

## Index

- ABCD1 gene mutations, 319, 321–22  
 abetalipoproteinemia, 341. *See also*  
   Bassen-Kornzweig disease  
     diagnosis, 344  
     pathology, 342–43  
     pathophysiology, 343–44  
     treatment for, 344–45  
 Acadian Friedreich ataxia, 339  
 acanthocytosis, 329–30  
   Bassen-Kornzweig disease and,  
   342  
 aceruloplasminemia, 325, 379, 382  
   clinical features, 382  
   CP protein mutations, 383–84  
   diagnosis, 384  
   pathology, 382–83  
   pathophysiology, 383–84  
   treatment for, 384  
 acetazolamide, 158–59, 355  
 acid maltase deficiency. *See* infantile  
   acid maltase deficiency  
 aconitase deficiency, 55–56  
 acrodynia, 469  
 acute axonal degeneration, 33  
 acute necrotizing encephalopathy  
   clinical features, 261–62  
   pathology, 262  
   pathophysiology, 262–63  
   RANBP2 gene mutations, 261–63  
   treatment for, 263  
 Addison disease, 319. *See also* x-linked  
   adrenoleukodystrophy  
 adolescent disorders. *See specific*  
   disorders  
 adolescent drug abuse. *See* drug abuse  
 adrenal insufficiency, 319  
 adult free sialic acid storage disorder,  
   125  
 adult neuronal ceroid lipofuscinosis.  
   *See* Kufs disease  
 Aicardi-Goutières syndrome  
   clinical features, 214–16  
   diagnosis, 216  
   pathology, 216  
   pathophysiology, 216  
   phenotypes for, 215–16  
 albuterol, 199  
 aldehyde oxidase, 70  
 Alexander disease, 184  
   astrocyte dysfunction and, 184–86  
   clinical features, 184  
   diagnosis, 186  
   pathology, 184–85  
   pathophysiology, 185–86  
   treatment for, 187  
 ALG1-CDG disorder, 96  
 ALG2-CDG disorder, 96  
 ALG3-CDG disorder, 96  
 ALG6-CDG disorder, 96  
 ALG8-CDG disorder, 96  
 ALG9-CDG disorder, 96  
 ALG11-CDG disorder, 96  
 ALG12-CDG disorder, 96  
 Alpers-Huttenlocher disease, 141, 252  
   clinical features, 141–42  
   diagnosis, 143–44  
   epilepsy and, 141–42  
   MELAS and, 143  
   MEMSA and, 143  
   pathology, 142  
   pathophysiology, 143  
   SANDO and, 143  
   treatment for, 144–45  
 alpha-fucosidosis, 112  
 α-mannosidosis, 112  
   clinical features, 297  
   diagnosis, 299  
   pathology, 298–99  
   pathophysiology, 299  
   type-2, 298  
 α-synuclein, 404  
 ALS2 genes, 399  
 amantadine, 391  
 aminoglycoside antibiotics, 335–36  
 aminoglycoside-induced hearing loss,  
   57  
 ammonia, 77–78  
 ammonium tetrathiomolybdate, 376–77  
 amphetamines, abuse of, 479–80  
 amyotrophic lateral sclerosis. *See*  
   juvenile amyotrophic lateral  
   sclerosis  
 Andersen disease. *See* infantile  
   Andersen disease  
 anemia, from chronic lead poisoning,  
   466  
 angiokeratoma corporis diffusum, 295  
 antibiotics. *See* aminoglycoside  
   antibiotics  
 anticonvulsants, 409  
   benzodiazepines, 413  
   carbamazepine, 413  
   clobazam, 413  
   cognitive effects of, 412–13  
   epileptic psychosis, 415–16  
   general principles for, 412  
   phenobarbital, 412  
   phenytoin, 412  
   valproate, 412  
 antiepileptic drugs, 373  
 anti-N-methyl-aspartate receptor  
   (NMDAR) encephalitis, 432  
 antiqutin deficiency, 84–85  
 antisense therapy, 400  
 apoptosis, 30  
   with mitochondrial disorders, 260  
 aprataxin deficiency, 249  
 arginine-glycine amidinotransferase  
   deficiency  
   clinical features, 132–33  
   diagnosis, 135  
   pathology, 133  
   pathophysiology, 134–35  
   treatment for, 135  
 argininemia, 76  
   ammonia and, 77–78  
   clinical features, 75–77  
   diagnosis, 78  
   glutamine and, 78  
   hyperammonemia and, 75–77  
   nitric oxide production, 78  
   pathology, 77  
   pathophysiology, 77–78  
   treatment for, 78  
 argininosuccinate lyase deficiency, 76  
   ammonia and, 77–78  
   clinical features, 75–77  
   diagnosis, 78  
   glutamine and, 78  
   hyperammonemia and, 75–77  
   nitric oxide production, 78  
   pathology, 77  
   pathophysiology, 77–78  
   treatment for, 78

## Index

- arginyl-transfer RNA synthetase (RARS1) mutations, 60  
 Arnold-Chiari malformations, 424  
 ascorbic acid. *See* vitamin C  
 ASD. *See* autism spectrum disorder  
 aspartylglucosaminuria, 112  
 astrocyte dysfunction, 184  
 ataxia, 249. *See also* Friedreich ataxia  
   childhood, 346  
   with vitamin E deficiency, 340, 342  
 ataxia teleangiectasia  
   brain development with, 333  
   clinical features, 331–32  
   diagnosis, 335  
   pathology, 332–33  
   pathophysiology, 333–35  
   treatment for, 335–36  
 ataxia teleangiectasia mutated (ATM)  
   protein, 331, 333–35  
 ATP7A-related distal motor  
   neuropathy, 164–68. *See also*  
   Menkes disease  
 ATP13A2 proteins, 403  
 auditory loss. *See* visual and auditory  
   loss  
 auditory reflex responses, 17  
 autism spectrum disorder (ASD),  
   417–18, 444  
   epilepsy in, 418  
 autoimmune diseases. *See* systemic  
   inflammatory diseases  
 autophagy, 31  
 autosomal dominant disorders. *See*  
   Aicardi-Goutières syndrome;  
   maple syrup urine disease  
 autosomal recessive disorders. *See*  
   *specific disorders*  
 axonal degeneration, 32–34  
   acute, 33  
   chronic, 34  
   dying back, 34  
   Wallerian, 34  
  
 B4GALT1-CDG disorder, 96–97  
 baclofen, 355  
 Baltic myoclonus. *See* Unverricht-  
   Lundborg disease  
 Bassen-Kornzweig disease, 341  
   acanthocytosis and, 342  
   clinical features, 341–42  
   MTTP genes, 341–42  
   vitamin E deficiency and, 341–42,  
   456  
 benzodiazepines  
   in anticonvulsant therapy, 413  
   for spinocerebellar ataxias, 355  
   for Unverricht-Lundborg disease,  
   233–34  
 beta ketothiolase deficiency, 104  
  
 betaine, 225–26  
 beta-propeller protein-associated  
   neurodegeneration, 379  
 $\beta$ -blockers, 355, 391  
 $\beta$ -mannosidosis, 112  
   clinical features, 297  
   pathology, 298–99  
   pathophysiology, 299  
 biotin therapy, for familial infantile  
   bilateral striatal necrosis, 223  
 biotinidase deficiency, 79  
   biotin-dependent enzymes, 80  
   clinical features, 79–80  
   diagnosis, 80  
   pathology, 80  
   pathophysiology, 80  
   treatment, 81  
 biotin-thiamine responsive basal  
   ganglia disease  
   clinical features, 368  
   diagnosis, 369  
   pathology, 368–69  
   pathophysiology, 369  
   treatment for, 369  
 bone marrow transplantation  
   for Farber lipogranulomatosis, 124  
   for fucosidosis, 296  
   for GM1 gangliosidosis, 304  
   for mannosidoses, 299–300  
   for metachromatic leukodystrophy,  
   182  
   for multiple sulfatase deficiency,  
   182  
   for Niemann-Pick type A/type  
   B disease, 110  
 Boston naming test, 19  
 botulinum toxin, 355  
 brain development  
   with ataxia teleangiectasia, 333  
   with Canavan disease, 155–56  
   familial infantile bilateral striatal  
   necrosis and, 222  
   fucosidosis and, 296  
   with Hartnup disease, 312  
   juvenile neuronal ceroid  
   lipofuscinosis and, 246–47  
   with Menkes disease, 165  
   MR imaging, 22–23  
   MR spectroscopy, 23  
   Spielmeier-Vogt disease and,  
   246–47  
 brain irradiation. *See* cranial irradiation  
 brivaracetam, 233–34  
 Brown-Vialetto-van Laere disease, 198  
  
 calcium, 462  
 calcium disodium  
   ethylenediaminetetraacetic acid  
   (CaNa<sub>2</sub>EDTA), 467  
  
