Dwarfs: Pathophysiology and Anesthetic Implications

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FOR MANY CENTURIES, dwarfs have been considered medical and social curiosities. In ancient cultures, these profoundly short and deformed individuals, who possessed an aura of mystery, were highly valued and even deified. People of the middle ages saw them as the keepers

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of jewels and jesters for royalty, and they played a prominent role in the literary folklore and mythology of American and many European cultures.[1] Dwarfs became particularly prominent in the entertainment field in the early 1900s. In the latter half of this century they have attempted to integrate into mainstream society despite the pressures of a culture that places a premium on conventional beauty, body proportions, and height.[2] The physiognomy and the frequently associated physiologic abnormalities of the respiratory, circulatory, and neurologic systems of dwarfs dictate, however, that from an anesthesiologist's point of view, they must be considered different from the norm.[3]

This review provides an overview of the classification of the syndromes associated with dwarfism and a discussion of the disturbed physiology of the respiratory, cardiovascular, neurological, and other organ systems. An understanding of this pathophysiology will facilitate the delivery of safe anesthesia in this group of patients.

Classification

Patients with dwarfism must not be regarded as having a single disease entity. There are, in fact, greater than 100 different types of dwarfism, many of which have specific implications for the anesthesiologist. Although each particular disorder is relatively rare (for instance, achondroplasia, the most common, occurs in only approximately 1.5 per 10,000 births),[4] the large number of dwarfs ensures that any practicing anesthesiologist is likely to encounter these patients. Indeed, in 1989, Scott estimated that there were 35,000 dwarfs in the United States.§

People with severe short stature have generally been divided into two categories: 1) those with proportionate growth and a normal ratio of trunk-to-limb length (formerly called "midgets," which now is considered a derogatory term) and 2) those with short stature and disproportionate development, characterized either by short limbs or short trunks that in many cases are deformed. Those in the latter group are referred to as "dwarfs".

Most proportionately short-statured persons are not dysmorphic and do not pose anesthetic problems aside

§ Scott CI: Personal communication, 1989.

from those associated with an underlying etiologic disease. Their growth deficiency is caused either by constitutional factors or by various endocrine deficiencies, metabolic disorders, or chronic cardiac, renal, neurologic, or gastrointestinal diseases.[5] In other normally proportioned patients, short stature is a component of a dysmorphic syndrome of unknown cause or is associated with chromosomal abnormalities.[5] Only a small number of these syndromes—for instance, the Smith-Lemli-Opitz syndrome (tiny mouth) or the Russel-Silver syndrome (micrognathia)—have important anesthetic implications.

In this review, we emphasize the anesthetic management of patients with disproportionate short stature—a manifestation of congenital, generalized, diseases of bone which present problems during or after anesthesia.

Under the International Nomenclature of Constitutional Diseases of Bone,[6] (table 1) disorders that produce disproportionate short stature are found in the osteochondrodysplasias (abnormalities of cartilage and/or bone growth and development) and in a group of primary metabolic diseases that involve the skeleton.[6] Abnormal bone growth that predominantly affects the axial skeleton produces short-trunk dwarfism, whereas a greater involvement of the appendicular skeleton characterizes short-limb dwarfism.

The nomenclature of the osteochondrodysplasias frequently reflects the clinical and roentgenographic features of the dysplasia (table 2). Rhizomelia, mesomelia, and acromelia describe limbs in which the shortening involves the proximal, middle, or distal segments, respectively. The names of some dysplasias are derived from the Greek terms describing the phenotype. For example, diastrophic dysplasia, from the Greek "diastrophos" meaning "tortuous, twisted," refers to the kyphoscoliosis and deformed extremities that are prominent features of this dysplasia. Camptomelic dysplasia, characterized by severe extremity deformities, is derived from the Greek "camptos," meaning "bent," and "melos," meaning "limb".

Since dwarfs tend to have several abnormalities that have anesthetic implications, we offer a general approach to the preoperative evaluation and suggest guidelines for the anesthetic management of these patients. The appendix summarizes the clinical manifestations and the anesthetic implications of the more common syndromes associated with dwarfism.

Anatomic and Physiologic Abnormalities Associated with Dwarfism

AIRWAY ABNORMALITIES

The anesthetic management of a variety of dwarfs is frequently complicated by upper airway obstruction and difficulties with direct laryngoscopy,[7-16] problems that

TABLE 1. Classification of Disproportionate Short Stature

Osteochondrodysplasias (Abnormalities of Cartilage and/or of Bone Growth and Development)	Primary Metabolic Abnormalities
Defects of growth of tubular bones and/or spine	Calcium and/or phosphorous
Identifiable at birth	Hypophosphatemic rickets
Achondroplasia	Hypophosphatasia
Camptomelic dysplasia	
Chondrodysplasia punctata	Complex carbohydrates
Diastrophic dysplasia	Mucopolysaccharidosis
Metatropic dysplasia	Mannosidosis
Chondroectodermal	Fucosidosis
dysplasia (Ellis-van	
Creveld syndrome)	
Asphyxiating thoracic	
dysplasia (Jeune	
syndrome)	
Spondyloepiphyseal	
dysplasia congenita	
Kniest dysplasia	
Mesomelic dysplasia (types	
Nievergelt, Langer,	
Robinow, Rheinardt,	
and others)	
Acromesomelic dysplasia	
Identifiable in later life	
Metaphyseal chondroplasia	
(types Jansen, Schmid,	
McKusick, Schwachman,	
and others)	
Spondylometaphyseal	
dysplasia (type	
Kozlowski and others)	
Pseudoachondroplastic	
dysplasia	
Spondyloepiphyseal	
dysplasia tarda	
Abnormalities of density of cortical diaphyseal structure and/or metaphyseal modeling Osteogenesis imperfecta	

