

## Index

- acetone-killed vaccines 327  
 acid tolerance response 189–190  
 adhesins 74–75  
 amoxicillin 11–12  
 ampicillin  
   resistance 39  
     *S. enterica* serovar Typhi 5, 29–30  
     *S. enterica* serovar Typhimurium 37, 38  
 typhoid fever treatment 11–12  
 amplified fragment length polymorphism (AFLP) 118  
 animal reservoirs 94–96  
 anti-melanoma DNA vaccines 349–350  
 antibiotic treatment  
   resistance *see* drug resistance  
   typhoid fever 11–15, 16  
     carriers 16  
   *see also specific antibiotics*  
 antibody responses 226  
   in cattle 305–306  
   in chickens 304  
   in human immunity 234, 235–237  
   in sheep 307  
   secondary infections 228, 229  
   to heterologous antigens 344–345  
   *see also* immunity  
 antigen-delivery systems 337  
   *see also* heterologous antigens  
 apoptosis 218–219  
 Artemis 119–120  
*asd* gene 339–340  
 AvrA 76–77, 152  
 azithromycin 12  
 B cell lymphoma (BCL) 352  
 B-cells 235–237  
   responses in cattle 305–306  
   responses in chickens 304  
   responses in sheep 307  
   T-cell interactions 227  
 bacteraemia, typhoid fever 6  
 bacteriophages 132–133  
   phage typing 118  
 birds 68–73  
   epidemiology 68  
   pathogenesis 69–71  
     molecular basis 71–72  
   salmonellosis characteristics 69  
   *see also* poultry  
 blood cultures, typhoid fever 10  
 bone marrow cultures, typhoid fever 10  
 bursectomy 304  
 cancer therapy 348–349, 352, 353  
 caspase-1 152, 208–209  
 cathepsin D 257  
 cattle 58–64, 94  
   adaptive immunity 305–306  
     B-cells 305–306  
     T cells 306  
   epidemiology 58–59  
     carriers 58–59

- cattle (*cont.*)  
 innate immunity 302–303  
   early interactions 302  
   macrophage/dendritic cell interactions 302–303  
 milk as vehicle of infection 96–97  
 molecular basis of pathogenesis 60–64  
   intestinal invasion 60–75  
     *Salmonella*-induced enteritis 62  
 salmonellosis characteristics 59–60  
 vaccines 309–310, 311
- cephalosporins, typhoid fever treatment 12  
 drug resistance 33
- chickens *see* poultry
- chloramphenicol  
 resistance  
   *S. enterica* serovar Typhi 5, 27–30  
   *S. enterica* serovar Typhimurium 38  
 typhoid fever treatment 5, 11, 12
- chromosomal integration of foreign genes 341–342
- chronic granulomatous disease (CGD) 232, 260
- ciprofloxacin  
 resistance 39  
   *S. enterica* serovar Typhimurium 38–39  
 typhoid fever treatment 12
- Cluster 121
- co-trimoxazole, typhoid fever treatment 11–12  
 drug resistance 29–30
- ColiBase 120
- common variable immunodeficiency (CVID) 235
- comparative genomics *see* genomics
- complement activation 210
- contamination, food 92–93
- cross-contamination 93–94  
 poultry 98–99
- CVD908 vaccine 327–328
- CXC chemokines 193
- cytokines 208–209, 215–216, 219–220, 223  
 balance between activation and  
   suppression of immunity 222–223  
 cancer therapy 352  
 heterologous expression 348–349  
 in chickens 300–301  
 in human immunity 233–234  
 in secondary infections 229–230  
 in sheep 307  
 production by dendritic cells 288–289  
 recruitment and activation of phagocytes 221–222  
 therapeutic immune response modulation 348–349
- cytolytic T-cells (CTLs) 226–227  
 heterologous antigen responses 346–347
- delayed type hypersensitivity (DTH) 226
- dendritic cells (DC) 227–228, 279–280, 285, 291  
 functions 280  
 in cattle 302–303  
 maturation 280  
*Salmonella* interactions  
   invasion and 281–282  
   liver 289–291  
   mesenteric lymph nodes 284–286  
   Peyer's patches 282–284  
   spleen 286–289
- dexamethasone 13
- DFI (differential fluorescence induction) 184–185
- diagnosis, typhoid fever 9–11
- diarrhea, intestinal invasion and 192–193
- differential fluorescence induction (DFI) 184–185
