Review article

CLINICAL AND EXPERIMENTAL VACCINE RESEARCH

Milestones in history of adult vaccination in Korea

Clin Exp Vaccine Res 2012;1:9-17
http://dx.doi.org/10.7774/cevr.2012.1.1.9
pISSN 2287-3651 • eISSN 2287-366X

Myoung-don Oh[1], Jong-Koo Lee[2]
Departments of [1]Internal Medicine and [2]Family Medicine, Seoul National University College of Medicine, Seoul, Korea

Received: May 13, 2012
Revised: June 8, 2012
Accepted: June 15, 2012

Corresponding author: Jong-Koo Lee, MD
Department of Family Medicine, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 110-744, Korea
Tel: +82-2-2072-2215, Fax: +82-2-2072-0318
E-mail: docmohw@snu.ac.kr

No potential conflict of interest relevant to this article was reported.

Vaccination is one of the most effective and cost-benefit interventions that reduced the mortality. Major vaccine preventable diseases have decreased dramatically after the introduction of immunization program in Korea. In this article, we review milestones in history of immunization program, especially in adult vaccination.

Keywords: Vaccination, Immunization, Adult, Immunization programs

Introduction

The impact of vaccination on the health of people is hard to exaggerate. With exception of safe water, no other modality has had such an enormous effect on the mortality reduction. Table 1 shows that major vaccine preventable diseases have decreased dramatically after the introduction of immunization program in Korea. Previous studies reviewed history of national immunization program [1,2] and immunization policies in Republic of Korea [1,3]. In this article, we update milestones in history of immunization (Table 2), and review adult vaccination in Korea.

Brief History of Adult Vaccination in Korea

Smallpox

The first vaccination in Korea was against smallpox. In 1790, Jaega Park brought a book on smallpox vaccination from China. In 1780, he was successful in inoculation of "smallpox vaccine," which was made of crusts from smallpox patients. In 1835, Yakyong Jung inoculated vaccines taken from lesions of cowpox. But he kept it secret and did not practice widely [4]. It was Seokyong Jee who introduced smallpox vaccination and opened a vaccine production site in Seoul in 1880. It was 1882 when provincial governments began to establish offices for smallpox vaccination campaign, which was the first national immunization program in Korea [5].

In 1912, the government established Department of Hygiene, and Division of Bacteriology was responsible for the production of smallpox vaccine. In 1954, Contagious Disease Prevention Act was legislated, and the Law designated 8 communicable diseases to be included into the National Immunization Program. With the help of smallpox vaccination campaign, the number of smallpox cases had decreased dramatically year by year, and the last case was reported in 1961. Finally, smallpox vaccination

Table 1. Impact of immunization on the incidence of major vaccine preventable diseases in Korea

Vaccine preventable disease	Peak cases (year)	Cases in 2010	Reduction (%)
Diphtheria	2,534 (1961)	0	100.0
Pertussis	20,157 (1956)	27	99.9
Tetanus	16 (1983)	14	12.5
Measles[a]	30,792 (1962)	114	99.6
Mumps	7,269 (1961)	6,094	16.2
Rubella[b]	128 (2001)	43	66.4
Polio, paralytic	2,486 (1956)	0	100.0
Smallpox	43,213 (1951)	0	100.0

[a]In 2001, 32,647 cases of measles reported because of a measles epidemic between January 2000 and July 2001.
[b]Rubella became reportable disease since 2000.

was discontinued in 1979, one year before the declaration of smallpox eradication by World Health Organization.

As number of susceptible persons accumulated after the discontinuation of smallpox vaccination, some experts raised concern that smallpox virus might be used as a potential biological weapon. This concern was heightened in 2001 when the event of anthrax bioterrorism occurred soon after the 911 attack of World Trade Center in the USA. To be better prepared for bioterrorism, the government stockpiled a first-generation vaccine (Lancy-Vaxina) purchased from a Swiss pharmaceutical company. We conducted a single-blind, randomized trial of 2 dilutions (1:1 or 1:10) of Lancy-Vaxina vaccine [6]. The results of the study showed that a 1:10 dilution of the vaccine can be successfully given to the vaccine naïve

