

Despite over thirty years of vaccine research following the isolation of HIV in 1983, no candidates are close to prophylactic use in humans [68]. However, much has been learnt about the immunopathogenesis of the virus, informing vaccine development efforts. One vaccine candidate that demonstrated limited efficacy against HIV-1 in adults in Thailand [69], is being further investigated. Only one pediatric trial, that has not begun recruitment, is registered on clinicaltrials.gov, utilising a killed HIV-1 viral particle vaccine (REMUNE™, BioPharma) [70].

Influenza

Seasonal epidemics of influenza occur globally with an annual attack rate estimated at 20–30 % in children [71]. Current vaccines, while moderately effective in all ages >6 months, induce strain specific immunity and have to be updated yearly because of antigenic drift [72]. They include injected inactivated influenza vaccines (IIV), and a nasally administered live-attenuated influenza vaccine (LAIV) [72], which have 56–64 %, and up to 80 % efficacy, respectively [73]. New quadrivalent influenza virus (QIV) vaccines (both as IIV and LAIV) contain a second influenza B strain in addition to the two influenza A and single B lineage in the trivalent, and will offer greater protection in years in which both or a mismatched B lineages circulate. QIVs are being incorporated into programs worldwide. The MF59 adjuvanted seasonal vaccine (e.g. Fluad®, Novartis) has been licensed for the elderly population but has had limited use in pediatrics [74].

Strategies to advance the speed and scale of influenza vaccine production include recombinant vaccines, the use of virus like particles, DNA vaccines, and virus-vectored vaccines [72]. The trivalent seasonal recombinant haemagglutinin vaccine (e.g. Flublok®, Protein Sciences) produced in insect cells has already been licensed in the USA [72]. Progress is also being made towards the development of a universal influenza virus vaccine [75], a major milestone facilitated by identification of neutralising antibodies to the conserved parts of the haemagglutinin protein, including the stalk. Clinical trials to test this hypothesis have been initiated [75].

Respiratory Syncytial Virus (RSV)

RSV was initially isolated in 1957 [76], and the quest for a vaccine has been underway since. It remains the most common acute lower respiratory tract illness in children <5 years of age worldwide, accounting for 33.8 million cases annually, and 3.4 million hospitalisations [77], with infants most severely affected.

A candidate formalin-inactivated RSV vaccine in the 1960s paradoxically resulted in more severe disease in a phase 3 clinical trial [78, 79], setting back progress on vaccine development for decades. Passive immunisation of high risk infants via monthly infusions of RSV-specific immunoglobulin (Palivizumab) has some efficacy, but is limited by cost and complexity [80]. Vaccine development is now focused on either maternal vaccination to protect infants in the first months of life (another form of 'passive immunisation') or active immunisation of infants and young children. Better understanding of RSV immunopathogenesis, and particularly delineation of the antigenic epitopes of the RSV F (fusion) protein responsible for entry into the host cell [81•], has led to a resurgence in vaccine development, with 16 vaccine candidates in active clinical trials (including two in Phase III studies) by December 2015 [82, 83]. Current vaccine candidates include RSV F nanoparticle vaccines, live-attenuated, particle-based, subunit-based and gene-based vectors [83].

Two live intranasal RSV vaccine candidates (MEDI-534 and -559) showed immunogenicity in a Phase 1 clinical trials in young children [84, 85]. Additionally, in a Phase II study in 330 non-pregnant women of childbearing age a 2-dose recombinant RSV fusion protein nanoparticle vaccine (RSV F vaccine) candidate was safe and immunogenic [86]. Post-hoc analysis demonstrated reduction in RSV infections in these women by 50 % over the following 112 days. Studies in pregnant women are currently in recruitment phase [87].

Human Papillomavirus (HPV)

Discovery of HPV's central role in the development of cervical and anogenital cancers, as well as approximately 60 % of head and neck cancers, prompted development of a vaccine against HPV; the second cancer preventing vaccine after hepatitis B. The first two HPV vaccines have been available for a decade and include oncogenic HPV genotypes 16 and 18, responsible for approximately 70 % of cervical cancer worldwide with the quadrivalent vaccine also including non-oncogenic types 6 and 11, responsible for external genital lesions (warts) [88, 89]. Both vaccines

have now shown efficacy in prevention of pre-cancerous lesions in males and females [90, 91•, 92, 93] and effectiveness in preventing high grade cervical lesions [94, 95] and genital warts [96, 97]. While continued progress is needed on vaccine implementation in low–middle income countries where cervical screening programs are not well established, a next generation 9-valent HPV vaccine has recently been licensed. It contains 5 additional oncogenic HPV types and is estimated to prevent approximately 90 % of all cervical cancers [91, 98]. The safety profile of this 9-valent vaccine appears similar to the quadrivalent, but incremental cost effectiveness may limit uptake.

Another major development in HPV vaccination has been evidence supporting the move from 3- to 2-dose schedules in young adolescent females and males. Those aged 9–15 years who receive two vaccine doses 6 months apart, have a comparable immune response to older persons (16–26 years) given three vaccines doses over the same time course. This schedule is now recommended by the WHO for HPV vaccination of girls in this age group [99], and will hopefully improve acceptability and uptake.