 Canavan disease, 155  
   brain development with, 155–56  
   clinical features, 155  
   diagnosis, 158  
   pathology, 155–56  
   pathophysiology, 156–58  
   treatment for, 158–59  
 cancer treatments. *See also* cranial  
   irradiation  
   chemotherapy, sequelae of, 448–49  
 cannabinoids, abuse of, 480  
 carbamazepine, 413  
 carbamoyl phosphate synthetase  
   deficiency, 76  
   ammonia and, 77–78  
   clinical features, 75–77  
   diagnosis, 78  
   glutamine and, 78  
   hyperammonemia and, 75–77  
   nitric oxide production, 78  
   pathology, 77  
   pathophysiology, 77–78  
   treatment for, 78  
 carbidopa, 154  
 carnitine, 199  
 caspase activation, 355  
 cell transplantation therapy, 404  
 central nervous system, degeneration  
   in, 29–31  
   axonal degeneration, 32–34  
   acute, 33  
   chronic, 34  
   dying back, 34  
   Wallerian, 34  
   neural cell death, 30–31  
   apoptosis, 30  
   autophagy, 31  
   necrosis, 30–31  
   pyruvate carboxylase deficiency and,  
   53  
 cerebellar ataxia, 59–60  
 cerebellar atrophy, 249  
 cerebrotendinous xanthomatosis, 385  
   clinical features, 385–86  
   diagnosis, 386–88  
   pathology, 386  
   pathophysiology, 386  
   treatment for, 388  
 ceroid lipofuscinosis. *See* infantile  
   ceroid lipofuscinosis; juvenile  
   neuronal ceroid lipofuscinosis;  
   Kufs disease  
 ceruloplasmin (CP) protein, 383–84  
 Charcot-Marie-Tooth (CMT) disease,  
   357. *See also* Déjérine-Sottas  
   disease  
   clinical features, 357–59  
   diagnosis, 359–60  
   pathology, 359

- pathophysiology, 359  
 phenotypes, 358  
   CMT1, 358  
   CMT2, 358–59  
   CMT3, 359  
   CMT4, 359  
   CMTX, 359  
 treatment for, 360  
 type 3, 204  
 chelation therapy, 376–77  
   with iron, 381  
 chemotherapy, sequelae of, 448–49  
 chenodeoxycholic acid, 388  
 child abuse. *See* medical child abuse  
 child development  
   through EEG assessment, 20–21  
   language development, 14  
   neural performance assessment,  
     15–18  
   through neurological examination,  
     16–18  
   through neurological history, 16  
   neurological development, 12–13  
   for intelligence variability, 13  
   muscle tone, 17–18  
   after neonatal insults, 12–13  
   through positive reinforcement, 13  
   for reflex responses, 12, 16–17  
   neuropsychological assessment, 19  
   through intelligence tests, 13, 19  
   psychological development, 12–13  
 childhood ataxia, 346  
 chloroquine, 294  
 chromosomal mutations, 199  
 chronic axonal degeneration, 34  
 chronic lead poisoning. *See* lead  
   poisoning  
 chronic mercury poisoning. *See*  
   mercury poisoning  
 chronic progressive external  
   ophthalmoplegia (CPEO), 252  
   clinical features, 255–56  
   diagnosis, 256–59  
   pathology, 256–59  
 chronic psychosis, from epilepsy, 415  
 citrullinemia, 76  
   ammonia and, 77–78  
   clinical features, 75–77  
   diagnosis, 78  
   glutamine and, 78  
   hyperammonemia and, 75–77  
   nitric oxide production, 78  
   pathology, 77  
   pathophysiology, 77–78  
   treatment for, 78  
 CLN6 genes, 396  
 clobazam, 413  
 CMT disease. *See* Charcot-Marie-  
   Tooth disease  
 cobalamin, 225–26, 458–59  
   deficiency, 459  
 cocaine, abuse of, 479–80  
 Cockayne syndrome  
   clinical features, 160–61  
   diagnosis, 162–63  
   pathology, 162  
   pathophysiology, 162  
   Type I, 162  
   Type II, 162  
   Type III, 162  
 coenzyme A synthetase protein-  
   associated neurodegeneration,  
     379  
   clinical features, 379  
 coenzyme Q10 deficiency, 59–60, 150,  
   248  
   clinical features, 248–49  
   diagnosis, 249–50  
   pathology, 249  
   pathophysiology, 249  
   primary, 249  
   secondary, 248–49  
   treatment for, 250  
 COG6-CDG disorder, 96–97  
 cognitive development  
   anticonvulsants and, 412–13  
   after cranial irradiation, 447  
   with multiple sclerosis dementia, 428  
   with Rasmussen encephalitis, 372  
 common maple syrup urine disease,  
   86–87  
 complex I deficiency, 59–60  
 congenital disorders of glycosylation,  
   128  
   adult phase, 129  
   clinical features, 128–29  
   diagnosis, 131  
   infantile multisystem form, 129  
   pathology, 129–30  
   pathophysiology, 130–31  
   treatment for, 131  
 continuous spike waves of sleep. *See*  
   electrical status epilepticus in  
   sleep  
 conversion disorder, 439  
   diagnosis, 439  
 copper metabolism, 462  
   Menkes disease and, 165–68  
 corticosteroids, 409, 422  
 CP protein. *See* ceruloplasmin protein  
 CPEO. *See* chronic progressive external  
   ophthalmoplegia  
 cPMP. *See* cyclic pyranopterin  
   monophosphate  
 cranial irradiation  
   cognitive development after, 447  
   delayed radiation encephalopathy,  
     447  
   delayed vascular injury after, 448  
   neurological deterioration after,  
     447–49  
   radiotherapy effects from, 447  
 creatine, 199  
 creatine deficiency syndromes, 132  
   clinical features, 132–33  
   diagnosis, 135  
   pathology, 133  
   pathophysiology, 134–35  
   treatment for, 135  
 CTMIO therapy, 335  
 cyclic pyranopterin monophosphate  
   (cPMP), 74  
 cyclodextrans, 273–75  
 cystatins, 233  
 cytochrome c oxidase deficiency,  
   58–59  
   reversible infantile myopathy from,  
     59  
 Dandy-Walker syndrome, 424  
 DAT deficiency. *See* infantile dopamine  
   transporter deficiency  
 DDOST-CDG disorder, 96–97  
 deafblindness. *See* visual and auditory  
   loss  
 deafness, 444  
 death and palliation, from  
   neurodegenerative disorders,  
     24–26  
   communication of death  
     expectations, 25  
   feeding and nutrition issues, 26  
   management of manifestations,  
     25–26  
   pain assessment, 25–26  
 deferiprone, 381  
 Déjérine-Sottas disease, 204  
   clinical features, 204  
   diagnosis, 206  
   pathology, 204  
   pathophysiology, 206  
   treatment for, 206–7  
 delayed radiation encephalopathy, 447  
 delayed vascular injury, 448  
 dementia, in DS, 420  
 desferrioxamine, 340  
 desipramine, 196  
 dextromethorphan, 196, 400  
 dichloroacetate, 51  
 dietary insufficiency, 249  
 dihydrofolate reductase deficiency, 228  
   pathophysiology, 229  
 dimercaprol, 466–67  
 disorders of pyridoxine metabolism, 82  
   clinical features, 82–83  
   diagnosis, 85  
   pathology, 83–84

