
Index

A

- Acetylcholine, 49, 86
- Acid-sensing ion channels (ASICs), 134
- Active standing test, 47, 48
- Acute painful diabetic neuropathy, 66
- AL amyloidosis, 85
 - clinical manifestation, 85
 - electrophysiology, 85, 86
 - pathogenesis, 86
 - pathology, 86
 - treatment and prognosis, 86
- Allodynia, 4, 36, 135
- Alloknesis, 5
- Alpha-synuclein, 143–145
- Ambroxol, 174
- American Diabetes Association, 60
- Amitriptyline, 168
- Amyloid, 20
- Amyloid neuropathy
 - AL amyloidosis, 85
 - clinical manifestation, 85
 - electrophysiology, 85, 86
 - pathogenesis, 86
 - pathology, 86
 - treatment and prognosis, 86
 - FAP
 - transthyretin, 87
 - TTR familial amyloid polyneuropathy, 87
 - skin denervation in, 92
- Amyloidosis, 84
- Amyotrophic lateral sclerosis (ALS), 40, 142, 145, 146
- Analgesic system, disturbance in, 167
- Anhidrosis, 5
- Anterior cingulate cortex (ACC), 156, 158
- Antidepressants, 7
- Antiepileptic drugs, 7
 - sodium channel blockers, 169, 170
 - voltage gated calcium channels, α 2 δ ligands of, 169
- Antisense oligonucleotide therapy, 94
- A β -fibers, 37
- Autoimmune diseases, 110
 - rheumatoid arthritis, 112
 - Sjögren's syndrome, 110, 111
 - SLE, 111

VGKC, 111, 112

- Autonomic function testing, 44
- Autonomic nervous system, 44
 - dysfunction, 142
- Autonomic neuropathy, 4, 62, 110

B

- Baroreflex sensitivity (BRS), 46
- β -pleated sheet, 84, 86
- Bladder pain syndrome/interstitial cystitis (BPS/IC), 132
- Blood pressure recovery time (PRT), 46
- Blood-oxygen-level dependent (BOLD), 157
- Botulinum toxin (BoNT)/A in detrusor overactivity, 136
- Brain stimulation therapies, 160
- Burning mouth syndrome, 135

C

- α 2 δ calcium channel ligands, 62
- Calcitonin gene related peptide (CGRP), 17
- Cannabinoid derivatives, 170, 171
- Cannabinoid receptor 1 (CB1), 136
- Capsaicin, 172, 173
- Carbamazepine, 169
- Carboplatin, 103
- Cardiac autonomic neuropathy (CAN), 64, 112
- Cardiovascular autonomic reflex testing
 - active standing test, 47, 48
 - head up tilt table testing, 47
 - heart rate variability with deep breathing, 44, 45
 - normative data, 44
 - testing method, 44
 - Valsalva maneuver, 45–47
- Carpal tunnel syndrome, 78
- Celiac disease, 112, 113
- Central nervous system, maladaptive plasticity, 155–157, 159
- Central nucleus of the amygdala (CeLC), 156
- Central sensitization, 133, 155–157, 167
- Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), 20, 147
- C-fibers, 4, 12, 17, 26, 37, 124, 125

