

# Index

- acute stroke 5, 104–11  
 cerebral hemodynamic changes 106–8, 111  
 CPAP therapy 108–9, 110, 123  
 deterioration 104–5  
   pathogenic mechanisms 106–8  
   predictors 106  
   sleep apnea predicting 105–8, 133–5  
 intracranial arterial blood steal 107–8  
 management of sleep apnea 109–10, 135–6  
 noninvasive ventilation 108–9  
 oxidative stress 16  
 sleep apnea prevalence 128, 129, 130  
 vascular inflammation/oxidized LDL 17
- adenotonsillectomy  
 blood pressure after 56, 58  
 pulmonary artery pressure after 59
- adhesion molecules 22–3
- affective disorders, restless legs syndrome and 147–8
- age differences  
 hypertension and sleep apnea association 52  
 patent foramen ovale incidence 85–6  
 stroke and patent foramen ovale association 86–7
- airway obstruction  
 pathophysiological effects 99  
 sleep apnea, mechanisms 98
- amnesia, transient global 88
- angiotensin II (Ang II) 19
- antioxidant activity, reduced 14
- antithrombotic therapy 93
- anxiety, restless legs syndrome and 147–8
- apnea/hypopnea index (AHI) 12  
 cardiovascular disease risk and 65  
 hypertension risk and 52  
 stroke patients 127–31, 133–4  
 stroke risk and 12, 65, 67, 131–3
- arousals  
 mechanisms 71–6  
 personal story of stroke 152, 153  
 RLS/PLMS and 141, 145–6  
 stroke pathogenesis 71, 72–5  
 upper airway obstruction 3, 71–6, 99
- arrhythmias *see* cardiac arrhythmias
- arterial blood flow steal, intracranial 107–8, 110–11
- atherosclerosis 24–5  
 induction by oxidized LDL 17  
 intracranial atherosclerotic disease (IAD) 105
- atrial arrhythmias 87–8
- atrial fibrillation 3, 80–3  
 CPAP therapy and 5, 122  
 epidemiology 80–1  
 management 82–3  
 patent foramen ovale and 87–8  
 pathophysiology 81–2  
 stroke pathogenesis 70
- autonomic function  
 atrial fibrillation pathogenesis 81–2  
 effects of CPAP 55, 117  
 normal sleep 34–6, 48  
 RLS/PLMS 144–6  
 sleep apnea 2, 33–44, 48–9, 100  
 stroke pathogenesis 68–70, 75
- Bainbridge reflex 100
- baroreflex function 39–43, 100
- baroreflex sensitivity index (BRSI) 41–2
- Berlin questionnaire 53–4
- $\beta$ 2-integrins 22
- bilevel positive airway pressure (BiPAP), acute stroke 108–9, 110
- blood pressure (BP)  
 CPAP therapy and 5, 55–6, 116–19  
 nondipping 2, 37, 49, 53  
 normal sleep (dipping) 48, 49  
 RLS/PLMS and 145–6  
 sleep apnea 2, 36–8, 48–9, 100, 116  
 sleep duration and 147  
 variability 48–9  
*see also* hypertension
- C-reactive protein, high-sensitivity (hsCRP) 17–19
- Canadian Neurological Scale 104
- cardiac arrhythmias 70, 87–8  
*see also* atrial fibrillation
- cardiac consequences, sleep apnea 99–100
- cardiovascular disease (CVD)  
 RLS/PLMS and 139–48  
 epidemiology 140–4  
 possible mechanisms 144–8  
 sleep apnea and  
   autonomic mechanisms 33–44  
   proatherogenic mechanisms 26  
   protective mechanisms 25  
 risk factor status 11, 65, 131  
*see also* cerebrovascular disease; hypertension; stroke
- carotid body, oxygen sensing 41
- catecholamines 70, 100, 116
- CD40 ligand, soluble (sCD40L) 70

- central sleep apnea (CSA)  
 poststroke patients 130  
 stroke risk and 133
- cerebral hemodynamics  
 acute stroke deterioration 5,  
 106–8  
 sleep apnea 4–5
- cerebral ischemia  
 on awakening 92  
*see also* stroke; transient  
 ischemic attack
- cerebral protective mechanisms  
 25
- cerebral small-vessel disease 4,  
 97–102
- cerebral white matter lesions  
 patent foramen ovale  
 89–90  
 sleep apnea 98
- cerebrovascular disease  