Meningococcus

Neisseria meningiditis, a common coloniser of the nasopharynx, can cause rapidly evolving meningitis or meningococcemia. There are 12 known serotypes; vaccines now exist against the five most common (A, C, Y, W-135, and B) disease causing strains. The first polysaccharide vaccines were effective in outbreak scenarios, but did not reduce nasal carriage or provide long-term immunity, and were ineffective in young children [100, 101]. Following the success of protein-polysaccharide conjugated *Hemophilius influenza type B* vaccines, conjugated meningococcal vaccines against serotype A or C alone, or A,C,Y,W-135 together were developed. These vaccines have demonstrated a major impact on serotype specific invasive meningococcal disease (particularly serotype C disease) when used in population-based programs [102, 103]. Country-specific recommendations are highly variable, depending on the local disease epidemiology, serotype prevalence and individual risk factors (e.g. underlying immunodeficiency). The recent introduction of a low-cost type A conjugate vaccine in the Sub-Saharan African 'meningitis belt' has had a major impact in that region, with a 94 % decrease in invasive meningococcal disease incidence following vaccination of 1.8 million people in a 10-day period in Chad [104].

Development of a type B vaccine proved highly challenging, because of capsular polysaccharide homology with polysilic acid structures present on human neural cells [105]. Two recent serogroup B vaccines used 'reverse vaccinology', where the sequenced genome was scanned for the most universally applicable antigen candidates, which were then manufactured using recombinant technology and tested in prototype vaccines. A four-antigen component vaccine (Bexsero®, GSK, previously Novartis) is now licensed for use in a four dose schedule in infants (or two doses in older children and adults), but population level programs have only been implemented in one community in Canada since May 2014 and country-wide in the UK since November 2015 [106, 107]. Vaccine cost effectiveness and the need to use prophylactic paracetamol to prevent post vaccination fever in infants have been factors influencing the decision not to publicly fund the vaccine in other countries where meningococcal B disease is prevalent, such as Australia [108]. The bivalent recombinant vaccine, rLP2086 (Trumenba®, Pfizer), has also been approved in the USA for adolescents [109].

Other Vaccines

Many vaccine candidates against common pediatric pathogens are in the developmental pipeline; including against Group B *Streptococcus* (GBS, *Streptococcus agalactia*), Group A *Streptococcus* (GAS, *Streptococcus pyogenes*), *S. aureus* and cytomegalovirus (CMV). Vaccines against ebola and zika virus infection have also been a focus of development after recent outbreaks.

Maternal vaccination against GBS was proposed approximately 40 years ago [110]. However, only 4 of 15 currently registered clinical trials have reported results. A multi-national phase II study reported safety and immunogenicity of a trivalent GBS vaccine administered to pregnant women; antibodies were measurable in mothers, and in infants for up to 91 days [13]. GAS-related disease has been described since the 1600s [111] with great variability in manifestations. Both disease and sequelae, including acute rheumatic fever, cause considerable morbidity and mortality; a 2005 study estimated that worldwide prevalence of serious GAS disease was at least 18.1 million, with 1.78 million new cases annually [112]. There are at least 18 current vaccine candidates, with three of these in Phase 1 or 2 trials [113]. *S. aureus* is a ubiquitous bacteria that causes a wide range of disease from skin and soft tissue infections to endocarditis to toxin-mediated illness. The increasing prevalence of methicillin-resistant *S. aureus* and diminishing antimicrobial treatment options underlines the importance of vaccine development. However, there are currently no pediatric clinical trials; most vaccine candidates have been evaluated in high risk adult patients but with limited success.

Cytomegalovirus is the most common congenital infection, occurring in 0.5–2 % of all live births but with

a variable phenotype. CMV has been the subject of attempts at vaccine development for decades, with limited success; current candidates include live-attenuated, subunit, and vectored vaccines. Phase I and II clinical trials are underway in women of childbearing age, and would especially target those with a toddler in the home [114].

The recent catastrophic ebola outbreak in 2014–2015 in Africa accelerated vaccine research and development. There are currently 45 clinical trials of vaccine candidates, with the two main candidates being rVSV-ZEBOV, a recombinant vesicular stomatitis vaccine, and ChAd3-EBO-Z, a chimpanzee adenovirus-3 vaccine. In 2015, rVSV-ZEBOV was evaluated in a cluster-randomised trial that employed 'ring' vaccination, where all near contacts of the index case are immunised. Interim results suggest both efficacy and safety [115•]. The ChAd3-EBO-Z vaccine recently completed phase 1b testing in adults and was found to be safe, thus supporting moving to phase 2/3 trials [116]. The emergence of zika virus in South and Central America as a new infectious cause of congenital neurologic disease, hallmarked by microcephaly, and as a trigger for Guillain-Barré syndrome resulted in the WHO declaring a global health emergency on 1 February 2016 [117]. Work on DNA-based, live-attenuated, and recombinant VSV vaccine candidates is proceeding, although gaps in knowledge around the disease itself need to be filled [118]. While this will take some time, it is possible that similar fast-tracking of clinical trials may occur as was the case with ebola vaccines.

Conclusions

Vaccine research and development is in a state of continual change and evolution. The number of infectious diseases for which regular vaccination is now offered has doubled within the past 25 years and will continue to grow. For the pediatrician, this can be readily observed by changes in clinical practice; cases of epiglottitis are now rare, and meningitis although still present, is much less common. As antimicrobial resistance continues to increase, and with new emerging infectious diseases, such as zika virus, vaccines are poised to provide an even greater impact on eliminating childhood disease.

Compliance with Ethics Guidelines

Disclosure Jeannette L Comeau, Jocelyn Chan, and Kristine K Macartney declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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