Adapted from Maroteaux P: International nomenclature of constitutional diseases of bones with bibliography. Birth Defects Original Article Series 22:1–54, 1986

are major causes of perioperative morbidity and mortality.[9,13-16]

The anesthesiologist caring for the patient with one of the mucopolysaccharidoses (MPS) (most notably MPS IH, MPS IH/IS, MPS II, MPS IV, MPS VI) (table 2) is frequently challenged by a difficult airway that tends to become obstructed with sedation or general anesthesia.[7-15] Copious nasal secretions, a large tongue, large tonsils and adenoids, stiff temporomandibular joints, thickened pharyngeal and laryngeal structures, and narrowed nasal passages from mucopolysaccharide deposition lead to upper airway obstruction even in the unanesthetized state (fig. 1A, B), and contribute to difficulty in visualizing the larynx. Once the larynx has been exposed, tracheal narrowing from infiltration of glycosaminoglycans in some

TABLE 2. Abbreviations and Glossary

OI	Osteogenesis Imperfecta
MPS	Mucopolysaccharidoses
MPS I-H	Hurler syndrome
MPS IH/IS	Hurler-Scheie syndrome
MPS II	Hunter syndrome
MPS IV	Morquio syndrome
MPS V	Scheie syndrome
Diastrophic	Derived from the Greek "diastrophos" meaning "tortuous, twisted"
Camptomelic	Derived from the Greek "camptos" meaning "bent" and "melos" meaning "limb"
Metatropic	Derived from the Greek "metatropos" meaning "different shape"; refers to the striking change in body proportion that develops with age
Spondyloepiphyseal	Refers to bone dysplasia characterized primarily by involvement of epiphyses of the spine
Chondrodysplasia punctata	Refers to bone dysplasia characterized by speckled calcification of cartilage

MPS[17-19] may make the passage of an endotracheal tube difficult (fig. 1.A). In contrast, although the patient with achondroplasia may have narrow nasal passages and pharyngeal hypoplasia as a result of dysplasia and angulation of the cranial base and hypoplasia of the maxilla, his airway can readily be managed with a face mask.[20]

Other airway anomalies, such as laryngomalacia, (chondrodysplasia punctata,[21] diastrophic dysplasia,[22] and camptomelic dysplasia), laryngotracheal stenosis (rarely in spondyloepiphyseal dysplasia),[23] and micrognathia

(mesomelic dysplasia, severe diastrophic dysplasia, and Russel-Silver syndrome)[24] can contribute to upper airway obstruction. Airway patency may, in addition, be affected by position. Some patients with achondroplasia,[25] Morquio syndrome,[26] and metatropic dysplasia[27] maintain a patent airway with the neck extended whereas flexion produces airway obstruction.

Cervical abnormalities contribute to difficult laryngoscopies. Dwarfs with short necks (Morquio syndrome, metatropic dysplasia, or spondyloepiphyseal dysplasia) or with cervical kyphosis (diastrophic dysplasia) are particularly difficult to intubate.[2,11] The sternal prominence associated with pectus carinatum in Morquio syndrome, metatropic dysplasia, and forms of spondyloepiphyseal dysplasia can interfere with the midline positioning of the laryngoscope. Odontoid hypoplasia with cervical instability, or the presence of cervical traction or other stabilization devices that limit neck extension, make direct laryngeal exposure difficult. Although occasional abnormalities of the base of the skull may limit neck extension, only rarely does this interfere with laryngoscopy and intubation.[16]