## Index

- disorders of pyridoxine metabolism (cont.)  
   pathophysiology, 84–85  
   antiquitin deficiency in, 84–85  
   treatment for, 85  
   through lysine restriction, 85  
   vitamin B6 and, 84–85  
 DNAJC5 genes, 396  
 DOLK-CDG disorder, 96  
 DOPA-responsive dystonia (DRD), 366  
 Down syndrome (DS), 419–20  
   dementia in, 420  
 DPAGT1-CDG disorder, 96  
 DPM1-CDG disorder, 96  
 DRD. *See* DOPA-responsive dystonia  
 drug abuse, in adolescents, 478–80  
   of amphetamines, 479–80  
   of cannabinoids, 480  
   of cocaine, 479–80  
   encephalopathies from, 479  
   of methamphetamines, 479–80  
   psychosis from, 479  
 DS. *See* Down syndrome  
 dwarfism, 295  
 dying back degeneration, 34  
 dysostosis, 295  
 dystonia  
   with infantile DAT deficiency, 152  
   Segawa disease, 365  
   clinical features, 365–66  
   diagnosis, 366–67  
   pathology, 366  
   pathophysiology, 366  
   treatment for, 367  
 ears. *See* auditory reflex responses;  
   visual and auditory loss  
 EEG assessment. *See*  
   electroencephalogram  
   assessment  
 eIF2B proteins, 349–50  
 electrical status epilepticus in sleep  
   clinical features, 410  
   treatment for, 410–11  
 electroencephalogram (EEG)  
   assessment, 20–21, 245  
   with Landau-Kleffer syndrome, 409  
 electron transferring-flavoprotein  
   dehydrogenase (ETFDH)  
   deficiency, 249  
 encephalomyopathy, 59–60  
   with myoglobinuria, 249  
 enzyme replacement therapy, 281, 300  
   for Fabry disease, 310  
 enzyme substitution therapy, 101–2  
 epilepsy  
   Alpers-Huttenlocher disease and,  
     141–42  
   anticonvulsants, 409. *See also specific  
     drugs*  
     cognitive effects of, 412–13  
     general principles for, 412  
     psychosis from, 415–16  
   antiepileptic drugs, 373  
   in ASD, 418  
   electrical status epilepticus in sleep,  
     410–11  
   fictitious, 476  
   Landau-Kleffer syndrome, 408–9  
   psychosis from, 414–16  
     from anticonvulsants, 415–16  
     chronic, 415  
     clinical features of, 414  
     episodic, 414–15  
     forced normalization, 415  
     temporal lobectomy, 415  
   Rett syndrome and, 196  
   episodic psychosis, from epilepsy,  
     414–15  
   ETFDH deficiency. *See* electron  
     transferring-flavoprotein  
     dehydrogenase deficiency  
   ethyl mercury, 469–70  
   evidence-based medicine, progressive  
     brain disorders and, principles  
     for, 7  
   excitotoxicity, 62–66  
   eyes. *See* infantile Refsum disease;  
     visual and auditory loss; visual  
     reflex responses  
 FA2H-associated degeneration, 325,  
   379  
   clinical features, 378–79  
   pathophysiology, 380  
 Fabry disease, 305  
   clinical features, 305–6  
   diagnosis, 309–10  
   pathology, 306–8  
   pathophysiology, 308–9  
   GLA gene mutations, 308–9  
   treatment for, 310  
 familial infantile bilateral striatal  
   necrosis  
   brain development and, 222  
   clinical features, 221–22  
   diagnosis, 223  
   pathology, 222  
   pathophysiology, 223  
   treatment for, 223  
 Farber bodies, 123–24  
 Farber lipogranulomatosis, 122  
   clinical features, 122–23  
   diagnosis, 124  
   pathology, 123–24  
   pathophysiology, 124  
   treatment for, 124  
 fatal hepatocerebral syndrome, 60  
 feeding and nutrition. *See also*  
   malnutrition; starvation  
   with neurodegenerative disorders, 26  
   with urea cycle defects, 78  
 fictitious epilepsy, 476  
 folate disorders. *See* hereditary folate  
   disorders  
 folic and folinic acids, 225–26, 459  
   deficiency, 459  
   intoxication from, 459  
 FOLR1 deficiency, 228  
   pathophysiology, 229  
 forced normalization psychosis, from  
   epilepsy, 415  
 frataxin proteins, 339–40  
 Friedrich ataxia, 337  
   Acadian, 339  
   clinical features, 337–39  
   diagnosis, 340  
   late-onset, 338  
   motor development with, 339  
   pathology, 339  
   with retained reflexes, 338  
   treatment for, 340  
   very late-onset, 338  
 fucosidosis, 295  
   brain development, 296  
   clinical features, 295  
   diagnosis, 296  
   pathology, 295–96  
   pathophysiology, 296  
   treatment for, 296  
 fumarate hydratase mutations, 56  
 FUS genes, 399  
 gabapentin, 199  
 galactosialidosis, 112, 114  
   clinical features, 114–15  
   phenotypes, 114  
   diagnosis, 116  
   pathology, 115  
   pathophysiology, 115–16  
   types of, 114–15  
 galactosylceramidase deficiency,  
   174–77  
 GAN gene. *See* gigaxonin gene  
 Gaucher disease, 264  
   clinical features, 264–66  
   diagnosis, 268  
   pathology, 266  
   pathophysiology, 266–68  
   treatment for, 268  
   types of, 265–66  
 genomics, in neurological practice, 4  
 gephrin protein, 72–73  
 giant axonal neuropathy, 361  
   clinical features, 361  
   diagnosis, 364

- neurological development, 363  
 pathology, 362–63  
   Rosenthal fibers, 362–63  
 pathophysiology, 363–64  
 treatment for, 364  
 gigaxonin (GAN) gene, 361  
   mutations of, 363–64  
 GLA genes, 308–9  
 globoid cell leukodystrophy. *See*  
   Krabbe disease  
 glutamine, 78  
 glutaric acidemia, 62  
   clinical features, 61–62  
   diagnosis, 66  
   excitotoxicity, 62–66  
   incidence rates, 61  
   pathology, 62  
   pathophysiology, 62–66  
   treatment for, 66–67  
 glutaric acidemia type II, 104  
 glycine encephalopathy, 90  
 glycogen storage diseases. *See also*  
   Pompe disease  
   infantile Andersen disease, 217  
     clinical features, 217  
     diagnosis, 219–20  
     pathology, 218  
     pathophysiology, 218–19  
   glycogen synthesis, defects of,  
     38  
 glycosylation disorders. *See* congenital  
   disorders of glycosylation  
 GM1 gangliosidosis, 301  
   chronic, 302  
   clinical features, 301–2  
   diagnosis, 303–4  
   infantile, 301  
   juvenile, 302  
   pathology, 302–3  
   pathophysiology, 303  
   treatment for, 304  
 GM2 gangliosidosis, 276  
   clinical features, 276–77  
   diagnosis, 281  
   pathology, 277–78  
   pathophysiology, 278–81  
   treatment for, 281–82  
 guanidinoacetate methyltransferase  
   deficiency  
     clinical features, 132–33  
     diagnosis, 135  
     pathology, 133  
     pathophysiology, 134–35  
     treatment for, 135  
 Hallervorden-Spatz disease, 325  
 haloperidol, 391  
 Haltia-Santavuori disease. *See* infantile  
   ceroid lipofuscinosis  
 Hartnup disease, 311  
   brain development and, 312  
   clinical features, 311–12  
   diagnosis, 313  
   pathology, 312  
   pathophysiology, 312–13  
   treatment for, 313  
   tryptophan production, 312–13  
 HDLs. *See* high density lipoproteins  
 HELLP syndromes, 38–39  
 hematopoietic stem cell transplantation  
   (HSCT)  
     for GM2 gangliosidosis, 281–82  
     for metachromatic leukodystrophy,  
       180–81  
     for mucopolysaccharidoses, 291, 294  
     for multiple sulfatase deficiency, 182  
     for x-linked adrenoleukodystrophy,  
       323  
 heparan sulphate, 290  
 hepatolenticular degeneration. *See*  
   Wilson disease  
 hepatorenal tyrosinemia. *See*  
   tyrosinemia type 1  
 hepatosplenomegaly, 107–8, 276, 295  
   clinical features, 276–77  
 hereditary folate disorders  
   clinical features, 227–28  
   diagnosis, 230  
   dihydrofolate reductase deficiency,  
     228–29  
   FOLR1 deficiency, 228–29  
   methylenetetrahydrofolate reductase  
     deficiency, 227–29  
   pathology, 228  
   pathophysiology, 228–30  
   proton-coupled folate transporter  
     deficiency, 228–29  
   treatment for, 230  
 hereditary motor sensory neuropathy  
   type III, 204. *See also* Déjérine-  
   Sottas disease  
 hereditary spastic paraplegias (SPGs),  
   392  
   age of onset for, 394  
   classifications for, 392–93  
   clinical features, 392–94  
   diagnosis, 394  
   modes of inheritance, 393  
   pathology, 393–94  
   pathophysiology, 394  
 high density lipoproteins (HDLs), 344  
 HIV-associated cognitive disorder,  
   434–35  
 holocarboxylase synthetase deficiency,  
   79  
   biotin-dependent enzymes, 80  
   clinical features, 79–80  
   diagnosis, 80  
   pathology, 80  
   pathophysiology, 80  
   treatment, 81  
 HSCT. *See* hematopoietic stem cell  
   transplantation  
 Hunter-Scheie syndrome, 283–86  
 Huntington disease. *See* juvenile  
   Huntington disease  
 Hurler syndrome, 283–86  
   pathophysiology, 290  
 hyaline inclusion disease. *See* neuronal  
   intranuclear inclusion disease  
 hyaluronidase deficiency, 289  
 hydrocephalus, 423–26  
   causes of, 424  
   clinical manifestations of, 424–25  
   diagnosis, 425–26  
   pathology, 425  
   pathophysiology, 425–26  
   treatment for, 426  
   X-linked, 425–26  
 hydroxyglutaric acidemia, 62  
   clinical features, 61–62  
   diagnosis, 66  
   excitotoxicity, 62–66  
   incidence rates, 61  
   pathology, 62  
   pathophysiology, 62–66  
   treatment for, 66–67  
 hydroxyglutaric aciduria, 104  
 hydroxyurea, 199  
 hypocalcemia, 456  
 hypoplasia of corpus callosum, 38, 40  
 hypotonia  
   with infantile DAT deficiency, 152  
   Pelizaeus-Merzbacher disease and,  
     188  
   spinal muscular atrophy and, 197  
 hysteria. *See* conversion disorder  
 immunization, progressive brain  
   disorders and, 5  
 immunoglobulin therapy, 409  
 impaired folate metabolism, 38  
*in utero* disorders  
   phenylketonuria, 40  
   prenatal inborn metabolic disorders,  
     38–39  
   HELLP syndromes, 38–39  
   hypoplasia of corpus callosum, 38,  
     40  
 inborn errors of amino acid  
   metabolism, 90  
   clinical features, 90–93  
   glycine encephalopathy, 90  
   lysine protein intolerance,  
     90–93  
   tyrosinemia type 1, 93  
 infantile acid maltase deficiency, 139

