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Two centuries of immunisation in the United Kingdom (Part II)

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Introduction

In Part I of this series we reviewed the developments over the first 150 years of immunisation in the UK that led to the eradication of smallpox and the introduction of vaccines to control the important childhood diseases, smallpox, diphtheria, tetanus, pertussis and polio. In Part II of this historical review, we consider the formation of the Joint Committee on Vaccination and Immunisation (JCVI) in 1963 and the subsequent efforts to improve public health through immunisation, building on the success of the first immunisation programmes. As a result of technological advances in vaccine development and scientific advances in immunology and microbiology over the 56 years since then, and the formation of a comprehensive public health surveillance system for vaccine-preventable disease, the NHS immunisation programme now covers 18 serious diseases of childhood, with an astonishing impact on child health. Today, for children, there are only a small number of antigens which might still be added to a routine universal immunisation programme,and future developments are likely to focus on particular risk groups and the needs of an ageing population.

Formation of the Joint Committee on Vaccination and Immunisation (JCVI)

The 1950s polio epidemics spurred a coordinated national approach to immunisation, with the formation of the Joint Committee for Polio Vaccination. Literature from the late 1950s documents the call for a national immunisation advisory body to be established, with a broader remit than polio vaccination.[1] In 1963, the Joint Committee for Polio Vaccination was replaced with the Joint Committee on Vaccination and Immunisation (JCVI). The JCVI became a statutory body in 1977.

The JCVI currently exists as an Independent Departmental Expert Committee that advises the UK health departments on immunisation for prevention of infectious disease.[2] The JCVI provides independent, evidence-based advice and recommendations and works closely with the Departments of Health (DH)

that procures vaccines. Negotiating vaccine prices to be within the levels that are deemed cost effective is essential for their introduction. JCVI terms of reference (Appendix 5) considers uncertainty in vaccine evaluation and procurement.[2]

All historical minutes from JCVI meetings are available online:

- 1963–2012: http://webarchive.nationalarchives.gov.uk/20120907090205/http://www.dh.gov.uk/ab/JCVI/index.htm
- 2012–current: https://www.gov.uk/government/groups/joint-committee-on-vaccination-and-immunisation#minutes

The UK immunisation schedule continues to evolve under the expert guidance of the JCVI, with the last 25 years seeing an unprecedented number of programmes introduced or adapted based on its advice.

Measles, mumps and rubella

Measles vaccination was introduced in 1968 and given in the second year of life; previously there were around 400,000 notifications and 86 deaths annually (10 year average).[3, 4]

Rubella vaccination was introduced in 1970, for girls aged 11-14 years.[5] The policy for the vaccination of adult women evolved between 1972 and 1976 from vaccinating women of childbearing age in specified occupational risk groups who were susceptible to rubella to extending rubella vaccination to all serologically rubella negative women before their first pregnancy.[6—8]

Even with high rates of rubella vaccination, some women remained susceptible to infection during pregnancy and rubella continued to circulate in the population. A switch to universal vaccination using MMR required high uptake to be successful. Up until 1987, coverage of measles vaccine had been low in the UK. If rubella vaccine uptake was as low as measles

coverage, mathematical modelling predicted that rubella transmission would be supressed but not eliminated[9]. This would lead to a shift in age of infection to occur when susceptible women would be pregnant, increasing congenital rubella syndrome compared with the previous policy of unrestricted circulation of rubella amongst young children (when there was an adolescent girl vaccination programme). This latter was designed to protect susceptible adolescent females before they became pregnant.

By 1987, coverage of measles vaccine was sufficiently high to avoid these risks and in 1988, the measles vaccine was replaced with MMR vaccine, given at 13 months of age to boys and girls, in order to extend protection against all three diseases and eliminate congenital rubella syndrome.[10,11] Rubella vaccination for school girls continued until October 1995.[12,13]

The importance of post licensure surveillance was demonstrated in 1992, leading to the withdrawal of two brands of MMR vaccine. These contained the Urabe mumps strain and were associated with an increased risk of aseptic meningitis 15 to 35 days after vaccination.[14]