PULMONARY ABNORMALITIES

Respiratory symptoms and dysfunction occur frequently in dwarfs, particularly when they are children. Several pathologic entities are responsible for these respiratory complications. Thoracic cage dystrophy from rib hypoplasia[25,28-30] and progressive kyphosis, scoliosis,
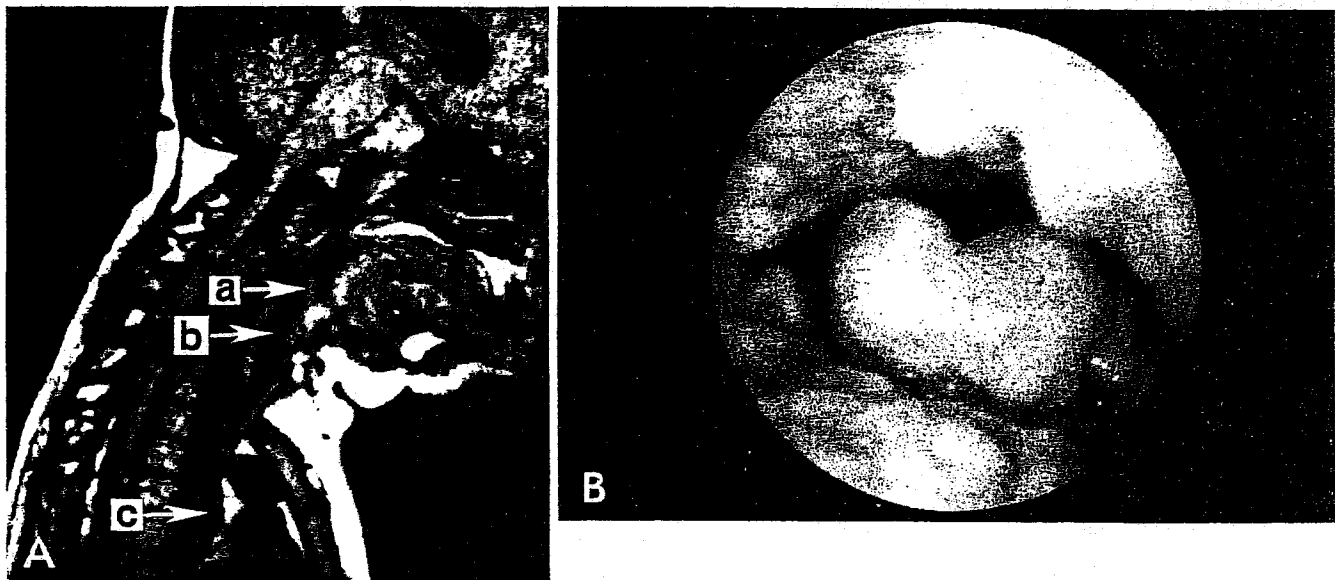

FIG. 1. (A) Sagittal thoracic magnetic resonance image of a 35-yr-old patient with Hurler-Scheie syndrome who developed severe airway obstruction after sedation for planned fiberoptic intubation. Note thickened, indurated epiglottis (a), marked glottic and subglottic narrowing (b), and diffuse tracheal stenosis (c). (B) Preoperative fiberoptic endoscopic view of thickened, deformed epiglottis and aryepiglottic folds of the same patient. (Courtesy of Bernard Marsh, M.D., The Johns Hopkins Hospital.)

and thoracic lordosis cause most of the cases of restrictive lung disease. Sleep apnea, with obstructive, central, and mixed components,[25,31–34] leads to substantial morbidity and even sudden death.[35–39] Structural abnormalities, with thickening and narrowing of the walls of the trachea and bronchi, particularly in the MPS, may be responsible for intrathoracic obstruction.[17–19,40] Coincidental chronic pulmonary diseases, such as asthma, recurrent atelectasis, chronic aspiration, and pneumonia can also contribute to respiratory morbidity.[25]

Restrictive Lung Disease

The small narrow chest wall of thoracic dystrophy from rib hypoplasia is associated in its worst form with lethal entities such as thanatophoric dwarfism, Saldino-Noonan syndrome, and Majewski syndrome.[22] Less severe forms

FIG. 3. Chest radiograph of a 12-yr-old girl with diastrophic dysplasia, chronic respiratory insufficiency, and moderate compression myelopathy. Note the "syphon-shaped" extremely severe, thoracic kyphoscoliosis.
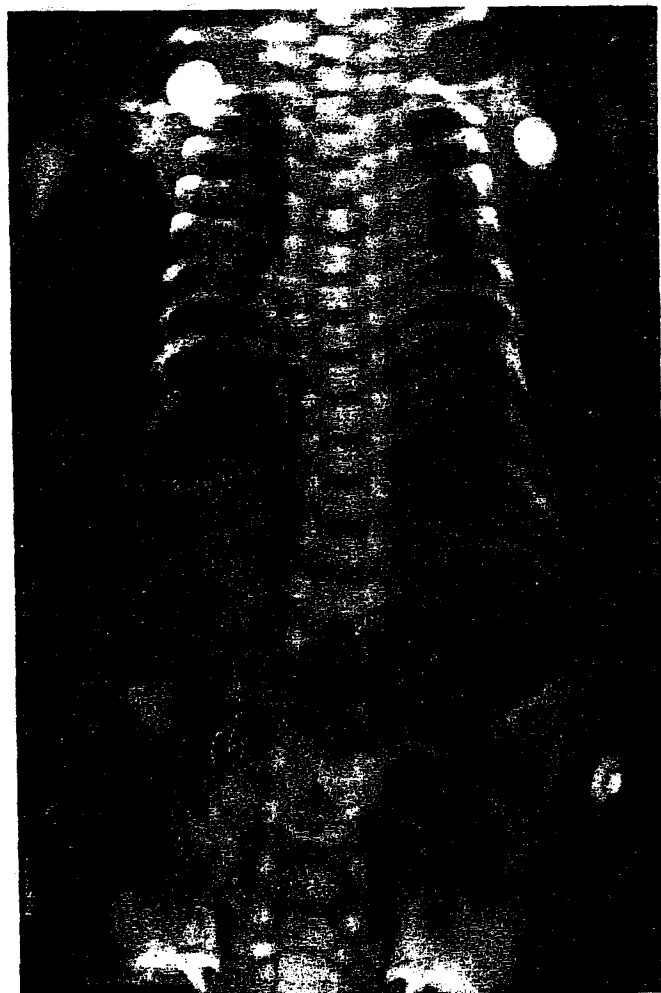

