
Index

- acetylcholine
 bone blood flow response 132, 133, 136, 137
 synovial blood flow response 47–9
- achondroplasia 30
- acid phosphatase 122, 123
- acro-osteolysis 82
- activator protein 1 (AP-1) 10, 11, 89
- adjuvant-induced arthritis 16, 63
 NOS inhibitors 64, 65–6, 72
 selective COX-2 inhibitors 73
 synovial blood flow 48–9
- alkaline phosphatase 109
- alveolitis, pulmonary 15
- aminoguanidine 12
 allograft survival and 14
 bone metabolism and 119
 in experimental arthritis 64, 66
 in experimental diabetes 15
 in experimental inflammation 75
- angiotensin II 43
- animal models of arthritis, *see* experimental models of arthritis
- apoptosis
 articular chondrocytes 98
 osteoblasts 110
 osteoclast progenitors 118
- L-arginine 3, 4, 11
 effects on lymphocytes 12
 synovial blood flow and 47, 48
- argininosuccinate synthetase 11
- arthritis
 infective 81
 inflammatory, *see* inflammatory arthritis
 see also osteoarthritis; rheumatoid arthritis
- aseptic loosening of hip prostheses, *see* hip prostheses, aseptic loosening
- athletes 141
- ATP production 98
- autoimmune diseases 15, 53
- blood flow
 bone, *see* bone blood flow
 synovial joint 41–50
 bone
- allograft preservation 137
- biology 21–37
- disease, role of NO 119–20
- erosions in rheumatoid arthritis, *see*
 rheumatoid arthritis, bone erosions/
 synovitis
- fluid flow, *see* fluid flow, in bone
- growth 22
- matrix proteins 22
- organ cultures, mechanical loading 154–6
- vascular anatomy 129–30, 131
- bone blood flow 129–39
 adrenergic control 130–2
 anatomical basis 129–30, 131
 endothelial-dependent control 132–3
 mechanical influences 163
 pathophysiology 136–8
 role in bone physiology 133–5, 141–2
- bone cells
 cultured, mechanical responses 156–8, 174,
 175–6
 cytokine production 25
 differentiation and function 22–7
 effects of NO 117–19
 fluid flow responses 157, 175–6
 ion channels 163
 mechanical strain responses 154–64, 169–76
 NOS expression 116–17, 144, 154, 161–2
 NOS inhibition *in vivo* 162–3
 see also osteoblasts; osteoclasts; osteocytes
- bone formation 23, 105
 effects of NO 118
 mechanical strain inducing 152, 158, 169,
 170–6
 venous pressure and 134–5
 see also bone resorption
- bone marrow stromal cells 25, 26, 116
- bone metabolism 21–2
 effects of NO 119
 regulation in health and disease 34–6
 regulatory factors 24, 27–33
 role of microcirculation 133–4
- bone morphogenetic proteins (BMPs) 23, 25,
 32, 85

- bone remodelling 21, 22, 27, 84
 fluid flow-mediated 143–4, 146
 mechanically induced 151–2
see also bone formation; bone resorption
- bone resorption 23, 105
 around hip prostheses 178–82
 factors affecting 24, 84–7
 linking (coupling) to formation 25–7, 105
 mechanical strain effects 151–2
 oestrogen lack and 137
 phase 122, 124
 reactive oxygen species and 85, 86–7,
 90–1, 92
 role of NO 92, 117–18, 123–5
 uncoupling from formation 93
- Borrelia burgdorferi*, murine 63, 64
- brachypodism 32
- bradykinin 85
- calcitonin 85, 123–4, 146
- calcitonin gene-related peptide (CGRP) 44–5,
 82, 130
 in fracture healing 138
- calcium
 concentration, NOS activity and 8, 11
 intracellular, in osteoclasts 122, 123–4
 metabolism, regulation 21
- calcium channels, voltage-gated 163
- calmodulin 3, 8
- capillaries
 in bone 130
 pressure, bone formation and 134–5
