

Contents lists available at ScienceDirect

Understanding Modern Vaccines: Perspectives in Vaccinology



Index

Note: Page numbers followed by 'f' and 't' denote figures and tables, respectively.

Adaptive immune receptors, diversity of, 36 Adaptive immune system, 28f, 30, 36-51 see also Immune system antibodies, effector functions of, 40-41, 42f antigen-presenting cells, role of, 36-38.47-48 B cells, 40-41 CD4⁺ T cells, 38-39 CD8⁺ T cells. 39-40 cytokines, role of, 43 distinguished from innate immune system, 46 immunological memory, 44-46 regulatory T cells, 43 T-cell activation, 38 Addiction, prophylactic and therapeutic vaccines for 187-189 Adjuvant combinations, in licensed vaccines, 102-106 Adjuvants, 13-14, 153-160 achievements of, 153-155

antigen identification and purification, new approaches to, 155-159 antigen selection and stability, new approaches to, 155 role in future vaccines, 155, 154f, 156t - 157tin vaccines, 89-111, 90f aluminium salts, 91, 93t, 95-97, 97t AS01, 107-110 AS03, 94t, 105-106, 106f AS04, 93t, 103-105, 104f AS15, 110 benefits of, 92 defined. 89-91 emulsions, 92, 93t, 99-101, 100f first use of, 91 on immune mechanisms, impact of, 94-95, 96f innovative adjuvants, need for, 92

microbial DNA immunostimulatory sequences, 107, 108f Montanide™ ISA51, 93t, 107 natural immune-defence triggers, mimicking, 95 persistence of, 95 role of, 92, 95, 111 safety profile of, 110-111 selection of, 91 synthetic MPL (RC-529), 93t thermo-reversible oil-in-water emulsion, 94t virosomes, 93t Administration of vaccines, 167-171 Advanced market commitments (AMCs), 119 Adverse events and vaccination, temporal associations between. 145 Adverse events of special interest (AESI), 137t, 139 Aerosol delivery, 172 AIDSVAX[™], 182

© 2011 Elsevier B.V. Open access under CC BY-NC-ND license.

