

# Subject Index

- acid glycoprotein 238
- acute phase reactant proteins 238–239
- adenosine 56 (table), 81, 208, 219–220
  - antagonists 219
- adenosine triphosphate 114
- adenylate cyclase 169, 182
- adrenaline 122, 151–152
  - chemical structure 188 (fig.)
  - therapeutic action 187–189
- $\beta$ -adrenergic hyporeactivity 243
- adrenergic innervation 151
- adrenergic mechanisms 151–154
- $\alpha$ -adrenoceptors 153–154
- $\beta$ -adrenoceptor(s) 152–153, 167–185
  - anti-inflammatory action in
    - asthmatic airways 179
  - $\text{Ca}^{2+}$  extrusion 127
  - $\text{Ca}^{2+}$  influx inhibition 122–124
  - $\text{Ca}^{2+}$  release inhibition 125–126
  - $\text{Ca}^{2+}$  sensitivity (responsiveness) 121–122
  - $\text{Ca}^{2+}$  sequestration promotion 126–127
- cyclic adenosine monophosphate
  - role 120
- density/destruction in lung 170–172
  - autoradiography 171
  - parenchyma 171–172
  - radioligand binding 170–171
  - trachea 171
- desensitization 169–170
- function in asthma 179–183
  - autoradiography 181–183
  - isolated human bronchi 181–182
  - isolated human leukocytes 180–181
  - in vivo studies 180
- regulatory proteins 169
- sites of action 172–179
  - airway smooth muscle 172–173
  - cholinergic nerves 175
  - cilia 173–174
  - eosinophils 176–177
  - lymphocytes 177
  - macrophages 178
  - mast cells 175–176
  - platelets 178
  - polymorphs 178
  - secretory cells 173–174
  - subtypes 168–169
  - tracheobronchial microvessels 174–175
- $\beta_2$ -adrenoceptors
  - efficacy 184–185
  - selectivity 183–184
- $\beta$ -adrenoceptor agonists 120–127, 167–195
  - adverse reactions 185–187
    - cardiac 185–186
    - hypersensitivity 187
    - neuropharmacological 187
    - $\text{PaO}_2$  186
    - plasma constituents 186
    - skeletal muscle tremor 185
  - clinical application 191–193, 194 (table)
  - prodrugs 191
  - selective 190–191
  - therapeutic actions 187–193, 194 (table)
- $\beta_2$ -adrenoceptor agonists 35
- AFG cells 15
- airway epithelial damage 54
- airway smooth muscle 13
  - biochemical basis of contraction 114–119
  - crossbridge formation 114
  - excitation-contraction coupling 107–119
    - extracellular activator  $\text{Ca}^{2+}$  109
    - intracellular activator  $\text{Ca}^{2+}$  111
    - intracellular  $\text{Ca}^{2+}$  release 111–113
  - mechanisms 108
  - receptor-operated channels 110–111
  - voltage-operated channels 109–110