Table 2. Milestones in history of immunization in Korea

Year	Target diseases	Events
1882	Smallpox	Office for smallpox vaccination established in Jeolla Province
1895	Smallpox	Regulation on smallpox vaccination introduced
1912	Smallpox, cholera	Department of Hygiene established and vaccines produced by Division of Bacteriology
1946	Cholera	18.9 million doses of cholera vaccine produced by Joseon Research Institute for Communicable Disease Prevention
1948	Tuberculosis	BCG produced
1954	Smallpox, diphtheria, pertussis, typhoid fever, paratyphoid fever, typhus fever, tuberculosis	Contagious Disease Prevention Act legislated; The eight communicable diseases were included by the law into National Immunization Program
1958	Diphtheria, pertussis, tetanus	DPT produced domestically and used
1958	Polio	Inactivated polio vaccine (IPV) introduced; IPV was inoculated to children with fee for service
1961	Polio	IPV discontinued; Oral, live attenuated polio vaccine introduced
1963	Tuberculosis	BCG vaccination after tuberculin skin test for preschool and school children
1965	Measles	Live attenuated measles vaccine introduced
1971	Japanese B encephalitis	Japanese B encephalitis vaccine introduced, and some people were vaccinated
1976	Typhus fever, paratyphoid	Immunization against typhus fever and paratyphoid excluded from National Immunization Program
1976	Cholera, tetanus	Immunization against cholera and tetanus included into National Immunization Program
1979	Smallpox	Vaccination discontinued since January 1979
1980	Measles, mumps, rubella	MMR vaccines introduced
1983	Cholera, typhoid	Excluded from National Immunization Program; Continued as supplementary immunization activity
1983	Measles, polio	Immunization against measles and polio included into National Immunization Program
1985	Japanese B encephalitis	Immunization against Japanese B encephalitis included into supplementary immunization activity; children of 3 to 15 years of age immunized annually
1985	Hepatitis B	Immunization against hepatitis B virus introduced as a supplementary immunization activity
1988	Leptospirosis	Immunization against leptospirosis introduced as a supplementary immunization activity
1989	Diphtheria, tetanus, pertussis	DPT replaced with acellular pertussis vaccine (DTaP)
1990	Cholera	Immunization discontinued
1992	Hemorrhagic fever with renal syndrome	Immunization introduced as a supplementary immunization activity
1994	Rubella	Rubella vaccination to high school girls of 15 years of age (until year 2000)
1995	Japanese B encephalitis	Immunization schedule changed from every year to every 2 years

(Continued to the next page)

 http://dx.doi.org/10.7774/cevr.2012.1.1.9

Table 2. *(Continued from the previous page)* Milestones in history of immunization in Korea

Year	Target diseases	Events
1995	Hepatitis B	Immunization against hepatitis B removed from supplementary immunization activity, and included into National Immunization Program
1995	Typhoid fever	Inactivated vaccine replaced with purified Vi polysaccharide vaccine
1997	Measles, mumps, rubella	Second dose recommended at the age of 4-6 years
1997	Influenza	Immunization introduced as a supplementary immunization activity
1997	Leptospirosis	Excluded from supplementary immunization activity
1997	Hemorrhagic fever with renal syndrome	Immunization recommended only to high risk group
1997	Typhoid fever	Immunization recommended only to high risk group
2000	Mumps, rubella	Immunization included into National Immunization Program
2000	Measles, mumps, rubella	MMR vaccines containing Hoshino and Urabe strains were discontinued
2001	Polio	Inactivated polio vaccine introduced
2001	Measles	Measles immunization catch-up campaign with MR vaccine launched as a part of the "5-Year Measles Elimination Program"
2002	Measles, mumps, rubella	MMR vaccines containing Rubini strain discontinued according to the WHO recommendation
2002	Japanese B encephalitis	Live attenuated vaccine introduced
2004	Tetanus, diphtheria	Td vaccine introduced
2004	Polio	OPV replaced with IPV
2005	Chickenpox	Immunization included into National Immunization Program
2005	Tetanus, diphtheria	Td immunization included into National Immunization Program
2006	Measles	Measles elimination declared
2008	Hepatitis B	WHO granted certification of control of vertical transmission of hepatitis B virus
2009	Influenza	Egg-based vaccine against 2009 H1N1 influenza produced by a domestic pharmaceutical company; This vaccine was licensed by Korea FDA and used for immunization campaign for pandemic influenza 2009
2012	Tuberculosis, hepatitis B, diphtheria, tetanus, pertussis, polio, measles, mumps, rubella, varicella, Japanese B encephalitis	Immunization cost for the 10 vaccines (BCG [intradermal], HepB, DTaP, Td, Tdap, IPV, DTaP-IPV, MMR, Var, JEV) reimbursed when the vaccines were given according to the National Immunization Program (January 1, 2012)
2012	Meningococcal infection	Mandatory vaccination against meningococcal infection introduced for military recruits

BCG, Bacillus Calmette-Guérin; DPT, diphtheria, pertussis, tetanus; MMR, measles-mumps-rubella; MR, measles-rubella; WHO, World Health Organization; Td, tetanus and diphtheria toxoid; OPV, oral polio vaccine; IPV, inactivated polio vaccine; FDA, Food and Drug Administration; HepB, hepatitis B; DTaP, diphtheria, tetanus, acellular pertussis; Tdap, tetanus, reduced diphtheria, acellular pertussis; JEV, Japanese encephalitis virus.
Source: adapted and modified from Korea Centers for Disease Control and Prevention [3].

and previously vaccinated persons.