## Index

- infantile Andersen disease, 217  
 clinical features, 217  
 diagnosis, 219–20  
 pathology, 218  
 pathophysiology, 218–19  
 missense mutations, 219
- infantile ascending hereditary spastic paraplegia, 178  
 clinical features of, 178  
 pathology, 179  
 pathophysiology, 179
- infantile ceroid lipofuscinosis, 117. *See also* late infantile neuronal ceroid lipofuscinosis  
 clinical features, 117–18  
 neuronal types, 118  
 late-onset, 120  
 pathology, 118–20  
 pathophysiology, 120  
 severity of, 120
- infantile dopamine transporter (DAT) deficiency, 152  
 clinical features, 152–53  
 diagnosis, 153–54  
 dystonia and, 152  
 hypotonia and, 152  
 language development and, 153  
 motor development and, 153  
 pathology of, 153  
 pathophysiology, 153  
 treatment for, 154
- infantile multisystemic disease, 59–60, 249
- infantile neuroaxonal dystrophy, 201, 379  
 clinical features, 201  
 diagnosis, 202–3  
 pathology, 201–2  
 pathophysiology, 202  
 treatment for, 203
- infantile organic acidemias, 103  
 clinical features, 103–4  
 types of, 104
- infantile Refsum disease, 171  
 clinical features, 171  
 diagnosis, 172  
 neonatal adrenoleukodystrophy and, 171  
 pathology, 171–72  
 treatment for, 172  
 Zellweger disease and, 171
- infantile sialic acid storage disease, 125  
 clinical features, 125–26  
 diagnosis, 127  
 pathology, 126  
 pathophysiology, 126–27
- infections, progressive brain disorders and, 5
- inherited cobalamin deficiency  
 clinical features, 224–25  
 diagnosis, 225  
 infantile forms of, 224  
 late-onset, 225  
 pathology, 225  
 pathophysiology, 225  
 MMACHC gene protein, 225  
 treatment for, 225–26
- inherited peroxisomal disorders. *See* x-linked adrenoleukodystrophy
- intelligence quotients (IQ)  
 measurements, 13. *See also* Stanford-Binet Intelligence Scale
- intelligence tests, 19  
 Stanford-Binet Intelligence Scale, 13, 19  
 WISC-III, 19  
 WPPSI, 19
- intentional poisonings, as child abuse, 477
- intermediate maple syrup urine disease, 86–87
- intermittent maple syrup urine disease, 86–87
- iodine, 462
- IPX066 therapy, 404
- IQ measurements. *See* intelligence quotients measurements
- iron, 462
- iron chelation therapy, 381  
 for aceruloplasminemia, 384
- irradiation. *See* cranial irradiation
- isolated myopathy, 59–60
- isovaleric acidemia, 104
- Jansky-Bielschowsky disease. *See* late infantile neuronal ceroid lipofuscinosis
- juvenile amyotrophic lateral sclerosis  
 clinical features, 397–98  
 diagnosis, 399–400  
 pathology, 398  
 pathophysiology, 398–99  
 ALS2 gene mutations, 399  
 FUS gene mutations, 399  
 phenotypes for, 398  
 treatment for, 400
- juvenile Huntington disease  
 clinical features, 389–90  
 diagnosis, 391  
 pathology, 390  
 pathophysiology, 390–91  
 treatment for, 391
- juvenile neuronal ceroid lipofuscinosis, 395  
 Batten disease and, 246  
 brain development and, 246–47  
 clinical features, 246  
 diagnosis, 247  
 pathology, 246–47  
 pathophysiology, 247  
 treatment for, 247
- juvenile Parkinson disease  
 causes of, 402  
 clinical features, 401–2  
 diagnosis, 403  
 KRS and, 402  
 Lewy bodies and, 402–3  
 pathology, 402–3  
 pathophysiology, 403  
 ATP13A2 proteins, 403  
 treatment for, 403–4
- Kanzaki disease. *See* Schindler disease
- Kearns-Sayre syndrome, 252  
 diagnosis, 256–59  
 pathology, 256–59
- kidney transplantation. *See* renal transplantation
- kinky hair disease, 164. *See also* Menkes disease
- Kinsbourne encephalopathy. *See* opsoclonus-myoclonus syndrome
- Korsakoff syndrome, 457
- Krabbe disease, 173  
 clinical features, 173–74  
 axonopathy, 176–77  
 diagnosis, 177  
 galactosylceramidase deficiency, 174–77  
 pathology, 174  
 pathophysiology, 174–77  
 treatment for, 177
- Kufor-Rakeb disease (KRS), 325, 379  
 clinical features, 378–79  
 juvenile Parkinson disease and, 402  
 pathophysiology, 380
- Kufs disease, 395  
 clinical features, 395–96  
 diagnosis, 396  
 forms of, 395  
 Parry disease and, 395–96  
 pathology, 396  
 pathophysiology, 396
- lactic acidosis, 52, 60
- Lafora bodies, 236–39
- Lafora disease, 235  
 clinical features, 235–36  
 diagnosis, 239–40  
 pathology, 236–38  
 pathophysiology, 238–39  
 treatment for, 240