- excitation-contraction uncoupling
  - mechanism 119–133
- hyperplasia 29
- latchbridges 115–117
- muscle cell 107–108
- pharmacology 107–134
- A-kinase 120
- alkylxanthines 127–133
  - Ca<sup>2+</sup> extrusion 133
  - Ca<sup>2+</sup> influx inhibition 129–130
  - Ca<sup>2+</sup> release inhibition 130–132
  - Ca<sup>2+</sup> sensitivity (responsiveness) 129–130
  - Ca<sup>2+</sup> sequestration promotion 132–133
- cAMP accumulation 127–129
- relaxation induced in vitro 127
- $\alpha$ -aminobutyric acid 159
- aminophenazone 294
- aminophylline 127
  - see also* alkylxanthines
- anaphylatoxins
  - C3a 298
  - C5a 298
- annexins 228
- $\alpha_1$ -antichymotrypsin 238
- anti-inflammatory proteins 237, 238
  - (table)
- APUD cells 15
- arachidonic acid 299 (fig.), 301–303
- aspirin (acetylsalicylic acid) 291, 293
  - (fig.)
  - allergic mechanisms 297
  - guaiacolic ester 293
  - protein acetylation by 298
- aspirin-induced asthma 291–309
  - bradykinin receptors in 297–298
  - complement involvement 298
  - cyclo-oxygenase theory 298–305
    - compartmentalization of eicosanoids in lungs 304
    - leukotriene involvement 301–303
    - platelet involvement 303–304
    - viral infection 304–305
  - diagnosis 306–307
  - prevention 307–309
  - protein acetylation in 298
  - therapy 307–309
- asthma
  - death rate increase 183
  - inflammatory component 167
  - nocturnal 245
  - $\beta$ -receptor function impairment 152–153
  - steroid-resistant 247
- ATPase 114
- autonomic nervous system 14
- axon reflex mechanisms 158–159
- bambuterol 188 (fig.), 191
- basophils 27, 35–37
  - glucocorticosteroids effect on 240–241
- betamethasone 296
- bradykinin 29, 56 (table), 78–80
  - airways effects 79–80
  - formation 78–79
  - metabolism 78–79
  - receptors 79
    - abnormal reactivity 297–298
    - role in asthma 80
- bronchial arteries 16
- bronchial circulation 16–17
- bronchial epithelium 2
  - between asthma attacks 2–4
  - during asthma attack 10–11
  - epithelial regeneration 12–13
  - nerves 14–15
  - shedding 4, 27
- bronchial glands 13–14
- bronchial hyperresponsiveness 33
  - transient 19
- bronchial vascular bed leakage 17–19
- bronchitis, chronic eosinophilic
  - desquamative 33
- bronchodilator drugs, future trends 133–134
- budenoside 245, 246
- caffeine 210
- calcimedins 228
- calcitonin gene-related peptide 157–158
- calectins 228
- calmodulin 115
- calpactins 228
- captopril 79
- catecholamines, circulating 151–152
- CD18 240
- ceruloplasmin 238
- chemotactic factors 86–87
- choline magnesium trisalicylate 293–294
- choline phosphotransferase 69–70
- cholinergic mechanisms 145–151
  - acetylcholine release increase 147
  - in:
    - asthma 148
    - chronic obstructive airways disease 148
    - reflex bronchoconstriction 145–147
    - vagal tone increase 145
- cholinergic nerves 175

- chromobinodins 228
- chronic eosinophilic desquamative bronchitis 33
- chronic obstructive airways disease 145
  - cholinergic mechanisms in 148
  - xanthines for 213–215
- cimetidine 58, 59
- Clara cells 174
- coffee 207
- complement fragments 56 (table), 82–85
  - airway effects 83–85
  - bronchial hyperresponsiveness 84–85
  - cell activation 84
  - chemotaxis 84
  - mucus secretion 84
  - smooth muscle contraction 83–84
  - vascular 84
- metabolism 82–83
- origin 82–83
- receptors 83
- role in asthma 85
- concanavalin A-induced suppressor cell function 39
- corticosteroids 53
- CR3 (C3bi receptor protein) 240
- C-reactive protein 238
- Creola body 2, 28
- cromakalin 134
- cromoglycate 261–272
  - animal pharmacology 267–269
    - anaphylactic bronchospasm 267–268
    - sensory reflexes 268–269
  - biochemical pharmacology 266–267
  - effect on:
    - eosinophils 264, 265
    - mast cells 262–263
    - monocytes 264
    - neutrophils 264, 265
    - platelets 265
    - secretagogues 263–264
    - human pharmacology 269–272
    - pharmacological analysis 278–279
- cyclic adenosine monophosphate (cAMP) 120, 125
- cyclooxygenase 298–299
  - theory of aspirin intolerance 299–305
- cyclooxygenase inhibitors 294–295
- diacylglycerol 113
- diflunisal 293
- [<sup>3</sup>H]dihydroalprenolol 170
- disodium cromoglycate 33, 35, 129, 175, 176
- dopamine 151
- eicosanoids 304
- enalapril 79
- endonexins 228
- enprofylline 210, 211, 214
  - adverse reaction 211
- eosinopenia 239
- eosinophil(s) 7–10, 16, 32–34, 54
  - $\beta$ -adrenoceptor action 176–177
  - glucocorticosteroid effect 259–260
  - in aspirin-sensitive asthmatics 302
  - 15-lipoxygenase pathway activation 66
- eosinophil activating factor 239
- eosinophil cationic protein 10, 32, 33
- eosinophil chemotactic factor 6–7
- eosinophil-derived neurotoxin 32
- eosinophilic major basic protein 9
- ephedrine 189
- fenoterol 188 (fig.)
- Feyrter cells 15
- fibrinogen 238
- fibronectin 12–13
- forskolin 182
- glucocorticosteroids 227–251
  - adverse reactions 295–297
  - clinical use 247–250
    - acute asthma 250
    - chronic asthma 250
  - effects on:
    - $\beta$ -adrenoceptors 242–243
    - airway function 243–247
    - basophils 240–241
    - cell activation/recruitment 239–241
    - eosinophils 239–241
    - lymphocytes 241
    - macrophages 241
    - mast cells 240–241
    - neutrophils 240
    - vascular endothelium 242
    - vascular permeability 242
  - mechanism of action 227–247
    - protein synthesis induction 227–229
  - pharmacokinetics 247
  - routes of administration 248
  - side-effects 249–250
- $\beta$ -glucuronidase 37
- G-protein 120
- granule-containing (neuroendocrine-like) cells 15–16
- granulocyte/macrophage-colony stimulating factor (GM-CSF) 34