To avoid unwanted immune responses to calf-derived material and to prevent bovine prion transmission, a cell-culture derived smallpox vaccine (CJ-50300) was developed by a Korean pharmaceutical company. A randomized, double-blind, controlled clinical trial demonstrated that CJ-50300 effectively evoked a cutaneous take reaction, and was not associated with any serious adverse reaction [7]. The vaccine has been licensed by Korea Food and Drug Administration in 2008.

Hemorrhagic fever with renal syndrome

The etiologic agent of hemorrhagic fever with renal syndrome (HFRS) was identified by Lee et al. [8] in 1978, and the etiologic agent, Hantaan virus, was successfully propagated in a cell line of human origin in 1983 [9]. In 1988, Lee and Ahn [10] reported that an inactivated Hantaan virus vaccine was developed. The seed virus for the vaccine, ROK84-105-1, was isolated from blood of a HFRS patient directly in Vero E6 cell culture. The virus was passaged 3 times in the brain of ICR suckling mice to increase virus yield. Then, pool of 5% suspension of suckling mice brain in phosphate buffered saline was inactivated with 0.05% formalin. This inactivated vaccine, named Hantavax, was the world's first HFRS vaccine. It got approved in 1990 under the condition of further clinical trials.

A field trial of Hantavax was conducted in HFRS endemic areas in Yugoslavia from 1996 to 1998 [11]. Three thousand and nine hundred people living in the endemic areas were randomized into placebo or vaccination group, and followed for 2 years to monitor HFRS development. The researchers reported that they found no HFRS case among 1,900 vaccinees, whereas they confirmed 20 HFRS cases among 2,000

non-vaccinated controls. Any remarkable local or systemic side effects were not reported in the study.

Park et al. [12] conducted a case-control study to evaluate the protective effectiveness of Hantavax. This study enrolled 57 soldiers with HFRS as cases, and matched controls were selected among the other patients at the same military hospital where the case patient had been admitted. They suggested that effectiveness increased as the number of doses increased: 25% for one dose, 46% for two doses, and 75% for three doses. However, all 95% confidence intervals overlapped zero; therefore, the findings could be due to mere chance [12].

The immunological response to Hantavax was evaluated in human volunteers in several studies [13-19]. Table 3 summarizes the results of the clinical trials. Because the seroconversion rate is low with single dose of Hantavax, a two dose series of primary vaccination is recommended. As shown in Table 3, seroconversion rates were greater than 90% after 2 doses of primary vaccination. In contrast, Sohn et al. [17] reported that neutralizing antibody responses were suboptimal, and they suggested the vaccine should be improved to produce a higher protective immune response. Some authors suggested that booster vaccination is necessary at 1 year after the primary vaccination [16,19]. However, it is not known which immunological parameters are correlated with the protective immunity against HFRS. Well-designed field trials are warranted to resolve the issues surrounding the efficacy and persistency of protective immunity conferred by Hantavax.

Leptospirosis

In early 1980s, outbreaks of hemorrhagic pneumonia occurred among farmers working in rice paddy. The etiology of the outbreaks was identified as leptospirosis. Most of the isolates were *Leptospira* icterohemorrhagiae serovar lai. *L.* icterohaemorrhagiae strain HY-10 [20], isolated from a patient in Yeoju, Gyeonggi Province, was used to develop an inactivated vaccine. Korea National Institute of Health conducted studies on immunogenicity and safety of the candidate vaccine between 1985 and 1987. The seroconversion rate was 80.8%, and serious side effect was not reported. The protective efficacy of the vaccine was not evaluated [21].