- Landau-Kleffer syndrome  
 clinical features, 408–9  
 EEG for, 409  
 treatment for, 409
- language development  
 Boston naming test for, 19  
 cultural transmission through, 14  
 in developing child, 14  
 infantile DAT deficiency and, 153  
 syntax in, 14
- late infantile neuronal ceroid  
 lipofuscinosis, 395  
 clinical features, 244  
 pathology, 244–45
- late-onset Friedreich ataxia, 338
- late-onset infantile ceroid  
 lipofuscinosis, 120  
 diagnosis, 120, 245  
 Niemann-Pick type C disease and, 244–45  
 pathophysiology, 245  
 TPP1 and, 245  
 treatment, 120–21  
 treatment for, 245
- lead poisoning, chronic, 465–67  
 clinical manifestations, 465–66  
 anemia, 466  
 diagnosis, 466  
 mechanisms for, 465  
 sources of, 465  
 treatment for, 466–67
- Leber's hereditary optic neuropathy (LHON), 252  
 clinical features, 255–56
- Leigh syndrome, 56, 59–60, 146, 252  
 causes of, 149  
 clinical features, 146–47  
 coenzyme Q10 deficiency, 150  
 complex I deficiency, 148  
 complex II deficiency, 149  
 complex IV deficiency, 149–50  
 complex V deficiency, 150  
 diagnosis, 151  
 pathology, 147  
 pathophysiology, 148–51  
 pyruvate dehydrogenase deficiency and, 150–51  
 treatment for, 151
- leucine, 89
- levetiracetam, 240
- levodopa, 154, 367, 403–4
- Lewy bodies, 402–3
- LHON. *See* Leber's hereditary optic neuropathy
- limbic encephalitis, 431–32
- lithium citrate, 158–59
- lithium therapy  
 for Alexander disease, 187  
 for juvenile Huntington disease, 391
- liver diseases. *See* Wilson disease
- liver transplantation  
 for organic acidemias of the newborn, 67  
 for pyruvate carboxylase deficiency, 54  
 for urea cycle defects, 78
- loss of sensory organs, 443–45. *See also* visual and auditory loss
- lupus encephalopathy. *See* neuropsychiatric systemic lupus erythematosus
- lysine restriction, 85
- lysine protein intolerance, 90–93
- lysosomal storage disorders, 112. *See also* Farber lipogranulomatosis; fucosidosis; metachromatic leukodystrophy; multiple sulfatase deficiency; sialidosis
- magnesium, 462–63
- magnetic resonance (MR) imaging, 22–23  
 of Alexander disease, 186  
 for cerebrotendinous xanthomatosis, 386  
 for giant axonal neuropathy, 362–63  
 for infantile sialic acid storage disease, 126  
 for inherited cobalamin deficiency, 225  
 for Niemann-Pick type A/type B disease, 109  
 for Rasmussen encephalitis, 372  
 for vanishing white matter disease, 346–49  
 for Vici syndrome, 212  
 for x-linked adrenoleukodystrophy, 319–21
- magnetic resonance spectroscopy, 23
- malnutrition, 451–53  
 clinical features of, 451–52  
 somatic growth and, 451
- manganese, 463
- mannosidoses. *See also*  $\alpha$ -mannosidosis;  
 $\beta$ -mannosidosis  
 clinical features, 297  
 diagnosis, 299  
 pathology, 298–99  
 pathophysiology, 299  
 treatment for, 299–300
- maple syrup urine disease, 86  
 clinical features, 86–87  
 common, 86–87  
 diagnosis, 89  
 dihydrolipoamide dehydrogenase deficient, 86–87  
 intermediate, 86–87  
 intermittent, 86–87
- pathology, 87  
 pathophysiology, 87–89  
 leucine in, 89  
 thiamine-responsive E2 deficient, 86–87  
 treatment for, 89  
 types of, 87
- marijuana. *See* cannabinoids
- Maroteaux-Lamy syndrome, 286–88
- measles virus, 435–36
- MeCP2 mutations, 193–95
- medical child abuse  
 fictitious epilepsy, 476  
 intentional poisoning, 477  
 Munchausen syndrome, 476–77
- Mediterranean myoclonus. *See* Unverricht-Lundborg disease
- megalocephaly, 184. *See also* Alexander disease
- meganeurites, 244–45
- MELAS. *See* mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes
- MEMSA. *See* myoclonic epilepsy, myopathy and sensory ataxia
- Menkes disease, 164  
 clinical features of, 164–65  
 symptoms, 165  
 copper metabolism and, 165–68  
 diagnosis, 168–69  
 mottled/brindled mutant mice and, 169–70  
 pathology, 165  
 brain development, 165  
 pathophysiology, 165–68  
 treatment, 169–70  
 Wilson disease and, 376
- mercury poisoning, chronic, 468–70  
 clinical manifestations, 468–69  
 tremor mercurialis, 469  
 diagnosis, 469  
 mechanisms of, 468  
 sources, 468  
 treatment for, 469–70
- MERRF syndrome. *See* mitochondrial epilepsy with ragged-red fibers syndrome
- metachromatic leukodystrophy, 180  
 clinical features, 180–81  
 diagnosis, 182  
 pathology, 181  
 SUMF1 mutations, 181–82  
 pathophysiology, 181–82  
 subtypes, 181  
 treatment for, 182
- methamphetamines, abuse of, 479–80

## Index

- methotrexate, 449  
 methylbutyryl-CoA dehydrogenase deficiency, 104  
 methylenetetrahydrofolate reductase deficiency, 227–28  
   pathophysiology, 229  
 methylglutaconic acidemia, 104  
 methylmalonic aciduria and homocystinuria type C (MMACHC) protein, 225  
 methylmalonic acidemia, 62  
   clinical features, 61–62  
   diagnosis, 66  
   excitotoxicity, 62–66  
   incidence rates, 61  
   pathology, 62  
   pathophysiology, 62–66  
   treatment for, 66–67  
 methylprednisolone, 422  
 mexiletine, 209–10, 355  
 microcephaly, 38, 40  
   phenylketonuria and, 99–100  
 microsomal triglyceride transfer protein (MTTP) genes, 341–42  
 miglustat, 273–75  
 mimentine, 355  
 mineral deficiencies. *See also specific minerals*  
   nervous system development and, 462–63  
 MIRAS. *See* mitochondrial recessive ataxia syndrome  
 mitochondrial amidoxime reducing component, 70  
 mitochondrial disorders, in children.  
   *See also specific disorders*  
   clinical features, 251–56  
   diagnosis, 256–59  
   LHON, 252, 255–56  
   MNGIE, 252  
   NARP, 252  
   pathology, 256–59  
   pathophysiology, 259–60  
     apoptosis regulation, 260  
     NO deficiency, 260  
   Ramsay-Hunt syndrome, 255  
   retinitis pigmentosa, 171, 252  
   treatment for, 260  
   Wolff-Parkinson-White excitation syndrome, 251–55  
 mitochondrial disorders, in newborns, 58. *See also* coenzyme Q10 deficiency  
   aminoglycoside-induced hearing loss, 57  
   clinical features, 57–60  
   complex I deficiency, 59–60  
   cytochrome c oxidase deficiency, 58–59  
     reversible infantile myopathy from, 59  
   diagnosis for, 60  
   fatal hepatocerebral syndrome, 60  
   GRACILE syndrome, 57–58  
   Leigh syndrome, 56, 59–60  
   pathology, 60  
   pathophysiology, 60  
   Pearson syndrome, 57–58  
   RARS1 mutations, 60  
   thymidine kinase 2 mutations, 60  
   treatment for, 60  
 mitochondrial DNA depletion, 249  
 mitochondrial encephalomyopathy,  
   lactic acidosis and stroke-like episodes (MELAS), 143, 150, 252  
   clinical features, 251–55  
   diagnosis, 256–59  
   pathology, 256–59  
 mitochondrial epilepsy with ragged-red fibers (MERRF) syndrome, 150, 252  
   clinical features, 255  
   diagnosis, 256–59  
   pathology, 256–59  
 mitochondrial membrane protein-associated neurodegeneration (MPAN), 379  
   clinical features, 378–79  
   pathophysiology, 380  
 mitochondrial neurogastrointestinal encephalomyopathy (MNGIE), 252  
 mitochondrial recessive ataxia syndrome (MIRAS), 255–56  
 MMACHC gene protein. *See* methylmalonic aciduria and homocystinuria type C protein  
 MNGIE. *See* mitochondrial neurogastrointestinal encephalomyopathy  
 MOGS-CDG disorder, 96–97  
 molybdenum cofactor deficiency, 70  
   clinical features, 70–71  
   diagnosis, 73  
   enzymes, 70  
   pathology, 71  
   pathophysiology, 71–73  
     gephrin protein, 72–73  
     mutations in, 71–72  
   treatment for, 73–74  
     with cPMP, 74  
 Morquio syndrome, 286–88  
 motor development. *See also* myotonic dystrophy; Rett syndrome  
   with Friedreich ataxia, 339  
   infantile ascending hereditary spastic paraplegia, 178  
     clinical features of, 178  
     pathology, 179  
     pathophysiology, 179  
   infantile DAT deficiency and, 153  
   with infantile neuroaxonal dystrophy, 201, 379  
     clinical features, 201  
     diagnosis, 202–3  
     pathology, 201–2  
     pathophysiology, 202  
     treatment for, 203  
   pathophysiology, 339–40  
   socioeconomic status as factor for, 13  
 motor neuron diseases. *See* juvenile amyotrophic lateral sclerosis  
 mottled/brindled mutant mice, 169–70  
 MPAN. *See* mitochondrial membrane protein-associated neurodegeneration  
 MPI-CDG disorder, 96  
 MPU1-CDG disorder, 96  
 MPZ. *See* myelin protein-zero  
 MR imaging. *See* magnetic resonance imaging  
 MR spectroscopy, 23  
 MTTP genes. *See* microsomal triglyceride transfer protein genes  
 mucopolysaccharidoses, 283, 285  
   clinical features, 283–89, 292–93  
   diagnosis, 291  
   Hunter-Scheie syndrome, 283–86  
   Hurler syndrome, 283–86  
     pathophysiology, 290  
   hyaluronidase deficiency, 289  
   Maroteaux-Lamy syndrome, 286–88  
   Morquio syndrome, 286–88  
   pathology, 289  
   pathophysiology, 289–90  
   Scheie syndrome, 283–86  
   Sly disease, 288–89  
   treatment for, 291, 294  
   type II, 293  
     clinical features, 292–93  
     diagnosis, 293–94  
     pathology, 293  
     pathophysiology, 293  
   type III, 293  
     clinical features, 293  
     diagnosis, 293–94  
     pathology, 293  
     pathophysiology, 293  
   type IV, 293  
     clinical features, 293  
     diagnosis, 293–94  
     pathophysiology, 293

