NOTES
CEREBROSPINAL MALFORMATIONS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Disorders affecting normative central nervous system (CNS) development/ function
- Varying severity, intensity

CAUSES

- Primary
  - Genetic mutation/idiopathic
- Secondary
  - E.g. trauma, infection, neoplasm, environmental factors

RISK FACTORS

- Cerebral ischemia, delivery trauma, premature birth, teratogenic substance exposure (prenatal)
- Supportive structure (bone, connective tissue) malformation → physically obstructs CNS development

SIGNS & SYMPTOMS

- Developmental milestones
  - Not met
- Motor dysfunction
  - Ataxia, paresis, unsteady gait, speech impairment, poor coordination
- Dysautonomia
- Intellectual disability
  - Learning/memory issues
- Dementia

DIAGNOSIS

DIAGNOSTIC IMAGING

- CT scan, MRI

OTHER DIAGNOSTICS

- Neurological exam

TREATMENT

- Mostly supportive

SURGERY

- In some cases; see individual disorders

ARNOLD–CHIARI MALFORMATION

osms.it/arnold-chiari-malformation

PATHOLOGY & CAUSES

- Insufficient posterior fossa growth → developmental cerebellum, brainstem, craniocervical junction malformation
- Affects cerebellar structure, position
- AKA Chiari malformation type II (types I, III, IV—no specific name)
- *Chiari malformations:* similar presentations, different mechanism development
- *Accompanying findings:* aqueductal stenosis, upward cerebellar displacement, cerebellar dysplasia
- Cerebellar tonsil protrusion through foramen magnum
- *Associations:* lumbosacral myelomeningocele, Pierre Robin syndrome, neurofibromatosis type I, Noonan syndrome
- Commonly accompanies spina bifida

RISK FACTORS

- Hydrocephalus (congenital/acquired)
- Ehlers–Danlos syndrome, Marfan syndrome → craniocervical joint instability → cerebellar tonsil displacement
- Posterior cranial fossa malformation (agenesia, craniosynostosis, osteopetrosis)
- Posterior cranial fossa pathology (tumor, abscess, cyst, hematoma)

COMPLICATIONS

- Aqueductal stenosis → impaired CSF flow → non-communicating hydrocephalus → lateral, third ventricle dilatation
- Fourth ventricle obstruction → non-communicating hydrocephalus → aqueduct dilatation; lateral, third ventricles
- Brainstem, spinal cord compression
- Syringomyelia (hydrocephalus → distention, dilation of spinal cord's central canal)

SIGNS & SYMPTOMS

- Nausea, vertigo, nystagmus, unsteady gait
- Lumbosacral/thoracic myelomeningocele presence
- Medulla oblongata compression → dysautonomia (↓ ↑ heart/breathing rate, neurogenic bladder, sleep apnea, pupillary dilation, etc.)
- Paralysis/dysesthesia below spinal compression
- Valsalva maneuver → symptoms worsen (increased intracranial pressure)

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan, MRI

- Findings include presence of myelomeningocele, cerebellar tissue (downward displacement) through foramen magnum, small fourth ventricle, tectal beaking, atlas assimilation

OTHER DIAGNOSTICS

- Neurological exam

TREATMENT

SURGERY

- Open neural tube defect closure
- Shunt placement (relieves hydrocephalus)
- Bone removal (↓ brain structure pressure)

OTHER INTERVENTIONS

- *Address complications:* neurogenic bowel, bladder; neonatal feeding difficulty; respiratory failure, apnea

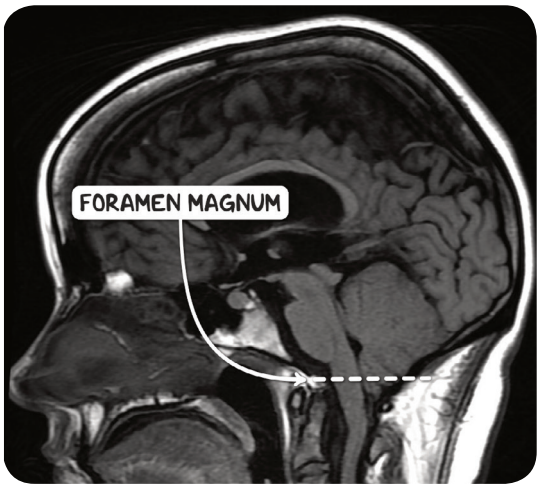

Figure 66.1 An MRI scan of the head in the sagittal plane of an individual with an Arnold-Chiari malformation. There is a small posterior fossa and partial descent of the brainstem and the cerebellar tonsils through the foramen magnum.