- carrageenan injection models
 knee joint 44, 47–8
 rat paw 71, 72–3, 74–5
 rat subcutaneous air pouch 72, 75
- cartilage
 matrix, effects of NO 65, 96–7
 NO production 61–3, 95–6
 in arthritis 98–9
 regulatory factors 24, 27–33
see also chondrocytes
- cartilage-derived morphogenetic proteins
 (CDMPs) 23, 32
- chondrocytes
 effects of NO 97–8
 NO and COX interactions 45
 NO synthesis 42, 95–6
 in arthritis 55, 61–3
see also cartilage
- L-citrulline 3, 4
- eNOS, *see* constitutive nitric oxide synthase
- collagen-induced arthritis 53, 63
 NOS inhibitors 64, 66
- collagen synthesis 97, 170–1
- collagenase (MMP-1) 27, 89
- colony-stimulating factors (CSFs) 23, 24, 25,
 28–9
 bone resorption and 85, 86
- complement, NO interaction 15
- constitutive nitric oxide synthase (eNOS) 8, 107
 in bone cells 144, 154, 161–2, 182
 in experimental inflammation 71
 in immune responses 9
 mechanical stimuli activating 158, 173
see also endothelial nitric oxide synthase
 (eNOS); neuronal nitric oxide synthase
 (nNOS)
- corticosteroids, *see* glucocorticoids
- COX, *see* cyclooxygenase
- cyclic AMP (cAMP), fluid shear stress and 144
- cyclic GMP (cGMP) 5, 41
- cyclooxygenase (COX) 70
 constitutive isoform (COX-1) 70
 activation by NO 75, 76–7
 hypoxia-mediated induction 88
 inducible isoform (COX-2) 33, 70–1
 activation by NO 73–5, 76, 77, 111–12
 in experimental inflammation 72–3, 74–5
 inhibition of induction by NO 97–8
 loosening of hip prostheses and 181–2
 mechanical stimuli inducing 172
 selective inhibitors, *see* non-steroidal anti-
 inflammatory drugs (NSAIDs), COX-2-
 selective
 NO interactions 71, 73–7, 111–12
 synovial blood flow and 45
- cytochrome *c* oxidase 5
- cytochrome P450 reductase 3, 8
- cytokines 5
 actions on bone cells 107, 108, 117
 bone formation and 23
 bone resorption and 23, 84–6, 92
 gene polymorphisms 34
 hypoxia-mediated release 88
 iNOS activation 9, 11
 in loosening of hip prostheses 180
 NO effects on production 13
 NO as mediator of effects 116–20
 oestrogen interactions 35–6
 production by bone cells 25
 receptors 34
 regulating bone and cartilage 24, 27–33
 in rheumatoid arthritis 58
 systemic vs local effects 34–5
see also specific cytokines
- dexamethasone 72, 76
- dextran-induced oedema in rat skin/paw 71
- diabetes mellitus, insulin-dependent (IDDM) 15
- 1,25-dihydroxy vitamin D 25, 84, 85, 117
- diphenylene iodonium chloride (DPI) 64
- eicosanoids 33
- electrokinetic migration 144
- endothelial cells
 fluid flow responses 146, 158–9
 ion channels 163
 in ischaemia/reperfusion injury 136, 137
 oestrogen receptors 137
 prostaglandin release 152–3
 in rheumatoid arthritis 88
 synovial, NO production 63
- endothelial nitric oxide synthase (eNOS) 3, 4, 8
 in bone cells 108, 116–17, 161–2, 164
 in bone–hip implant interaction 182

- expression 4–5
- in fracture healing 138
- in inflammation 70
- knock-out mice 164
- in osteoclastic bone resorption 122, 124
- regulation of activity 11
- endothelial permeability 12, 71
- endothelin-1 58
- endothelium-derived relaxing factor (EDRF) 8, 12, 41
- endotoxin, *see* lipopolysaccharide
- eNOS, *see* endothelial nitric oxide synthase
- epidermal growth factor 85
- experimental allergic encephalomyelitis (EAE) 15, 53
- experimental models of arthritis 16, 53, 61–7, 119