- directed mutagenesis 135
- dmsA* promoter 341
- DNA vaccines 332  
 anti-melanoma vaccines 349–350  
   *S. enterica* as delivery system 349–351
- domestic animals *see* cattle; pigs; poultry; sheep
- drug resistance 25–27  
 causes of 43–48  
   antibiotic withdrawal effects 44–48  
 definitions of terms 27  
 enteric fevers other than typhoid 36  
 impact on human health 26  
 non-typhoid *S. enterica* serovars (NTS) 36–43  
   *S. enterica* serovar Typhimurium 37–39, 42–43, 47  
 transmission routes 42–43

- plasmids 33–36, 46, 131  
*S. enterica* serovar Typhi (typhoid fever)  
 5–6, 13, 27–31, 36  
 molecular analysis of resistance plasmids  
 33–36  
 multidrug resistance 5, 12,  
 29–30  
 resistance beyond MDR 30–33  
 surveillance of 47  
*see also* multidrug resistance (MDR)
- ectodermal dysplasia with immunodeficiency  
 (EDA-ID) 237
- eggs and egg products, as vehicles of infection  
 100–105  
 contamination rates 102–105  
 infection routes 102–105  
*S. enterica* serovar Enteritidis pandemic  
 101–102
- endosomes 256
- endotoxin  
 endotoxic shock 219–220  
 typhoid fever 6
- enteric fevers 1  
 antibiotic resistance (other than typhoid)  
 36  
*see also* typhoid fever
- enterocolitis, in pigs 65, 66
- EnvZ-regulated genes 190–191
- epidemiology  
 in birds 68  
 in cattle 58–59  
 in pigs 64–65  
 salmonellosis 89  
 recent trends 90–92  
 typhoid fever 2–6  
 hygiene and sanitation relationships  
 4–5
- evolution  
*Salmonella* pathogenicity island 1 (SPI-1)  
 148–151  
 virulence 147
- Fenton reaction 262
- fever, in typhoid 7
- fimbrial gene variability 133–134
- flow typhoid (FT) 69
- fluoroquinolones  
 resistance  
*S. enterica* serovar Choleraesuis 42  
*S. enterica* serovar Typhi 13, 30–33  
*S. enterica* serovar Typhimurium 38–39  
 typhoid fever treatment 5–6, 12–13  
 drug resistance 13, 30–33
- follicle-associated epithelium (FAE) 281–282
- food contamination 92–93  
 cross-contamination 93–94, 98–99  
 eggs and egg products 102–105  
 meat and meat products 97–98  
 poultry meat 98–100  
 milk and milk products 96–97
- foreign genes, chromosomal integration  
 341–342
- fowl *see* poultry
- furazolidone resistance 37
- fusion proteins 342–344
- gall bladder infection, typhoid fever 7
- gene expression  
 global changes, microarray analysis 185  
 modulation by Nramp1 260  
*Salmonella* pathogenicity island-1 153  
*Salmonella* pathogenicity island-2 157–158  
 virulence genes 185–191  
 acid tolerance response 189–190  
 genes regulated by OmpR/EnvZ 190–191  
 invasion phenotype expression 188–189  
 PhoPQ and global regulator 186–188  
 temperature change response 191
- gene therapy 351–352
- Genespring 120–121
- genetic variation  
 fimbrial and pilus genes 133–134  
 microarray analysis 134–135  
*see also* genomics
- genomics 117  
 bacteriophages 132–133  
 comparative genomics 118–119  
*in silico* tools 119–120  
 microarray technology 120–121, 134–135  
 sequenced genomes as tools 121–124  
 fimbrial and pilus gene variability 133–134  
 full genome sequences 117–118, 121–124  
 functional genomics 135–136

- genomics (*cont.*)  
*in silico* analysis 124–130  
 large-scale genomic rearrangements  
 125–127  
 pseudogenes 127–128  
*Salmonella* pathogenicity islands (SPI)  
 128–130  
 plasmids 130–131  
 sequencing projects 122  
 Glimmer 120  
 Good's syndrome (GS) 236  
 granuloma formation 221  
 green fluorescent protein (GFP) 184–185
- heterologous antigens 338  
 expression systems 338–344  
 chromosomal integration of foreign  
 genes 341–342  
 fusion proteins 342–344  
 plasmids 339–341  
 problems 339  
 immune responses against 344–349  
 antibody responses 344–345  
 cytotoxic T-cell responses 346–347  
 effect of prior immunity 347–348  
 T-helper cell activation 345–346  