CEREBRAL PALSY (CP)

osms.it/cerebral-palsy

PATHOLOGY & CAUSES

- Wide disorder group; non-progressive cerebral lesions impair motor, postural function/muscle tone
- Most common motor disorder, 2.1 per 1000 babies affected, ages 0–3 years
- Varying severity, complexity
- Often accompanied by mental function impairment, epilepsy

MNEMONIC: PALSY

Main characteristcs of CP

Paresis
Ataxia
Lagging motor development
Spasticity
Young

CAUSES

- *Primary:* genetic (autosomal recessive glutamate decarboxylase-1 deficiency)
- *Secondary:* preterm birth (most common cause), CNS injury, intrauterine growth restriction, intrauterine infection, antepartum hemorrhage, severe placental pathology, multiple pregnancy

RISK FACTORS

- Prenatal/perinatal
  - CNS trauma (pregnancy/birth)
  - Cerebrovascular insult (infarction, thrombosis, hypoxic-ischemic injury)
  - CNS infection
  - Radiation exposure
  - Methylmercury/alcohol (prenatal exposure)
  - Maternal smoking/obesity
  - Infections during pregnancy

- Postnatal
  - Stroke, CNS trauma, hypoxia (drowning), sepsis/meningitis, kernicterus

SIGNS & SYMPTOMS

- Motor symptoms (type-dependent)
  - Paresis, ataxia, spasticity, irregular posture, orthopedic contracture, scoliosis, seizure, neurogenic bladder/bowel, impaired vision/speech, difficulty feeding/swallowing

CLASSIFICATION OF CEREBRAL PALSY

	SPASTIC	ATAXIC	ANTHETOID	MIXED
SYMPTOMS	Hypertonia, spasticity	Hypotonia, poor movement coordination	Athetosis, dystonia, chorea	Mixed
LESION LOCATION	Upper motor neuron	Cerebellum	Basal ganglia	Mixed

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan, MRI

- Type-dependent
  - Hypoxic-ischemic lesions (e.g. periventricular leukomalacia/basal ganglia lesions); cortical malformation; hydrocephalus

Ultrasound

- In young infants with open anterior fontanelle

OTHER DIAGNOSTICS

- Neurological exam
- Diagnostic tests
  - Differentiate from other motor dysfunction disorders (e.g metabolic disorders, stroke, hydrocephalus, hematomas)

TREATMENT

- No definitive treatment

MEDICATIONS

- Benzodiazepines → myorelaxation, anxiety relief
- Spasmolytics → muscle-spasticity relief
- Anticonvulsants → seizure treatment, prevention
- Pain medication

SURGERY

- Posture correction

OTHER INTERVENTIONS

- Physical, occupational, speech therapy
- Posture correction
  - Braces/other orthotic devices

DANDY–WALKER SYNDROME (DWS)

osms.it/dandy-Walker-malformation

PATHOLOGY & CAUSES

- Neurodevelopmental disorders; affect cerebellar vermis, fourth ventricle
- Classical triad
  - Vermis hypoplasia/agenesis, cystic dilatation (fourth ventricle), posterior fossa enlargement
- Accompanying disorders (wide range)
  - Cortical dysplasia, syringomyelia, schizencephaly, corpus callosum dysgenesis, cleft palate, etc.
- Associated with posterior fossa malformations–hemangiomas–arterial anomalies–cardiac defects–eye abnormalities–sternal cleft and supraumbilical raphe syndrome (PHACES)

MNEMONIC: DWS

Components of DWS

Dilated 4th ventricle
Water on the brain
Small vermis

CAUSES

- Genetic, environmental factors
  - Meckel syndrome
  - Chromosomal aneuploidy (e.g. 45X, triploidy)
  - Rubella infection/warfarin exposure during pregnancy
  - Maternal alcohol consumption
  - Congenital heart defect
  - Neural tube defect
  - Holoprosencephaly

COMPLICATIONS

- Foramina (Magendie, Luschka) atresia → hydrocephalus

SIGNS & SYMPTOMS

- Macrocephaly, developmental milestones not met (mental, motor), impaired motor coordination, unsteady gait, seizure, lower limb spasticity, eye/ear involvement (rarely)