 - NO production 61–5, 72
 - NOS inhibitors 64, 65–7, 72
 - role of NO in pathophysiology 65
 - synovial blood flow 44, 47–9
- fibroblast growth factors (FGF) 23, 25, 30, 85
- fibroblasts
 - COX-2/NO interactions 74
 - synovial
 - NO synthesis 42, 56, 63
 - in rheumatoid arthritis 87–8
- fibronectin, chondrocyte interactions 98
- fluid flow
 - in bone 142–3, 174
 - hormonal control 145–6
 - bone cell responses 157, 175–6
 - bone remodelling and 143–4
 - shear stress induced by, *see* shear stress, fluid flow-induced
 - vs* mechanical strain 147, 175–6
- c-fos* 89, 146
 - activation by NO 173
 - mechanically induced expression 170, 171–2
- fracture repair 134, 138, 141–2
- G proteins 145
- giant cells, foreign body 179
- glucocorticoids 85
 - in experimental inflammation 72, 76
 - hip prosthesis loosening and 182
 - regulation of iNOS 11
 - in rheumatoid arthritis 66, 82
- glucose 6-phosphate dehydrogenase (G6PD) 152–3, 159–60, 162–3, 173
- gout 55
- graft rejection 14–15
- graft versus host disease (GVHD) 15–16
- granulocyte-macrophage colony-stimulating factor (GM-CSF) 28–9, 36, 85, 86
- granulomas, foreign body 179
- growth factors
 - receptors 34
 - regulating bone and cartilage 24, 25, 27–33, 85
- GTP cyclohydroxylase I 11
- guanylyl cyclase 4, 5, 111
- haem 3–4, 5
- haemoglobin 6
- Haversian canals 130
- head-down tilt 142, 156–7
- hemiplegia 82
- heparin 85
- hip prostheses, aseptic loosening 178–82
 - cytokines and NO mediating 180
 - future developments 182
 - iNOS and COX-2 181–2
 - proposed model 182
 - pseudomembrane formation 179
 - wear debris and 179–80
- Howship's lacunae 90
- hydrochloric acid 122, 123
- hydrogen peroxide 91, 92, 180
- hydronephrosis, experimental 72, 75
- 15-hydroperoxyicosatetraenoic acid 159
- hydroxyl radical 74, 93
- hypercalcaemia of malignancy 32
- hypoxia
 - in rheumatoid joints 87
 - role in rheumatoid erosions 83, 87–91
 - xanthine oxidoreductase upregulation 92
- hypoxia-inducible factor (HIF) 88, 92
- hypoxia-response elements 10, 88, 89
- IFN- γ , *see* interferon- γ
- IFN- γ -related transcription factor-1 (IRF-1) 10
- IGFs, *see* insulin-like growth factors
- immune-complex-mediated disease 15–16
- immune responses 8–16, 65
 - in vivo*, NO and 13–16
 - NOS regulation during 9–12
- indomethacin 76
 - in experimental arthritis 66
 - hip prosthesis loosening and 182
 - mechanical strain and 152, 159, 172, 173
- inducible nitric oxide synthase (iNOS) 3–4, 107
 - activating factors 9
 - in acute and chronic inflammation 70, 71
 - in bone cells 107, 116–17, 154, 161–2
 - cells expressing 5, 8–9
 - in chondrocytes 96
 - constitutive expression 5, 10
 - in experimental arthritis 72
 - in experimental inflammation 71, 74–5
 - in fracture healing 138
 - gene promoter/enhancer sites 10–11, 89
 - in human arthritides 55–6, 57, 62, 99, 109
 - inhibitory agents 10
 - knockout mice 14, 65, 72
 - loosening of hip prostheses and 180, 181–2
 - mRNA stability 11
 - post-translational regulation 11
 - regulation of expression 9–12
 - in rheumatoid arthritis 54, 89, 92, 119
 - selective inhibition 76, 182
 - in synovial joints 42
- infections, immune responses to 13–14
- infective arthritis 81
- inflammation
 - NO and prostaglandin interactions 70–7

- inflammation (cont.)