 heterologous expression of cytokines  
 348–349  
 heterophils 300–301  
 high pathogenicity island (HPI) 164  
 HilA transcriptional regulator 188–189  
*his* operon 341  
 HIV infection 236–237  
 HlyA secretion system 343  
*hok* genes 340  
 horizontal gene transfer 146  
 host specificity 57–58  
 determinants 73–76  
 early interactions 74–75  
 environmental and genetic differences  
 73–74  
 host intestinal inflammatory response  
 75–76  
 dissemination to systemic tissues 77–79  
 stealth strategy of host-specific serovars  
 76–77  
*see also specific hosts*
- human defensin 5 (HD5) 232  
 hygiene  
 food 92–93  
 cross-contamination 93–94  
 typhoid epidemiology relationships 4–5  
 immunity to *S. enterica* 207, 231, 237–239  
 adaptive immune response 220–224,  
 304–307  
 balance between activation and  
 suppression signals 222–223  
 cattle 305–306  
 cell migration and granuloma formation  
 221  
 chickens 304–305  
 LPS responsiveness 223  
 non-dependence on T-cells and B-cells  
 220  
 phagocyte antibacterial functions and 223  
 phagocyte recruitment and activation  
 221–222  
 pigs 306–307  
 sheep 307  
 transient immunosuppression 224  
 antigen specific immunity 225–228  
 antibody responses 226  
 dendritic cells (DCs) and 227–228  
 T-cell responses 226–227  
 T-cell/B-cell interactions 227  
 dynamics of bacterial spread and  
 distribution 211–214  
 escape from infected cells 214  
 growth characteristics 212–214  
 segregation to phagocytes within infected  
 tissues 211–212  
 early events 208–210, 232, 300, 302  
 dissemination to systemic tissues 210  
 invasion and inflammatory responses  
 208–210  
 heterologous antigen responses 344–349  
 antibody responses 344–345  
 cytotoxic T-cell responses 346–347  
 effect of prior immunity 347–348  
 T-helper cell activation 345–346  
 human immunity 230–237  
 antibody responses 234, 235–237  
 cytokines and 233–234

- early defence in gut 232  
 immunodeficiency effects 235–237  
 phagocyte deficiencies and 232–233  
 T-cell responses 234, 235–237
- innate immunity 215–219, 300–303  
 activation 265–268  
 cattle 302–303  
 chickens 300–302  
 control of bacterial growth 217–218  
 evasion of killing by phagocytes 218–219  
 Nramp1 divalent metal transporter role 258–260  
 pigs 303  
 reactive oxygen intermediates 217, 223  
 recognition of *S. enterica* by phagocytes 215–216  
 role of *Slc11a1* gene 216–217  
 sheep 303
- intracellular bacterial occurrence 210–211  
 models 207–208  
 primary infection clearance 224–225  
 genetic control 225  
 T-cell requirement 224–225  
 secondary infections 228–230  
 antibody responses 228, 229  
 cytokines and 229–230  
 protective antigens 230  
 T-cell responses 229  
*see also* phagocytes
- immunodeficiencies 235–237  
 clinical syndromes and 237  
 common variable immunodeficiency (CVID) 235  
 ectodermal dysplasia with  
 immunodeficiency (EDA-ID) 237  
 Good's syndrome (GS) 236  
 HIV infection 236–237  
 MHC class II deficiency 235–236  
 X-linked agammaglobulinaemia (XLA) 235  
 X-linked hyper IgM syndrome 236
- in vivo* expression technology (IVET) 181–183  
 IncHI plasmids 33–36  
 incubation period 92  
 inducible nitric oxide synthase (iNOS) 262–263, 264  
 infectious dose 105–107
- inflammatory response *see* intestinal inflammatory response  
 interferon gamma (IFN $\gamma$ ) 221–222, 233–234  
 macrophage activation 268–269  
*see also* cytokines
- interleukins (IL) 221–223, 233–234  
*see also* cytokines
- intestinal inflammatory response 192–193, 208–209  
 host specificity and 75–77  
 stealth strategy of host-specific serovars 76–77
- intestinal interaction  
 in cattle 60–75  
 in humans 232  
 virulence gene functions 191–193  