- guanosine 5'-triphosphate 169  
 guanyl nucleotide binding stimulatory proteins 169
- 15-HETE 54, 65
- histamine 29, 56 (table), 57–61  
 airway effects 59–60  
 chemotaxis to inflammatory cells 60  
 metabolism 58  
 receptors 58–59  
 role in asthma 60–61  
 synthesis 58  
 T cell suppressor cell function stimulation 60
- hydrocortisone, adverse reactions 296
- impromidine 59
- inflammation 27  
 pathological evidence in asthma 28–29
- inflammatory cells 27–28  
 between attacks 2–10
- inositol-1,4,5-triphosphate 111–113
- interleukins  
 IL-1 34, 239, 241  
 IL-2 241  
 IL-5 (interleukin-S-like factor) 34, 241  
 IL-6 239
- <sup>125</sup>I-iodocyanopindolol 170
- isobutylmethylxanthine 128
- isoprenaline 122, 189–90  
 cardiac arrhythmia induced by 184  
 chemical structure 188 (fig.)  
 over-reliance on 183
- kallidin (lysine-bradykinin) 78
- ketotifen 272–278, 280  
 animal pharmacology 274–275  
 human pharmacology 275–278  
 blockade of responses to  
 spasmogens/allergens 275  
 double-blind trials 276–278  
 reversal of  $\beta$ -adrenergic receptor tachyphylaxis 275–276  
 pharmacology in vitro 272–273
- kinin(s) 78–80  
 airway effects 79–80  
 formation 78–79  
 metabolism 78–79  
 receptors 79  
 role in asthma 80
- kininogenases 78–79
- Kulchitsky cells 15
- late-phase asthmatic reactions 35–36, 40–41
- leukotrienes 29, 65, 241  
 involvement in aspirin-induced asthma 301–303  
 A4 65  
 B4 31, 54, 56 (table), 301  
 C4 10, 34, 56 (table), 66, 67, 241  
 D4 56 (table), 301  
 E4 56 (table), 301
- lipocortins 228–237  
 anti-inflammatory action 231–237  
 presence in lung 231  
 synthesis/release 229–231
- lipomodulin 238 (table)
- lipoxins 65–66  
 A 67
- lipoxygenase products 65–69  
 airway effects 67–68  
 bronchial responsiveness 68  
 cellular activation 68  
 secretion 67  
 smooth muscle 67  
 vascular 67  
 metabolism 65–66  
 receptors 66  
 role in asthma 68–69  
 synthesis 65–66
- lymphocytes 39–42, 241  
 $\beta$ -adrenoreceptor action 177  
 atypical intraepithelial 39
- lysine-bradykinin (kallidin) 78
- lysine-acetylsalicylate 293 (fig.)
- macrocortin 238 (table)
- macrophages (mononuclear phagocytes) 37–38, 54, 241  
 $\beta$ -adrenoreceptor action 178
- major basic protein 10, 32, 33
- mast cells 4–7, 16, 35–37, 53  
 $\beta$ -adrenoreceptor action 175–176  
 glucocorticosteroid effect on 240–241
- mediators 53–88  
 antagonists 57  
 cellular origin 53–54  
 effects 54–55, 56 (table)  
 interactions 57  
 receptors 55
- membrane phospholipid-derived mediators 33
- mepyramine (pyrilamine) 58
- N*-methylhistamine 35
- methylprednisolone 244
- mono-HTEs 65
- mononuclear phagocytes; *see* macrophages
- microvascular leakage 29–30
- monocytes 37–38
- mucociliary transport 174