In 1994, despite good uptake of MMR (92%), modelling based on measles sero-epidemiology identified sufficient susceptibly among school aged individuals to predict that a measles epidemic was likely to occur.[15,16] A school based immunisation programme for children aged 5-16 years was put in place urgently. More than 6.5 million children received measles/rubella vaccine.[16]This campaign interrupted endemic transmission of measles.[16]A second dose of MMR was introduced in 1996 at pre-school age providing protection to the 10% of vaccinated persons who do not respond to a first measles dose of MMR.[17]

Like pertussis vaccine in the 1970s, the MMR programme faced major challenges from the mid 1990s due to concerns about vaccine safety. The subsequent media coverage, which questioned the safety of the vaccine and the policy for combined vaccination, shook confidence in the MMR vaccination programme amongst the public and some health care workers. Uptake fell to

80% or even lower in some districts by 2003.[18] National policy remained constant during this period with continued reassurance of MMR vaccine safety. This approach, combined with increasing evidence to counter the safety concerns, began to restore confidence in the programme. In 2018 coverage in England of one dose of MMR at five years was 95.3%.[19] Addressing vaccine confidence and supporting parental decision-making are key aspects of immunisation policies.[20,21]

In the 21st century large outbreaks of measles have occurred in part due to the pools of susceptible individuals in the population.[22,23,24] Focused MMR vaccine catch-up campaigns have been aimed to reduce the pool of susceptible persons in the population.[22,25] These catch up programmes, combined with increasing vaccine confidence, have allowed the UK to achieve WHO elimination status for rubella and measles.[26,27] However by the end of October 2018 over 800 cases of measles have been confirmed in England, with several outbreaks and a clear link to the measles outbreaks reported in 2017 and into 2018 throughout Europe.[28]

Haemophilus influenzae type b (Hib) vaccine

In 1992, Hib vaccination was introduced into the routine infant schedule for infants prior to the peak incidence of Hib disease, which occurred between 10 and 12 months of age.[29]

A decrease in the incidence of Hib disease was observed in vaccine eligible children, from 862 confirmed cases in 1991 to 33 in 1998.[30] This reduction was not sustained however with cases rising from 62 in 1999 to 236 in 2003.[30] This rise was attributed to declines in immunity in children vaccinated in the initial catch up, the lack of a booster dose at a year of age, and reduced immunity among a recent cohort who had been vaccinated in infancy with a acellular pertussis containing vaccine (DTaP/Hib) that produced lower Hib immunity than did the previously used whole cell pertussis containing vaccine.[31,32]

A Hib vaccine catch up programme was put in place in 2003 for children aged six month to four years that successfully reduced cases of Hib amongst all age groups.[33] In 2006 a booster dose of Hib was introduced for infants at 12 months of age (combined with Men C) and a catch up took place for the children who had never had Hib vaccine beyond infancy.[32-35] Confirmed cases of Hib in England fell to 12 in 2014.[30]

Hib vaccine was initially given as a separate injection alongside the other primary vaccinations. From 1996, Hib was combined with diphtheria, tetanus and pertussis as a “four–in-one” vaccine (DTP-Hib).[36] The four-in-one vaccine (DTP-Hib) was replaced in 2004 with five-in-one vaccine (DTaP/Hib/IPV), and replaced with a six-in-one vaccine (DTaP/Hib/IPV/HepB) in 2017.[37,38]

The evolution of the UK routine immunisation schedule

Few individuals working in immunisation today will recall a time without national leadership on immunisation and without published recommended schedules. This however was the reality for those practising during the 1940s and 50s. The inconsistencies in provision of immunisation programmes between Local Health Authorities (LHA) across England was further complicated by the range of vaccines available for diphtheria, pertussis and tetanus, including different formulations of diphtheria vaccine, single antigen vaccines, adjuvanted and plain tetanus toxoid vaccines and both combined double (DT) or triple vaccines (DTP).

Letters published in 1958 claimed that confusion surrounded immunisation practice and the letters’ authors called for clarity from the government.[39] Individual doctors, LHAs and groups such as the British Medical Association (BMA) lobbied the Ministry of Health (MoH) to establish a standardised approach to childhood immunisation. Guidance was requested on how best to provide early protection against whooping cough, whether the use of combined vaccines provoked paralytic polio and how to address concerns that

more injections led to lower uptake.[40] Clarification was also requested on protection against tetanus, with both vaccine and anti-serum (associated with serum sickness reactions) in use.[40]