*see also* intestinal inflammatory response; invasion
- intestinal perforation, in typhoid fever 8–9  
 management 13
- invasion 151–152, 208–210  
 dendritic cells and 281–286  
 dissemination to systemic tissues 77–79, 210  
 dynamics of spread and distribution 211–214  
 host specificity and 77–78  
 in cattle 60–75  
 in pigs 66–67  
 in poultry 70–71  
 intestinal interaction 192  
 invasion phenotype expression 188–189
- IS200 typing 118  
 IVET (*in vivo* expression technology) 181–183  
*ivi* genes 182–183
- Kauffmann-White scheme 118
- lethal infections 219–220
- lipopolysaccharide (LPS)  
 activation of innate defences 265–268  
 O-antigen 230  
 responsiveness, adaptive innate immunity and 223  
 role in lethal infections 219–220

- liver 289
  - invasion 78–79
  - Salmonella*/dendritic cell interactions 289–291
- livestock *see* cattle; pigs; poultry; sheep
- lysosomes 256
- M cells 66–67, 281–282
- macrophages 208–209, 255
  - activation 221–222, 265–269
    - IFN $\gamma$  268–269
    - TNF $\alpha$  268
  - toll-like receptors (TLR) 265–268
- balance between activation and suppression 222–223
- control of bacterial growth 217–218
- endosomal pathway interactions 256–258
- evasion of killing by 218–219
- in cattle 302–303
- in chickens 301–302
- oxygen-dependent killing 260–264
  - inducible nitric oxide synthase cell biology 264
  - NADPH oxidase 260–261
  - ROS biological chemistry 261–262
- recruitment 221–222
- see also* phagocytes
- magnesium transport system (Mgt) 159
  - role in systemic infection 194–195
- malaria 232
- mannose 6-phosphate receptors (M6PR) 256, 259–260
- MD2 protein 265
- meat and meat products, as vehicles of infection 97–98
  - poultry meat 98–100
- Megan Vac 1 vaccine 330–331
- melanoma 349–350, 352, 354
- mesenteric lymph nodes (MLN) 78
  - Salmonella*/dendritic cell interactions 284–286
- MHC (major histocompatibility complex) 225, 346–347
  - MHC class II deficiency 235–236
- microarray techniques 119, 120–121
  - functional genomics 135–136
  - global changes in gene expression 185
  - Salmonella* genome analysis 134–135
- milk and milk products, as vehicles of infection 96–97
- msbB* mutation 353
- multidrug resistance (MDR)
  - role of *Salmonella* genomic island 1 (SGI-1) 163–164
  - S. enterica* serovar Typhi (typhoid fever) 5, 12, 29–30
  - S. enterica* serovar Typhimurium 37–39
  - see also* drug resistance
- multilocus enzyme electrophoresis (MLEE) 118–119
- multilocus sequence typing (MLST) 119
- MUMmer 120
- NADPH-oxidase 217, 260–262
- nalidixic acid resistance, *S. enterica* serovar Typhi 30
- nirB* promoter 340–341
- nitric oxide (NO) 262–263
  - in pathogenesis 263–264
- Nramp1 divalent metal transporter 258–260
  - modulation of host cell gene expression 260
  - nutritional effects 259
  - vesicular trafficking effects 259–260
- ofloxacin, typhoid fever treatment 12
- OmpR-regulated genes 190–191
- osmolarity responses 190–191
- oxygen-dependent killing 260–264
  - inducible nitric oxide synthase (iNOS) 262–263, 264
  - NADPH oxidase 260–261
  - nitric oxide biological chemistry 263–264
  - ROS biological chemistry 261–262
  - S. enterica* defences against NO stress 264
- pagC* promoter 341
- paratyphoid fever 1, 36, 323
  - antibiotic resistance 36
- pathogen associated molecular patterns (PAMPs) 193
- pathogenesis 207
  - dynamics of spread and distribution within host 211–214

- escape from infected cells 214
- growth characteristics 212–214
- segregation to different infected phagocytes 211–212
- early interactions with host immune system 208–210
  - dissemination to systemic tissues 210
  - invasion and inflammatory response 208–210
- in birds 69–71
  - molecular basis 71–72
- in cattle 60–64
- intracellular occurrence in phagocytes 210–211