- Channelopathy, 74, 174
 Charcot-Marie-Tooth disease (CMT disease), 74, 103
 Chemotherapy, 86, 94, 102
 Chemotherapy-induced peripheral neuropathy (CIPN), 101–103
 Chronic inflammatory demyelinating polyneuropathy (CIDP), 100, 101
 Complex regional pain syndrome (CRPS), 122
 Compound muscle action potential (CMAP), 68, 85, 91, 104
 Congenital insensitivity, 76
 Contact heat evoked potentials (CHEP), 26, 28, 29, 143, 154
 Contactin-associated protein-like 2 (CASPR2)-IgG, 111
 Corneal confocal microscopy (CCM), 124, 125, 143
 Coupling, 166
 Cranial neuropathies, 68, 69
 Cryoglobulinemia, 114
 Cryoprotection, 13
- D**
- Desipramine, 168
 Detrusor overactivity (DO), 135, 136
 Diabetes, 38, 59
 diagnostic criteria for, 60
 Diabetes Control and Complications trial (DCCT), 66
 Diabetes-related neuropathies
 cranial neuropathies, 68, 69
 DAN, 63–66
 diabetic neuropathy, screening for, 69
 distal symmetric polyneuropathy, 60, 61
 distal symmetric small fiber neuropathy, 62, 63
 mixed, 61, 62
 DLRPN, 67, 68
 mononeuropathies, 68
 syndromes of, 60
 TIND, 66, 67
 Diabetic 6th nerve palsy, 68
 Diabetic amyotrophy, 67
 Diabetic autonomic neuropathy (DAN)
 cardiovascular autonomic involvement, 64
 complications, 65
 consequence, 64
 diagnosis, 65
 management, 65, 66
 significant data, 64
 sweating, 65
 symptom, 64
 vision loss, 65
 Diabetic lumbosacral radiculoplexus neuropathy (DLRPN), 67, 68
 Diflunisal, 93
 Distal axonal polyneuropathy, 114
 Distal paraesthesias, 78
 Distal symmetric polyneuropathy, 60, 61, 115
 distal symmetric small fiber neuropathy, 62, 63
 mixed, 61, 62
 Distal symmetric small fiber neuropathy
 diagnosis, 63
 management, 63
 presentation, 62
 symptoms, 62
 thermal sensation and autonomic function, 62
 Dorsal root ganglia (DRG), 12, 74, 115
 Duloxetine, 169, 172
 Dysautonomia, 6–7, 44
- E**
- Ehlers-Danlos syndrome, 128
 Electrical spinal cord stimulation (ESCS), 160
 Electrical stimuli evoked potentials, 26, 27
 Electrodiagnostic testing, 61
 Erythropoietin, 174
 Evoked potentials, 26, 122
 Evoked somatosensory potentials, 26
 Excitatory postsynaptic currents (EPSCs), 156
 Excitatory postsynaptic potential (EPSP), 156
- F**
- Fabry disease, 7, 18, 38, 39, 77, 174
 Familial amyloid cardiomyopathy (FAC), 87
 Familial amyloid neuropathy, 20, 27
 Familial amyloid polyneuropathy (FAP), 78
 amyloid neuropathy
 transthyretin, 87
 TTR familial amyloid polyneuropathy, 87
 Fentanyl, 171
 Fibromyalgia, 133
 Fibromyalgia syndrome (FMS), 123
 CCM, 124
 evoked potentials, 122, 123
 microneurography, 124, 125
 QST, 122
 skin biopsy studies, 123, 124
 Skin innervation, 123
 small fiber findings, 125, 126
 small fiber impairment, 126
 small nerve fiber tests, 126
 Free-floating method, 13
 Friedreich's ataxia, 146, 147
 Functional gastrointestinal disorders (FGIDs), 134, 135
- G**
- Gabapentin, 169, 172
 Gabapentinoids, 172
 γ -aminobutyric acid (GABA), 156
 Ganglionopathy, 16
 Gastrointestinal autonomic neuropathy, 64
 Gastro-oesophageal reflux disease (GORD), 134
 Gastroparesis, 64, 65
 Genetic small fiber sensory neuropathy
 congenital insensitivity, 76
 Fabry disease, 77
 FAP, 78
 paroxysmal extreme pain disorder, 75–77
 primary erythromelalgia, 75
 sodium channel blockers, 74
 Tangier's disease, 78

Genitourinary autonomic neuropathy, 64
 Genitourinary disorders, 135, 136
 Global anhidrosis, 50
 Globotriaosylceramide (GL-3), 77
 Growth-associated protein 43 (GAP-43), 124
 Guillain-Barré syndrome (GBS), 40, 100, 101