FIG. 2. Chest radiograph of infant with asphyxiating thoracic dystrophy (Jeune's syndrome). Note the short hypoplastic ribs and very narrow dystrophic chest. (Courtesy of John Dorst, M.D., The Johns Hopkins Hospital.)

of this deformity are responsible for restrictive pulmonary dysfunction in many other types of dwarfs, including those with achondroplasia,[25] chondroectodermal dysplasia,[21,28] Jeune syndrome,[28,29] metatropic dysplasia,[27] and camptomelic dysplasia[41] (fig. 2). Whether lung hypoplasia with reduced number of bronchioles and alveoli is associated with thoracic dystrophy and contributes to impaired lung function remains to be investigated. Preliminary evidence suggests, at least in Jeune syndrome, that it may be a factor.[42] Of the above syndromes, achondroplasia is by far the most likely to be encountered by the anesthesiologist. Thoracic dysplasia in achondroplasia is a problem essentially confined to young children.[25] In a study that included measurements of chest wall dimensions in adults with achondroplasia, Stokes *et al.*[43] demonstrated no difference from that of average-statured control patients in the shape of the adult achondroplast thorax, except for a slight reduction in the anteroposterior chest diameter in men.

Scoliosis and/or kyphosis is a common clinical finding in dwarfs.[44] Spinal deformity must be moderately severe before it interferes with respiratory function. Such severe scoliosis frequently develops in diastrophic and metatropic dysplasia and in some forms of osteogenesis imperfecta (figs. 3 and 4). Less severe scoliosis develops in patients
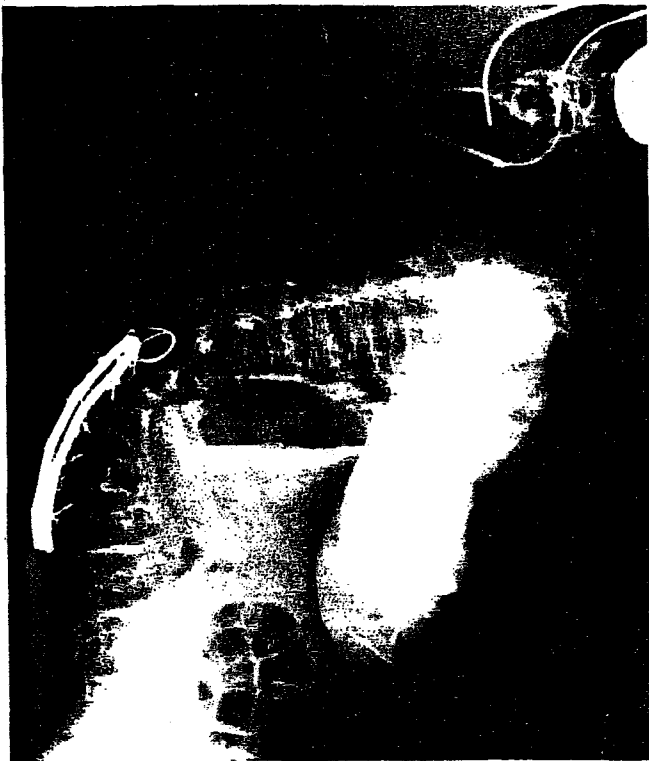
FIG. 4. Lateral chest and abdomen radiograph of a 12-yr-old boy with metatropic dysplasia and chronic respiratory failure. Note the severe narrowing of the transverse dimension of the chest due to rib hypoplasia. The spinal segment between the distal end of an occipito-C3 fusion and the L1–L3 fusion progressively developed a horizontal "swan-neck" deformity. The thoracic spine (T1–T10) became ankylosed almost parallel to the diaphragm, compressing the lungs into a small wedge.

with camptomelic dysplasia, pseudoachondroplastic dysplasia, spondyloepiphyseal dysplasia congenita, and spondylometaphyseal dysplasia. Thoracic lordosis cephalad to thoracolumbar kyphosis also compromises respiratory function in patients with achondroplasia and MPS I, II, and IV.[45] Restrictive lung disease with reduced vital capacity and functional residual capacity characterizes thoracic dystrophy and kyphoscoliosis. These reduced lung volumes predispose toward airway closure accompanied by subsequent ventilation perfusion mismatching, increased alveolar–arterial gradient, and recurrent, scattered atelectasis.[25,46,47] Only with advanced, severe restrictive disease does hypoventilation with retention of carbon dioxide develop.[47] Interference with normal intercostal muscle function may also contribute to the disturbed physiology.[46] Massive hepatosplenomegaly in some patients with MPS and the exaggerated thoracolumbar lordosis or gibbus formation observed in some patients with skeletal dysplasias can compromise diaphragmatic motion and aggravate the restrictive defect. Interstitial pulmonary deposition of glycosaminoglycans contribute

to both the restrictive disease and a diffusion deficit.[31] In patients with MPS, recurrent atelectasis and aspiration of purulent nasopharyngeal secretions predispose patients to recurrent, potentially life-threatening pneumonias.