In 1959 an international symposium on childhood immunisation was held in London. Sponsored by the Wellcome Foundation, it was organised by an independent steering committee under Brigadier Sir John Boyd.[39] The symposium aimed to resolve conflicting viewpoints on immunisation practice and to recommend an acceptable immunisation schedule. Five sessions were held that led to the expert committee at the symposium recommending two alternative childhood schedules, giving guidance on sterilization of needles and record keeping and the recommendation that a national immunisation advisory body should be established.[1] The schedules agreed at the symposium formed the basis of the first national routine infant and childhood schedules, published in 1961.[41]

First national routine childhood schedules published: 1961

The two schedules from the symposia were subject to further development by the MoH in consultation with the BMA, the Society of Medical Officers and LHA associations.[41,42] The final schedules received approval from the Central Health Services Council's Standing Medical Advisory Committee (SMAC - a non-departmental body) and the Joint Committee on Poliomyelitis Vaccine.[43]

In September 1961, the MoH published a memorandum 'Routine Immunisation Against Infectious Disease – summary of advice by the Standing Medical Advisory Committee'.[44] This detailed two alternative schedules of vaccination for diphtheria, pertussis, tetanus (DPT), polio, smallpox and BCG. The schedules were designated as P & Q (Table 1 and Table 2).[44]

Schedule P commenced from 1 month of age with infants receiving seven injections by 21 months of age; schedule Q commenced at six months of age

and infants received six injections by 21 months of age. A third schedule, ‘R’, was drafted but was excluded during the final approval stages.

Establishing effective immunisation programmes took time. In 1962 rates of vaccine uptake in England ranged from 11-93% across LHAs.[45]

Changes to the routine childhood immunisation schedule

The first significant revision of the routine childhood schedule occurred in August 1968 (Table 3), when schedules P and Q were replaced with a single schedule of vaccination.[46]The primary infant schedule was refined; three doses of DPT and polio vaccines were to be administered from three to six months of age with intervals of six to eight weeks between doses to balance an optimal immune response with early protection from disease. DTP boosters in the second year of life ceased, as did the diphtheria booster given to eight to 12 year olds. Five doses of polio and tetanus were scheduled; three primary infant doses with boosters at pre school age and adolescence.[46]

The primary infant schedule was further revised when an accelerated primary schedule was introduced in England and Wales in June 1990.[47]Primary immunisation against DPT and polio commenced at two months of age, the interval between each dose being reduced to one month. [47]

The rationale for this acceleration was to improve early protection against pertussis and to mitigate the mobility of young families that was a major reason for low vaccine coverage. Clinic attendance rates were also known to decline by the time a child reached seven to eight months and thus the move to an accelerated schedule would increase the proportion of infants completing three doses.[48] This also offered early protection against pertussis, most serious in young infants. Early completion was also considered important for protection against *Haemophilus influenzae* type b, as this vaccine was due to be introduced in 1992. The Joint Committee on Vaccination and Immunisation (JCVI) was aware that schedules starting at the age of two months in Canada and the USA were associated with lower rates

of febrile convulsions and it considered that it was likely that the revised schedule would be associated with fewer febrile convulsions.[49] A four-fold reduction in febrile convulsions attributed to DTwP was subsequently observed in UK studies.[50]

The eight, 12 and 16 week schedule was expected to be adequately immunogenic given the evidence that was available for the WHO recommended schedule of 6, 10 and 14 weeks.[51] UK studies confirmed that an accelerated schedule provided satisfactory immunogenicity and lower levels of reactogenicity than the previously recommended extended schedules.[52,53]

The rate of introductions and programme changes has increased substantially, as highlighted in Figure 1, a summary of immunisation programme introductions for infants and children across the 19th, 20th and 21st centuries.

During the late 20th and early 21st centuries, major landmarks have included the introduction of new vaccines against two further major bacterial pathogens of childhood (capsular group A, B, C, W and Y *Neisseria meningitidis* and 13 sero-types of *Streptococcus pneumoniae); rotavirus (*the major cause of diarrhoea in early childhood); a leading cause of cancer in women (human papillomavirus); universal influenza vaccination in children; hepatitis B; and to prevent shingles and pneumococcal disease in the elderly.[34,38,54-63] Innovative programmes of vaccination of pregnant women have improved health in mothers and newborns, protecting infants from pertussis and reducing the maternal and infant morbidity associated with influenza. [64-66]

The UK immunisation programme continues to evolve; with the HPV programme soon to be expanded to boys and the continued extension of the universal influenza programme for children.