H

Head up tilt table testing, 47
 Hepatitis C, 114
 Hereditary erythromelalgia, 174
 Hereditary neuropathies, 103
 Hereditary sensory and autonomic neuropathies (HSN/HSAN), 73–74
 Herpes, 114, 115
 Herpes simplex virus (HSV), 115
 Human immunodeficiency virus (HIV) infection, 113, 114
 Hyperalgesia, 5, 28, 38, 39, 135, 154
 Hyperknesis, 5
 Hypersensitivity mechanisms, 132–134
 Hyperventilation, 44
 Hypoglycemia, 65
 Hypohidrosis, 5

I

Idiopathic detrusor overactivity (IDO), 135
 Idiopathic rapid eye movement sleep behavior disorder (iRBD), 20
 IENF density (IENFD), 7, 154, 155, 158
 Immune globulin, 68
 Immunoreactive axons, 14
 Immunotherapy, neuropathic pain, 159
 Impaired glucose tolerance, 38
 Infectious diseases, 113
 hepatitis C and cryoglobulinemia, 114
 HIV infection, 113, 114
 leprosy, 115
 Lyme disease, 115
 VZV, 114, 115
 Inflamed human bowel neurotrophin-3, 134
 Inflammation, 19, 155
 Inflammatory diseases
 Celiac disease, 112, 113
 sarcoidosis, 112
 Inflammatory neuropathies, small fiber nerve degeneration in, 100, 101
 Inguinal postherniorrhaphy pain, 127
 Inherited neuropathies, 73, 74
 Insulin neuritis, 66
 Interscalene block, 28
 Interstitial cystitis/painful bladder syndrome, 133
 Intraepidermal nerve fiber density (IENFD), 100, 122, 134, 143
 microscopy, quantification and documentation, 14
 nerve fiber density, skin biopsy analysis of, 51
 Intraepidermal nerve fibers (IENFs), 4, 74, 100

Ion-channel blockade, 159
 Irritable bowel syndrome (IBS), 132, 134

K

Kennedy's disease, 147

L

Lacosamide, 170
 Lamotrigine, 170
 Large fiber dysfunctions, 5
 Large fiber motor, 6
 Large fiber neuropathy, 39, 40, 100
 functional correlations, 103, 104
 GBS and CIDP, 100, 101
 hereditary neuropathies, affecting, 103
 small fiber nerve degeneration in, 101–103
 Laser evoked potentials (LEP), 26–28, 122, 154
 Lepromatous leprosy, 115
 Leprosy, 115
 Lidocaine, 171, 173
 Light chain amyloidosis, 85, 86
 Limbic system, 157
 Liver transplantation, 93
 Low-threshold sensory fibres, 133
 Lyme disease, 115

M

Maladaptive plasticity, 155–159
 Mechanical detection thresholds, 37, 154
 Mechanical hyperalgesia, 38, 102
 Meissner's corpuscles, 12, 143
 Melphalan, 83, 86
 Methadone, 171
 Methylprednisolone, 68
 Microneurography, 124, 125
 Microvascular ischemia, 68
 Mixed distal symmetric polyneuropathy, 61
 diagnosis, 61
 management, 61, 62
 symptoms, 61
 Monofilaments, 61
 Mononeuropathy, 68
 Multiple mononeuropathies, 112
 Multiple system atrophy (MSA), 142
 Musculoskeletal chest pain, 132
 Myelin abnormalities, 143
 Myenteric plexus, 77, 134

N

Nabilone, 170
 Nav1.8 expression, 135
 Nerve fiber, skin biopsy analysis
 IENFD, 51
 nerve fiber density, skin biopsy analysis of, 51, 52
 pilot motor nerve fibers, 52, 53
 sudomotor nerve fibers, 51, 52