Tracheobronchial Obstruction

In addition to upper airway obstruction and restrictive lung disease, positionally dependent[26,27] or fixed intrathoracic airway obstruction[31] is now recognized as an important cause of respiratory morbidity and even death in patients with MPS, particularly MPS IH, II, IV, and VI. Narrowing of the trachea and mainstem bronchi to produce airway compromise[17–19] can result from focal enlargement and thickening of tracheal rings and thickening of the mucosa and periluminal connective tissue by glycosaminoglycan deposition (fig. 1A). Tracheobronchial narrowing may even occur below the level of a tracheostomy that has been performed because of upper airway obstruction. Peters et al.[40] demonstrated that 15% of patients with MPS have an abnormally narrow trachea, a finding that can be easily observed from a frontal chest radiograph.

Sleep Apnea

Sleep apnea with obstructive, central, or mixed components has become recognized as an insidious but treatable cause of severe morbidity and even death in some dwarfs, and especially in children. It has been described with several different types of dwarfism but appears to be of particular importance in patients with achondroplasia,[25,33–37] metatropic dysplasia,[27] and several of the MPS.[31,32] Obstructive sleep apnea is more common than central apnea in patients with achondroplasia.[34] Abnormal craniofacial bone growth that results in brachycephaly, facial and pharyngeal hypoplasia, flattening of the nasal bridge, and constricted upper airways causes upper airway obstruction in achondroplasia. Hypotonia of muscles of the upper airway, a component of the generalized hypotonia common in young children with achondroplasia, may also contribute to functional upper airway obstruction during sleep.[25] Obstructive sleep apnea in patients with MPS also demonstrates both fixed and dynamic components of obstruction.[31] The causes of upper airway obstruction in these patients have been discussed above and include macroglossia, tonsillar and adenoidal enlargement, and infiltration of the pharyngeal mucosa and laryngeal structures with glycosaminoglycans.

Central apnea in patients with achondroplasia is caused by compression of the distal medulla and upper cervical cord at the craniovertebral junction by foramen magnum stenosis[34] (see the section on neurologic abnormalities, below). Episodes of central apnea and hypoxia in these patients can be occult, without other clinical evidence of

ord compression, or may be so severe as to occur when
he patient is awake. In addition, a few children with
chondroplasia and cervicomedullary compression exhibit
espiratory distress and even hypoxia that cannot be ac-
counted for by pulmonary or thoracic pathology. Marked
mprovement after suboccipital decompression[54] suggests
hat these respiratory problems are neurogenic in origin.
Central apnea is relatively uncommon in patients with
MPS despite the frequent demonstration of odontoid hy-
poplasia and cervical spine subluxation.

CARDIAC ABNORMALITIES

Cardiovascular abnormalities, both congenital and ac-
quired, frequently confront the anesthesiologist respon-
sible for the anesthetic management of dwarfs.[41,48,49]

Congenital Heart Disease

Atrial septal defect, ventricular septal defect, or cleft
mitral valve occur more frequently in patients with chon-
droectodermal dysplasia than in the general population.[22]
An atrial septal defect is an anomaly occasionally asso-
ciated with Robinow mesomelic dysplasia and with camp-
tomelic dysplasia.[5]

Valvular Heart Disease

Aortic root dilatation, aortic insufficiency, and mitral
valve prolapse occasionally occur in patients with osteo-
genesis imperfecta.[48,50,51] In some patients with MPS, col-
lagen and fibroblasts distended with glycosaminoglycans
lead to valvular thickening with insufficiency and/or to
stenosis and calcification at an early age.[19,48,52] Patients
with MPS IH (Hurler syndrome) and MPS II (Hunter
syndrome) frequently have both mitral and aortic regur-
gitation, although the tricuspid and pulmonary valves
rarely become involved.[19,52-54] Severe infiltrative valvular
involvement is less common in MPS IV (Morquio syn-
drome), but aortic insufficiency has been noted.[19,52] Se-
vere aortic stenosis has been described in patients with
MPS VI (Maroteaux-Lamy syndrome).[56]

Cardiomyopathy

In addition to acquired valvular disease, some dwarfs
with MPS can develop a cardiomyopathy as a result of
glycosaminoglycan deposition in the myocardium. Others
manifest asymmetric septal hypertrophy.[52,57]

Coronary Artery Disease

In some patients with MPS, particularly in those with
MPS IH and II, concentric intimal and medial thickening
of extramural coronary arteries, by storage cells contain-
ing glycosaminoglycans, can lead to severe narrowing and
ischemic heart disease.[53] Brosius and Roberts[58] found at
necropsy that five of six children with MPS IH had greater
than 75% narrowing in one or more coronary arteries.
These findings may explain why half of the deaths in pa-
tients with MPS IH are due to sudden cardiovascular col-
lapse or progressive congestive heart failure.[53,55]