XXXVIII INDEX

Alliance for Case Studies for Global Health, 186	viral vector vaccines, 161, 162 <i>f</i> , 163 <i>t</i> —164 <i>t</i>	Biologics License Application (BLA), 131, 136
Aluminium hydroxide, 95, 97 <i>t</i> Aluminium hydroxyphosphate	Antigen-specific cancer immunothera- peutics (ASCI), AS15 for, 110	Bordetella pertussis infection, 193
sulphate, 97t	Antitoxin, as immune serum, 13, 62	Calmette, Albert, 14
Aluminium phosphate, 95, 97 <i>t</i> Aluminium salts, 91, 92, 93 <i>t</i> , 95–97, 97 <i>t</i>	AS01, 107—110, 156t, 179 AS03, 94t, 105, 155	Canarypox vector vaccine (ALVAC™), 182
limitation of, 97	structure of, 106 <i>f</i>	Cancer
Anopheles spp mosquito, 178f	AS04, 92 <i>t</i> —93 <i>t</i> , 103—105, 104 <i>f</i> , 155,	cervical, 19, 84
Antibiotics, 180	157 <i>t</i> , 176	infectious diseases associated with,
Antibodies, 37f, 52–54, 64, 82f, 83, 91,	-adjuvanted HPV-16 vaccine,	188 <i>t</i> —189 <i>t</i>
92, 134, 142, 159, 164, 174, 184	125—126	immunotherapeutics, antigen-
anti-diphtheria toxin, 26	-adjuvanted HPV-18 vaccine,	specific, 110
anti-HAV, 142, 144	125—126	non-small-cell lung, 107
discovery of, 12, 26	AS15, 157 <i>t</i>	prophylactic and therapeutic
effector functions of, 39-40, 42f, 53	for antigen-specific cancer	vaccines for, 187–189,
Anti-diphtheria toxin antibodies, 26	immunotherapeutics, 110	188 <i>t</i> —189 <i>t</i>
Antigenic drift, 179–180	Association of University Technology	prostate, 167
Antigen-presenting cells (APCs), 28,	Managers (AUTM), 186	Cathelicidins, 31
30, 34, 57, 94, 98, 101, 155	Attenuation	CD4 ⁺ T cells, 38-39
role of, 36-38, 46-47	of live vaccines, loss of, 69	help, induction of, 53
Antigens	of pathogens, 10, 65, 128	CD8 [÷] T cells, 39-40
bacterial vector vaccines, 162-165,	of vaccines, 10, 22	Cell culture era, 14-15
165 <i>f</i> , 166 <i>t</i>	Autism, MMR vaccination and,	Center for Biologics Evaluation and
delivery, new approaches of,	146—147	Research (CBER), 131, 132
160—167	Autoimmune diseases, 125, 149	Centers for Medicaid and Medicare
dendritic cell vaccines, 167	definition of, 142	Services (CMS), 139
DNA vaccines, 165–167	Autoimmunity and vaccines, 144-145	Chamberland—Pasteur filter, 15
identification and purification, new		Charles IV of Spain, 8
approaches to, 155-159	Bacille Calmettee Guérin (BCG)	Chemokines, 32, 34, 95, 105
pathogen peptide libraries, 159	vaccine, 14, 69, 170, 173	Circulating recombinant forms (CRFs),
poly-epitope vaccines and MHC	Bacterial pathogen, 55-56	182, 183 <i>f</i>
restriction, 158	Bacterial vector vaccines, 162–164, 165f	Clinical assessment or development, of
reverse vaccinology, 158	advantages and disadvantages of,	vaccines
presentation, issues affecting,	169 <i>t</i>	overview of, 123-124
160—161	in clinical development, 163t—164t	Phase I trial, 123
research and discovery, key areas of,	Balmis, Francisco Xavier de, 8	Phase II trial, 123
157t	B cell receptors (BCR), 40-42	Phase III trial, 123
selection and stability, new	B cells, 40–42	Phase IV trial, 123
approaches to, 155	Behring, Emil von,12	safety evaluation, 124, 124 <i>f</i>
stability, 159–160	Bill & Melinda Gates Foundation, The,	Cocaine candidate vaccine, 187
vaccine see Vaccine antigens	163 <i>t</i> —164 <i>t</i> , 183	Cold chain, 119, 152, 159

INDEX XXXIX

Committee for Medicinal Products for ingredients, safety concerns of, Emulsions in vaccines. 98–102f. 147-148 Human Use (CHMP), 129, 134 Complement system, 34-36 modern elements of, 153f oil-in-water, 79, 93t, 100-102, 100f, Conditional approval, for vaccines, 135 pathogens, identification and 101*f* Council for International Organizations selection, 120 water-in-oil, 92, 100, 100f, 107 of Medical Sciences, 136 post-licensure surveillance. 136-137 Enders, John, 15 Cowpox vaccination, for smallpox, 6 case study, 139-140 Epithelial cells. 31 see also Vaccination preclinical evaluation, 120-121 Epitope-based vaccines, 158 CpG 7909, 107, 108f principles of, 117-120 Epitope mapping, 158 Current good manufacturing practices production of vaccines, 126-136 Europe, variolation in, 4 (cGMP), 122 safety assessment, improvement in, European Commission (EC), 129 Cutter incident, 15 148 European Medicines Agency (EMA), Cytokines, 32, 34, 37f, 38-40, 42-43, Diphtheria, 22 129, 139 45, 47, 48, 82, 93, 94*f*, 101, 141 bacillus, 13 European Union (EU), vaccine Cytomegalovirus (CMV), 56, 71, burden of, 14 licensing procedures, immunotherapy of, 14, 26 173 - 175129. 130f reactivation of, 176 Disease burden, assessment of, centralized procedure, 129 Cytotoxic T cells, 49, 50 117-120 mutual recognition and decentralmedical need and economic ised procedures, 129-132 resources, 118 Evolution of vaccines. 1-24, 12f Damage-associated molecular recent science and technology Exotoxins, 12 see also Toxins patterns (DAMPs), 97 discoveries, 119-120 Defensins, 31 vaccine programmes, funding, Dendritic cell (DC) vaccines, 167, 169t Fibroblasts, 31 118-119 advantages and disadvantages of, Flagellin, 156t-157t DNA expression libraries, 159 169t - 170tFollicular helper cells, 39 DNA recombinant vaccines, 18-19, Dendritic cells (DCs), 34,38, 94 Food and Drug Administration (FDA), 165-166 Department of Defense (DOD), 122, 136 advantages and disadvantages of, 139 - 140Investigational New Drug (IND) 169t - 170tDepot effect, 91 application, 122, 131 in clinical development, 168t Development of vaccines, 63f, 116 Formaldehyde inactivation, in case study, 125-126 vaccines, 11, 15 challenges to, 143-144, 146-147 Effector(s) Future vaccines, 149 autoimmunity and vaccines, adaptive immune, 37f, 39-41 adjuvants, 153-160 144-145 cells, selection and targeting of, antigen delivery, new approaches of, case study, 54-55, 142-147 53 - 54160 - 167protective effects, measurement functions of antibodies, 40-41, 42f complex and challenging targets, of, 142-143 innate immune, 34-36, 35f new vaccines for 172-187 temporal associations between Ehrlich, Paul, 13, 26, 64 non-infectious conditions, vaccines adverse events and vaccination. Elderly, vaccines for, 193 for. 187-191 145-147 Embryonated eggs, 14 specific populations, vaccines for, clinical evaluation, 123-125 Emergency procedure, pandemic 191-195 using immune correlates of influenza vaccines authorisation vaccine administration, new protection, 143 using, 134f, 135-136 approaches to, 167-171

