Index

Note: Numbers in bold refer to Figures and Tables.

ABCDE resuscitation principles 109
abdominal compartment syndrome 123
abdominal injury, whole-body CT scanning 117
abdominal sonography, ultrasound 114
activated partial thromboplastin time 61–2
activated protein C (APC), recombinant (drotrecogin alfa) 58, 69, 151–5
absolute/relative contraindications 155
anti-inflammatory properties 152–3
clinical studies 153–4
future developments 156
practical considerations 155
adipose tissue, and insulin therapy 188
aerobic Gram-negative bacilli (AGNB) 161–2
alcohol dependence lifetime prevalence 197
withdrawal prophylaxis and treatment 205
aldosterone antagonists, chronic heart failure 92
amphetamine 206
anaesthetic agents inhalational vs i.v. 80
interaction with ischaemic injury 78
and myocardial protection 77–88
potential harmful mechanisms 85–6
reperfusion injury 78–80
anaesthetic-induced cardioprotection 85–6
see also substance use disorders
analgesia, chest trauma 119–120
angina, and preconditioning 81
angiotensin converting enzyme (ACE) inhibitors 19, 20
chronic heart failure 91
angiotensin II receptor antagonists, chronic heart failure 92
anticoagulants 69–70
antidepressants 26
antimicrobials, enteral/parenteral 164
aorta, traumatic rupture 107
apolipoprotein E 20
ARDS, post-traumatic 118
arterial blood pressure, variations 143–6
ATP-binding cassette (ABC) 94
automatic implantable cardioverter defibrillators (AICDs) 92
azathioprine 4
barbiturates and anaesthesia 206
blockade of potassium channel 85
bendrofluazide, heart failure 92
benzodiazepines 206
β-2 adrenergic receptor 20
beta-blockers, chronic heart failure 91–2
bioinformatics 2, 21–2
defined 23
bisoprolol, chronic heart failure 91–2
bleeding disorders, recombinant factor VIIa 70–1
blood pressure, ACE inhibitors 19
blunt chest trauma see chest trauma
bovine adrenal medulla peptide-22 (BAM-22) 44
brain natriuretic peptide 91
human recombinant (nesiritide) 96
bronchial wounds 106
bumetamide, heart failure 92
buprenorphine 45
butorphanol 45
C-reactive protein, lipid metabolism 182
calcium antagonists, and heart failure 93
cAMP 40, 197
cAMP-response-element-binding proteins (CREBs) 40, 43, 197
candesartan 92
cannabis (marijuana) 207
cardiac markers, assays 115–6
cardiac resynchronization therapy (CRT) 94
cardiac transplantation 95
cardioprotection see myocardial protection
cardiopulmonary resuscitation 119
cardiopulmonary 119
cardiopulmonary failure 104
cardiovascular injuries 107
haemodynamic care 122–3
carrier proteins (membrane transporters) 15–18
carvedilol, chronic heart failure 91–2
cDNA, expressed sequence tags (ESTs) 21
cefortaxime 165
cervical spine, standard X-rays 110
chest trauma 103–31
assessment and diagnosis 108–16
abdominal sonography 114
Organ Injury Scaling 103, 104
physical examination 109
secondary assessment and surgery prerequisites 117–9
sonographic assessment 110–15
standard X-rays 109–10
transcranial Doppler 114–5
ultrasound-guided vascular access 115
whole-body CT scanning 117–8
cardiovascular complications 107
chest wall injuries 104–6
secondary surgery 118–9
therapeutic strategy 119–23
analgesia 119–20
cardiopulmonary resuscitation 119
cardiovascular care 122–3
deep venous thrombosis prevention 123
haemodynamic stability 120
intercostal drainage 121
mechanical ventilation 121–22
pain management 120
post-traumatic goal-directed therapy 122–3
regional analgesia 120
respiratory care 121–2
systemic analgesia 119
thoracic aorta rupture 107