The government introduced immunization against leptospiroris as a supplementary immunization activity in 1988. A 2 dose series of vaccination, with 7-10 days interval, was recommended during April and May, before the rainy season in Korea. Domestic pharmaceutical companies (Green

Table 3. Summary of immunological response to Hantavax in clinical trials reported in the literature

Author (year)	Time after vaccination	Seroconversion rate			
		IFA	ELISA IgG	HDPA	PRNT
Lee et al. [19] (1992)	1 mo after 1st dose	66/74 (89.2)			
	1 mo after 2nd dose	72/74 (97.3)			
	12 mo after 2nd dose	27/74 (36.5)			
	1 mo after 3rd dose	73/74 (98.6)			
Chu et al. [14] (1998)	1 mo after 2nd dose	16/17 (94.1)		16/17 (94.1)	13/17 (76.5)
	1 yr after 2nd dose	25/40 (62.5)		18/40 (45.0)	9/40 (22.5)
	1 mo after 3rd dose	8/8 (100)			8/8 (100)
	20 mo after 3rd dose	11/12 (91.7)			9/12 (75.0)
	3 mo after 4th dose	7/7 (100)			6/7 (85.7)
Cho and Howard [15] (1999)	30 day after 1st dose	51/64 (79.7)	40/64 (62)		3/23 (13)
	30 day after 2nd dose	62/64 (96.9)	62/64 (96.9)		24/32 (75)
	1 yr after 2nd dose	9/24 (37.5)	10/23 (43.5)		2/14 (14.2)
	30 day after 3rd dose	15/16 (93.8)	16/16 (100)		7/14 (50)
Woo et al. [16] (2000)	1 yr after 2nd dose	11/21 (52.3)	20/21 (95.2)	10/21 (47.6)	6/21 (28.6)
	1 mo after 3rd dose	13/13 (100)	13/13 (100)	13/13 (100)	13/13 (100)
	1 yr after 3rd dose	11/13 (84.6)	12/13 (92.3)	11/13 (84.6)	9/13 (69.2)
Sohn et al. [17] (2001)	4 wk after 1st dose		14/30 (46.7)	10/30 (33.3)	2/30 (6.7)
	4 wk after 2nd dose		23/30 (76.7)	23/30 (76.7)	10/30 (33.3)

Values are presented as number (%).
IFA, immunofluorescent assay; ELISA, enzyme-linked immunosorbant assay; HDPA, high density particle agglutination; PRNT, plaque reduction neutralizing antibody test.
Source: adapted from Shon JW, Kim HY. Hantaan virus. In: Korean Society of Infectious Diseases, editor. Vaccination for adult. 2nd ed. Seoul: MIP; 2012.

 http://dx.doi.org/10.7774/cevr.2012.1.1.9

Cross, Boryong, Hankook Vaccine, CJ Pharmaceutical, and SK Chemical) produced inactivated vaccines. The vaccines were inoculated to 200,106 persons in 1988, 145,276 persons in 1989, 283,616 persons in 1990, 541,300 persons in 1991, 825,104 persons in 1992, 780,579 persons in 1993, and 490,608 persons in 1994.

The immunization activity was discontinued in late 1997, because of the following reasons: 1) booster vaccination was required every 6 months as the vaccine-induced antibody waned rapidly; 2) serotypes of leptospira might vary according to the geographic areas, previous vaccination, and animal reservoirs; 3) alternative preventive measures, such as chemoprophyaxis, early detection and treatment, education for exposure reduction, were more cost-effective than vaccination; 4) the incidence of leptospirosis decreased dramatically in 1990s.

Influenza

Seasonal influenza

Vaccination against seasonal influenza was introduced as a supplementary immunization activity in 1997. Persons who had high-risk conditions for complication of influenza were recommended annual influenza vaccination. The high-risk groups included persons of 6 months of age or older who had 1) lung or heart diseases; 2) chronic illness residing nursing facilities; 3) chronic illness requiring regular clinic visit, such as metabolic disease (diabetes mellitus), renal disease, chronic liver disease, malignancy, immunocompromised conditions, hemoglobinopathy, and children of 6 months to 18 years of age taking aspirin; 4) persons of 65 years of age and older; 5) healthcare workers and family member of patients. The high-risk groups were expanded to include pregnant women and persons of 50 to 64 years old in 2003; children 6-23 months old, farmers working at chicken, pig, and duck farm and primary responders to avian influenza in 2004 [22]. In 2010, after the outbreak of 2009 pandemic influenza, children of 24 to 59 months of age and persons with neuromuscular diseases were also included. Among high-risk groups, vaccine coverage rates in 2006 were estimated 56% in children and 64% in adults.

2009 Pandemic influenza A (H1N1)

The first case of 2009 pandemic influenza A (H1N1) was identified on 1 May 2009 in Republic of Korea. The pandemic influenza peaked in late October (44th week) 2009. A total of 763,759 cases were reported and 270 patients died of the pandemic influenza [23].