XL INDEX

	1101/2	<u> </u>
Gene—environment interaction, 187	HSV-2 glycoprotein D (gD2) candidate	Immunoevasion, 71
Genital HSV-2 infection, 175–176	vaccine, 176	Immunological impediments to
Genocea	Human Hookworm Vaccine Initiative	vaccination, 57
T-cell antigen discover y technology,	(HHVI), 186	Immunological memory, 44–46
159, 160 <i>t</i>	Human immunodeficiency virus (HIV),	responses, kinetics of, 45f
German measles see Rubella	92, 143, 152	Immunological requirements, of
Germ theory of disease, 8	vaccines, 55	vaccines
Glenny, Alexander, 13, 91, 97	candidates, targets of, 184	antigen, identification and selection
Global Advisory Committee on Vaccine	development of, 183	of, 52
Safety (GACVS), 139	Human immunodeficiency virus 1	CD4 ⁺ T-cell help, induction of, 53
Global Alliance for Vaccines and	(HIV-1), 182	effector cells, selection and targeting
Immunisation (GAVI),	subtypes, 183f	of, 53-54
118–119	Human leukocyte antigens (HLA), 38	innate immune responses, induction
Global Solutions for Infectious	Human Microbiome Project, The, 187	of, 52–53
Diseases, 182	Human papilloma virus (HPV), 19	Immunological senescence, 79
Glycerine, 6	L1 synthesis, in yeast expression	Immunology of vaccines, 25–59
Goodpasture, Ernest, 14	system, 77f	history of, 26–28
Group A streptococcus, 183–184	recombinant antigens for vaccines	Immunostimulatory sequences (ISS),
Guérin, Albert, 14	against, 84	107, 156 <i>t</i>
	vaccines, 76	Immunotherapy, 12—14
H1N1 pandemic influenza, 135, 139,	AS04-adjuvanted, 105	Inactivated polio vaccine (IPV), 15
192	1004794 4504	Independent Data Monitoring
Haemophilus influenzae type b (Hib)	IC31™, 156t	Committees (IDMCs), 124
vaccine, 20, 81, 86t, 118–119	Immune correlates of protection,	Influenza vaccines, 18, 73, 182t
Heads of Medicines Agencies (HMA),	54-55	antigens for, 78–79
131	vaccine development by, 142	pandemic, 79
Helper T cells, 38–39	Immune system, 28–46	seasonal, 78–79
Hepatitis A vaccines, 143–144	adaptive, 28f, 30, 36–51	types of, 77f
active immunization, 144	innate, 28f, 30–36, 46–51	Innate immune system, 28f, 30–36,
passive immunization, 144	interaction of vaccines with, 58–59	46–51, 144 see also Immune
Hepatitis B virus (HBV) vaccine,	organs and tissues of, 29f	system cells of, 30-31
18—19, 69, 76, 125	Immunisation, 13, 118–119,	complement system, 34–36
antigen, recombinant proteins for,	136, 194	distinguished from adaptive immune
83–84	active, 144	system, 46
Herpes simplex virus (HSV), 71,	neonatal, 193	
175—177	passive, 144	innate response, effectors of, 34–36, 35 <i>f</i>
vaccines, possible effects and	polio, 17 RRR-TV, 140	pathogens, detection of, 31–34
consequences of, 176t		Inoculation, 4, 7f
Host—pathogen interactions, 55	Immunity, 3	Interferon-gamma (IFN _γ), 39
diseases with complex, 142	adaptive, 30	Interleukin-4 (IL-4), 39
HPV-16, 19	innate, 30	Interleukin-4 (IL-4), 39 Interleukin-5 (IL-5), 39
HPV-18, 19	Immunocompromised individuals,	
HPV L1 coat protein, 19	vaccines for, 194-195	Interleukin-13 (IL-13), 39