troponin concentration 116
coagulation 55–74
acquired disorders 67–70
anticoagulants 69–70
dilutional coagulopathy 68–70
disseminated intravascular coagulation (DIC) 69
factor deficiencies 71
intractable haemorrhage 67–8
bleeding disorders 70–1
effects of critical illness 182–4
haemostasis, normal 56–62
hereditary disorders 63–5
of fibrinolysis 66
of haemostasis 62–7
importance in sepsis 151–2
model 59
tests of coagulation 61–2
thrombotic disorders 66–7
cocaine 206
codeine, CYP2D6 phase-I metabolism 4, 8–9
cor pulmonale 133–4
critical illness see intensive care and
critical illness
CT see whole-body CT scanning
CYP2A6, phase-I metabolism, and
smoking 12–13
CYP2C9, warfarin 9–12
CYP2C19, proton-pump inhibitors 12
CYP2D6 locus, debrisoquine: 4-
hydroxydebrisoquine ratio 9
CYP450 enzymes
microarrays 24
phase-I metabolism 7–13
cystic fibrosis, CFTR 17
debri squoquin: 4-hydroxydebrisoquine
ratio, CYP2D6 locus 9
deductive genomics 24
deep venous thrombosis, prevention
in chest trauma 123
defibrillators, AICDs 94
depression, drug targets 17–18
desflurane, interaction with ischaemic
injury 78, 80
desmopressin (DDAVP) 64, 71
diabetes mellitus
glycaemic control, improved
outcomes with tight control 179–82
metabolic management in intensive
care 186–7
and myocardial infarction 181
renal failure 182
sensory neuropathy 182–3
diaphragmatic injury 105–106
digestive tract see selective
decontamination
digoxin, heart failure 93
dilutional coagulopathy 68–70
disseminated intravascular
coagulation (DIC) 69
diuretics, heart failure 92
DNA microarrays, gene expression
studies 22–4
dobutamine, heart failure 96
dopamine, heart failure 96
dopamine receptor 20
Doppler, transcranial 114–5
drotrecogin alfa see activated
protein C
drug development 21–4
bioinformatics 21–2
databases 22
definitions 23
microarrays and gene expression
studies 22–4
recent trends 24
drug metabolizing enzymes (DMEs),
7–8
drug response variability 1–33
carrier proteins (membrane
transporters) 15–18
ethical and legal issues 25
and future health care 25–6
interindividual variability 4–8
drug metabolizing enzymes
(DMEs) 7–8
mutations 4–5
pharmacokinetic variability 5–8
phase-I P450 enzymes 8–9
see also pharmacogenomics
ECG recording 115–6
echocardiography 114, 136
Edinger–Westphal nuclei 46
dendorphins 44
derorphins 43
endothelial adhesion factors 152
denflurane, interaction with ischaemic
injury 77, 78
enoximone, heart failure 96
epileptone 92
evidence-based medicine (EBM), ICU recommendations 166
expressed sequence tags (ESTs) 21

factor deficiencies
coagulation disorders 64–5, 70
recombinant VIIa 71
VIII and IX 64–7
factor V Leiden 67
fentanyl, structure 35–7
fexofenadine 16
fibrin, generation in haemostasis 56–60
fibrinogen, hypofibrinogenaemia 69
fibrinogen degradation products 60–1
fibrinolysis 60–1
flail chest 104
fluid responsiveness see functional haemodynamic monitoring
frameshift mutation 5
Frank–Starling relationship 134–137, 140
frusemide, heart failure 92
functional haemodynamic monitoring 133–50
algorithm, treatment of instability 147
left ventricular stroke volume variations 142–143
positive-pressure ventilation 138–141
protocol 147
right atrial pressure variations 142
spontaneous variation in BP 136–138
static measures of cardiovascular status 134–136
systemic arterial blood pressure variations 143–146
systolic pressure and pulse pressure variations 143–146
usefulness 141–143
velocity and flow variations 146

G-protein-coupled receptor kinases (GRKs) 42