An inactivated, split vaccine against 2009 influenza A (H1N1), GreenFlu S, was developed by a domestic pharmaceutical company (Green Cross Cooperation). The vaccine was produced in embryonated chicken eggs. A prospective, open-label, multicenter clinical trial was conductive to evaluate safety and immunogenicity of the vaccine [24]. The study enrolled 251 healthy Korean children from 6 months to <18 years of age. The vaccine contained 7.5 μg (for children <3 years of age) or 15.0 μg (children 3 to <18 years of age) of hemagglutinin antigen per dose. Twenty one day after 2-dose series of vaccination, hemagglutinin inhibition titers of 1:40

Table 4. Vaccination coverage rate for pandemic influenza A (H1N1) 2009 in Korea

		Target population	No. of persons vaccinated	Coverage rate (%)
Priority groups		22,901,461	12,456,962	54.4
	Healthcare workers	800,000	615,341	76.9
	Elementary-high school students	7,471,857	6,173,321	82.6
	Children aged 6 mo to 6 yr	3,017,313	1,747,737	57.9
	Pregnant women	434,529	88,858	20.9
	Caregivers for infants aged <6 mo	600,000	38,113	6.4
	Nursing home residents	200,000	127,912	64.0
	Military personnel	750,000	623,771	83.2
	Persons with chronic medical conditions	3,912,132	972,374	24.9
	Elderly persons aged 65 yr or older	5,267,708	2,001,794	38.0
	Others	457,922	67,741	14.8
Persons not belong to the priority groups		26,871,664	539,660	2.0
Unknown		-	361	-
Total		49,773,145	12,996,983	26.1

Source: adapted from Lee et al. [26].

Vaccine \ Age group	19-29	30-39	40-49	50-64	≥65
Tetanus-diphtheria-pertussis	1-time dose of Tdap for Td booster; then boost with Td every 10 yr (strength I)		First dose with Tdap, Td at 1-, and 6-mo; then Td booster every 10 yr (strength I) (Tdap only for age of 65 or less)		
Influenza	1 dose annually (strength III)			1 dose annually (strength I)	
Hepatitis A	2 doses (at 0 and 6 mo) (strength II)	For seronegative, 2 doses (at 0 and 6 mo) (strength II)		For high-risk group[a], seronegative, 2 doses (at 0 and 6 mo) (strength II)	
Hepatitis B	When 3 doses of immunization uncertain, check HBsAb and vaccinate seronegatives (strength III)			For high-risk group[b] with uncertain immunization history, check HBsAb and vaccinate seronegative (strength III)	
Measles-mumps-rubella	For high-risk group[c], at least 1 dose; check rubella IgG for women who is planning pregnancy (strength III)				
Varicella	For high-risk group[d], check serology; 2 doses for seronegatives (strength II)				
Human papillomavirus	Female (strength II)				
Meningococcal	For high-risk group[e], 1 or 2 doses				
Pneumococcal	For high-risk group[f], 1 dose (strength I)				1 dose (strength I)
Zoster				1 dose (strength U)	1 dose (strength III)

Strength of recommendation

I. Very strongly recommended; Immunization may reduce mortality, have cost-benefit effect. Most countries recommend the vaccination.
II. Strongly recommended; Immunization may reduce mortality, Cost-benefit effect in Korea is unknown, Most of developed countries recommend the vaccination.
III. Recommended; Immunization may reduce morbidity rather than mortality. Cost-benefit effect in Korea is unknown.
U. Recommendation reserved; Limited evidence for recommendation.

Color code	For all persons in this category who meet the age requirement	Recommended if some other risk factor is present	No recommendation

Fig. 1. Adult immunization schedule 2012, recommended by the Korean Society of Infectious Diseases.

Td, tetanus and diphtheria toxoid; Tdap, tetanus, reduced diphtheria, acellular pertussis; HBsAb, hepatitis B surface antibody; IgG, immunoglobulin G.

[a] Hepatitis A (high-risk group): persons with chronic liver disease; persons working at child-care facilities; medical personnel and laboratory workers with potential risk of exposure to hepatitis A virus; food handlers working at restaurants; persons traveling to or working in countries where hepatitis A is endemic; persons who receive blood products frequently; men sex with men; IV drug users; persons who contact with acute hepatitis A patients within 2 wk.

[b] Hepatitis B (high-risk group): men sex with men; sexually active persons with more than one partner; human immunodeficiency virus (HIV) patients; IV drug users; household contacts and sexual partners of persons with hepatitis B virus (HBV) carrier; patients with chronic renal failure; patients with chronic liver disease; workers who are frequently exposed to HBV; clients and staff members of institutions for persons with developmental disabilities.