Pulmonary Hypertension

Pulmonary hypertension, leading to cor pulmonale, is
probably the most common cardiovascular disturbance
that develops in dwarfs. Restrictive lung disease,[26,59] con-
genital heart disease with left-to-right shunts,[60] chronic
upper airway obstruction,[61,62] and sleep apnea all con-
tribute to the development of pulmonary hypertension
and cor pulmonale in dwarfs. Chronic upper airway ob-
struction is associated with pulmonary hypertension, al-
though the pathophysiology is not clearly understood.
Chronic or recurrent hypoxemia, carbon dioxide reten-
tion, and negative intrathoracic pressures with increased
vascular transmural pressures and increased left and right
ventricular afterload all may play a role.[63] Pulmonary hy-
pertension can also be due either to increased pulmonary
blood flow from a left-to-right intracardiac shunt or to a
reduction in the cross-sectional area of the pulmonary
vascular bed that leads to increased pulmonary vascular
resistance.[64] The latter results from either fixed, structural
changes of the pulmonary vascular bed (which occurs with
severe thoracic dystrophy)[42] or from reactive, partially
reversible pulmonary arterial vasoconstriction in response
to a variety of stimuli such as hypoxia, hypercarbia, and
acidosis. Carefully planned and performed anesthesia in
patients with pulmonary hypertension can prevent acute
elevations of pulmonary arterial pressure that initiate a
vicious cycle of right-sided heart failure, decreasing car-
diac output, myocardial ischemia, acidosis, and further
aggravation of pulmonary hypertension.[60,64]

NEUROLOGIC ABNORMALITIES

The two major categories of neurologic complications
commonly associated with dwarfism are hydrocephalus
and compressive spinal cord and nerve root syndromes.
Compression of the spinal cord and nerve roots may result
from one or more of the following lesions: foramen mag-
num stenosis, odontoid hypoplasia with cervical instability,
thoracolumbar and generalized spinal stenosis, and severe
kyphosis and scoliosis. Common surgical procedures to
alleviate the neurologic symptoms include suboccipital
craniectomy for foramen magnum stenosis, laminectomy
for spinal stenosis, cervical fusion for cervical instability,
and ventriculoperitoneal shunts for hydrocephalus.

Macrocephaly and Hydrocephaly

The disproportionately large head that so frequently
is a finding in the patient with achondroplasia may be a

reflection of macrocephaly, hydrocephaly, or both. Macrocephaly results from an accelerated rate of head growth and is generally accompanied by mild dilation of the ventricles, but without elevated intracranial pressure.[65,66] Macrocephaly, in contrast to hydrocephaly, has no physiologic implications for the anesthesiologist. Progressive hydrocephalus with signs of elevated intracranial pressure (ICP) may necessitate decompressive ventriculoperitoneal shunting.[65] Hydrocephalus in patients with achondroplasia is probably due to intracranial venous hypertension[67-69] or to obstruction of the cerebrospinal fluid pathways at the level of the foramen magnum. It usually is associated with other neurologic signs of cervical cord compression.[65,68] Progressive hydrocephalus can also complicate the course of patients with MPS, particularly those with MPS IH and MPS II.[19]

Spinal Cord and Nerve Root Compression Syndromes

Odontoid dysplasia, a frequent finding in many of the osteochondrodystrophies, is occasionally complicated by atlantoaxial instability and cord compression.[70-76] The odontoid process arises perpendicularly from the superior surface of the body of the second cervical vertebra (C2) and lies in the facet of the anterior arch of the first cervical vertebra (C1). This allows the head to be flexed and extended on the neck. If the odontoid process is hypoplastic, C1 may dislocate anteriorly and cause spinal cord compression.[70] Odontoid dysplasia with atlantoaxial instability occurs more frequently, although not exclusively, in syndromes primarily affecting the axial skeleton. Odontoid dysplasia and atlantoaxial instability are common in patients with Morquio syndrome, spondyloepiphyseal dysplasia congenita, metatropic dysplasia, and spondylometaphyseal dysplasia, and occur less frequently in patients with chondrodysplasia punctata, MPS IH, MPS II, and multiple epiphyseal dysplasia.[45,71-73]

Foramen magnum stenosis, thoracolumbar stenosis, and generalized spinal stenosis may develop in patients with achondroplasia.[65,77-80] These spinal neurologic complications cause the majority of hospital admissions for achondroplastic dwarfs.[77] Foramen magnum stenosis results from hypertrophy of the bony margins of the foramen magnum. An axial computerized tomographic (CT) study of 26 children with achondroplasia and neurologic or respiratory symptoms[81] demonstrated that in 25 of 26 cases, the foramen magnum was smaller than 3 standard deviations from the mean for age-matched normal-stature controls. This bone encroachment narrows the upper cervical spinal canal and subarachnoid space, potentially impinging on the medulla and upper cervical cord.[34,72,73] The compression of the cervicomedullary junction can be demonstrated by CT, CT myelography,[81,82] or magnetic resonance imaging (MRI)[68] (fig. 5).

In thoracolumbar and generalized spinal stenosis, the spinal cord, conus medullaris, and cauda equina are compressed by a spinal canal that is narrowed either by abnormally shaped vertebrae or congenitally hyperplastic intervertebral discs.[78] Endochondral bone formation is affected in achondroplasia and results in vertebral bodies that are abnormally shallow and vertebral arches that are considerably underdeveloped. As a result, the spinal canal is constricted throughout its length, a condition that leads to narrowing of the subarachnoid and epidural spaces.[83] In addition, the congenitally hyperplastic intervertebral discs in persons with achondroplasia tend to bulge laterally and posteriorly. Multiple protruded discs are common in the adult achondroplastic dwarf. Disc prolapse into a congenitally stenotic canal may cause neural compression, usually involving the cauda equina.[84] Neurologic presentations include acute or slowly progressing paraparesis, quadriparesis, sensory deficits, and sphincter dysfunction.[85,86] Severe thoracic or lumbar kyphoscoliosis and cervical scoliosis only infrequently produce cord compression.