- multiple sclerosis dementia, 426  
   cognitive deficits from, 428  
   natural history, 428  
 multiple sulfatase deficiency, 180  
   clinical features, 180–81  
   diagnosis, 182  
   pathology, 181  
     SUMF1 mutations, 181–82  
   pathophysiology, 181–82  
   SUMF1 mutations, 181  
   treatment for, 182  
 multiple system atrophy, 249  
 multisystemic disease. *See* infantile  
   multisystemic disease  
 Munchausen syndrome, 476–77  
 muscle tone, 17–18  
 mutations  
   ABCD1 genes, 319, 321–22  
   ALS2 genes, 399  
   ATP13A2 proteins, 403  
   in Canavan disease, 156–58  
   chromosomal, 199  
   CP proteins, 383–84  
   frataxin proteins, 339–40  
   fumarate hydratase, 56  
   FUS genes, 399  
   of GAN gene, 363–64  
   GLA genes, 308–9  
   in infantile Andersen disease, 219  
   MeCP2, 193–95  
   Menkes disease and, 169–70  
   in molybdenum cofactor deficiency,  
     71–72  
   MTTP genes, 341–42  
   PLP, 188, 190  
   progressive brain disorders and,  
     principles for, 7  
   RANBP2 gene, 261–63  
   tolerability of, 7  
 mycophenolate mofetil, 247  
 myelin protein-zero (MPZ), 206  
 myelin-related diseases and disorders.  
   *See* Déjérine-Sottas disease;  
   Krabbe disease; Pelizaeus-  
   Merzbacher disease  
 myoclonic epilepsy, myopathy and  
   sensory ataxia (MEMSA),  
   143  
 myoclonus epilepsies, 232. *See also*  
   Lafora disease; Unverricht-  
   Lundborg disease  
 myopathy, 249  
 myotonia, 208–9  
 myotonic dystrophy, 208  
   clinical features, 208–9  
   later-onset, 209  
   diagnosis, 209  
   pathology, 209  
   pathophysiology, 209  
   treatment, 209–10  
   type 1, 208–9  
 naltrexone, 196  
 NARP. *See* neurogenic weakness with  
   ataxia  
 NBIA. *See* neurodegenerative  
   syndromes with brain iron  
   accumulation  
 necrosis, 30–31. *See also* acute  
   necrotizing encephalopathy;  
   familial infantile bilateral  
   striatal necrosis  
 neglect, maltreatment through, 474  
 neonatal adrenoleukodystrophy  
   clinical features, 47  
   diagnosis, 47  
   infantile Refsum disease and, 171  
   pathology, 47  
   pathophysiology, 47  
 neonates. *See* mitochondrial disorders,  
   in newborns  
 nephrotic syndrome, 249  
 nervous system development, 455  
 neural cell death, 30–31  
   apoptosis, 30  
   autophagy, 31  
   necrosis, 30–31  
   spinocerebellar ataxias, 354–55  
 neuregulin-1, 360  
 neurodegenerative disorders, death and  
   palliation in, 24–26  
   communication of death  
   expectations, 25  
   feeding and nutrition issues, 26  
   management of manifestations,  
   25–26  
   pain assessment, 25–26  
 neurodegenerative syndromes with  
   brain iron accumulation  
   (NBIA), 325, 378–79  
   clinical features, 378–79  
   diagnosis, 381  
   pathology, 379–80  
   pathophysiology, 380  
   treatment for, 381  
 neuroferritinopathy, 325, 378–79  
   pathology, 379–80  
   pathophysiology, 380  
 neurogenic weakness with ataxia  
   (NARP), 252  
 neurological development, 11–13  
   after cranial irradiation, 447–49  
   in developing child, 12–13  
   for intelligence variability, 13  
   after neonatal insults, 12–13  
   through positive reinforcement,  
   13  
   for reflex responses, 12, 16–17  
   with giant axonal neuropathy, 363  
   Niemann-Pick type C disease and,  
     269–70  
 neurological practice, genomics  
   in, 4  
 neuronal intranuclear inclusion  
   disease, 241  
   autonomic dysfunctional form,  
     241–42  
   clinical features, 241–43  
   diagnosis, 243  
   gastrointestinal dysfunction form,  
     241–42  
   pathology, 243  
   pathophysiology, 243  
 neuropsychiatric systemic lupus  
   erythematosus, 422  
   pathology, 422  
   treatment for, 422  
 newborn congenital glycosylation  
   disorders, 95  
   clinical features, 95–97  
 niacin, 457–58  
   deficiency, 458  
 nicotinamide supplements, 313  
 Niemann-Pick type A/type B disease,  
   107  
   clinical features, 107–8  
   diagnosis, 110  
   hepatosplenomegaly and, 107–8  
   pathology, 108–9  
   MR imaging for, 109  
   pathophysiology, 109–10  
   mutations in, 109–10  
   sphingomyelin in, 109–10  
   Tay-Sachs disease and, 107–8  
   treatment for, 110  
 Niemann-Pick type C disease, 244–45,  
   269  
   clinical features, 269–70  
   diagnosis, 273  
   neurological development and,  
     269–70  
   NPC proteins and, 271–73  
   pathology, 270–71  
   pathophysiology, 271–73  
   spleen and, 271  
   treatment for, 273–75  
 nigericin, 294  
 nitric oxide (NO) production, 78  
   mitochondrial disorders and, 260  
 NMDAR encephalitis. *See* anti-  
   N-methyl-aspartate receptor  
   encephalitis  
 NO production. *See* nitric oxide  
   production  
 Nogo protein, 400  
 nose. *See* olfactory reflex responses  
 NPC1/NPC2 proteins, 271–73