CLASSIFICATION OF DANDY–WALKER MALFORMATION

	PATHOLOGY
MALFORMATION	Posterior fossa enlargement, elevated tentorium, vermis agenesis, cystic dilatation (fourth ventricle) Often accompanied by spina bifida, hydrocephalus
VARIANT	Hypoplastic vermis, posterior fossa enlargement, fourth ventricle dilated
MEGA CISTERNIA MAGNA	Posterior fossa enlargement, cisterna magna enlargement, hypoplastic vermis fourth ventricle dilated

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI, prenatal ultrasound

- Characteristic findings
  - Cerebellar vermis agenesis/hypoplasia, cystic dilatation (fourth ventricle), posterior fossa enlargement; hydrocephalus, absent corpus callosum may also be present

LAB RESULTS

- Amniocentesis

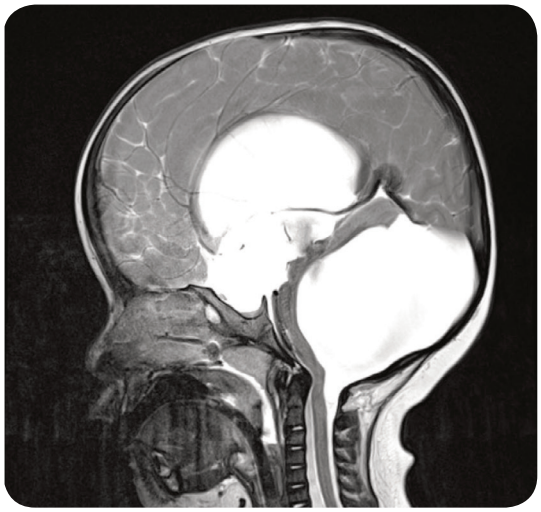

Figure 66.2 An MRI scan of the head in the sagittal plane demonstrating a Dandy-Walker malformation in a one-year-old boy. There is accompanying gross hydrocephalus.

TREATMENT

- No definitive treatment

SURGERY

Ventricular-peritoneal shunt

- Manages hydrocephalus

OTHER INTERVENTIONS

- Physical, occupational therapy

NORMAL PRESSURE HYDROCEPHALUS (NPH)

osms.it/normal-pressure-hydrocephalus

PATHOLOGY & CAUSES

- Cerebrospinal fluid (CSF) accumulation → progressive lateral ventricle enlargement
- AKA Hakim's syndrome
- Intracranial pressure (ICP) not normal (name is misnomer)

CAUSES

- Slight–moderate elevation → classical ↑ ICP symptoms (nausea, vomiting, photophobia, neck pain, stiffness) not evident
- ↑ CSF → ↑ ICP → lateral ventricle dilation → pressure on corona radiata
  - Urinary incontinence), brainstem structure (magnetic gait), periventricular limbic system (dementia)
- Idiopathic/secondary
  - Cerebrovascular insult, meningitis, trauma, tumor

RISK FACTORS

- Prevalence largest among elderly (common onset approx. 60 years old)

SIGNS & SYMPTOMS

- Unsteady gait
  - Described as magnetic or "glue-footed"
- Urinary incontinence
- Cognitive impairment

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI/CT scan

- Ventriculomegaly, enlarged Sylvian fissures, enlarged sulci with no cortical atrophy

OTHER DIAGNOSTICS

- High-volume lumbar puncture/lumbar drain trial
  - Improved functionality with CSF removal
- Neurological exam

TREATMENT

SURGERY

- In some situations

Ventriculoperitoneal shunt

- ↑ ICP relief

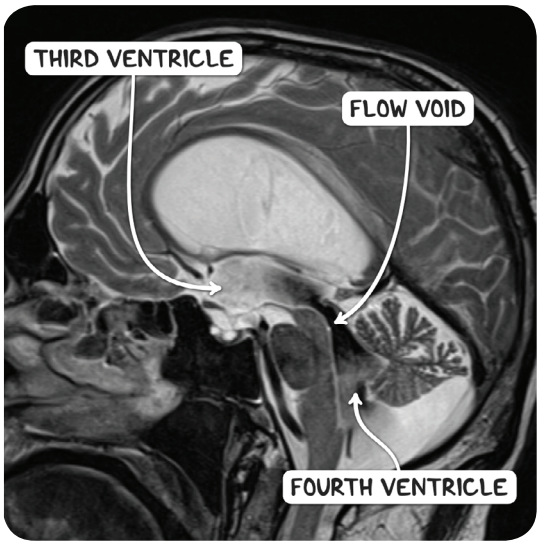

Figure 66.3 An MRI scan of the head in the sagittal plane demonstrating hydrocephalus. There is a prominent flow void in the sylvian aqueduct, suggesting a normal-pressure hydrocephalus.