G-protein-coupled receptors 38–40
SNSRs 44
G-proteins, interactions with opioids 41
gene chips see microarrays
gene expression analysis 22–4
gene therapy, ethical and legal issues 25
genetic markers, SNPs 18–19
genomics defined 23
see also pharmacogenomics
Glanzmann’s thrombasthenia 63–4
gliblenclamide, blockade of potassium channel 85
gluconeogenesis, phosphoenolpyruvate carboxykinase (PEPCK) 187
glucose 6-phosphate dehydrogenase deficiency 3
glucose, regulation see glycaemic control
glucose transporter-4 (GLUT-4) 178
glucuronidation, phase-II metabolism 14
glycaemic control 177–194
diabetes improved outcomes with tight control 180–182
metabolic management during critical illness 186–187
hyper-, normo- or hypocalorific nutrition 185–186
hyperglycaemia, defined 177–178
hyperglycaemia in critical illness 182–184
associated neuropathy 182–183
associated renal failure 182
historical rationale for management 178–179
immune system impairment and risk of infection 183–184
impairment of lipid metabolism 184
### Index

| Improvement of outcome with normoglycaemia | 178–180 |
| Infections | 180 |
| Insulin therapy | 187–189 |
| Effects on inflammation and coagulation | 184–186 |
| Trauma/critical illness | 177–178 |
| Haemodynamic monitoring | |
| Functional haemodynamic monitoring | |
| Haemophilia | 64–5 |
| Acquired | 70 |
| Haemorrhage, intractable, in hospital practice | 67–8 |
| Haemostasis | 56–62 |
| Fibrin generation | 56–60 |
| Fibrinolysis | 60–1 |
| Hereditary disorders | |
| Clinical features | 63–4 |
| Treatment | 64 |
| Inhibition of coagulation after clotting | 58–60 |
| Primary haemostasis | 56 |
| Haemothorax | 107, 113 |
| Drainage | 121 |
| Halothane, and reperfusion injury | 78 |
| Heart failure | 89–95 |
| Aetiology | 89–90 |
| Epidemiology | 88 |
| Investigations | 90–91 |
| Pathophysiology | 90 |
| Heart failure, acute | |
| Non-invasive ventilation | 97 |
| Therapy, recent advances | 96–97 |
| Heart failure, chronic | |
| Cardiac resynchronization therapy (CRT) | 94 |
| Cardiac transplantation | 95 |
| Device therapy | 94–95 |
| Disease-modifying therapy | 91–92 |
| Left ventricular assist devices (LVADs) | 94–95 |
| Lifestyle modification | 94 |
| Non-pharmacological intervention | 94 |
| Pharmacological therapy | 91–93 |
| Surgical options | 95 |
| Symptomatic therapy | 92 |
| Heparins | 69–70 |
| Heroin and other opioids | 200–201 |
| Continuation of opioid maintenance programmes | 202 |
| Opioid antagonists | 204 |
| Transient perioperative administration of methadone | 202 |
| Withdrawal prophylaxis and treatment | 202 |
| HIV infection and AIDS, PGP polymorphisms and therapy enhancement | 16 |
| 5-HTT gene, serotonin transporter | 18 |
| Hydralazine, chronic heart failure | 92 |
| Hydroxytryptamine receptor | 20 |
| Hyperglycaemia | see glycaemic control |
| Hypoglycaemia, effects and complications | 186–187 |
| Hypoglycaemic agents, blockade of cardioprotection | 85 |
| Hypoprothrombinaemia, acquired | 70 |
| Inflammation, effects of critical illness | 184 |
| Insulin therapy and adipose tissue | 188 |
| Effects on inflammation and coagulation | 184 |
| Endotoxin scavenging | 184 |
| See also glycaemic control |
| Insulin-like growth factor binding protein-1 (IGFBP-1) | 187 |
| Intensive care/critical illness diabetes | 180 |
| Improved outcomes with tight control | 180 |
| Metabolic management | 186 |
| Evidence-based medicine (EBM) | 166 |
| Glycaemic control | 177 |
| Hyper-, normo- or hypocaloric nutrition | 184 |