- Neurodegenerative disorders
 ALS, 145, 146
 autonomic failure, 145
 distal and unmyelinated nerve, 146
 MSA, 145
 Parkinson's disease, 142, 143, 145
 small-fiber function and pathology, 146
 somatosensory and autonomic nerve fiber loss, 146
 synucleinopathies, 145
- Neurogenic detrusor overactivity (NDO), 136
- Neuroinflammation, 166
- Neurokinin-1 (NK1) receptor, 156
- Neuronopathies, 39–40
- Neuropathic pain, 61, 102, 154
 alternative treatment strategies, 159
 brain stimulation therapies, 160
 ESCS, 160
 guidelines, pharmacological treatment of, 168
 immunotherapy, 159
 noninvasive brain stimulations
 tDCS, 161
 TMS, 160, 161
 pathogenesis of
 central nervous system, maladaptive plasticity,
 155–157, 159
 peripheral nerve damage, 155
 pathophysiological mechanism of, 166
 PENS, 159, 160
 pharmacological treatment, 159
 starting and maintenance dose, drugs used in, 173
 treatment of, 62
- Neuropathy, diagnostic criteria, 60
- Neuroprotection, 174
- Nociceptive nerve fibers
 amyloid and deposits in skin, 20
 biopsy, 12, 13
 choice of site, and method, 12, 13
 fixation and staining, 13
 IENFD, microscopy, quantification and
 documentation of, 14
 intraepidermal nerve fiber density
 normative values, 14, 15
 SFN, findings in, 15, 16
 normal innervation of skin, 12
 skin biopsy, yield of inflammation, 19
 subepidermal nerves, 18
 subtyping nerve fibers, 16, 17
- Nociceptor dysfunction, 26
- Non-infectious diseases, *see* Inflammatory diseases
- Noninvasive brain stimulations
 tDCS, 161
 TMS, 160, 161
- Noninvasive neuroimaging techniques, 156
- Non-peptidergic axons, 16
- Non-peptidergic C-fibers, 17
- Non-steroidal anti-inflammatory drug (NSAID), 93
- Nortriptyline, 168–169
- Number needed to treat (NNT), 167, 168
- O**
- Obstetric brachial plexus injury, 29
- Oesophagitis, 133
- Opioids, 171
- Overactive bladder syndrome, 133
- Oxaliplatin, 102
- Oxcarbazepine, 170
- Oxycodone, 171
- P**
- P2X3-immunoreactive nerve fibers, 136
- Paclitaxel, 102, 103
- Paclitaxel neuropathy, 102
- Paclitxel, 103
- Pain evoked potentials, 26, 100
 CHEP, 28, 29
 electrical stimuli evoked potentials, 26, 27
 laser-evoked potentials, 27, 28
- Pain matrix, 157, 160
- Pain related evoked potentials, 122, 123, 134
- Pain syndromes, *see* Small fiber pathology
- Pain thresholds, 35
- Painful neuropathy, 4, 5, 74
- Pain-related evoked potentials (PREP), 7, 123, 134
- Parkinson's disease, 144
 alpha-synuclein deposits in skin nerve fibers,
 143, 145
 autonomic denervation, 142
 non-motor symptoms, 142
 orthostatic hypotension, 142
 peripheral autonomic system, 142
 sensory function, 143
 somatosensory system, 142, 143
- Paroxysmal extreme pain disorder (PEPD), 75–77
- Participant Neurotoxicity Questionnaire (PNQ), 102
- Peptidergic fibers, 13, 16, 17
- Peptidergic innervation, 17
- Percutaneous electrical nerve stimulation (PENS),
 159, 160
- Peripheral nerve, 84–86
- Peripheral nerve damage, 155
- Peripheral neuropathy, 66, 78, 84, 87, 91, 111, 115, 143
- Phosphorylated alpha-synuclein in skin, 144
- Phospho-alpha-synuclein, 145
- Pilomotor nerve fibers, 52, 53
- Pinprick stimulators, 36
- Plasma cell dyscrasia, 85
- Polyneuropathy, 38, 60–62, 78, 85, 112–114
- Polyneuropathy, organomegaly, endocrinopathy,
 monoclonal gammopathy and skin
 hyperpigmentation (POEMS), 101
- Postherpetic neuralgia (PHN), 114, 125, 127
- Postsurgical pain, 127–128
- Postural tachycardia syndrome (POTS), 47
- Precuneus, 158
- Prediabetes, 60, 62
- Predonine, 86