 autonomic mechanisms  
 33–44  
 CPAP therapy and 122–4  
 proatherogenic mechanisms  
 11, 26  
 protective mechanisms 25  
*see also* stroke; transient  
 ischemic attack
- chemoreceptor reflexes 40–1,  
 99, 100
- Cheyne-Stokes breathing 130
- children *see* pediatric patients
- chronic kidney disease  
 139–40
- chronic obstructive pulmonary  
 disease (COPD) 89
- circadian rhythms  
 hormone levels 36  
 stroke timing and 70
- cognitive dysfunction 4, 97,  
 101–2
- continuous positive airways  
 pressure (CPAP) 5–6,  
 12, 115–24  
 acute stroke 108–9, 110, 123,  
 135–6  
 arousal threshold after 71  
 atrial fibrillation 5, 122  
 blood pressure changes after  
 5, 55–6, 116–19  
 glucose metabolism after  
 119–21  
 oxidative stress markers and  
 15  
 patent foramen ovale 92–3
- poststroke sleep apnea 6,  
 67–8, 135
- pregnancy 58
- pulmonary artery pressure  
 effects 59
- stroke occurrence after  
 122–4
- stroke risk factors and 5,  
 115–22
- coronary artery bypass surgery  
 80–1
- cortisol 36, 100, 146–7
- CPAP *see* continuous positive  
 airways pressure
- cytokines, proinflammatory  
 21–2
- daytime sleepiness *see* excessive  
 daytime somnolence
- decompression illness 88
- deep vein thrombosis (DVT)  
 87, 92, 154
- dementia 98, 102  
*see also* cognitive dysfunction
- depression, restless legs  
 syndrome and 147–8
- diabetes mellitus  
 restless legs syndrome and  
 144, 147  
 type 2, CPAP therapy  
 119–21
- diuretics 57
- dyslipidemia, CPAP therapy  
 121
- E-selectin 22
- ecstasy (methylenedioxy-  
 methamphetamine;  
 MDMA) 74–5
- edema, peripheral, treatment  
 56–7
- endothelial cells, adhesion  
 molecules 22–3
- endothelial dysfunction 23–4,  
 44
- endothelial progenitor cells  
 (EPCs) 24
- endothelin 100
- epinephrine (adrenaline) 100
- Epworth sleepiness scale (ESS)  
 53
- erythropoietin (EPO) 20
- European Cooperative Acute  
 Stroke Study (ECASS)  
 104
- excessive daytime somnolence  
 (EDS)  
 acute stroke deterioration  
 and 108  
 autonomic impairment 42–3
- factor V Leiden gene mutation  
 88
- fat embolism syndrome 89
- fatal familial insomnia 97
- fibrinogen 19
- fibrinolysis 19
- foramen ovale 85–6  
 patent *see* patent foramen  
 ovale
- four-variable screening tool 54
- gender differences, vascular  
 inflammation 18
- glucose metabolism, effects of  
 CPAP 119–21
- heart failure 57, 145
- heart rate (HR)  
 normal sleep 48  
 RLS/PLMS and 145–6  
 sleep apnea 36–7  
 variability 38–9, 146
- heart transplant recipients 145
- hemodynamic changes  
 sleep apnea 36–7, 48–9, 100  
*see also* blood pressure
- high-altitude pulmonary edema  
 (HAPE) 89
- high density lipoprotein (HDL)  
 dysfunction 17
- homocysteine, plasma levels  
 101
- hormones, during sleep 36
- hyperaldosteronism, treatment  
 56–7
- hypercapnia  
 arousal response 72–5, 99  
 sympathetic activation 41
- hypercholesterolemia, CPAP  
 therapy 121
- hypercoagulability 19, 102
- hypertension 2, 100  
 autonomic instability and  
 41–2, 49, 59, 116  
 baroreflex function and 41  
 daytime 49–50  
 daytime sleepiness and 43  
 effects of CPAP 5, 55–6,  
 116–19

- effects of OSA treatment 55–7  
 morning 49  
 nocturnal 49  
 obesity and sleep apnea 51  
 populations at risk 51–3  
 predictors of sleep apnea 51–5  
 pregnancy 57–8  
 resistant 50, 52, 57, 119  
 RLS/PLMS and 144–5  
   epidemiology 140–4  
   possible mechanisms 144–8  
   screening for OSA 53–5  
*see also* blood pressure  