INDEX

International AIDS Vaccine Initiative Live vector vaccine. 184 Mycobacterium leprae. 69 Mycobacterium tuberculosis (IAVI), 186 LT. 156t Intramuscular vaccination, 50-51, 51f LuJo virus, 186 (M. tuberculosis), 55, 71, 173, ISCOM[™] (immune-stimulating complex Lysozymes, 31 174t consisting of cholesterol and phospholipids), 109 Naïve T lymphocytes, 38 Macrophages, 94 ISCOMATRIX™, 156t Madhava Nidana. 4 NanoBio Corp., 155 Major histocompatibility complex Nanoemulsions, 155 (MHC), 38-39 NanoStat™, 156t Jenner, Edward, 5, 7f, 62, 152 restriction, 158 National Regulatory Authorities (NRA). Measles-mumps-rubella (MMR) 132 Killed/inactivated pathogen vaccines, vaccine, 17, 119, 144-145 10, 11, 17, 60, 64, 68-69, Natural immunity to infection, 13 Measles vaccine, aerosolised. Natural killer (NK) cells. 71 89-90 170 Neisseria gonorrhoeae, 53 characteristics of, 72t Neisseria meningitides, 81 Meningococcal polysaccharide influenza, 17 vaccines. 19-20 Neonatal infants, vaccines for, 193 Pneumococcus, 19 Metchnikoff, Élie, 13, 26 Neonatal tetanus, 13 see also Tetanus polio, 15 $MF59^{TM}$, 93t, 101–102, 155, 156t–157t, New onset of chronic disorders Kitasato, Shibasaburo, 13 175, 193 see also Oil-in-water (NOCDs), 125 Koch. Robert. 6. 8. 26. 62 emulsions New vaccines, for complex and postulates, 8 structure of, 101f challenging targets, 172-187 Microbes, 8 neglected tropical and non-tropical Large-scale vaccine manufacturing, Microbial DNA immunostimulatory diseases, 185-186 127 sequences, 107 pathogens Latency, 71 structure of, 108f with complex life cycle, 177-179 Lederberg, Joshua, 186 Microbiome, 186 exhibiting antigenic variability, Licensing procedures, for vaccines Microneedles, 171f 179-184 (in EU), 129-132, 130f novel and emerging, 186 Mock-up procedure, pandemic centralised procedures, 129 influenza vaccines authorisation persistent infections and maligemergency procedure, 134f. using, 132-134, 133f, 134t nancy, 172-177 135-136, 135t undesirable immune responses. 185 Monocytes, 94 mock-up procedures, 130-131, Monophosphoryl lipid A (MPL), 103, Nicotine vaccine, 189 130f, 132t 104f. 157t Nigera, polio outbreak in, 22 mutual recognition and decentral-Montague, Mary Wortley, 5f Non-infectious conditions, vaccines for. ised procedures, 129-132 Montanide[™] ISA51, 93*t*, 107, 157*t* 185*t*—186*t*, 187—191, Lipkin, lan, 186 see also Water-in-oil emulsions 188*t*—189*t* Lipopolysaccharide (LPS), 33 Montanidec ISA720, 156t addiction, prophylactic and therachemical structure of, 103, 104f Multifactorial vaccine development peutic vaccines for, 187-189 Liposomes. 98-99 cancer, prophylactic and therapeutic structure of, 98f process, 121 Multiple puncture method, 7-8, 8f vaccines for, 189-191 Live, attenuated pathogen vaccines, Mumps, 146-147 North America, variolation in, 4 10, 14, 15, 21, 65, 68, 77, 170, Mycobacterium bovis bacillus, 14, Novartis Vaccines Institute for Global 184, 192 173 Health, 186 characteristics of, 72