- mucus hypersecretion 27
  - muscarinic receptor(s) 147–148
    - autoreceptors 148–149
    - subtypes 148
  - muscarinic receptor agonists 125
  - myosin 114
    - phosphorylation 114–115
  - NANC nerves 154
    - bronchoconstriction modulation 159
    - excitatory 155
    - inhibitory 154
  - nedocromil 261
    - biochemical pharmacology 266
    - human pharmacology 269
    - pharmacological analysis 278–280
  - neural mechanisms in asthma 143–159
  - neural pathways 14–16
  - neuroendocrine-like (granule-containing) cells 15–16
  - neuroepithelial bodies 15–16
  - neurokinin A 56 (table), 155, 156
  - neuropeptides 154, 155 (table)
    - K 156
  - neutrophils 10, 30–32, 54
    - $\beta$ -adrenoreceptor action 178
    - chemotactic activity 87
    - glucocorticosteroid effect on 240
    - high molecular weight chemotactic activity 31
  - noradrenaline 151
  - noramindopyrine 294
  - OKY046 64–65
  - orciprenaline 188 (fig.), 190
  - oxygen radicals 56 (table), 87–88
  - paracetamol 294
    - adverse reactions 294
    - hypersensitivity 294
  - pathology of asthma 1–19
    - investigations 1–2
  - pentoxifylline 217
  - phenylbutazone 294
  - phorbol dibutyrate 113
  - phorbol ester tumour promoters 113
  - phorbol myristate acetate 113
  - phosphatidyl-2-acetylhydrolase 70
  - phosphodiesterases 209
  - phosphoramidon 157
  - platelet(s) 38, 54, 303–304
    - $\beta$ -adrenoceptor action 178
    - platelet activating factor (PAF) effect 74
  - platelet activating factor (PAF) 10, 31, 56 (table), 69–78
    - airway effects 71–75
    - bronchial hyperresponsiveness 74–75
    - inflammatory cells 73–74
    - secretions 72
    - smooth muscle 71–72
    - vascular 72–73
  - antagonists 77–78
  - cellular origin 70
  - eosinophil generated 34
  - metabolism 70
  - microvascular leakage due to 29
  - receptors 71
  - release in asthma 75–76
  - synthesis 69–70
- polymorphonuclear leucocytes 178
  - prednisolone 247, 296
  - prednisone 244, 296
  - prodrugs 191
  - prophylactic anti-asthma drugs 261–280
  - prostaglandins 31, 61–65
    - airways effects 63–64
    - inflammatory 64
    - secretion 64
    - smooth muscle 63–64
  - receptors 63
  - role in asthma 64–65
  - D2 56 (table), 62–64
  - E1 63
  - E2 56 (table), 62, 63, 301
  - F2 56 (table), 61, 62, 64
  - G2 61
  - H2 61
  - I2 62
  - $\alpha_1$ -proteinase inhibitor 238
  - pulmonary veins 16
  - pyrilamine (mepyramine) 58
  - protein(s), anti-inflammatory 237, 238 (table)
  - protein kinase C 113–114
  - pyralazones 294–295
  - ranitidine 58, 59
  - renocortin 238 (table)
  - ritmeterol 188 (fig.), 191
  - salbutamol 35, 175–176, 190
    - adverse reactions 185–186
    - chemical structure 188 (fig.)
  - salicylates 292–294
  - salicylsalicylic acid (salsalate) 293
  - serotonin 56 (table), 85–86
  - SKF 96365 110–111
  - sodium salicylate 293
  - sputum examination 1–2
  - steroid-resistant asthma 247
  - steroid withdrawal syndrome 249
  - submucosal oedema 242

- substance P 18, 29, 56 (table), 155–157
- sulfinpyrazone 294
- sulphidopeptide leukotriene 29, 68
- surfactant 173–174
  
- tachykinins 155–157
- tartrazine 295
- T cells 39–42
  - lymphokines 28 (fig.)
  - natural killer activity 39
  - suppressor 39
- terbutaline 122, 190
  - adverse reaction 211
  - chemical structure 188 (fig.)
- tetodium salicylate 298
- 12-*O*-tetradecanoyl-phorbol-13-acetate 113
- theobromine 208
- theophylline 128, 130, 133, 182, 207–208
  - cardiac effects 218
  - maintenance treatment 212
  - T cell number/activity 217
  - tracheal relaxant action 127
  - unwanted effects 133
  - see also* alkylxanthines
- thiorphan 157
- thromboxanes 31, 56 (table)
  - A2 62–64
- tumour necrosis factor 239
- type 1 allergic reaction 36
  