 hypothalamic–pituitary–adrenal (HPA) axis, restless legs syndrome 146–7  
 hypoxemia  
   obstructive sleep apnea 99  
   patent foramen ovale 89  
 hypoxia  
   arousal response 76  
   intermittent *see* intermittent hypoxia  
 hypoxia-inducible factor-1 $\alpha$  (HIF-1 $\alpha$ ) 21
- inflammation, vascular 1–2, 16–23, 44, 101  
 inherited prothrombotic disorders 88  
 inspiration, respiratory 98  
 insulin resistance, effects of CPAP 119–21  
 integrins,  $\beta$ 2 22  
 intercellular adhesion molecule-1 (ICAM-1) 22  
 interleukin-6 (IL-6) 21  
 interleukin-10 (IL-10) 21–2  
 interleukin-12 (IL-12) 22  
 intermittent hypoxia (IH)  
   carotid body effects 41  
   endothelial progenitor cells 24  
   oxidative stress 14–16  
   proatherogenic mechanisms 11, 26  
   sympathetic activation 40–1  
   vascular inflammation 16, 20  
 International Restless Legs Syndrome Study Group (IRLSSG) 141, 144  
 intracranial arterial blood flow steal 107–8, 110–11  
 intracranial atherosclerotic disease (IAD) 105  
 intrathoracic pressure, fluctuations 82, 99–100  
 ischemia/reperfusion injury, oxidative stress 13–14  
 ischemic preconditioning (IPC) 11–25
- kidney disease, chronic 139–40
- L-selectin 22  
 lacunar stroke 98  
 lectin-like oxidized LDL receptor-1 (LOX-1) 17  
 left atrial enlargement 82, 100  
 left ventricular wall thickening/diastolic dysfunction 100  
 leptin 51, 101  
 leukocytes, adhesion molecules 22–3  
 lipid peroxidation 15  
 lipids, blood, effects of CPAP therapy 121  
 low density lipoprotein (LDL) 14–16  
   oxidized (oxLDL) 16–17
- melatonin 36  
 memory 97  
 metabolic syndrome  
   restless legs syndrome and 144  
   sleep apnea association 52, 54, 101  
   stroke pathogenesis 68  
 methylenedioxy-methamphetamine (MDMA; ecstasy) 74–5  
 migraine with aura 88  
 Mueller maneuver 2, 48, 92, 99  
 multi-infarct dementia 98  
 myocardial infarction 89
- NADPH oxidase 15  
 National Institutes of Health Stroke Scale (NIHSS) score 104–5  
 nitric oxide (NO) 13, 23, 24  
 nitrosative stress 13, 15  
 noninvasive ventilation  
   acute stroke 108–9, 110  
   *see also* continuous positive airways pressure  
 non-rapid eye movement (NREM) sleep  
   arousal response 71  
   autonomic function 34, 35–6  
 norepinephrine (noradrenaline) 38, 100, 116  
 nuclear factor-kappaB (NF- $\kappa$ B) 20
- obesity  
   C-reactive protein 18  
   insulin resistance and CPAP therapy 120  
   restless legs syndrome and 147  
   sleep apnea and 97, 101  
   sleep apnea and hypertension 51, 52, 54  
 obesity hypoventilation syndrome (OHS) 58–9  
 obstructive sleep apnea (OSA)  
   12–13  
   acute stroke deterioration and 105–8, 133–5  
   acute stroke patients 129, 130  
   arousal response *see* arousals  
   atrial fibrillation and 3, 80–3  
   autonomic changes 2, 33–44, 48–9, 100  
   cardiovascular risk 65, 131  
   cerebral small-vessel disease 4, 97–102  
   characteristics 12, 33–4  
   definition 12, 98  
   hemodynamic consequences 36–7, 48–9, 100  
   hypertension *see* hypertension  
   paradoxical embolism and 91–2  
   patent foramen ovale and 91–2  
   pathogenic mechanisms 99  
   proatherogenic mechanisms 11, 26  
   protective mechanisms 25  
   stroke patients *see* post-stroke sleep apnea  
   as stroke risk factor 12–13, 64–7, 90–1, 128, 131–3  
   treatment *see* treatment of obstructive sleep apnea  
 oral appliance (OA) therapy, blood pressure effects 56  
 OSA *see* obstructive sleep apnea  
 oxidative stress 13–16

- oxidative stress (cont.)  