ABNORMALITIES OF THERMAL REGULATION

Patients with osteogenesis imperfecta (OI) display evidence of a generalized disturbance of energy metabolism[87,88] This hypermetabolic state is characterized by episodic elevations of body temperature, elevated oxygen consumption, and diaphoresis. The increased heat and oxygen consumption has been attributed to an uncoupling of oxidative phosphorylation with increased adenosine triphosphate (ATP) breakdown.[87-89] This produces elevated serum pyrophosphate levels, a frequent laboratory finding in these patients.

Under anesthesia, patients with osteogenesis imperfecta[90-92] occasionally manifest a rise in body temperature. These episodes are not associated with features of malignant hyperthermia such as muscle rigidity, arrhythmias, metabolic and respiratory acidosis, or hyperkalemia, and should not be diagnosed as malignant hyperthermia.[90,91] Atropine has been blamed for temperature elevation in patients with OI and in other dwarfs, but such an adverse effect is not proven.[93]

COAGULATION ABNORMALITIES

Although not a problem with other osteochondrodystrophies, some patients with OI demonstrate easy bruisability and a mild bleeding tendency that is not usually a clinical problem during surgery.[94] Several case reports, however, describe substantial postoperative bleeding in OI patients after open heart surgery.[95-97] The precise nature of this coagulopathy is not defined. Hathaway et al.[94] have demonstrated that this bleeding diathesis is caused by platelet dysfunction, which may be another
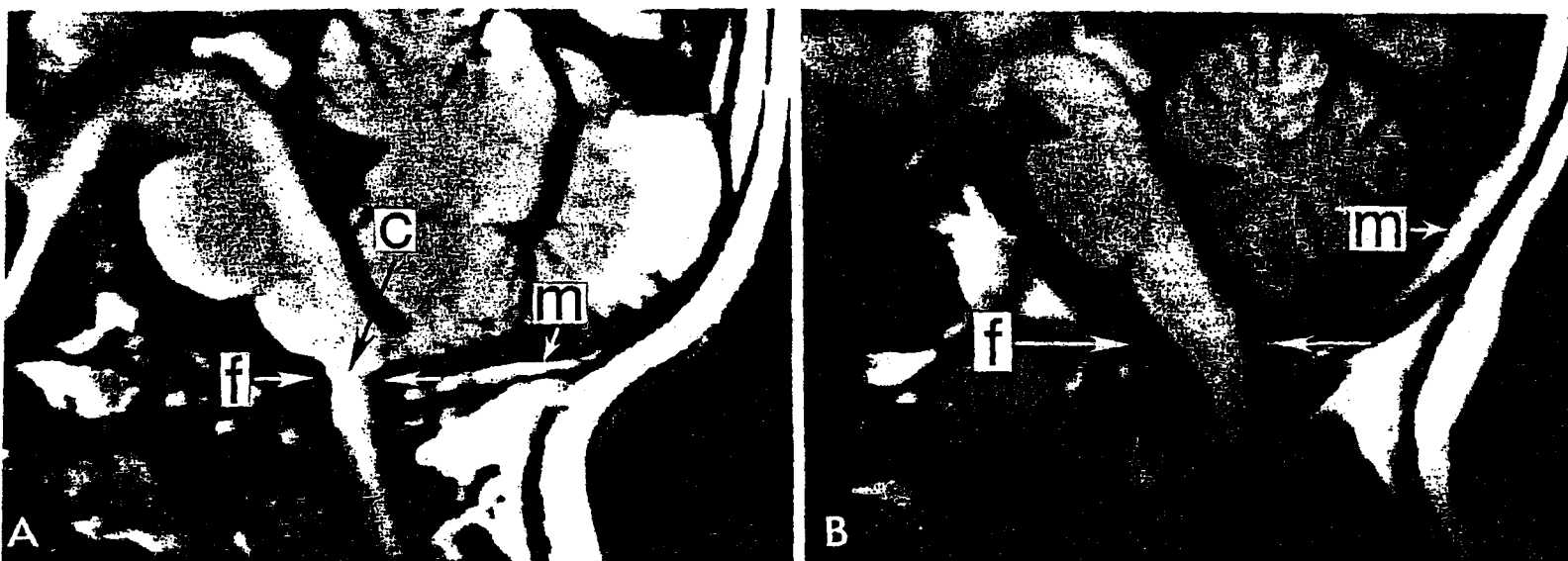
FIG. 5. Sagittal cranial magnetic resonance images demonstrating the foramen magnum and cervico-medullary junction. (A) Patient with chondroplasia. Scan demonstrates foramen magnum stenosis with impingement of hypertrophied bony margins of the foramen magnum (f) on the cervico-medullary junction (c) and marrow space (m). (B). Normal patient. Note the wide subarachnoid space between foramen magnum and spinal cord. (Courtesy of Henry Wang, M.D., The John Hopkins Hospital.)

manifestation of altered ATP metabolism. This coagulopathy is characterized by one or more of the following abnormalities on *in vitro* tests of platelet function: defective release of platelet factor III and impaired platelet aggregation to ADP, or, less frequently, impaired aggregation on collagen stimulation. Approximately 30% of patients with OI also demonstrate prolonged bleeding time, enhanced capillary fragility, decreased platelet retention, and a reduction of factor VIII.[98] These studies indicate that tissue friability, platelet aggregation abnormalities, and coagulation factor deficiencies all play a role in the hemostatic defect of patients with OI.