 NOS regulation during 9–10
 role of NO 12, 65
- inflammatory arthritis 41–50
 experimental models, *see* experimental models of arthritis
 human, NO production 53–8, 61, 62, 71–2, 109
 role of NO in pathophysiology 65
see also osteoarthritis; rheumatoid arthritis
- inflammatory bowel disease (IBD) 15–16
- iNOS, *see* inducible nitric oxide synthase
- insulin like growth factor I (IGF-I) 23, 30
 gene, mechanically induced expression 170–3
- insulin-like growth factor II (IGF-II) 23, 30, 160
- insulin-like growth factors (IGFs) 25, 30, 85
- integrins, in rheumatoid arthritis 88
- interferon- γ (IFN- γ)
 actions on bone/cartilage 29–30, 86
 actions on osteoblasts 108, 109
 iNOS induction 9, 10
 NO effects on production 13
 regulation of iNOS expression 10, 11
- interleukin 1 (IL-1)
 actions on bone/cartilage 27, 29, 85, 86, 118
 actions on osteoblasts 108, 109, 110
 β (IL-1 β), iNOS regulation 9, 11
 chondrocyte responses 95, 96
 IL-6 induction 28
 in loosening of hip prostheses 180
 oestrogens and 35, 36
 in rheumatoid erosions 88–9, 92, 119
- interleukin 1 receptor antagonist (IL-1 ra) 27–8
- interleukin 2 (IL-2) 86
- interleukin 3 (IL-3) 86
- interleukin 4 (IL-4) 10, 11, 86
 NO effects on production 13
- interleukin 6 (IL-6) 23, 25
 actions on bone and cartilage 28, 85, 86
 effects of NO on production 97, 118
 oestrogens and 36, 137
- interleukin 8 (IL-8) 86
- interleukin 10 (IL-10) 10, 88
- interleukin 11 (IL-11) 23, 25, 85, 86
- interleukin 12 (IL-12) 16
- intraosseous vascular pressure 130, 141–2
- ion channels, bone cells 163
- ischaemia/reperfusion injury
 in bone 136–7
 in rheumatoid joints 87
- joints, synovial
 blood flow 41–50
 effects of inflammation 47–9
 regulation 42–5
 sites of NO synthesis 42, 43, 61–3
 sympathetic-mediated vasoconstriction 45–6, 47
- c-jun* 89
- lactic acid 98
- LAP (latency associated protein) 32
- laser Doppler perfusion imaging 47, 48
- Leishmania major* infections 13, 14
- leukocytes, synovial, NO production 42, 63
- leukotrienes 33
- lipopolysaccharide (LPS, endotoxin) 5, 9, 14
 actions on osteoblasts 108
 COX-2 induction 73
 IL-6 induction 28
 iNOS induction 73
- locomotion
 fluid shear stress 146
 mechanical strain effects 151
 long-term potentiation/depression 153–4, 164
- Lyme disease, murine 63, 64
- lymphocytes 88
see also T lymphocytes
- macrophage colony-stimulating factor (M-CSF) 29, 85, 86
- macrophages
 COX-2/NO interactions 73
 cytokine production 13
 iNOS expression 8, 9
 loosening of hip prostheses and 179, 180, 181
 NO-dependent activity 13–14
 regulation of iNOS expression 10
 in rheumatoid arthritis 88
- matrix metalloproteinases (MMPs) 27, 97, 119
- mechanical strain 34, 151–64, 169–76
 adaptive bone responses 141, 151–2, 169
 cultured bone cells 156–8, 174, 175–6
 fluid flow induced by 143, 174
 hip prosthesis-associated 181–2
 NO production induced by 135, 154–64, 173
 bone cells responsible for 160–3
 by non-load-bearing bones 160
 prostaglandin production and 159–60, 173
 NOS expression and 108, 161–2
 prostaglandin production and 152–3, 159–60, 172–3, 174
 rat tail vertebra model 170
 vs fluid flow 147, 175–6
- mechanotransduction 145, 152, 170–3
- M-CSF, *see* macrophage colony-stimulating factor
- memory, strain 153–4, 157, 164
- metalloproteinases, matrix (MMPs) 27, 97, 119
- metaphyseal dysplasia, Jansen type 33
- methylene blue 74
- MMPs, *see* matrix metalloproteinases
- mononuclear cells, peripheral blood
 cytokine production 13