## Index

- occipital horn syndrome, 164. *See also* Menkes disease
- olanzapine, 391
- olfactory reflex responses, 17
- olivopontocerebellar atrophy, 351–53
- opsoclonus-myoclonus syndrome, 431
- oral reflex responses, 17
- organic acidemias. *See* infantile organic acidemias
- organic acidemias of the newborn, 61  
 clinical features, 61–62  
 diagnosis, 66  
 excitotoxicity, 62–66  
 incidence rates, 61  
 pathology, 62  
 pathophysiology, 62–66  
 treatment for, 66–67  
 types of, 62
- ornithine transcarbamoylase  
 deficiency, 76  
 ammonia and, 77–78  
 clinical features, 75–77  
 diagnosis, 78  
 glutamine and, 78  
 hyperammonemia and, 75–77  
 nitric oxide production, 78  
 pathology, 77  
 pathophysiology, 77–78  
 treatment for, 78
- pain assessment, with  
 neurodegenerative disorders,  
 25–26
- PANK2 enzymes, 329
- pantothenate kinase deficiency, 324  
 clinical features, 324–25  
 diagnosis, 329–30  
 PANK2 enzymes, 329  
 pathology, 325–26  
 pathophysiology, 326–29  
 treatment for, 330
- pantothenate kinase-associated  
 neurodegeneration, 379
- paraneoplastic neurological syndromes,  
 431–32  
 limbic encephalitis, 431–32  
 NMDAR encephalitis, 432  
 opsoclonus-myoclonus syndrome,  
 431
- paraplegia. *See* infantile ascending  
 hereditary spastic paraplegia
- Parry disease, 395–96
- Pearson syndrome, 252
- Pelizaeus-Merzbacher disease  
 clinical features, 188  
 diagnosis, 190  
 hypotonia and, 188  
 pathology, 188–89  
 pathophysiology, 190
- PLP mutations, 188, 190  
 treatment for, 190
- pellagra, 458
- penicillamine, 376–77
- pernicious anemia, 459
- peroxysomal diseases and disorders, 43.  
*See also* neonatal  
 adrenoleukodystrophy;  
 rhizomelic chondrodysplasia  
 punctata; Zellweger disease
- peroxysomes, 44–46
- PEX genes. *See also* neonatal  
 adrenoleukodystrophy;  
 peroxysomes; rhizomelic  
 chondrodysplasia punctata  
 mutations in, 47
- phenobarbital, 412
- phenylbutyrate, 199
- phenylketonuria, 40, 99  
 clinical features, 99  
 diagnosis, 101  
 microcephaly and, 99–100  
 pathology, 99–100  
 pathophysiology, 100–1  
 treatment for, 101–2  
 with enzyme substitution therapy,  
 101–2
- phenytoin, 412
- phosphorous, 462
- phytanic acid storage, 171
- pimozide, 391
- pioglitazone, 340
- PLA2G6 associated neurodegeneration  
 (PLAN), 325
- plasma creatine kinase, 199
- PLP mutations. *See* proteolipid protein  
 mutations
- PMM2-CDG disorder, 96
- PMP22 protein, 206
- poisonings. *See also* lead poisoning;  
 mercury poisoning  
 intentional, 477
- Pompe disease, 136  
 clinical features, 136–37  
 diagnosis, 139  
 infantile acid maltase deficiency, 139  
 infantile form, 137  
 pathology, 137–38  
 pathophysiology, 139  
 treatment for, 139
- positive reinforcement, neurological  
 development influenced by, 13
- pramipexole, 154
- primary coenzyme Q10 deficiency, 249
- primary psychosis, 479
- principles, for progressive brain  
 disorders  
 with alternative statistical constructs,  
 7
- of early diagnosis and treatment, 5–7  
 with evidence-based medicine, 7  
 genomics in neurological practice, 4  
 for immunization factors, 5  
 for infective factors, 5  
 for later-onset disorders, variable  
 expression of, 4  
 for mutations, tolerability of, 7  
 for neural regression patterns, 4–5  
 neurodegenerative neurology,  
 localization in, 5  
 from primal injuries, 4  
 from secondary injuries, 4
- progressive multifocal  
 leukoencephalopathy, 436–37
- progressive myoclonic epilepsy type 1.  
*See* Unverricht-Lundborg  
 disease
- prolonged hospitalization,  
 psychological disturbances  
 from, 471–72  
 interventions for, 472
- propionic acidemia, 62  
 clinical features, 61–62  
 diagnosis, 66  
 excitotoxicity, 62–66  
 incidence rates, 61  
 pathology, 62  
 pathophysiology, 62–66  
 treatment for, 66–67
- propranolol, 391
- proteolipid protein (PLP) mutations,  
 188, 190
- proton-coupled folate transporter  
 deficiency, 228  
 pathophysiology, 229
- PRX genes, 206
- psychological development, in  
 developing child, 12–13
- psychosis  
 from adolescent drug abuse, 479  
 primary, 479
- Purkinje cells, 80
- pyridoxal isonicotinoyl hydrazone, 340
- pyridoxine, 84–85, 458
- pyridoxine-5'-phosphate-responsive  
 epileptic encephalopathy  
 clinical features, 82–83  
 diagnosis, 85  
 pathology, 83–84  
 pathophysiology, 84–85  
 antiquitin deficiency in, 84–85  
 treatment for, 85  
 through lysine restriction, 85  
 vitamin B6 and, 84–85
- pyridoxine-dependent epilepsy  
 clinical features, 82–83  
 diagnosis, 85  
 pathology, 83–84

- pathophysiology, 84–85  
   antiquitin deficiency in, 84–85  
   treatment for, 85  
   through lysine restriction, 85  
   vitamin B6 and, 84–85  
 pyrimethamine, 281–82  
 pyruvate carboxylase deficiency, 52  
   benign, 52  
   clinical features of, 52  
   clinical severity of, 53  
   diagnosis of, 53–54  
   infantile forms of, 52  
   pathology, 53  
   pathophysiology, 53  
   severe neonatal, 52  
   treatment for, 54  
     through liver transplantation, 54  
   types of, 53–54  
 pyruvate dehydrogenase deficiency, 48  
   biochemical variants of, 48  
   clinical features, 48–50  
   diagnosis of, 51  
   Leigh syndrome and, 150–51  
   pathology, 50  
   pathophysiology, 50–51  
   treatment for, 51
- quinidine, 400  
 quinine, 355
- Ramsay-Hunt syndrome, 255  
 RANBP2 gene mutations, 261–63  
 rapamycin, 187  
 RARS1 mutations. *See* arginyl-transfer  
   RNA synthetase mutations  
 Rasmussen encephalitis, 371  
   clinical features, 371–72  
   cognitive development, 372  
   diagnosis, 373  
   pathology, 372  
   pathophysiology, 372–73  
   treatment for, 373  
 reflex responses, 12  
   auditory, 17  
   olfactory, 17  
   oral, 17  
   tactile, 16–17  
   visual, 17  
 Refsum disease. *See* infantile Refsum  
   disease  
 renal transplantation, for organic  
   acidemias of the newborn, 66–67  
 retinitis pigmentosa, 171, 252. *See also*  
   infantile Refsum disease; Usher  
   syndrome  
 retinitis pigmentosa-deafness  
   syndrome, 444  
 Rett syndrome, 191  
   autism, 193
- clinical features, 191–93  
 diagnosis, 195–96  
 epilepsy and, 196  
 incidence rates, by gender, 191–93  
 MeCP2 mutations, 193–95  
 pathology, 193  
 pathophysiology, 193–95  
   treatment for, 196  
 reversible cytochrome c oxidase  
   deficient infantile myopathy,  
   59  
 RFT1-CDG disorder, 96  
 rhizomelic chondrodysplasia punctata  
   clinical features, 47  
   diagnosis, 47  
   pathology, 47  
   pathophysiology, 47  
 riboflavin deficiency, 457  
 riluzole, 199, 391, 400  
 risperidone, 391  
 rituximab, 373  
 RNA interference therapy, 355  
 ropinirole, 154
- Salla disease, 125–27  
 Sandhoff disease, 276  
   clinical features, 276–77  
   diagnosis, 281  
   pathology, 277–78  
   pathophysiology, 278  
   treatment for, 281–82  
 SANDO. *See* sensory ataxic  
   neuropathy, dysarthria and  
   ophthalmoplegia  
 Sanfilippo syndrome, 286–88  
 Scheie syndrome, 283–86  
 Schindler disease, 112, 314  
   clinical features, 314–15  
   diagnosis, 315–16  
   pathology, 315  
   pathophysiology, 315  
   treatment for, 316  
   type I, 314–15  
     diagnosis, 315  
     pathology, 315  
   type II, 314–15  
     diagnosis, 315  
     pathology, 315  
   type III, 315  
 scurvy, 459–60  
 secondary coenzyme Q10 deficiency,  
   248–49  
 Segawa disease, 365  
   clinical features, 365–66  
   diagnosis, 366–67  
   pathology, 366  
   pathophysiology, 366  
   treatment for, 367  
 selenium, 463
- SENDA. *See* static encephalopathy of  
   childhood with  
   neurodegeneration in  
   adulthood  
 sensory ataxic neuropathy, dysarthria  
   and ophthalmoplegia  
   (SANDO), 143  
   clinical features, 255–56  
 sialic acid storage disease. *See* infantile  
   sialic acid storage disease  
 sialidosis, 111–12  
   clinical features, 111–12  
   diagnosis, 113  
   pathology, 112–13  
   pathophysiology, 113  
 SLC35A2-CDG disorder, 96–97  
 SLC35C1-CDG disorder, 96–97  
 Sly disease, 288–89  
 SPGs. *See* hereditary spastic paraplegias  
 Spielmeyer-Vogt disease, 246, 395  
   Batten disease and, 246  
   brain development and, 246–47  
   clinical features, 246  
   diagnosis, 247  
   pathology, 246–47  
   pathophysiology, 247  
   treatment for, 247  
 spinal muscular atrophy  
   Brown-Vialetto-van Laere disease  
     and, 198  
   clinical features, 197  
   diagnosis, 199  
   hypotonia and, 197  
   pathology, 198–99  
   pathophysiology, 199  
     chromosomal mutations, 199  
   treatment for, 199–200  
   Type 1, 197–98  
   Type 2, 197–98  
   Type 3, 198  
 spinocerebellar ataxias, 351  
   clinical features, 351  
   diagnosis, 355  
   pathology, 351–53  
   pathophysiology, 353–55  
     calcium homeostasis, alterations  
       in, 354  
     neuronal death, 354–55  
     polyglutamine neurotoxicity,  
       353–54  
   phenotypes, 352–53  
   treatment for, 355  
 SRD5A3-CDG disorder, 96–97  
 Stanford-Binet Intelligence Scale,  
   13, 19  
 starvation. *See also* malnutrition  
   neurochemical consequences of, 452  
   neurological effects of, 451–52  
   recovery from, 452–53