Primary erythromelalgia, 75
 Primary Sjögren's syndrome (PSS), 110
 Proinflammatory cytokines, 155
 Protein gene product 9.5 (PGP 9.5), 11
 Pruritus, 4, 5
 Psychophysics, *see* Quantitative sensory testing (QST)
 Psychophysiological interaction (PPI), 158
 Purinergic receptor P₂X₃, 132

Q

Quality of life, 104
 Quantitative sensory testing (QST), 18, 33, 74, 122, 124, 125, 127, 133, 142, 154
 in consensus papers and guidelines, 36, 37
 distal symmetric small fiber neuropathy, 63
 Fabry disease, 77
 in SFN, 37, 38
 diabetes and impaired glucose tolerance, 38
 Fabry disease, 38, 39
 large fiber neuropathies/neuronopathies, 39, 40
 sarcoidosis, 39
 sodium channel mutations, 39
 method, 35, 36
 normal values, reproducibility, and sex differences, 36
 profiles, 35
 Quantitative sudomotor axon reflex testing (QSART), 48, 49, 63, 143

R

Ranvier nodes, 13, 18
 Rapid eye movement, 19
 Reference electrode, 48
 Regional anhidrosis, 50
 REM sleep behavior disorder (RBD), 143
 Resiniferatoxin (RTX), 136
 Restless legs syndrome, 5
 Rheumatoid arthritis (RA), 112
 RNA interference (RNAi), 94
 Ross syndrome, 51, 53, 147
 Rostroventromedial medulla (RVM), 156

S

Sarcoidosis, 39, 112
 Sedation, 172
 Sensory deafferentation, 157, 158
 Sensory phenotypes, 38, 102
 Sensory symptoms, 61, 89, 103, 145, 146
 Serotonin norepinephrine reuptake inhibitor (SNRI), 62, 169
 Sinus arrhythmia, 44, 45
 Sjögren's syndrome, 110, 111
 Skin biopsy
 analysis, 142
 large fiber neuropathy, 103, 104
 studies, 123, 124

Skin innervation, 12, 100, 103, 123, 127, 128, 142
 Sleep behavior disorder, 19, 143
 Small fiber nerve degeneration
 CIPN, 102, 103
 in inflammatory neuropathies, 100, 101
 Small fiber neuropathy, pathology of, *see* Nociceptive nerve fibers
 Small fiber neuropathy (SFN), 4, 122, 166
 antidepressants
 serotonin norepinephrine reuptake inhibitor, 169
 tricyclic antidepressants, 167–169
 antiepileptic drugs
 sodium channel blockers, 169, 170
 voltage gated calcium channels, $\alpha 2\delta$ ligands of, 169
 cannabinoid derivatives, 170, 171
 cause-/molecular target-specific treatment, 174
 central mechanisms
 analgesic system, disturbance in, 167
 central sensitization, 167
 clinical manifestation, 4, 5
 definition, 4
 diagnosis, 6, 7
 disease course, 5
 etiology, 6
 medication classes, 167
 medication efficacy, comparison of, 167
 natural course of, 5
 neuropathic pain (*see* Neuropathic pain)
 neuroprotection, 174
 opioids, 171
 patchy involvement, 5
 pathology, 5, 19
 peripheral mechanisms, sodium channels, ectopic firing, 166, 167
 presentations, 4
 prevalence, 4
 specific sodium channel subtype blockers, 174
 symptoms, 5
 therapy, combination of, 172
 topical agents, 171, 172
 treatment, 7, 8, 172, 173
 Small fiber pathology
 in CRPS, 122
 in FMS, 122–126
 in neurodegenerative disorders (*see* Neurodegenerative disorders)
 in PHN, 127
 with painful conditions, 128
 postsurgical pain, 127
 Small nerve fiber tests, 126
 Sodium channel(s), 166, 167
 Sodium channel blockers, 74, 169, 170
 Sodium channel mutations, 39
 Somatosensory-evoked potentials (SSEP), 26
 Somnolence, 168, 170, 172
 Spontaneous neuropathic pain, 154
 Stocking-glove pattern, 5
 Subepidermal nerves, 18