intensive care/critical illness (cont’d)
impairment of lipid metabolism 184
infections 161
endogenous/exogenous PPMs 161
normal/abnormal PPMs 160
inflammation and coagulation 184
interventions that reduce mortality 166
neuropathy 181–182
renal failure 182
selective decontamination of digestive tract (SDD) 161
see also glycemic control
intercostal drainage 121
intercostal nerve block 120
ischaemia see myocardial protection
isoflurane, interaction with ischaemic injury 78

ketamine, blockade of potassium channel 85
left ventricular assist devices (LVADs) 94
left ventricular stroke volume, variations 142
left ventricular systolic dysfunction 89–101
see also heart failure
leucotriene receptor 20
levosimendan 96–97
lipid metabolism, impairment in critical illness 184
5-lipoxygenase (ALOX5) gene 19, 20
long QT syndrome 19
lung contusion 104, 117
lysergic acid diethylamine (LSD) 207–208
mediastinum, standard X-rays 109–110
α-melanocyte stimulating hormone (MSH) 44
membrane transport proteins 15–18
single nucleotide polymorphisms 4–5, 17
meningococcal sepsis
PAI-1 levels 69
protein C 69, 151
mercapturine 4
methadone, structure 36–37
metolazone, heart failure 90, 92
metoprolol, chronic heart failure 89–91
microarrays, and gene expression studies 22–4
midazolam, effect on potassium channel 85
milrinone, heart failure 96
mitogen-activated protein kinases (MAPKs) 85
monocyte chemoattractant protein-1 (MCP-1) 153
morphine
binding 47–48
clinical features 63–64
epidural infusion 120
glucuronides 46
structure–activity 35–7
MRSA, ICU infections 162–169
multidrug resistance gene (MDR1) 15–16
multiple organ failure 122
myocardial contusion 107, 114
myocardial infarction, and diabetes 180, 181
myocardial protection 77–88
blockade by anaesthetics and oral hypoglycaemic agents 85
opioid-induced 84
preconditioning 78–83
N-acetyltransferase (NAT)
NAT1 and NAT2 15
phase-II metabolism 13
N-methyl-D aspartate (NMDA) receptors 42, 43
nalbuphine 45
nalorphine, structure 36–37
Index

naloxone 35–7, 43, 48
naltrexone 45
nesiritide, heart failure 96
neuropathy, and insulin therapy in critical illness 182–3
nitrates
  acute heart failure 92
  chronic heart failure 92
  volatile (substance use) 205
NMDA receptor antagonists 43
nociceptin 38
NSAIDs, and heart failure 93
nuclear factor (NF-κB) 152
nutrition, hyper-, normo- or hypocaloric nutrition 185–186
oesophageal trauma 107
oestrogen receptor alpha 20
opioid receptor antagonists 37
opioid receptors 37–43, 20
  molecular cloning 37–8
  ORL-1 38
  peripheral receptors and inflammation 47–8
  signal transduction 40–3
  SNPs 18
  structural features 38–40
  topology 39
  trafficking 42–3
  types 37–8
opioids 35–53
  cellular mechanisms of action 40–3
  functional effects 45–9
  history 35
  inflammation and endogenous peptides 48
  ligands 43–5
    endogenous ligands 43–4
    exogenous receptor agonists 44–5
  nausea and vomiting 46
  opioid-induced cardio protection 84
  peripheral opioids and clinical implications 48–9
peripheral sites 46–9
structure–activity 35–7
substance use disorders (SUD) and anaesthesia 200–204
supraspinal and spinal sites 45–6
Organ Injury Scaling 104, 105
orphanin FQ 38
P450 enzymes, phase-I metabolism 7–13, 10–11
P-glycoprotein (PGP), substrates (drugs) 16
P-glycoprotein (PGP) multidrug transporter 15–16
pain management, chest trauma 120
paravertebral block 120
pentazocine 45
pharmacodynamic variability, receptors 18–20
pharmacogenetics
defined 2, 23
history 2–3, 4