- nitric oxide biological chemistry 263–264
- plasmid role 63–64, 72, 194
- progressive growth leading to lethal infection 219–220
  - see also* invasion
- pathogenicity islands (PAI) 146
  - definition 147
  - high pathogenicity island (HPI) 164
  - role in virulence evolution 147
  - see also* *Salmonella* genomic island 1 (SGI-1); *Salmonella* pathogenicity islands (SPI)
- perforation *see* intestinal perforation
- peroxynitrite 263–264
- Peyer's patches 66–67, 281–282
  - in typhoid fever 6
  - Salmonella*/dendritic cell interactions 282–284
- phage typing 118
- phagocytes 255
  - antibacterial functions 223
    - control of bacterial growth 217–218
  - bacterial segregation to 211–212
  - balance between activation and suppression 222–223
  - deficiencies, innate immunity and 232–233
  - evasion of killing by 218–219
  - intracellular occurrence of *S. enterica* 210–211
  - recognition of *S. enterica* 215–216
  - recruitment and activation 221–222
  - see also* macrophages; polymorphonuclear phagocytes (PMNs)
- phagosomes 256–258
  - acidification 257
- pHCM1 plasmid 33–35
- PhoPQ, global regulation of gene expression 186–188
- pigeons 72–73
- pigs 64–66, 67, 94
  - adaptive immunity 306–307
  - epidemiology 64–65
  - innate immunity 303
  - pathogenesis 66–67
    - molecular basis 67
  - salmonellosis characteristics 65–66
  - vaccines 310–311
- pilus gene variability 133–134
- PIPs (pathogenicity island encoded proteins) 63
- plasmids 130–131
  - cryptic 131
  - drug resistance 46, 131
    - S. enterica* serovar Typhi 33–36
  - heterologous antigen expression systems 339–341
  - role in pathogenesis 63–64, 72, 194
  - virulence 130–131, 194
- Plasmodium falciparum* malaria 232
- polymorphonuclear phagocytes (PMNs) 208–209, 221
  - control of bacterial growth 217–218
  - see also* phagocytes
- polytope 329–330
- poultry 94
  - adaptive immunity 304–305
    - B-cells 304
    - T-cells 304–305
  - as reservoir of infection 95
  - epidemiology 68
  - innate immunity 300–302
    - early interactions 300
    - heterophils 300–301
    - macrophage role 301–302
  - meat contamination 98–100
    - cross-contamination 98–99
  - pathogenesis 69–71
    - molecular basis 71–72
  - reproductive tissue infection 102–103
  - salmonellosis characteristics 69

- poultry (*cont.*)  
 sources of infection 99–100  
 vaccines 308–309, 311–312, 330–331  
*see also* eggs and egg products
- pregnancy, typhoid fever and 9, 13
- pseudogenes 127–128
- pullorum disease (PD) 69
- pulse-field gel electrophoresis (PFGE) 118
- purl* gene mutations 353–355
- R27 plasmid 33–35
- reactive nitrogen substances (RNS) 223
- reactive oxygen species (ROS) 217, 223  
 biological chemistry 261–262
- restriction fragment length polymorphism  
 (RFLP) analysis 118
- RhoP protein 189–190
- ribotyping 118
- RpoS factor 189
- SAL1* gene 302
- Salenvac vaccine 331
- Salmonella* centisome 6 genomic island (SCI)  
 160–161  
 functions 161  
 structure and evolution 160–161
- Salmonella enterica* 89  
 animal reservoirs 94–96  
 as delivery system  
 for DNA vaccines 349–351  
 for gene therapy 351–352  
 strains that replicate in distinct  
 anatomical sites 353
- control 107–108
- epidemiology 89  
 recent trends 90–92
- heterologous antigen expression 338  
 expression systems 338–344
- human disease 92  
 outbreaks 96
- infectious dose 105–107
- intestinal interaction 191–193
- transmission 92–94  
*see also* immunity to *S. enterica*
- Salmonella enterica* serovars 57–58, 89–90
- Choleraesuis, drug resistance 42  
*see also* pigs
- Dublin *see* cattle
- Enteritidis  
 drug resistance 39–40  
 epidemiology 101  
 in poultry 69  
 pandemic 101–102
- Gallinarum *see* poultry
- Hadar, drug resistance 39
- Newport, drug resistance 40–42
- Paratyphi (paratyphoid fever) 1  