- Substance P, 13, 133, 156
- Sudomotor function testing
 QSART, 48, 49
 SSR, 48
 TST, 50, 51
- Sudomotor innervation, 93
 loss of, 147
- Sudomotor nerve dysfunction, 65
- Sudomotor nerve fibers, 51–52
- Sudoscan, 102
- Superior parietal lobule (SPL), 158
- Sweat gland, 49
- Sweat gland innervation, 52
- Sweat gland nerve fiber density (SGNFD), 51–53
- Sweating, 49, 50, 65
- Sympathetic skin response (SSR), 48, 77
- Sympathetic sprouting, 166–167
- Synucleinopathies, 145
- Systemic lupus erythematosus (SLE), 111
- Systolic orthostatic hypotension, 103
- T**
- Tafamidis, 93
- Tangier's disease, 78
- Tensor-based morphometry, 158
- Thermal hyperalgesia, 35, 38
- Thermal sensory testing device, 35
- Thermodes, 26, 35
- Thermoregulatory sweat testing (TST), 50, 51
- Thermotesting, 37
- Third nerve (oculomotor) palsy, 68
- Tilting table testing, 47
- Tooth pulp-evoked potentials (TPEPs), 26–27
- Topical phenytoin, 172
- Topiramate, 76, 170, 173
- Total Neuropathy Score clinical version (TNSc), 102
- Tramadol, 27, 171
- Transcranial direct current stimulation (tDCS), 161
- Transcranial magnetic stimulation (TMS), 160, 161
- Transient receptor potential vanilloid type 1 (TRPV1), 132, 155
- Transthyretin (TTR), 87
 genetic evidence of, 90
 genetics of, 87, 88
 majority of, 87
 phenotypes of, 87
 TTR-FAP
 clinical features of, 88, 89, 91
 neurophysiology of, 91
 pathogenesis of, 88
 pathology of, 91, 92
 treatment of, 93, 94
- Transthyretin gene, 20
- Treatment induced neuropathy of diabetes (TIND), 66
 associated autonomic features, 66
 clinical presentation, 66
 diagnosis, 66, 67
 management, 67
- Tricyclic antidepressants
 diabetes-related neuropathies, 62
 SFN, 167–169
- Trinucleotide repeat disorder, 146
- TRPM8, 136
- TRPV1 expression, 135
- TRPV1 sensory nerve fibers, 134
- TRPV1(+) nerve fibers, 134
- Tuberculoid leprosy, 115
- Type 1 diabetes, 69
- U**
- Unsharp mask filter photographic technique, 51
- V**
- Valsalva maneuver, 45–47
- Valsalva test, 101
- Varicella zoster virus (VZV), 114, 115
- Vasculitic inflammatory infiltrates, 146
- Vasculitic neuropathy, 100
- Vasculitis, 6
- Vasoactive intestinal peptide (VIP), 51
- Vincristine, 102, 103
- Visceral pain, 132–134
- Visceral sensation (hypersensitivity)
 altered descending excitatory/inhibitory influences, spinal cord nociceptive neurones, 132
 enhanced nociceptor input, 133
 gastrointestinal afferent nerves, 132
 neuroimmune pathways, 132
 nociceptive conditioning stimulus, 133
 nociceptor activation, 132
 non-noxious sensation, 132
 pathophysiological mechanisms, 131–132
 peripheral and central afferents pathways, 132
 peripheral and central nervous pathways, 133
 persistent neuropathic pain, 131
 psychological and organic processes, 132
 spinal cord dorsal horn neurones, 132
 stimulus-response characteristics, 133
 tissue damage, 132
- Vision loss, 65
- Vitamin E, 174
- Voltage gated calcium channels, 169
- Voltage-gated-calcium channel antagonist, 172
- Voltage gated potassium channels (VGKC), 111, 112
- Voltage-gated sodium channels, 135
- Voltage-gated sodium channel 1.7 (Nav1.7), 174
- Vulvodynia, 132, 133, 135
- W**
- WHO quality of life (WHOQoL) scores, 104
- Windup ratio, 36