The routine childhood immunisation schedule in 1968 offered protection against seven diseases and required seven patient contacts. In 2018 the routine childhood schedule offers protection against 17 diseases whilst still only taking nine contacts (see Table 3).[29,46,67]

Policy publications

UK immunisation policy and guidance today is published on-line in Immunisation Against Infectious Disease, known as the 'Green Book'.[67] The first 18 page edition, which included both active and passive immunisation, was published in November 1968.[68] Subsequent editions were published in 1972, 1982, 1984, 1988, 1990, 1992 and 1996.[69–75] The final print edition was published in 2006.[133]

Immunisation from 1992 to the present day

Web-based resources and published descriptions of introductions after 1992 are readily available online and the developments over the last few decades are summarised below

The further development of conjugate vaccines

The success of the Hib programme provided confidence in development of protein-polysaccharide conjugate vaccines, paving the way for the development of meningococcal and pneumococcal vaccines. The capsular group C meningococcal vaccine (MenC) was the next of the conjugate vaccines to be introduced in 1999 in the UK. The MenC vaccine's inclusion in the infant programme and targeted catch up greatly decreased the incidence of cases of invasive MenC meningococcal disease from 883 cases in 1998 to 37 in 2016/17.[77] The conjugate vaccine extended protection to the wider population by reducing nasopharyngeal carriage in the vaccinated groups, blocking on-going transmission and inducing herd immunity.

Broader coverage against meningococcal disease was achieved in 2015, in response to an outbreak of MenW disease. MenACWY vaccine was introduced for adolescents with a large catch-up programme, which included vaccination of adolescents in a school's programme and young adults moving to higher education.[78] MenB vaccine was introduced in the UK in 2015 to provide control against the main disease-causing capsular groups of *Neisseria meningitidis,* the UK being the first country to do so as part of a routine immunisation programme.[79] MenB vaccine includes an outer membrane vesicle derived from a New Zealand meningococcal outbreak strain, combined with 3 recombinant proteins.[80] The vaccine is offered to all infants in a three dose schedule at two, four and 12 months of age and early observations show high effectiveness with at least a 50% reduction in disease in infants.[81]

A pneumococcal 7 valent conjugate vaccine (PCV7) was introduced for children in clinical risk groups in 2004; it was introduced into the routine schedule in 2006 with a dramatic impact reducing pneumococcal disease and nasopharyngeal carriage of the vaccine serotypes.[34] In 2010, PCV7 was replaced with PCV13 given at two, four and 12 months of age.[57]

Vaccination of individuals in risk groups over two years of age with the 23-valent plain polysaccharide vaccine (PPV23) was introduced in 1992 with further extensions to adults over 80 years in 2003, those over 75 years in 2004, and to the current policy for those over 65 years in 2005. [54,82-84]

Extension of the influenza immunisation programme

In 1961 the influenza immunisation programme was directed at protection of individuals at increased risk of disease and later expanded to include adults aged 75 years and older in 1998 and 65 years and older from 2000.[15,85,86] The programme was extended in 2010 to include all pregnant women in view of the morbidity and mortality associated with influenza in late pregnancy, highlighted by cases in the 2009 H1N1 pandemic.[64] We have not further considered pandemic influenza vaccines here but this important topic and concerns about

adverse events arising from the vaccines used in the 2009 pandemic have been extensively discussed elsewhere.[87,88]

Universal influenza vaccination was introduced in 2013 for children, initially for those aged two and three years and the programme in England has been extended each year to increase the annually vaccinated cohort of children.[63,89-92] This universal approach using a live attenuated influenza vaccine (LAIV) is expected to both directly protect vaccinated children whilst indirectly protecting the wider population by reducing transmission of the virus. The limited effectiveness of influenza vaccines in some seasons (especially in the elderly), and suboptimal uptake remains a challenge for control of the disease. Further changes in the vaccines used for influenza control continue, as quadrivalent, adjuvanted, cell-culture derived, recombinant and high dose influenza vaccines become available.