XLII INDEX

Oil-in-water emulsions, 79, 93t, 100, 100f see also Emulsions in vaccines MF59™, 93t, 99—100, 99f, 101—102, 101f thermo-reversible, 94t, 102 Oral polio vaccine (OPV), 15 Pan American Health Organization Revolving Fund for Vaccine Procurement, 119 Pandemic influenza vaccines, 77 see also Influenza vaccines EU authorization of, 132—136 using emergency procedure, 134f, 135—136, 135t using mock-up procedure, 133f, 134—135, 135t post-authorisation studies of, 133t, 136—142, 137t Parasites, 39, 56—57, 177, 185 Particulate antigens, 83—85 Pasteur, Louis, 8, 26, 62 Pathogen-associated molecular patterns (PAMP), 31 effectors, 33f recognition of, 94 sensors, 33f Pathogen peptide libraries, 159—160 Pathogens attenuation of, 8—11 causing persistent infections, 174t complexity, 70—71 with complex life cycle, 177—179 detection of, 31—34 exhibiting antigenic variability, 179—184 identification and selection, 120	whole organism vaccines for, 17–18 Pattern recognition receptors (PRRs),	QS21, 107—110 chemical structure of, 109f Quality-adjusted life years (QALYs), 117 Quality control (QC), of vaccines, 128—129 Ramon, Gaston, 12, 13, 91 Reassortant viruses, 21—22 Recombinant/DNA technology approaches to vaccine antigens, 64—66, 66f generation of short peptide antigens by, 76, 77f Recombinant modified vaccinia Ankara (rMVA), 161, 163t, 175t, 191t Reference Member State (RMS), 131 Regulatory T cells (Treg cells), 43 Resiquimod, 156t Respiratory syncytial virus (RSV) vaccines, 55, 67—68, 70, 182, 185 Reverse vaccinology, 74, 74f, 158 Rhesus rotavirus tetravalentvaccine (RRV-TV) (Rotashield™), 139—142, 145 Robbins, Frederick, 15 Rotarix™ (RV1), 141 RotaTeq™ (RV5), 141 Rotavirus infection, 140—142 vaccination previous attempts to, 140—141 recent attempts, 141—142 Rotavirus vaccine, 22 Roux, Émile, 8, 12 Royal Jennerian Society, 6 Royal Philanthropic Expedition, 8
179—184	80—81, 82 <i>f</i>	Royal Jennerian Society, 6