RETT SYNDROME

osms.it/rett-syndrome

PATHOLOGY & CAUSES

- Rare neurological disorder, impairs motor function (eating, walking, talking, breathing)
- AKA cerebroatrophic hyperammonemia
- Associated with prolonged QT syndrome

CAUSES

- X-linked autosomal dominant MeCP2 gene mutation (spontaneous)
- MeCP2 protein involved in forming neuronal connections, when only one gene is mutated, the other one can compensate to a degree

RISK FACTORS

- Young, individuals who are biologically female
- Extraordinarily, individuals who are biologically male with Klinefelter syndrome (XXY), otherwise fatal for biologically-male (XY) individuals

COMPLICATIONS

- Growth failure
- Seizure
- Fractures (related to ↓ bone mineralization)
- Cardiac abnormalities; e.g. prolonged QTc interval
- Autonomic nervous system dysfunction
- Sleep disturbances
- Behavioral issues; e.g. clapping, "pill-rolling" (due to extrapyramidal motor defects)

CLASSIFICATION OF RETT SYNDROME

	AGE	SYMPTOMS
EARLY ONSET (STAGE I)	6–18 months	Decreased playfulness, eye contact reduced/absent
RAPID DETERIORATION (STAGE II)	1–4 years	Massive speech/motor skill reduction, repetitive hand movement (clapping/clasping), hyperventilation/breath-holding, acquired microcephaly
PLATEAU (PSEUDO-STATIONARY) (STAGE III)	2–10 years	↑ attention span, eye contact, seizures, apraxia
LATE MOTOR DETERIORATION (STAGE IV)	10 years–life	Progressive muscle weakness, rigidity, spasticity, scoliosis, cognitive stability

SIGNS & SYMPTOMS

- Manifests after six months old → later, divided into four stages

DIAGNOSIS

LAB RESULTS

- Genetic test
  - *MeCP2* mutation

OTHER DIAGNOSTICS

- Clinically diagnosed (characteristic findings)
  - Loss of acquired purposeful hand skills, spoken language
  - Gait abnormalities
  - Stereotypic hand movements

TREATMENT

- No definitive treatment

MEDICATIONS

- SSRI (behavioral issues)

OTHER INTERVENTIONS

- Occupational, speech, physical therapy
- Nutritional support for fracture reduction

SEPTO-OPTIC DYSPLASIA (SOD)

osms.it/septo-optic-dysplasia

PATHOLOGY & CAUSES

- Congenital malformation triad
  - Underdeveloped optic nerve, hypopituitarism, absent septum pellucidum
- AKA de Morsier syndrome
- Most individuals have two of three components, some present with all three
- May also have encephalomalacia, schizencephaly, ectopic pituitary tissue

CAUSES

- Genetic
  - Spontaneous/inherited *HESX1*, *OTX2*, *SOX2*, *PAX6* mutation
- *In utero* sodium valproate, cocaine exposure

SIGNS & SYMPTOMS

- Nystagmus
- Visual impairment
- Intellectual impairment
- Seizure
- Growth hormone deficiency → short stature, hypoglycemia, micropenis (if biologically-male)
- Vasopressin deficiency → diabetes insipidus
- Hyperprolactinemia
- Hyperbilirubinemia → jaundice

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI

- Optic nerve hypoplasia, septum pellucidum, corpus callosum agenesis

LAB RESULTS

Genetic testing

- *HESX1*, *OTX2*, *SOX2*, *PAX6* mutations

OTHER DIAGNOSTICS

- Neurological exam

TREATMENT

MEDICATIONS

- Hormone replacement therapy
- Anticonvulsants → seizure treatment, prevention

OTHER INTERVENTIONS

- Treat complications
  - Ophthalmic, physical, and occupational therapy

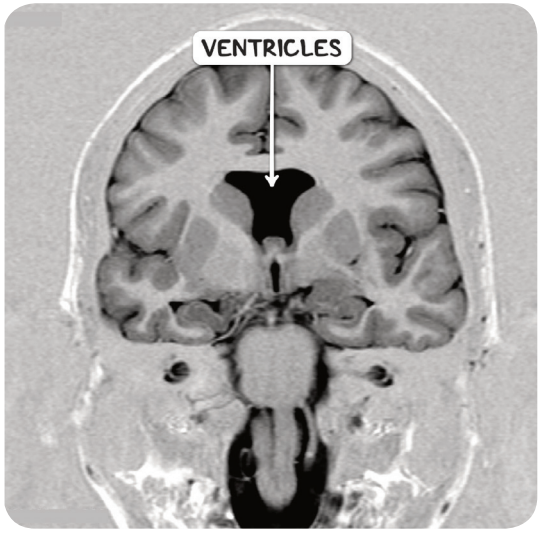

Figure 66.4 An MRI scan of the head in the coronal plane of an individual with septo-optic dysplasia. The septum pellucidum, which normally separates the two lateral ventricles, is absent.