[c] Measles-mumps-rubella (vaccination recommended for high-risk group): Although serological test (especially, for measles) can be done for laboratory evidence of immunity, vaccination without serologic test would be cost saving. High-risk group: healthcare personnel (serological test required, 2 doses); persons traveling to developing countries; family member who take care of immunocompromised patient; students who dwell in dormitory.

[d] Varicella: vaccination recommended for high-risk group if serological test reveal no evidence of immunity. High-risk group: healthcare worker; family contacts of immunocompromised patients; teachers and child-care employees; students; military personnel; residents of correctional institutions; non-pregnant women with expecting pregnancy; adolescent and adult living in households with children; international travelers.

[e] Meningococcal (high-risk group): persons with anatomical or functional asplenia; persons with complement component deficiencies; military personnel; (especially for recruits); laboratory workers exposed to meningococcus; persons who travel or live in an endemic area, particularly if their contact with local populations will be prolonged; college students living in dormitories. 2 dose series is recommended for adults with anatomical or functional asplenia, complement component deficiency, HIV infection; 2 doses should be administered at 0 and 2 mo. Revaccination with meningococcal conjugate vaccine every 5 yr for adults who remain at increased risk for infection.

[f] Pneumococcal (high-risk group): chronic lung disease (including asthma); chronic cardiovascular disease; diabetes; chronic liver disease; chronic renal failure; nephrotic syndrome; functional or anatomical asplenia; immunocompromised patients (congenital immunodeficiency, HIV infection; leukemia, lymphoma, Hodgkin's disease, multiple myeloma, other malignancy; solid organ transplantation), (vaccinate with 3 or 4 doses of protein conjugate vaccine for hematopoietic stem cell transplants); prolonged use of high-dose corticosteroids or immunosuppressive agents; cochlear implant. One-time revaccination is recommended for persons aged 65 years or older if they were vaccinated 5 or more years previously and they were less than 65 years of age at the time of primary vaccination. One-time revaccination after 5 years is recommended for patients with chronic renal failure, nephrotic syndrome, functional or anatomical asplenia, immunocompromised conditions, prolonged use of immunosuppressive agents.

Source: adapted from Korean Society of Infectious Diseases. Vaccination for adult. 2nd ed. Seoul: MIP; 2012.

 http://dx.doi.org/10.7774/cevr.2012.1.1.9

Table 5. List of vaccines licensed by Korea Food and Drug Administration, as of April, 2012

	Date of license
Vaccines for virus diseases	
Hemorrhagic fever with renal syndrome vaccine	January 18, 2005
Hepatitis A vaccine	April 10, 1998
Hepatitis B, recombinant vaccine	April 24, 1995
Human papillomavirus, recombinant	June 27, 2007
Influenza, HA	July 18, 1990
Influenza, live vaccine, cold adapted	October 8, 2002
Influenza, live vaccine, nasal spray	July 22, 2009
Influenza, split, 2009 pandemic	October 21, 2009
Influenza, split, adjuvant, 2009 pandemic	January 5, 2010
Influenza, split, adjuvant, prepandemic (H5N1)	January 5, 2010
Influenza, surface ag	May 27, 1992
Influenza, surface ag, MF59C.1 adjuvant	May 26, 2009
Inlfuenza, split	January 28, 1994
Japanese B encephalitis, inactivated vaccine	October 29, 1970
Japanese B encephalitis, live vaccine	May 16, 2002
MMR	July 26, 1982
Polio, inactivated vaccine	April 8, 2001
Polio, oral vaccine	September 18, 1980
Rota virus, oral, live attenuated	June 22, 2007
Rubella	March 12, 1982
Smallpox, cell culture, liophilized	December 31, 2008
Varicella, attenuated vaccine	September 13, 1993
Yellow fever, live attenuated	June 30, 2011
Zoster vaccine	April 17, 2009
Vaccines for bacterial diseases	
Cholera	March 31, 1989
Diphtheria and tetanus (adult Td)	October 21, 2003
Diphtheria and tetanus (DT)	April 24, 1974
Diphtheria, tetanus, acellular pertussis (adult DTaP)	June 22, 2009
Diphtheria, tetanus, acellular pertussis (DTaP)	February 24, 1983
Hemophilus influenzae type B	February 26, 1998
Leptospirosis	April 4, 1988
Pneumococcal, CRM197 protein conjugated	June 26, 2002
Pneumococcal, polysaccharide-23	December 15, 2000
Tuberculosis, BCG intradermal	September 29, 2003
Tuberculosis, BCG percutaneous	November 29, 2006
Typhoid, oral	January 10, 1992
Typhoid, Vi	December 19, 1990
Combined vaccines	
DTwP-HepB	March 10, 2006
DTwP-Hib-HepB	March 27, 2006
DTaP-HepB	April 28, 2008
DTaP-IPV	August 31, 2009
Hib-HepB	August 19, 1999