Universal hepatitis B vaccination

The introduction of universal hepatitis B vaccination for infants in 2017 aligned the UK with global WHO advice. The JCVI had considered a universal hepatitis B vaccine programme for many years, but demonstrating cost effectiveness had been a challenge due to the low incidence and prevalence of hepatitis B in the UK. In October 2014 JCVI advised the Health Departments to switch the infant programme from a pentavalent vaccine to a hexavalent hepatitis B containing vaccine, subject to suitable costs.[93]

Future developments

In the next decade immunisation programmes might include prevention of neonatal Group B streptococcal infection and RSV bronchiolitis, the leading cause of hospitalisation in infancy. Important other programmes that could be realised are vaccines to prevent nosocomial infections and vaccines that help avoid antimicrobial resistance. With control of most of the severe infections of childhood, a major focus will likely switch to improving the health through the ageing population with development of new vaccines with improved

immunogenicity in older adults, such as a new adjuvanted shingles vaccine, which appears to overcome immunosenesence and provide protection even for those over 80 years of age.[94] Other vaccines may prevent hospital-acquired infections such as *C. difficile*, norovirus, various Gram negative infections or *S.aureus* associated wound infection.

Conclusion

Starting in Part I, we have presented a comprehensive timeline of immunisation in the UK from the first use of smallpox vaccine to the routine programmes of the present day.

Between 1986 and 2013 there were more new vaccine introductions and programme changes than at any time previously. These came about as a result of the collaboration between the Departments of Health and successively the Public Health Laboratory Service, the Health Protection Agency (HPA) and Public Health England and the respective agencies in the devolved nations responsible for immunisation delivery. The former was responsible for programme management, vaccine procurement, vaccine distribution, communication and policy; the latter was responsible for the surveillance of vaccine preventable diseases and research on new vaccines, vaccine safety, modelling and economic analysis.

The timeline provides insights into the immunisation history of the current UK population. The history of the immunisation programme highlights the importance of sensitive surveillance to respond to changing epidemiology and central coordination through our National Immunisation Technical Advisory Committee, the JCVI. The immunisation programme has improved the health of the UK population by employing strategies to cover an ever-increasing range of diseases and using technologies to combine vaccines and reduce visits, protecting the most vulnerable through the life course including pregnant women, young infants, those at special risk of disease, and the elderly.

Conflicts of interest

Sarah Lang, Sarah Loving, Noel McCarthy and Mary Ramsay: we declare that we have no conflicts of interest.

David Salisbury: reports personal fees from vaccine manufacturers, outside the submitted work.

Andrew Pollard is Chair of UK Dept. Health's Joint Committee on Vaccination & Immunisation & the EMA scientific advisory group, on vaccines and is a member of the WHO's SAGE.

Contributors

Sarah Lang: Conceived idea of immunisation timeline, completed literature searches, sources and analysed available literature, designed, drafted and revised paper (and the immunisation timeline).

Sarah Loving: Revised draft papers and advised on design of the paper. Approved final version.

Noel McCarthy: Initiated collaborative timeline project. Advised on design of paper, revised draft paper. Approved final version

Mary Ramsay: Drafted sections of the paper, critically revised draft papers. Approved final version

David Salisbury: Critically revised draft papers, advised on interpretation of data. Approved final version.

Andrew Pollard: Initiated collaborative timeline project. Advised on design of paper, drafted sections of paper, critically revised draft papers. Approved final version.

Panel: Search strategy and selection criteria

The search strategy initially focused on sourcing primary references for the immunisation timeline before being expanded to support the analysis of programme introductions and changes. A catalogue of immunisation related circulars was not available to facilitate these searches.

Available web based materials were searched on the Department of Health Website including Chief Medical Officer (CMO) letters on immunisation, Immunisation Against Infectious Diseases (2006) and current and historical JCVI minutes. All CMO letters from 1995 were available on-line.
To identify primary references from 1938 to 1994 Google Scholar and Medline were searched for “immunisation programmes” and “vaccination programmes”. Results were searched to identify published circulars and further searches made to source these.

Further searches were necessary to access pre-1993 circulars. All available Ministry of Health Circulars (1919–1968) held at the Radcliffe Camera Library (Oxford) were accessed and reviewed. Internal government documents were examined; all open Ministry of Health, DHSS & War Office files pertaining to immunisation or vaccination programmes from 1920s onwards held at the National Archives, Kew, were searched and reviewed, including minutes of meetings, notes and published circulars. Searches at the National Archives were conducted over three days. Where circulars were not accessible, data in other primary references were cross-referenced.