SPINA BIFIDA

osms.it/spina-bifida

PATHOLOGY & CAUSES

- Congenital spinal column, meninges malformation
- Most common neural tube defect
- Improper vertebrae formation allows meninges/spinal cord to protrude dorsally out of spinal canal
- Occurs in fourth week of pregnancy
- Usually manifests in lumbar part of spinal column (can occur elsewhere)
- Most individuals with spina bifida have latex allergy (complicates medical procedures)
- Some individuals with spina bifida have intellectual impairment
- Can present with Arnold–Chiari malformation
- Associated with malformed corpus callosum, cerebellum, cerebral cortex

RISK FACTORS

- Multifactorial
  - Genetic, environmental factors
- Pregnancy
  - Folate deficiency, anticonvulsant use
- Obesity
- Poorly-managed diabetes mellitus

COMPLICATIONS

- Meningitis; neurogenic bladder, bowel; nerve damage paralysis; tethered cord syndrome; cognitive impairment; pressure ulcer; seizure; hydrocephalus; orthopedic problems

SIGNS & SYMPTOMS

- Lower-back pain, hip dysplasia, dysesthesia (below lesion), leg weakness, nystagmus, clubfoot, scoliosis

CLASSIFICATION OF SPINA BIFIDA

		PATHOLOGY	SYMPTOMS
SPINA BIFIDA OCCULTA		Improper vertebral arch fusion The meninges, spinal cord do not protrude from spinal canal	Improper vertebrae formation, Meninges herniate through opening, lining entire malformation and forming a CSF-filled sac
SPINA BIFIDA CYSTICA	MENINGOCELE	1–4 years	Massive speech/motor skill reduction, repetitive hand movement (clapping/clasping), hyperventilation/breath-holding, acquired microcephaly
	MYELOMENINGOCELE	2–10 years	Improper vertebrae formation, Meninges, spinal cord herniate through opening
	MYELOCELE (AKA OPEN SPINA BIFIDA)	10 years–life	Improper vertebrae formation, Spinal cord completely exposed

DIAGNOSIS

DIAGNOSTIC IMAGING

Prenatal ultrasound

X-ray, CT scan, MRI

- Show improper vertebral formation

LAB RESULTS

- ↑ alpha-fetoprotein
  - Spina bifida occulta does not show ↑
- Genetic tests

OTHER DIAGNOSTICS

- Visual examination
  - Visible meningocele, myelomeningocele at birth

TREATMENT

SURGERY

- Reposition meninges, spinal cord into spinal canal

OTHER INTERVENTIONS

- Resolve complications
  - Seizure, hydrocephalus, orthopedic problems
- Physical therapy

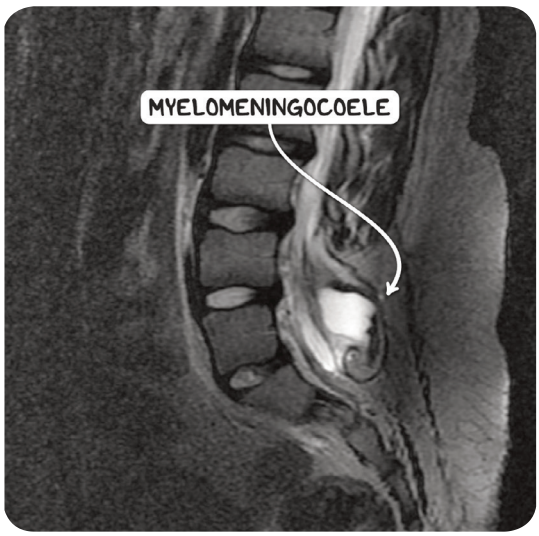

Figure 66.5 An individual with spina bifida and a an associated myelomeningocoele, also known as spina bifida cystica.