 cardiovascular morbidity and stroke 16  
 intermittent hypoxia models 14–16  
 obstructive sleep apnea 1–2, 14–16  
 oxidized low density lipoprotein (oxLDL) 16–17  
 oxygen desaturation index (ODI) 12  
 acute stroke patients 133  
 oxygen saturation, minimal arterial (MinO<sub>2</sub>) 12
- P-selectin 22  
 soluble (sP-selectin) 70  
 paradoxical embolism 85  
 patent foramen ovale 85, 86, 87  
 peripheral and coronary artery 89  
 sleep apnea and 91–2  
 paraoxinase-1 (PON1) 14  
 parasympathetic activity, normal sleep 48  
 patent foramen ovale (PFO) 3, 85–93  
 association with stroke 86–7  
 pathogenesis of stroke 87–92  
 prevalence 85–6  
 sleep apnea and 91–2  
 therapeutic closure 93  
 pediatric patients  
 blood pressure effects of sleep apnea surgery 56  
 hypertension and sleep apnea 58  
 PLMS and hypertension 145  
 pulmonary hypertension 59  
 pelvic deep vein thrombosis 87  
 periodic limb movement (PLM) index 139  
 periodic limb movements during sleep (PLMS) 6, 139–48  
 cardiovascular disease and 139–48  
 pathophysiological effects 141, 144–8  
 periodic limb movements while awake (PLMW) 139  
 peripheral embolism 89  
 peroxides 14  
 physician, personal experience of stroke 7, 151–4
- plasminogen activator inhibitor-1 (PAI-1) 19  
 platelet activation 70  
 platypnea–orthodoxia syndrome 89  
 PLMS *see* periodic limb movements during sleep  
 poststroke sleep apnea 6, 105–8  
 pathophysiology 106–8, 111  
 predicting neurologic deterioration 105–8, 133–5  
 prevalence 127–31  
 treatment 6, 67–8, 135  
*see also* acute stroke  
 pramipexole 146  
 pregnancy 57–8  
 proinflammatory vascular risk factors 1–2, 16–23  
 prothrombin gene G20210A mutation 88  
 pulmonary edema, high-altitude (HAPE) 89  
 pulmonary embolism 89, 92, 154  
 pulmonary hypertension (PHT) 58–9, 92  
 pulse rate *see* heart rate
- rapid eye movement (REM) sleep  
 arousal response 71  
 autonomic function 35–6  
 stroke pathogenesis 70  
 reactive oxygen species (ROS) 13  
 mechanisms of production 13–14  
 sleep apnea and intermittent hypoxia models 15  
 renin 36  
 renin–angiotensin system 44  
 respiratory disturbance index (RDI), stroke patients 134  
 respiratory inspiration 98  
 respiratory polygraphy, acute stroke 109–11  
 restless legs syndrome (RLS) 1, 6, 139–48  
 cardiovascular disease and 139–48  
 epidemiological studies 140–4  
 pathophysiological mechanisms 144–8
- reversed Robin Hood syndrome (RRHS) 5, 107–8, 110  
 RLS *see* restless legs syndrome
- Scandinavian Neurological Stroke Scale 104  
 screening, obstructive sleep apnea 53–5  
 selectins 22  
 selective serotonin reuptake inhibitors (SSRIs) 74–5  
 serotonin system 73–5  
 sleep  
 autonomic function during 34–6, 48  
 during stroke rehabilitation 154  
 sleep apnea 1  
 autonomic alterations 2  
 prevalence 1, 11  
 stroke risk 3–4, 12–13  
*see also* central sleep apnea; obstructive sleep apnea  
 sleep deprivation/loss  
 arousal threshold and 71  
 cognitive effects 97  