HA, hematogglutinin; MMR, measles-mumps-rubella; BCG, Bacillus Calmette-Guérin; DTwP, diphtheria, tetanus, and whole-cell pertussis; HepB, hepatitis B; Hib, haemophilus influenzae type b; IPV, inactivated polio vaccine.
Source: from website for Korea Food and Drug Administration. Accessed on 5 July 2012 (Visit http://www.kfda.go.kr/index.kfda?searchkey=title:contents&mid=70&searchword=백신&cd=&pageNo=1&seq=12836&cmd=v).

or greater was observed in 55.9% of children 6 months to <3 years of age, 69.5% of children 3 years to <9 years of age, and 90.5% of subjects 9 years to <18 years of age. No serious adverse reaction was observed [24]. The vaccine was licensed on 21 October 2009 by Korea Food and Drug Administration. MF59-adjuvanted vaccine, GreenFlu S Plus, was also developed and evaluated in a clinical trial [25].

Korea Centers for Disease Control and Prevention (KCDC) launched a vaccination campaign against 2009 pandemic influenza on 27 October 2009. The government purchased 25 million doses of GreenFlu S and GreenFlu S Plus to cover high risk groups. A total of 12,996,983 persons (26% of population) were vaccinated. Of those vaccinated, 95.8% were from high priority groups that included health care workers, students attending elementary, junior and high schools, children 6 months to 6 years of age, pregnant women, military personnel, persons living in welfare facilities, persons with chronic medical conditions, and elderly people of 65 years or older. Of 22,901,461 persons of the high priority groups, 54.4% were vaccinated [26]. Table 4 summarizes the coverage rate of vaccination against 2009 pandemic influenza.

Adult Vaccination Program in Korea

In 2006, KCDC recommended several vaccinations for adults [3]. The recommended vaccinations included vaccinations against influenza for persons of 50 years or older; pneumococcal infection for 65 years or older; hepatitis B, measles-mumps-rubella (MMR), tetanus and diphtheria toxoid (Td) and varicella for all adults who are susceptible to the infections. It also recommended hepatitis B virus, influenza, MMR and varicella vaccinations for healthcare workers. In 2007, Korean Society of Infectious Diseases (KSID) published a textbook on adult immunization, titled 'Vaccination for Adult.' In 2012, KSID published second edition of the book, and revised its previous recommendation on adult immunization. Fig. 1 shows the recommended adult immunization schedule by KSID. List of vaccines licensed by Korea Food and Drug Administration is shown in Table 5.

Adult immunization has become increasingly important for the following reasons: incomplete childhood immunization, waning immunity over time (e.g., diphtheria-pertussis-tetanus), changing epidemiology of some infectious diseases (e.g., hepatitis A virus), increase in overseas travel to endemic areas (e.g., meningococcal meningitis and yellow fever), introduction of newly developed vaccines (e.g., human pa-

pillomavirus and zoster vaccines), and increase in elderly persons and immunocompromised patients [27]. Although immunization has become a routine pediatric practice, it has not been as well integrated into routine clinic visits for adults. Besides influenza vaccine, most adult vaccines are severely under-utilized in Republic of Korea. A recent study reported the pneumococcal vaccination rate was less than 1% among elderly 65 years or older [28]. To raise coverage rate, multiple efforts including burden of disease study for vaccine preventable diseases, cost-benefit analysis for vaccination, education of physicians, and advertisement for adult vaccination are needed.