SYRINGOMYELIA

osms.it/syringomyelia

PATHOLOGY & CAUSES

- Cerebrospinal fluid-filled cyst around spinal cord's central canal
- Cyst in nerve tissue (syrinx); spinal cord (myelia)
  - E.g. brainstem syrinx (syringobulbia)
- As cyst forms, grows → fluid collects within spinal cord tissue → ↑ pressure within spinal cord → damage
- Symptoms progress slowly, often adult diagnosis

RISK FACTORS

- *Congenital:* Arnold–Chiari malformation, genetic mutation
- *Acquired:* trauma; spinal cord tumor, bleeding; scoliosis

SIGNS & SYMPTOMS

- Various locations, syringomyelia severity
- Chronic pain, dysesthesia, paresis/paralysis
- Suspended sensory level
  - Sensory perception defect only on body parts innervated by syringomyelia-affected structures

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI

- Syrinx visualization in spine

OTHER DIAGNOSTICS

Neurological exam

- For suspended sensory level

TREATMENT

SURGERY

- Cyst drainage; flow restoration

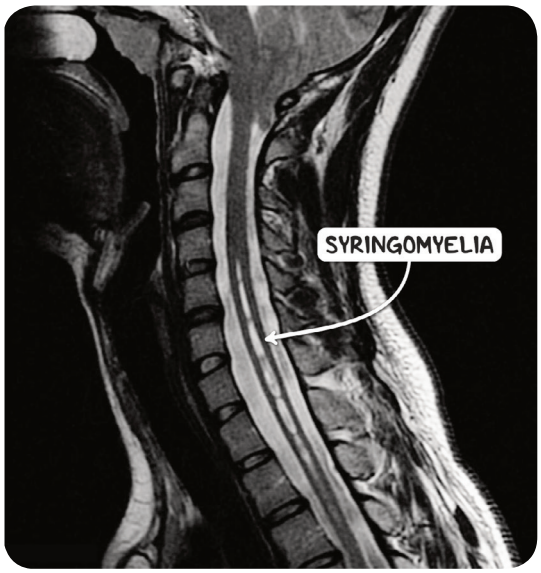

Figure 66.6 An MRI scan of the head and neck in the sagittal plane demonstrating syringomyelia extending from approximately the level of C4 to T3. There is also a Chiari I malformation.

TETHERED SPINAL CORD SYNDROME (TCS)

osms.it/tethered-spinal-cord-syndrome

PATHOLOGY & CAUSES

- Pathological spinal cord fixation to spinal canal wall
- AKA occult spinal dysraphism sequence
- Spinal cord movement restricted
  - Normally, spinal cord floats freely in CSF
  - *TCS:* restricted movement → physical strain → spinal cord damage

CAUSES

- *Primary:* congenital short filum terminale
- *Secondary:* surgery/trauma → scar tissue attachment; (myelo)meningocele

SIGNS & SYMPTOMS

- Lower-back pain, scoliosis, clubfoot, neurogenic bladder, bowel, paresis/paralysis below lesion

DIAGNOSIS

DIAGNOSTIC IMAGING

Spinal MRI

- Conus medullaris located below the normal L2–3 level

OTHER DIAGNOSTICS

- Neurological exam

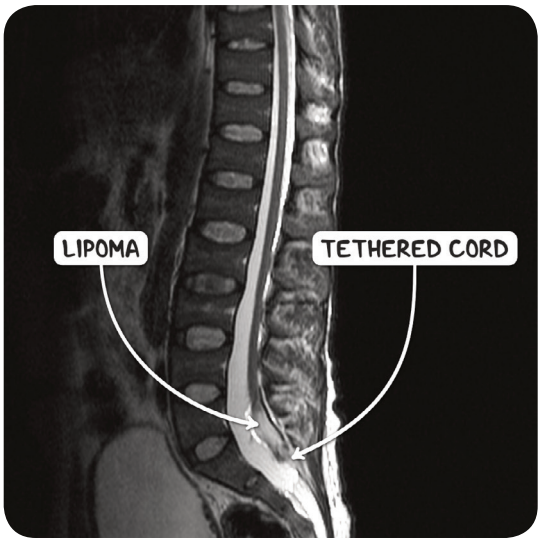

Figure 66.7 An MRI scan of the spine in the sagittal plane demonstrating a tethered spinal cord associated with a lipoma of the filum terminale.

TREATMENT

SURGERY

- Relieve spinal cord strain (if possible)
- Corrective orthopedic surgery

OTHER INTERVENTIONS

- Physical therapy