 NO production, in arthritis 54, 63
- MRL-*lpr/lpr* mice 16, 53, 63, 72
 NOS inhibitors 64
- c-myc* 89
- NADPH 3, 173
- L-NAME (L-*N*^ω-nitro-L-arginine methylester)
 in experimental arthritis 64, 66
 in experimental bone ischaemia 136
 in experimental inflammation 71
in vivo effects on bone cells 162
 mechanical loading responses and 173

- synovial blood flow and 43–4, 46, 47, 48
- natural killer (NK) cells 12, 14
- nerves
- in fracture healing 138
 - perivascular, in bone 130
 - rheumatoid erosions and 82
 - synovial, NO production 46
- neuronal nitric oxide synthase (nNOS) 3, 4, 8
- in bone cells 108, 116, 117, 144, 161–2
 - expression 4–5
 - novel form, in osteoarthritic joints (OA-NOS) 9, 63, 96
 - regulation of activity 11
 - in synovial joints 42, 46
- neuropeptides 24, 82, 130
- neutrophils 12, 88
- NF-IL6 10
- NF- κ B 10–11, 89, 97
- L-NIL (*N*-iminoethyl-L-lysine) 12
- in experimental arthritis 64, 66, 72
 - in experimental inflammation 71, 74–5
- nitrate:creatinine ratio, urinary 54
- nitrate, urinary, in arthritis 54, 72
- nitric oxide (NO)
- synthesis, *see* synthesis of NO
 - targets 5
 - transport 6
- nitric oxide (NO) metabolites
- serum, in arthritis 41, 54, 62
 - synovial fluid, in arthritis 41, 55, 62
 - urinary, in arthritis 54, 62, 72
- nitric oxide synthase (NOS) 3
- in bone cells 116, 144, 154, 161–2
 - constitutive isoforms (cNOS), *see* constitutive nitric oxide synthase
 - endothelial isoform (eNOS), *see* endothelial nitric oxide synthase
 - inducible isoform (iNOS), *see* inducible nitric oxide synthase
 - isoforms 3, 4–5, 8–9, 107
 - neuronal isoform (nNOS), *see* neuronal nitric oxide synthase
 - novel form, in osteoarthritic joints (OA-NOS) 9, 63, 96
 - in osteoblasts 108–9, 116–17
 - regulation in immune responses 9–12
- nitric oxide synthase (NOS) inhibitors 11–12
- actions on osteoblasts 108, 109, 112
 - adverse effects of non-selective 75, 76
 - in experimental arthritis 64, 65–7, 72
 - in experimental inflammation 71, 72
 - in vivo* effects on bone cells 162–3
 - isoform-specific 11–12, 76, 182
 - mechanical loading responses and 155, 173
 - prostaglandin release inhibition 73, 74–5
 - therapeutic potential 67
- nitrite
- production
 - in arthritis 55
 - osteoblasts 106, 107–8
 - serum, in arthritis 54, 72
 - synovial fluid, in arthritis 55, 61, 72
- nitrogen species, reactive
- bone resorption and 85, 86–7, 92–3
 - see also* peroxynitrite
- S-nitroso-acetylpenicillamine (SNAP) 56, 112
- nitroglutathione 6, 57
- nitrosothiols 6
- 3-nitrotyrosine
- loosening of hip prostheses and 181
 - serum, in arthritis 54, 72
 - synovial fluid, in arthritis 55, 72
- L-NMMA (*L*-*N*^ω-methylarginine) 11–12
- in experimental arthritis 53, 64, 66, 72
 - in experimental inflammation 71
 - in vivo* effects on bone cells 162
 - mechanical loading responses and 159, 173
 - synovial blood flow and 46
- L-NNA (*L*-*N*^ω-nitroarginine) 11–12, 112
- nNOS, *see* neuronal nitric oxide synthase
- non-obese diabetic (NOD) mouse 15, 53
- non-steroidal anti-inflammatory drugs (NSAIDs) 33
- COX-2-selective
 - in experimental arthritis 73
 - in experimental inflammation 72, 73
 - hip prosthesis loosening and 182
 - in experimental inflammation 72–3
 - in rheumatoid arthritis 83, 88
- noradrenaline
- bone blood flow and 130–2, 133
 - synovial blood flow and 45–6, 47
- NOS, *see* nitric oxide synthase
- nutrient artery 129
- oedema, inflammatory 71
- oestradiol 137
- actions on osteoclasts 123–4
- oestrogens
- cytokine interactions 35–6