References

1. Lee JK, Choi WS. Immunization policy in Korea. Infect Chemother 2008;40:14-23.
2. Korea Centers for Disease Control and Prevention. National immunization program. Mon Newsl Natl Immun Program 2007;5:117-8.
3. Korea Centers for Disease Control and Prevention, editor. Epidemiology and prevention of vaccine-preventable diseases. Seoul: Korea Centers for Disease Control and Prevention; 2011.
4. Chun CH. Overview of acute communicable diseases in Korea. Seoul: Newest Medicine Co.; 1975. p.85-8.
5. Korean Society of Infectious Diseases. History of communicable diseases in Korea. Seoul: Kunja Publishing Co.; 2009. p.319-410.
6. Kim SH, Yeo SG, Jang HC, et al. Clinical responses to smallpox vaccine in vaccinia-naive and previously vaccinated populations: undiluted and diluted Lancy-Vaxina vaccine in a single-blind, randomized, prospective trial. J Infect Dis 2005;192:1066-70.
7. Jang HC, Kim CJ, Kim KH, et al. A randomized, double-blind, controlled clinical trial to evaluate the efficacy and safety of CJ-50300, a newly developed cell culture-derived smallpox vaccine, in healthy volunteers. Vaccine 2010;28:5845-9.
8. Lee HW, Lee PW, Johnson KM. Isolation of the etiologic agent of Korean hemorrhagic fever. J Infect Dis 1978;137:298-308.
9. French GR, Foulke RS, Brand OA, Eddy GA, Lee HW, Lee PW. Korean hemorrhagic fever: propagation of the etiologic agent in a cell line of human origin. Science 1981;211:1046-8.
10. Lee HW, Ahn CN. Development of inactivated vaccine against hemorrhagic fever with renal syndrome. J Korean Soc Virol 1988;18:143-8.
11. Chu YK, Gligic A, Tomanovic S, et al. A field efficacy trial of inactivated Hantaan virus vaccine (Hantavax (TM)) against hemorrhagic fever with renal syndrome (HFRS) in the endemic areas of Yugoslavia from 1996 to 1998. J Korean Soc Virol 1999;29:55-64.
12. Park K, Kim CS, Moon KT. Protective effectiveness of hantavirus vaccine. Emerg Infect Dis 2004;10:2218-20.
13. Sohn YM, Roh HO, Kim HS. Neutralizing antibody response to two doses of formalin inactivated mouse brain-derived Hantaan virus vaccine (HantavaxR) in healthy adults. Korean J Infect Dis 1998;30:325-31.
14. Chu YK, Woo YD, Lee HW. Immune response and antibody persistence against Hantaan virus of vaccinees with Hantavax (TM). Korean J Infect Dis 1998;30:317-24.
15. Cho HW, Howard CR. Antibody responses in humans to an inactivated hantavirus vaccine (Hantavax). Vaccine 1999;17:2569-75.
16. Woo YD, Chu YK, Baek LJ, Lee HW. An immunoserological study of vaccine against haemorrhagic fever with renal syndrome. J Korean Soc Virol 2000;30:11-8.
17. Sohn YM, Rho HO, Park MS, Kim JS, Summers PL. Primary humoral immune responses to formalin inactivated hemorrhagic fever with renal syndrome vaccine (Hantavax): consideration of active immunization in South Korea. Yonsei Med J 2001;42:278-84.
18. Cho HW, Howard CR, Lee HW. Review of an inactivated vaccine against hantaviruses. Intervirology 2002;45:328-33.
19. Lee HW, Baek LJ, Woo YD. The persistence of immunity against hemorrhagic fever with renal syndrome among Hantaan virus vaccinees. J Korean Soc Microbiol 1992;27:73-7.
20. Shinozaki F, Sada E, Tamai T, Kobayashi Y. Characterization of Leptospira strains HY-1, HY-2, and HY-10 isolated in Korea by means of monoclonal antibodies and restriction endonuclease DNA analysis. Am J Trop Med Hyg 1992;46:342-9.
21. Kim MH, Park SC. Leptospirosis. In: Korean Society of Infectious Diseases, editor. Vaccination for adult. 2nd ed. Seoul: MIP; 2012. p.225-35.
22. Kim YT. Current situation and elimination plan of influenza. J Korean Med Assoc 2004;47:1116-28.
23. Korea Centers for Disease Cntrol and Prevention. Analysis

of reported pandemic influenza (A/H1N1 2009) virus infections in Korea: from April, 2009 through August, 2010. Public Health Wkly Rep 2010;3:637-42.
24. Oh CE, Lee J, Kang JH, et al. Safety and immunogenicity of an inactivated split-virus influenza A/H1N1 vaccine in healthy children from 6 months to <18 years of age: a prospective, open-label, multi-center trial. Vaccine 2010; 28:5857-63.
25. Cheong HJ, Song JY, Heo JY, et al. Immunogenicity and safety of the influenza A/H1N1 2009 inactivated split-virus vaccine in young and older adults: MF59-adjuvanted vaccine versus nonadjuvanted vaccine. Clin Vaccine Immunol 2011;18:1358-64.
26. Lee YK, Kwon Y, Kim DW, et al. 2009-2010 novel influenza A (H1N1) vaccination coverage in the Republic of Korea. Am J Infect Control 2012;40:481-3.
27. Oh MD. Adult vaccination: Why we need it? In: Korean Society of Infectious Diseases, editor. Vaccination for adult. 2nd ed. Seoul: MIP; 2012. p.2-6.
28. Lim J, Eom CS, Kim S, Ke S, Cho B. Pneumococcal vaccination rate among elderly in South Korea. J Korean Geriatr Soc 2010;14:18-24.