 RLS and PLMS 147  
 Sleep Heart Health Study  
 cardiovascular disease and sleep apnea 90, 131  
 hypertension and sleep apnea severity 43, 50, 52  
 restless legs syndrome 144  
 sleep apnea and stroke risk 67, 132–3  
 sleep studies  
 acute stroke 109, 110  
 personal story of stroke 152, 153  
 smoking, restless legs syndrome and 144, 148  
 steal, intracranial arterial blood flow 107–8, 110–11  
 STOP/STOP-BANG questionnaire 54  
 stroke  
 acute phase *see* acute stroke  
 arousal phenomena and 71–6  
 on awakening 92  
 CPAP for prevention 122–4  
 cryptogenic 86, 87  
 endothelial dysfunction 23–4  
 endothelial progenitor cells 24

- lacunar 98  
 oxidative stress 16  
 patent foramen ovale and 86–92  
 pathogenic mechanisms 68–70  
 personal experience 7, 151–4  
 prevention 92–3  
 rehabilitation 6, 127–36  
   early sleep apnea therapy 135–6  
   effect of sleep apnea 133–5  
   a personal story 154  
 risk factors 64–76  
   effects of CPAP 5, 115–22  
   mechanisms of sleep apnea association 68–70  
   obstructive sleep apnea 3–4, 12–13, 64–7, 90–1, 128, 131–3  
   *see also* atrial fibrillation; hypertension; patent foramen ovale  
 RLS/PLMS and risk 6, 139  
 sleep apnea after *see* post-stroke sleep apnea  
 vascular inflammation 17, 19, 20, 21–2, 23  
 surgical treatment of  
   obstructive sleep apnea 98  
 blood pressure changes after 56  
 pulmonary artery pressures after 59  
*see also* adenotonsillectomy
- sympathetic overactivity  
 atrial fibrillation  
   pathogenesis 81–2  
 effects of CPAP 117  
 hypertensive effects 41, 116  
 obesity 51  
 RLS/PLMS 144–6  
 sleep apnea 2, 37, 39–42, 48, 100  
 stroke pathogenesis 68–70, 75  
 sympathetic skin responses (SSRs) 35  
 syndrome Z 52
- thermoregulation, during sleep 35–6  
 thiobarbituric acid-reactive substances (TBARS) 14  
 thrombosis 102  
   *see also* deep vein thrombosis  
 thrombotic disorders, inherited 88  
 thyroid stimulating hormone 36  
 TIA *see* transient ischemic attack  
 tongue, upper airway obstruction 98  
 tracheostomy 68  
 transcranial Doppler (TCD)  
   acute stroke 108, 110–11  
   intracranial arterial blood flow steal 107  
 transcription factors, redox-regulated 20  
 transesophageal echocardiography 85
- transient global amnesia 88  
 transient ischemic attack (TIA)  
   64–7  
   CPAP therapy and 122–3, 135, 136  
   sleep apnea prevalence after 127–9  
 travel, prolonged 92  
 treatment of obstructive sleep apnea 12  
   blood pressure effects 55–7  
   pulmonary artery pressure effects 59  
   stroke patients 67–8, 135–6  
   stroke prevention 92–3  
   *see also* continuous positive airways pressure  
 tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) 21
- Valsalva maneuver 39, 87, 91, 92  
 vascular cell adhesion molecule-1 (VCAM-1) 22  
 vascular endothelial growth factor (VEGF) 20  
 vascular inflammation 1–2, 16–23, 44, 101
- weight loss 68  
 Wisconsin Sleep Cohort Study 49, 50, 132  
 work of breathing, increased 76  
 xanthine oxidase 15