JH Parish’s publications, A History of Immunisation (1965) and Victory with Vaccines (1968) [95.96,] provided further historical insights and additional primary references were identified from these publications.

Limitation of historical methods. This work used written records accessible through tracing references from key resources and systematic extensive searches in both the National Archive at Kew and the University of Oxford library ensuring good coverage of DH and JCVI documents. We have not

used any oral history approaches to supplement this work nor attempted to access less structured archives such as those describing policy development and disease surveillance work undertaken to inform the decisions and decision making discussions summarised in the DH statements and JCVI minutes that we have reviewed but which are outside the scope of this work.

Table 1 Schedule P

Schedule P				
Age	**Visit**	**Vaccine**	**Injection**	**Interval**
1 to 6 months	1	Diphtheria, Pertussis, Tetanus 1	1	4-6 weeks
	2	Diphtheria, Pertussis, Tetanus 2	2	4-6 weeks
	3	Diphtheria, Pertussis, Tetanus 3	3	
7 to 10 months	4	Poliomyelitis 1	4	4 weeks
	5	Poliomyelitis 2	5	
15 to 18 months	6	Poliomyelitis 3	6	
18 to 21 months	7	Diphtheria, Pertussis, Tetanus 4	7	
Smallpox during the first 2 years but preferably at 4-5 months (see Note h)				
School entry		Poliomyelitis 4 Diphtheria and Tetanus		
8 to 12 years		Diphtheria and Tetanus Smallpox re-vaccination		
Over 12 years		B.C.G.		

Table 2 Schedule Q

Schedule Q				
Age	**Visit**	**Vaccine**	**Injection**	**Interval**
6 to 8 months	1	Poliomyelitis 1	1	4 weeks
	2	Poliomyelitis 2	2	
9 to 12 months	3	Diphtheria, Pertussis, Tetanus 1	3	4-6 weeks
	4	Diphtheria, Pertussis, Tetanus 2	4	
15 to 18 months	5	Poliomyelitis 3	5	
18 to 21 months	6	Diphtheria, Pertussis, Tetanus 3	6	
Smallpox during the first 2 years but preferably at 4-5 months (see Note f)				
School entry		Poliomyelitis 4 Diphtheria and Tetanus		
8 to 12 years		Diphtheria and Tetanus Smallpox re-vaccination		
Over 12 years		B.C.G.		

Table 3 Comparison of routine infant and child immunisation schedules in 1968, 1992 and 2018

Age	1968	1992	2018
2 months	From 3-6 months of age, 3 doses of DTP, OPV at 6-8 week intervals	DTwP, Hib, OPV	DTaP/IPV/Hib,HepB PCV, MenB, Rotavirus
3 months		DTwP, Hib, OPV	DTaP/IPV/Hib,HepB Rotavirus
4 months		DTwP, Hib, OPV	DTaP/IPV/Hib,HepB PCV, MenB
2nd year of life	Measles, Smallpox		
12 months			Hib/MenC, PCV, MMR, MenB
12-18 months		MMR	
2-9 years			Influenza
3 years 4 months			d/DTaP/IPV, MMR
4-5 years		DT + OPV	
5 years	DT + OPV or DT + IPV, Smallpox		
10-13/14 years	B.C.G	Rubella (girls), B.C.G.	
12-13 years			HPV (girls)
14 years			Td/IPV, MenACWY
15-18 years	Tetanus, Polio, Smallpox	Tetanus, OPV	

MMR = measles, mumps and rubella; Hib = *Haemophilus influenzae* type b ;Td = tetanus and diphtheria; DTwP = diphtheria, tetanus and whole cell pertussis; DTaP = diphtheria, tetanus and acellular pertussis; IPV = inactivated polio vaccine; OPV = oral polio vaccine; PCV= pneumococcal conjugate vaccine; HepB= hepatitis B vaccine; HPV = human papilloma virus; Men B = capsular group B meningococcal vaccine; MenC = capsular group C meningococcal vaccine; Men ACWY = capsular group ACWY meningococcal vaccine; HCW = healthcare workers