- vasoactive intestinal peptide 154
- vasocortin 237, 238 (table)
- viral infection 19, 304–306
  
- wet nebulisers 192
  
- xanthines 207–221
  - chemistry 209–210
  - clinical use 211–215
    - acute severe asthma 211
    - chronic asthma 211–212
    - chronic obstructive pulmonary disorders 213–215
  - mode of action 215–220
    - airway anti-inflammatory 216–217
    - outside airway 217–218
    - smooth muscle relaxation/inhibition 213–214
    - subcellular mechanisms 218–219
  - subdivision 209–210
  - see also* alkylxanthines
  
- zymosan 178

---

# ***Handbook of Experimental Pharmacology***

Editorial Board: G. V. R. Born, P. Cuatrecasas, H. Herken

---

Volume 56

## **Cardiac Glycosides**

Part 1: **Experimental Pharmacology**

Part 2: **Pharmacokinetics and Clinical Pharmacology**

Volume 57

## **Tissue Growth Factors**

Volume 58

## **Cyclic Nucleotides**

Part 1: **Biochemistry**

Part 2: **Physiology and Pharmacology**

Volume 59

## **Mediators and Drugs in Gastrointestinal Motility**

Part 1: **Morphological Basis and Neurophysiological Control**

Part 2: **Endogenous and Exogenous Agents**

Volume 60

## **Pyretics and Antipyretics**

Volume 61

## **Chemotherapy of Viral Infections**

Volume 62

## **Aminoglycoside Antibiotics**

Volume 63

## **Allergic Reactions to Drugs**

Volume 64

## **Inhibition of Folate Metabolism in Chemotherapy**

Volume 65

## **Teratogenesis and Reproductive Toxicology**

Volume 66

Part 1: **Glucagon I**

Part 2: **Glucagon II**

Volume 67

Part 1: **Antibiotics Containing the Beta-Lactam Structure I**

Part 2: **Antibiotics Containing the Beta-Lactam Structure II**

Volume 68

## **Antimalarial Drugs**

Part 1: **Biological Background, Experimental Methods and Drug Resistance**

Part 2: **Current Antimalarias and New Drug Developments**

Volume 69

## **Pharmacology of the Eye**

Volume 70

Part 1: **Pharmacology of Intestinal Permeation I**

Part 2: **Pharmacology of Intestinal Permeation II**

Volume 71

## **Interferons and Their Applications**

Volume 72

## **Antitumor Drug Resistance**

Volume 73

## **Radiocontrast Agents**

Volume 74

## **Antiepileptic Drugs**

Volume 75

## **Toxicology of Inhaled Materials**



---

# ***Handbook of Experimental Pharmacology***

Editorial Board: G. V. R. Born, P. Cuatrecasas, H. Herken

---

Volume 76  
**Clinical Pharmacology of Antiangial Drugs**

Volume 77  
**Chemotherapy of Gastrointestinal Helminths**

Volume 78  
**The Tetracyclines**

Volume 79  
**New Neuromuscular Blocking Agents**

Volume 80  
**Cadmium**

Volume 81  
**Local Anesthetics**

Volume 82  
**Radioimmunoassay in Basic and Clinical Pharmacology**

Volume 83  
**Calcium in Drug Actions**

Volume 84  
**Antituberculosis Drugs**

Volume 85  
**The Pharmacology of Lymphocytes**

Volume 86  
**The Cholinergic Synapse**

Volume 87  
Part 1: **Pharmacology of the Skin I**  
Part 2: **Pharmacology of the Skin II**

Volume 88  
**Drugs for the Treatment of Parkinson's Disease**

Volume 89  
**Antiarrhythmic Drugs**

Volume 90  
Part 1: **Catecholamines I**  
Part 2: **Catecholamines II**

Volume 91  
**Microbial Resistance to Drugs**

Volume 92  
**Insulin**

Volume 93  
**Pharmacology of Antihypertensive Therapeutics**

Volume 94  
Part 1: **Chemical Carcinogenesis and Mutagenesis I**  
Part 2: **Chemical Carcinogenesis and Mutagenesis II**

Volume 95  
Part 1: **Peptide Growth Factors and Their Receptors I**  
Part 2: **Peptide Growth Factors and Their Receptors II**

Volume 96  
**Chemotherapy of Fungal Diseases**

Volume 97  
**Histamine and Histamine Antagonists**