 - receptors in bone 35, 137
- oophorectomy 125, 137
- op/op* mouse 29
- orthopaedic implant failure 141, 178–82
- osteoarthritis (OA) 81
- excessive NO production 54, 55, 62, 72, 98–9
 - novel form of NOS (OA-NOS) 9, 63, 96
 - synovial iNOS expression 56, 57
- osteoblasts 21, 84, 105–12
- cytokine production 25
 - differentiation 23, 29
 - effects of NO 109–10, 118
 - factors affecting 31
 - fluid flow effects 143, 144–6, 147, 157–8, 175–6
 - function 22, 23
 - in vivo* effects of NOS inhibitors 162–3
 - ion channels 163
 - load-related NO production 159–60, 161
 - load-related prostaglandin production 159–60
 - in loosening of hip prostheses 180, 181–2
 - mechanisms of NO actions 110–12
 - NO production 106, 107–10
 - NOS expression 108–9, 116–17, 162
 - osteoclast interactions 25–7, 91
- osteocalcin 109, 170–1

- osteoclast-activating factors (OAFs) 27
- osteoclasts 21, 84, 122–5
 cyclic activity 122, 124
 differentiation 23, 25, 26, 29, 118
 effects of NO 117–18, 123–4
 fluid flow effects 143–4
 function 22, 23, 26
 in loosening of hip prostheses 180
 mechanisms of bone resorption 90, 91
 NOS expression 116, 117
 osteoblast interactions 25–7, 91
see also bone resorption
- osteocytes
 fluid flow effects 143, 157–8, 175–6
in vivo effects of NOS inhibitors 162–3
 ion channels 163
 NOS expression 116, 162
 responses to mechanical loading 169,
 175–6, 181
 induced gene expression 170–2
 NO production 159–60, 161, 164, 173
 prostaglandin production 159–60, 172–3
- osteogenesis, *see* bone formation
- osteopontin 89, 147
- osteoporosis
 disuse 141
 pathogenesis 22, 35–6, 137
 possible therapeutic strategies 36
 postmenopausal 125, 137, 164
- osteosarcoma cells
 effects of NO 109
 NO production 106, 107–8
- ovariectomy 125, 137
- oxidants 89
- oxidative respiration 5
- oxygen-derived free radicals
 bone resorption and 85, 86–7, 90–1
 chondrocyte apoptosis and 98
 COX-2 activation 74
 in rheumatoid bone erosions 90–3
see also peroxynitrite; superoxide
- Paget's disease 27
- pannus 87–8
- parallel plate flow chamber 175
- parathyroid hormone (PTH) 23, 84, 117
 bone resorption and 25, 26, 84, 85
 fluid flow and 145–6
- parathyroid hormone-related peptides (PTH-RP)
 23, 32–3
- periosteal arteries 129–30
- peroxynitrite (ONOO⁻) 5, 71, 98
 in COX-2 activation 74
 cytotoxicity 110
 loosening of hip prostheses and 180
 in rheumatoid erosions 92–3
- phosphorylation, NOS isoforms 11
- plasminogen activator (PA) 26, 32
- plasminogen activator inhibitor (PAI) 32
- plasticity, signalling 153–4, 164
- platelet aggregation 12, 75
- platelet-derived growth factor (PDGF) 23, 25, 85
- poliomyelitis 82
- polymethylacrylate particles 179, 180
- posture maintenance 146
- potassium perchromate (K₃CrO₈)-induced
 arthritis 63, 64
- prednisolone 66
- prolyl hydroxylase 97
- prostacyclin (PGI₂) 153
 actions on bone 33
 fluid flow-induced release 157
 load-related release 152, 159–60
- prostaglandin E₂
 actions on bone 33, 85
 effects of NO on production 97–8
 fluid flow-induced production 145, 157
 load-related release 152, 153, 159–60
 loosening of hip prostheses and 180
 release by osteoblasts 112
- prostaglandins 25
 actions on bone 33, 86
 in experimental inflammation 72–3
 fluid flow-induced release 157, 175
 inhibition by NOS inhibitors 73, 74–5
 load-related release 152–3, 159–60, 172–3,
 174
 NO interactions in inflammation 70–7
 osteoblast production 111–12
 synovial blood flow and 42–3, 45
see also prostacyclin; prostaglandin E₂