## Index

- static encephalopathy of childhood  
 with neurodegeneration in  
 adulthood (SENDA), 325, 379  
 statin use, 249  
 Steiner disease, 208–9. *See also* type  
 1 myotonic dystrophy  
 stenosis of the aqueduct of Sylvius, 424  
 steroid therapy, 263  
 subacute sclerosing panencephalitis,  
 435–36. *See also* measles virus  
 clinical stages of, 435  
 substrate reduction therapy, 281  
 succinate dehydrogenase deficiency, 56  
 succinic semialdehyde dehydrogenase  
 deficiency, 104  
 sudanophilic leukodystrophy. *See*  
 Pelizaeus-Merzbacher disease  
 sulfatide modifying factor 1 (SUMF1)  
 mutations, 181–82  
 sulfite oxidase, 70  
 SUMF1 mutations. *See* sulfatide  
 modifying factor 1 mutations  
 syntax, in language development, 14  
 systemic inflammatory diseases,  
 421–22  
 neuropsychiatric systemic lupus  
 erythematosus, 422  
 pathology, 422  
 treatment for, 422
- tacrolimus, 373  
 tactile reflex responses, 16–17  
 Tay-Sachs disease, 107–8, 276  
 clinical features, 276–77  
 diagnosis, 281  
 pathology, 277–78  
 pathophysiology, 278  
 temporal lobectomy psychosis, from  
 epilepsy, 415  
 tetany, 456  
 thiamine, 457  
 activation, 369  
 deficiency, 457  
 thiamine-responsive E2 deficient maple  
 syrup urine disease, 86–87  
 thiomersal, 469–70  
 thymidine kinase 2 mutations, 60  
 tissue nonspecific isoenzyme of alkaline  
 phosphatase deficiency  
 clinical features, 82–83  
 diagnosis, 85  
 pathology, 83–84  
 pathophysiology, 84–85  
 antequitin deficiency in, 84–85  
 treatment for, 85  
 through lysine restriction, 85  
 vitamin B6 and, 84–85  
 tizanidine, 355  
 topiramate, 240
- touch. *See* tactile reflex responses  
 TPP1. *See* tripeptidyl peptidase 1  
 transplantation. *See* bone marrow  
 transplantation; hematopoietic  
 stem cell transplantation; liver  
 transplantation; renal  
 transplantation  
 tremor mercurialis, 469  
 tricarboxylic acid cycle disorders,  
 55  
 aconitase deficiency, 55–56  
 clinical features, 55–56  
 diagnosis of, 56  
 fumarate hydratase mutations, 56  
 Leigh syndrome, 56  
 pathology, 56  
 pathophysiology, 56  
 succinate dehydrogenase deficiency,  
 56
- trientine, 376–77  
 tripeptidyl peptidase 1 (TPP1), 245  
 tryptophan production, 312–13  
 type 1 myotonic dystrophy, 208–9  
 type 1 spinal muscular atrophy, 197–98  
 type 2 spinal muscular atrophy, 197–98  
 type 3 spinal muscular atrophy, 198  
 type A pyruvate carboxylase deficiency,  
 53–54  
 type B pyruvate carboxylase deficiency,  
 53–54  
 type C pyruvate carboxylase deficiency,  
 53–54  
 type I Cockayne syndrome, 162  
 type II Cockayne syndrome, 162  
 type III Cockayne syndrome, 162  
 type I Gaucher disease, 265–66  
 type II Gaucher disease, 265–66  
 type III Gaucher disease, 265–66  
 type I Schindler disease, 314–15  
 type II Schindler disease, 314–15  
 type III Schindler disease, 315  
 tyrosinemia type 1, 93
- Unverricht-Lundborg disease, 232  
 clinical features, 232–33  
 cystatins and, 233  
 diagnosis, 233  
 pathology, 233  
 pathophysiology, 233  
 treatment for, 233–34
- urea cycle defects, 75  
 ammonia and, 77–78  
 clinical features, 75–77  
 diagnosis, 78  
 glutamine and, 78  
 hyperammonemia and, 75–77  
 nitric oxide production, 78  
 pathology, 77  
 pathophysiology, 77–78
- related disorders, 76  
 treatment for, 78  
 Usher syndrome  
 clinical features, 444–45  
 types of, 444
- vagus nerve stimulator therapy, 233–34  
 valienamine, 304  
 valproate, 199, 240, 412  
 vanishing white matter disease, 346  
 clinical features, 346  
 diagnosis, 350  
 MR imaging for, 346–49  
 pathology, 346–49  
 pathophysiology, 349–50  
 ventricular hemorrhage, 424  
 very late-onset Friedreich ataxia, 338  
 very low density lipoproteins (VLDLs),  
 343
- Vici syndrome, 211  
 clinical features, 211  
 pathology, 212  
 pathophysiology, 212–13  
 treatment for, 213
- viral disorders, neural regression in,  
 434–37  
 HIV-associated cognitive disorder,  
 434–35
- progressive multifocal  
 leukoencephalopathy, 436–37  
 subacute sclerosing panencephalitis,  
 435–36  
 clinical stages of, 435
- visual and auditory loss, 444–45  
 deafblindness, causes of, 444  
 deafness, 444  
 Usher syndrome  
 clinical features, 444–45  
 types of, 444
- visual reflex responses, 17  
 vitamin A, 455–56  
 in abetalipoproteinemia treatments,  
 344–45  
 deficiency, 455  
 toxicity from, 455–56  
 vitamin B1. *See* thiamine  
 vitamin B2. *See* riboflavin deficiency  
 vitamin B6. *See* pyridoxine  
 vitamin B12. *See* cobalamin  
 vitamin C, 459–60  
 deficiency, 459–60  
 vitamin D, 456  
 deficiency, 456  
 toxicity from, 456  
 vitamin E, 456  
 deficiency  
 ataxia with, 340, 342  
 Bassen-Kornzweig disease and,  
 341–42, 456

- vitamin K, 456
- vitamins. *See also specific vitamins*
  - deficiencies and excesses, 454–60
  - nervous system development and, 455
- VLCFA coenzymes, 321–22
- VLDLs. *See* very low density lipoproteins
- Wallerian (axonal) degeneration, 34
- Wechsler Intelligence Scale for Children-III (WISC-III), 19
- Wechsler preschool and primary scale of intelligence (WPPSI), 19
- Wernicke syndrome, 457
- Wilson disease, 375
  - clinical features, 375–76
  - diagnosis, 376
  - Menkes disease and, 376
- pathology, 376
- pathophysiology, 376
- treatment for, 376–77
- WISC-III. *See* Wechsler Intelligence Scale for Children-III
- Wolff-Parkinson-White excitation syndrome, 251–55
- Woodhouse-Sakati syndrome, 379
  - clinical features, 379
- WPPSI. *See* Wechsler preschool and primary scale of intelligence
- xanthine oxidoreductase, 70
- xanthomas. *See* cerebrotendinous xanthomatosis
- x-linked adrenoleukodystrophy, 317
  - ABCD1 gene mutations, 319, 321–22
  - clinical features, 317–19
  - diagnosis, 322–23
  - pathology, 319–21
- progressive axonopathy, 319
- treatment for, 323
- VLCFA coenzymes, 321–22
- X-linked disorders. *See* Fabry disease; Menkes disease; Pelizaeus-Merzbacher disease
- X-linked hydrocephalus, 425–26
- Zellweger disease, 42–46
  - diagnosis of, 46
  - infantile Refsum disease and, 171
  - pathology of, 43–44
  - pathophysiology, 44–46
  - phytanic acid storage and, 171
  - symptoms of, 42–43
  - treatment of, 46
- zinc therapy, 300, 376–77
- for aceruloplasminemia, 384
- zonisamide, 240