 drug resistance 36
- Paratyphi B, drug resistance 42
- Pullorum *see* poultry
- Typhi (typhoid fever) 2  
 drug resistance 5–6, 27–31, 36  
 genome sequencing 121  
 identification 2  
 molecular analysis of resistance plasmids  
 33–36  
 multidrug resistance 5, 12, 29–30  
 vaccines 234  
*see also* typhoid fever
- Typhimurium  
 drug resistance 37–39, 42–43, 47  
 genome sequencing 124  
 microarray analysis 185  
*see also* birds; cattle; pigs; virulence  
 genes  
*see also* genomics
- Salmonella* genomic island 1 (SGI-1)  
 163–164  
 evolution 163  
 functions 163–164  
 structure 164
- Salmonella* pathogenicity islands (SPI)  
 147–148, 164–166  
 common features 165–166  
 comparative analyses 128–130, 165  
 future research 166
- SPI-1 60, 148–153  
 evolution 148–151  
 function and effector proteins 151–153,  
 191–193  
 gene expression regulation 153  
 role in inflammatory diarrhea 192–193  
 structure 151  
 variable effector loci 157

- SPI-2 154–158  
 evolution 154  
 functions 155–156, 193–194  
 gene expression regulation 157–158  
 in chickens 301  
 structure 155  
 variable effector loci 157
- SPI-3 158–159  
 evolution and structure 158  
 functions 158–159
- SPI-4 159  
 evolution and structure 159  
 functions 159
- SPI-5 63, 159–160  
 evolution and structure 159–160  
 functions 160  
 gene expression regulation 160
- SPI-6 (*Salmonella* centisome 7 genomic island) 160–161  
 evolution and structure 160–161  
 functions 161
- SPI-7 (major pathogenicity island) 161–162  
 evolution and structure 161–162  
 functions 162
- SPI-8 162
- SPI-9 162–163
- SPI-10 162, 163  
*see also* pathogenicity islands (PAI)
- Salmonella* translocated effector (STE)  
 proteins 156
- salmonellosis 299  
 epidemiology 89, 101  
 recent trends 90–92  
 human disease 92  
 in birds 69  
 in cattle 59–60  
 in pigs 65–66
- SAM 121
- sanitation, typhoid epidemiology  
 relationships 4–5
- septicaemia, in pigs 65–66
- sequence analysis *see* genomics
- serological tests, typhoid fever 10–11
- serotyping 118
- sheep 94  
 adaptive immunity 307
- B-cells 307
- T-cells 307
- innate immunity 303  
 vaccines 311
- Shigella dysenteriae* 28
- Shigella flexneri* 28
- sickle cell disease (SCD) 232–233
- signature-tagged transposon mutagenesis (STM) 135–136  
 virulence gene identification 183–184
- Sip proteins 152, 153  
 SipA 192
- Slc11a1* gene 216–217, 233
- sok* genes 340
- Sop proteins 152–153, 192  
 SopB 62  
 SopE 61, 192
- SopE* gene 132–133
- spleen 286  
 invasion 78–79  
*Salmonella*/dendritic cell interactions 286–289
- SptP 152–153
- spv* operon 64
- stealth strategy, host-specific serovars 76–77
- STM *see* signature-tagged transposon mutagenesis
- streptomycin, resistance 39  
*S. enterica* serovar Typhimurium 37, 38
- subtractive hybridization 119
- sulphamethoxazole resistance 5
- sulphonamides, resistance 39  
*S. enterica* serovar Typhimurium 37, 38
- systemic infection  
 dissemination to systemic tissues 77–79, 210  
 key genes needed for 193–195
- T-cells  
 heterologous antigen responses 345–347  
 cytotoxic T-cell responses 346–347  
 T-helper cell activation 345–346  
 primary infection clearance 224–225  
 CD4<sup>+</sup> TCRαβ<sup>+</sup> T-cells 224–225  
 TCRγδ<sup>+</sup> T-cells 225  
 responses 226–227  
 B-cell interactions 227

- T-cells (*cont.*)  
 dendritic cells and 227–228  
 in cattle 306  
 in chickens 304–305  
 in human immunity 234, 235–237  
 in sheep 307  
 secondary infections 229  
 temperature change response 191  
 TetC 344, 347  
 tetracycline resistance 39  
*S. enterica* serovar Typhimurium 37, 38  
 TlpA protein 191  
 toll-like receptors (TLR) 215–216, 265–268  
 TLR2 216, 267–268  
 TLR4 215–216, 265–267  
 TLR5 216, 268  
 TLR9 216, 268  