INDEX XLIII

Sabin, Albert, 15 Safety assessment or monitoring, of vaccines, 124f clinical safety evaluation,	Tetanus neonatal, 13 vaccination, 13 Theiler, Max, 14	discovery of, 64 future of, 85 HBV vaccine antigen, recombinant proteins for, 83–84
124–125 continuous improvement in, 148	Thermo-reversible oil-in-water emulsion, 94t, 102 see also	identifying and producing, 64–68, 63 <i>f</i>
vaccine ingredients, 147–148 Salmonella enterica, 56 Seasonal influenza vaccines, 78–79	Oil-in-water emulsions Thiomersal, 147—148 Toll-like receptors (TLRs), 31, 94	for influenza vaccines, 78–79 on nature, building and improving, 80
see also Influenza vaccines	mammalian, 32t	particulate antigens, 83
Serious adverse events (SAEs), 125 Serious unexpected suspected adverse events (SUSARs), 137	TORCH pathogens, 192 Toxins, 11–13 anatoxin, 13	peptide approaches to, 66, 67f polysaccharide conjugate vaccines, 80–81, 82f
Seroprotection rates, 142 Serotype replacement, 180	exotoxins, 12 Toxoids, 12, 62, 81	recombinant/DNA approaches to, 65–66, 66 <i>f</i>
Short peptide antigens direct synthesis of, 76	Transdermal microneedle patches,	short peptide antigens direct synthesis of, 76
generation of, by recombinant DNA technology, 76, 77f	Tuberculosis (TB), 4, 172–173 Tumour-associated antigens (TAA),	generation of, by recombinant DNA technology, 76, 77f
Sipuleucel-T, 167 Smallpox, 4f	189 Typhoid fever vaccine, 11	whole-pathogen-based Whole-pathogen-based
cowpox vaccination for, 6–7 variolation for, 4, 5 <i>f</i>	'Typhoid Mary', 11f	vaccines Vaccine Safety Data (VSD) link system,
inoculation procedure, 4, 7f	UK National Health Service (NHS), 146	139
Speckled monster, 4 Split-pathogen approaches to vaccine	United Nations Children's Fund (UNICEF), 132	Vaccines and Related Biological Products Advisory Committee
antigens, 17–18, 73, 128 see also Pathogens characteristics of, 75	United States impact of vaccines in, 21 <i>t</i>	(VRBPAC), 132 Vaccinology, immunological milestones of, 27t
Streptococcus pneumoniae, 81 Subunit antigens, 17–18, 21–22, 52,	Vaccination	Varicella zoster virus, 71 Variolation, 6f
61, 73, 128 characteristics of, 75 defined, 73–75	boosting in, 45 <i>f</i> cowpox, 4–6 evolution of, 3 immunological impediments to, 57	in Europe, 4 mortality associated with, 4 in North America, 6
limitations of, 75 Synthetic MPL (RC-529), 93 <i>t</i> Syphilis, 4	intramuscular, 51 <i>f</i> priming in, 45 <i>f</i> programme (first), 8	Vascular endothelial cells, 31 Veterans' Health Administration (VHA), 139
Tajikistan, polio outbreak in, 22	programmes, adherence to, 22 tetanus, 13	Viral vector vaccines, 161, 162 <i>f</i> , 163 <i>t</i> —164 <i>t</i>
T-cells activation of, 38	Vaccine Adverse Event Reporting System (VAERS), 139	advantages and disadvantages of, 169t-170t
antigen discover y technology, 159, 160 <i>f</i>	Vaccine antigens, 60–87 defined, 64	Virosomes, 93t, 98–99 structure of, 98f

XLIV INDEX

Viruses, 56 as infectious agents, 15 Vitamin E, 105

Water-in-oil emulsions, 92, 99, 98*f*see also Emulsions in vaccines
Montanide[™] ISA51, 93*t*, 107
Wellcome Trust Hilleman Laboratories,
186
Weller, Thomas, 15
Whole-pathogen-based vaccines,
17—18, 65*f*killed/inactivated pathogen

vaccines, 68-72, 72t

limitations of
attenuation of live vaccines, loss
of, 69
high reactogenicity, 69
latency and immunoevasion, 71
pathogen complexity, 70—71
reduced immunogenicity,
71—72
reversion, risk of, 70
unwanted immune response,
70
live, attenuated pathogen vaccines,
69, 70, 72t
split-pathogen, 17—18, 73, 128

subunit antigens, 18, 22, 52, 73, 90, 128, 158, 184
World Health Organization (WHO), 2, 132, 185
CHOICE (CHOosing Interventions that are Cost-Effective) project, 118
polio position paper, 15–17

Yersin, Alexandre, 12

Zoster vaccine, 172