Figure 1 Routine vaccine introductions for infants, children and adolescents

Abbreviations for Figure 1 : MMR = measles, mumps and rubella; Hib = *Haemophilus influenzae* type b ; DTwP = diphtheria, tetanus and whole cell pertussis; DTaP = diphtheria, tetanus and acellular pertussis; IPV = inactivated polio vaccine; OPV = oral polio vaccine; PCV13 = 13-valent

pneumococcal conjugate vaccine; HPV = human papilloma virus; Men B = capsular group B meningococcal vaccine; MenC = capsular group C meningococcal vaccine; Men ACWY = capsular group ACWY meningococcal vaccine; BCG = Bacille Calmette Guérin

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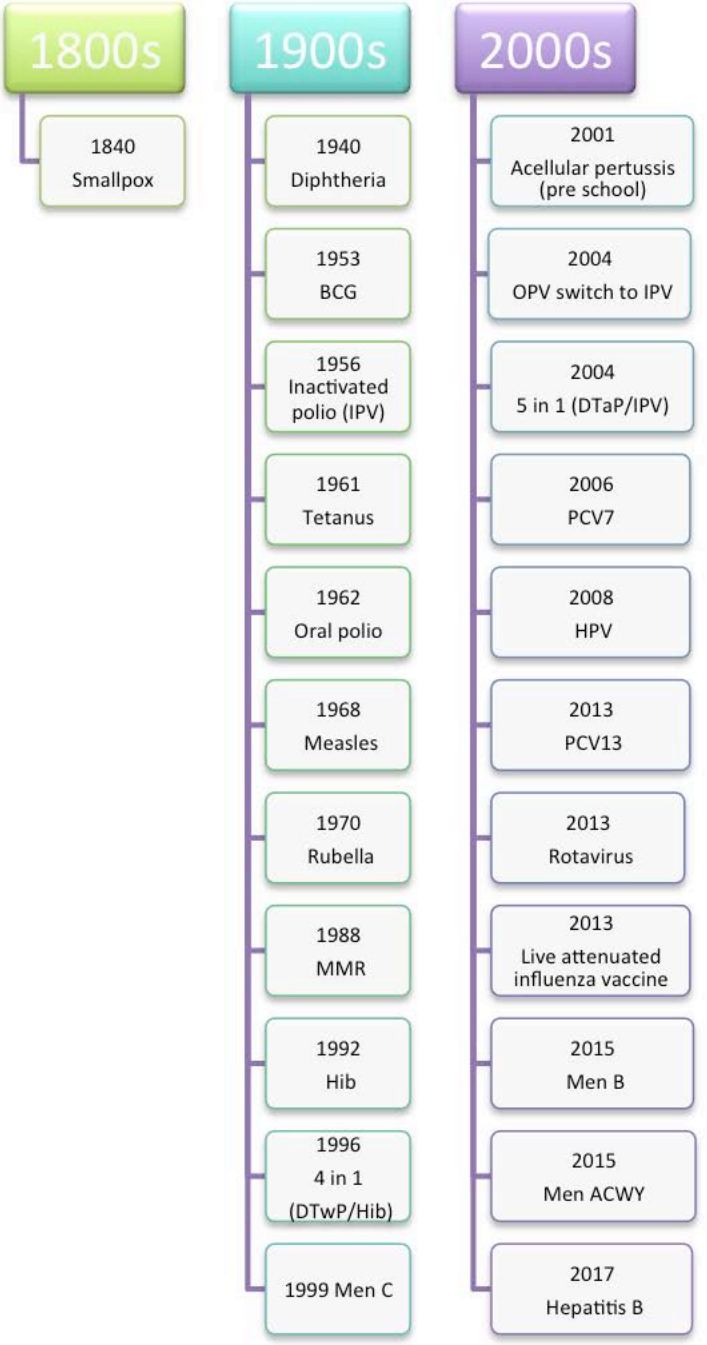
1800s
1840
Smallpox
1900s
1940
Diphtheria
1953
BCG
1956
Inactivated polio (IPV)
1961
Tetanus
1962
Oral polio
1968
Measles
1970
Rubella
1988
MMR
1992
Hib
1996
4 in 1 (DTwP/Hib)
1999 Men C
2000s
2001
Acellular pertussis (pre school)
2004
OPV switch to IPV
2004
5 in 1 (DTaP/IPV)
2006
PCV7
2008
HPV
2013
PCV13
2013
Rotavirus
2013
Live attenuated influenza vaccine
2015
Men B
2015
Men ACWY
2017
Hepatitis B