pharmacogenomics 1–33
carrier proteins (membrane transporters) 15–18
deductive genomics 24
defined 23
drug development 21–4
databases 22
ethical and legal issues 25
pharmacodynamic variability 18–20
pharmacokinetic variability 5–8
phase-I metabolism 8–13
CYP2A6 (smoking) 12–13
CYP2C9 (warfarin) 9–12
CYP2C19 (proton-pump inhibitors) 12
CYP2D6 (codeine, tramadol) 4, 8–9
CYP2E1 (volatile anaesthetic agents) 13
CYP P450 enzymes 7–8
phase-II metabolism 13–15
glucuronidation 14
N-acetyl transferase (NAT) 15
<table>
<thead>
<tr>
<th>Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>224</td>
</tr>
<tr>
<td>pharmacogenomics (cont’d)</td>
</tr>
<tr>
<td>phase-II metabolism (cont’d)</td>
</tr>
<tr>
<td>thiopurine S-methyl transferase (TPMT) 14–15</td>
</tr>
<tr>
<td>web sites 32–3</td>
</tr>
<tr>
<td>see also drug response, variability</td>
</tr>
<tr>
<td>pharmacokinetic variability 5–8</td>
</tr>
<tr>
<td>pharmacophylogenomics, defined 23</td>
</tr>
<tr>
<td>pharmacoproteomics, defined 23</td>
</tr>
<tr>
<td>phenylcyclidine 205–6</td>
</tr>
<tr>
<td>phosphoenolpyruvate carboxykinase (PEPCK), gluconeogenesis 187</td>
</tr>
<tr>
<td>phylogenomics 21</td>
</tr>
<tr>
<td>defined 23</td>
</tr>
<tr>
<td>plasminogen activation inhibitor-1 (PAI-1) 66, 71</td>
</tr>
<tr>
<td>platelet activating factor (PAF) 151</td>
</tr>
<tr>
<td>platelet function analyser (PFA100) 62, 64</td>
</tr>
<tr>
<td>platelets, activation and aggregation 56–7</td>
</tr>
<tr>
<td>pleural sonography 111–12</td>
</tr>
<tr>
<td>pneumothorax 104, 110</td>
</tr>
<tr>
<td>drainage 119</td>
</tr>
<tr>
<td>polymyxin E/tobramycin 164–6</td>
</tr>
<tr>
<td>potassium voltage-gated channel 20</td>
</tr>
<tr>
<td>blockade by barbiturates and ketamine 85</td>
</tr>
<tr>
<td>preconditioning 78–83</td>
</tr>
<tr>
<td>angina and 81</td>
</tr>
<tr>
<td>and myocardial protection 78–83</td>
</tr>
<tr>
<td>pharmacological, with anaesthetic agents 80–3</td>
</tr>
<tr>
<td>preload indicators, receiver–operator characteristic 145</td>
</tr>
<tr>
<td>preload responsiveness 133–4</td>
</tr>
<tr>
<td>pro-dynorphin (PDYN) 38, 43–4</td>
</tr>
<tr>
<td>pro-enkephalin (PENK) 44, 48</td>
</tr>
<tr>
<td>pro-opiomelanocortin (POMC) 44, 48</td>
</tr>
<tr>
<td>propofol effect on potassium channel 85</td>
</tr>
<tr>
<td>and myocardial function 78</td>
</tr>
<tr>
<td>protein C, activated protein C (APC) 38, 69, 151–5</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
## Index

1. **infection in intensive care unit**
   - 161–3
2. **protocol**
   - 164–5
3. **questions on use**
   - 166–8
4. **selective serotonin reuptake inhibitors (SSRIs)**
   - 18
5. **sensory neuron-specific G-protein-coupled receptor (SNSR)**
   - 44
6. **sensory neuropathy, in diabetes**
   - 182–3
7. **sepsis**
   - 151–6
   - APC (activated protein C)
     - 151–5
   - importance in coagulation
     - 151–2
   - pathogenesis
     - 151–5
8. **serotonin receptor 5-HT\textsubscript{4}**
9. **serotonin transporter, 5-HTT gene**
10. **sevoflurane**
    - interaction with ischaemic injury
      - 78, 79, 80
    - cardioprotection
      - 84
11. **signal transducer and activator of transcription factors (STAT)**
    - 47
12. **signal transduction, opioids**
    - 40–3
13. **single nucleotide polymorphisms (SNPs)**
    - 4–5, 17
14. **genetic markers**
    - 18–19, 20
15. **slow acetylators**
    - 3
16. **smoking, phase-I metabolism**
    - CYP2A6
    - 12–13
17. **spironolactone**
    - 90
18. **standard X-rays**
    - 109–10