- protein kinase, cAMP-dependent 11
- proteoglycans, cartilage 96–7
- pseudomembrane, loosened hip prostheses 179
- RA, *see* rheumatoid arthritis
- rat caudal vertebrae 155–6, 170, 172
- rat ulnar explants 155
- reperfusion, in rheumatoid joints 87
- rheumatoid arthritis (RA) 16, 41, 53
 bone erosions/synovitis 81–93
 movement and 82
 pathophysiology 84–93
 sites 81–2
 symmetry of distribution 82
 therapeutic intervention 82–4
 excessive NO production 41, 54–8, 62, 72,
 98–9
 glucocorticoid therapy 66, 82
 role of NO in pathophysiology 65, 67, 119
 synovial iNOS expression 55–6, 57, 63
 typus robustus arthritis 82
- sensory nerves, bone and periosteum 130
- septicaemia 13–14
- shear stress, fluid flow-induced 141–7, 156–7,
 174
 hip prosthesis-associated 181–2
 mediating bone remodelling 143–4, 146
 sensitivity to 146
 signal transduction 145
 vs streaming potentials 144–5
- sodium nitroprusside 47
- space flight 134–5
- c-src* 89
- Staphylococcus aureus* infections 13, 14

- steroids, *see* glucocorticoids; oestrogens
 'strain memory' concept 153–4, 157, 164
 streaming potentials 143, 144–5, 174
 streptococcal cell wall (SCW)-induced arthritis
 16, 53, 63
 NOS inhibitors 64, 65–6
 streptozotocin-induced diabetes 15
 stretch-shear cation channels 163
 stromelysin (MMP-3) 27, 32, 89
 subchondral cysts 81, 82
 substance P 44–5, 48, 82, 130
 superantigens, bacterial 9, 10, 14
 superoxide
 bone resorption and 90, 91, 180
 NO interaction 92, 98
 sympathetic nerves
 bone and periosteum 130
 vasoconstriction mediated by 45–6, 47,
 130–2
 synovial cells, type A 55
 synovial joints, *see* joints, synovial
 synovial tissue
 hypoxia, in rheumatoid arthritis 87–8
 NO production, in arthritis 55–6, 63
 synoviocytes, NO synthesis 42
 synovitis 81
 rheumatoid, *see* rheumatoid arthritis, bone
 erosions/synovitis
 synthesis of NO 3–4
 in cartilage 61–3, 95–6
 in osteoblasts 106, 107–10
 in synovial joints 42, 43, 61–3
 T helper type 1 (T_H1) cells 12–13, 65
 in rheumatoid arthritis 88
 T helper type 2 (T_H2) cells 13, 65
 T lymphocytes
 loosening of hip prostheses and 179
 NO effects on activation 12–13, 65
 regulation of iNOS expression 10
 in rheumatoid arthritis 88
 tetrahydrobiopterin 11
 thrombin 85
 thyroid hormones 85
 tibia, isolated perfused rabbit 132–3, 136–07
 tissue inhibitors of metalloproteinases
 (TIMPs) 32
 TNF, *see* tumour necrosis factor
 transforming growth factor β (TGF β) 10
 actions in bone/cartilage 30–2, 85, 86, 96
 regulation of iNOS expression 11
 in rheumatoid arthritis 88
 superfamily 23, 25
 transgenic animals 35
 tumour necrosis factor (TNF) 28, 29
 oestrogens and 35–6
 soluble receptors (p55 and p75) 28
 tumour necrosis factor α (TNF α) 9
 actions in bone/cartilage 28, 85, 86, 118
 actions on osteoblasts 108, 109
 in loosening of hip prostheses 180
 NO effects on production 13
 regulation of iNOS expression 11
 in rheumatoid arthritis 16, 88–9, 92
 tumour necrosis factor β (TNF β) 28
 tumours, iNOS expression 8–9
 turkey ulna model 146, 147
 vascular endothelial growth factor (VEGF) 88
 vascular permeability 12, 71
 vasoconstriction, sympathetic-mediated 45–6,
 47, 130–2
 vasodilatation, NO-induced 12, 41
 in acute and chronic inflammation 71
 in bone 132–3
 in synovial joints 43–4, 47–9
 venous pressure, bone formation and 134–5
 venous stasis, fracture repair and 141–2
 vitamin A 85
 wear debris, hip prostheses 179–80, 181
 weightlessness 134–5
 xanthine oxidoreductase (XOR) 89, 91–2, 93