 transcriptome analysis 135  
 transmission 92–94  
 animal reservoirs 94–96  
 typhoid fever 5  
*see also* vehicles of infection  
 transposon mutagenesis  
 virulence gene identification 174–181  
*see also* signature-tagged transposon mutagenesis (STM)  
 TRASH system 135–136  
 treeview 121  
 trimethoprim resistance  
*S. enterica* serovar Typhi 5  
*S. enterica* serovar Typhimurium 38–39  
 tumor amplified protein expression (TAPET)  
 353–354  
 TAPET-cytosine deaminase 354–355  
 tumor necrosis factor alpha (TNF $\alpha$ ) 217, 220,  
 221  
 macrophage activation 268  
*see also* cytokines  
 Ty21a vaccine 16–17, 234, 327  
 Ty800 vaccine 328  
 type III secretion systems (TTSS) 151, 154,  
 160  
 heterologous antigen delivery 343–344  
 TTSS-1 71–72  
 role in host inflammatory response  
 75–77, 192–193  
 role in intestinal invasion 60–61, 191–193  
 TTSS-2 62–63, 71–72, 155–156  
 effector proteins 156  
 expression regulation 157–158  
 in chickens 301  
 role in systemic infection 193–194  
 typhoid fever 1, 323  
 chronic carriers 9, 16  
 clinical features 7–9  
 complications 8  
 control and prevention 16–17, 230  
 diagnosis 9–11  
 drug resistance 5–6, 13, 27–31, 36  
 molecular analysis of resistance plasmids  
 33–36  
 multidrug resistance 5, 12, 29–30  
 resistance beyond MDR 30–33  
 epidemiology 2–6  
 in pregnancy 9, 13  
 management 11–15, 16  
 carriers 16  
 intestinal perforation 13  
 pathophysiology 6–7  
 transmission 5  
 vaccines 16–17, 230, 234, 323–326, 329  
 acetone-killed vaccines 327  
 CVD908 5  
 history 323–325  
 performance criteria 325  
 Ty21a 16–17, 234, 327  
 Ty800 328  
 Vi vaccine 17, 230, 234, 327  
 WT05 328  
 $\chi$  4073 328–329  
 ZH9 328  
 vaccination 230, 308–311, 329–330  
 DNA vaccines 332  
 anti-melanoma vaccines 349–350  
*S. enterica* as delivery system 349–351  
 domestic animals 330–331  
 cattle 309–310, 311  
 chickens 308–309, 311–312, 330–331  
 live vaccines 311–312  
 pigs 310–311  
 sheep 311  
 live vaccines in domestic animals  
 311–312

- protection by non-immune mechanisms 312
- protection by non-specific immune mechanisms 312–313
- non-typhoidal salmonellosis 329–330
- novel approaches 332
- S. enterica* expressing heterologous antigens 338
  - see also* heterologous antigens
- typhoid fever 16–17, 230, 234, 323–326, 329
  - history 323–325
  - performance criteria 325
  - see also* heterologous antigens
- vehicles of infection 95
  - eggs and egg products 100–105
  - food contamination 92–93
    - cross-contamination 93–94
  - meat and meat products 97–98
    - poultry meat 98–100
  - milk and milk products 96–97
    - see also* transmission
- vesicular trafficking 259–260
- Vi vaccine 17, 230, 234, 327
- virulence
  - horizontal gene transfer and 146
  - pathogenicity island evolutionary role 147
    - see also* *Salmonella* pathogenicity islands (SPI)
- virulence genes 173–174
  - expression regulation 185–191
    - acid tolerance response 189–190
    - genes regulated by OmpR/EnvZ 190–191
  - invasion phenotype expression 188–189
  - PhoPQ as global regulator 186–188
  - temperature change response 191
- functions 191–195
  - intestinal interaction 191–193
  - systemic infection 193–195
- identification of 174–179, 185
  - differential fluorescence induction (DFI) 184–185
  - in vivo* expression technology (IVET) 181–183
  - microarray analysis 185
  - signature-tagged transposon mutagenesis (STM) 183–184
  - traditional transposon mutagenesis 174–181
- virulence plasmids 130–131, 194
  - see also* plasmids
- VNP20009 353–354
- WT05 vaccine 328, 329
- χ 4073 vaccine 328–329
- X-linked agammaglobulinaemia (XLA) 235
- X-linked ectodermal dysplasia with immunodeficiency (EDA-ID) 237
- X-linked hyper-IgM syndrome 236
- ZH9 vaccine 328