19. **Staphylococcus aureus (methicillin-resistant, MRSA)**
    - 161–168
20. **statins, heart failure**
    - 93
21. **sternal fractures**
    - 104–105
22. **streptokinase**
    - 167
23. **substance use disorders (SUD) and anaesthesia**
    - 195–216
    - basic aspects of SUD
      - 195–199
    - clinical aspects of SUD
      - 200
24. **CNS-depressants**
    - 200–206
25. **alcohol**
    - 204
26. **barbiturates**
    - 206
27. **benzodiazepines**
    - 206
28. **fuels and solvents**
    - 205
29. **heroin and other opioids**
    - 200–204
30. **volatile nitrates**
    - 205
31. **CNS-stimulants**
    - 206–207
32. **amphetamine**
    - 206
33. **cannabis (marijuana)**
    - 207
34. **cocaine**
    - 206
35. **lysergic acid diethylamine (LSD)**
    - 207
36. **phencyclidine**
    - 207
37. **definitions**
    - 199
38. **physical dependence**
    - 199
39. **terminology**
    - 215–216
40. **tolerance**
    - 199
41. **drug-free recovery**
    - 207–210
42. **anaesthesia**
    - 208
43. **analgesia**
    - 208–209
44. **sulphonylurea, blockade of potassium voltage-gated channel**
    - 85
45. **sulphonylurea receptor**
    - 20
46. **terfenadine**
    - 16
47. **thiazolidinone**
    - 17
48. **tiopurine S-methyl transferase (TPMT), phase-II metabolism**
    - 14–15
49. **thoracic aorta, traumatic rupture**
    - 107
50. **thrombin**
    - 58–61, 151–152
51. **prothrombin time**
    - 61–2
52. **thrombin-activated fibrinolysis inhibitor**
    - 60
53. **thrombomodulin**
    - 58, 151–152
54. **thrombotic disorders**
    - 66–7
55. **deep venous thrombosis**
    - 123
56. **prothrombotic traits**
    - 66
57. **thromboxane**
    - 56
58. **tissue factor (TF)**
    - 56–8, 69
59. **tissue factor pathway inhibitor (TFPI)**
    - 57–8, 61
60. **torsade-de-pointes**
    - 19
61. **toxicogenomics, defined**
    - 23
62. **tracheal wounds**
    - 106
63. **tramadol, CYP2D6 phase-I metabolism**
    - 4, 8–9
<table>
<thead>
<tr>
<th>226</th>
<th>Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>transcranial Doppler</td>
<td>blunt chest trauma 114–115</td>
</tr>
<tr>
<td>trauma</td>
<td>altered glucose regulation 177–178</td>
</tr>
<tr>
<td>see also chest trauma</td>
<td>troponin 116</td>
</tr>
<tr>
<td>ultrasound</td>
<td>abdominal sonography 114</td>
</tr>
<tr>
<td></td>
<td>chest trauma 110–111</td>
</tr>
<tr>
<td></td>
<td>pleural 112–113</td>
</tr>
<tr>
<td></td>
<td>ultrasound-guided vascular access 115</td>
</tr>
<tr>
<td>Valsava manoeuvre, square wave</td>
<td>138</td>
</tr>
<tr>
<td>vancomycin</td>
<td>166</td>
</tr>
<tr>
<td>variable number tandem repeats (VNTRs)</td>
<td>4–5</td>
</tr>
<tr>
<td>ventilation</td>
<td>mechanical 121–122</td>
</tr>
<tr>
<td></td>
<td>non-invasive, heart failure 97</td>
</tr>
<tr>
<td>volatile anaesthetic agents, CYP2E1</td>
<td>phase-I metabolism 13</td>
</tr>
<tr>
<td>volatile fuels and solvents</td>
<td>205</td>
</tr>
<tr>
<td>von Willebrand disease</td>
<td>63–4</td>
</tr>
<tr>
<td>acquired</td>
<td>70</td>
</tr>
<tr>
<td>von Willebrand factor (vWF)</td>
<td>56–9</td>
</tr>
<tr>
<td>warfarin</td>
<td>CYP2C9 phase-I metabolism 9–12</td>
</tr>
<tr>
<td></td>
<td>reversal 70</td>
</tr>
<tr>
<td>whole-body CT scanning</td>
<td>associated abdominal injury 118</td>
</tr>
<tr>
<td></td>
<td>blunt aortic injury 117–118</td>
</tr>
<tr>
<td></td>
<td>lung contusion 117</td>
</tr>
<tr>
<td></td>
<td>spinal injury 118</td>
</tr>
<tr>
<td>xenobiotics</td>
<td>3</td>
</tr>
</tbody>
</table>