PSYCHOSOCIAL CONSIDERATIONS

Although the literature on the medical management of dwarfs is extensive, there are few studies that examine the psychosocial consequences of being profoundly short.[99–101] The studies that do exist have tended to evaluate patients with achondroplasia,[101–103] hypopituitarism,[104,105] or constitutional short stature,[106] although there are more than 100 different types of dwarfism. Although it is frequently assumed that patients with disproportionate short stature are retarded, numerous studies have demonstrated a normal range of intelligence in many dwarfs.[99] Motor milestones in early childhood may be delayed, and some dwarfs, particularly those with hypopituitarism, lag in psychosocial maturity. A very important concern in dealing with dwarf patients, particularly with older children and adults, is the need to avoid infantalization.[107] The interaction of the anesthesiologist with the patient must be appropriate to the age of the patient regardless of the patient's height.[99,107] This may require a

conscious effort, since the typical response of an averaged-sized person is to relate age and maturity to height and not to chronologic age.

Anesthetic Management

GENERAL CONSIDERATIONS

An understanding of the multiple abnormalities that affect dwarfs will facilitate the safe delivery of anesthesia in these patients. Monitoring and anesthetic techniques for optimal care should be dictated by the type of dwarf, the anatomic and physiologic aberrations of different organ systems, and the nature of the surgical procedure.

Although the potential for airway obstruction in some dwarfs is well-recognized, general anesthesia has traditionally been the technique of choice.[108] This may, in part, be due to technical challenges encountered during the performance of spinal and epidural anesthesia in many of these patients.[108] These difficulties result from a variety of spinal anatomical abnormalities, such as severe lumbar lordosis, kyphoscoliosis, and malformed vertebral bodies.[45,72,73] In patients with achondroplasia, prolapsed intervertebral discs and a relatively narrow spinal canal may exist in addition to these anatomic abnormalities. There are, however, several case reports of successfully performed spinal and epidural anesthetics for cesarean section in patients with several types of dwarfism, including achondroplasia,[109] osteogenesis imperfecta,[110] and spondylometaphyseal dysplasia.[111]

Accurate blood pressure measurement mandates the use of an appropriately sized blood pressure cuff, which should cover two thirds of the length of the upper arm.

Cuffs smaller than those usually used for average-sized patients of the same age must be used in rhizomelic dwarfs (achondroplasia or diastrophic dysplasia). In patients with severe OI, invasive blood pressure measurement by arterial cannulation may be preferable to the use of a blood pressure cuff, to reduce the risk of humeral fractures.

Establishing central or peripheral vascular access in dwarfs is often difficult. Obesity and the thickened, indurated subcutaneous tissues of patients with MPS make identification of veins and insertion of intravenous catheters a challenge. Cervical abnormalities in some dwarfs, including very short necks, cervical scoliosis, and the presence of a cervical stabilizing device, may make jugular vein cannulation difficult or even impossible; in such instances, the anesthesiologist may be compelled to use either femoral or subclavian veins for central line placement. Subclavian vein cannulation may also be unsuccessful or even hazardous, particularly when the upper thoracic anatomy is distorted by severe thoracic scoliosis and kyphosis.

Guidelines for the selection of the appropriately sized endotracheal tube for dwarfs are unclear.[20,108] Review of the data for patients with achondroplasia by Mayhew et al.[20] suggests that the age-based formula for selecting endotracheal tube size for children (tube size (mm ID) = [age (yr) + 16]/4)[112] usually predicts the correct endotracheal tube size. No information is available in regard to the size of endotracheal tubes that should be used for other types of dwarfs.

AIRWAY DYSFUNCTION

Preoperative Evaluation

In addition to knowledge of the airway abnormalities that might exist,[41] a careful search for symptoms of obstructive sleep apnea will alert the anesthesiologist to patients who are likely to develop upper airway obstruction after sedation or the induction of general anesthesia.[31,32] All available prior anesthetic records should be reviewed for information about airway management, such as difficulty with a mask airway or with laryngoscopy and intubation. Dwarfs born with short necks (spondyloepiphyseal dysplasia congenita, camptomelic dysplasia, or diastrophic dysplasia) may have a history of traumatic or prolonged perinatal intubation, which may have lead to subsequent subglottic stenosis. A physical examination of the airway should include evaluation of the size of the tongue, mouth, and mandible. Particular attention should be paid to evaluating the position of the larynx, the shortness of the neck, and the mobility of neck and jaw.[113] Cervical spine stability must be assessed, since odontoid hypoplasia is observed in many different dwarfs.[70-73] This evaluation is discussed in detail in the section on neurologic dysfunction.

The clinical impression of an anatomically abnormal upper airway or of tracheal narrowing should be confirmed by one or more of the following studies; lateral neck radiographs, xerography, tomography, CT scanning, or MRI techniques.[40,114] If the patient seems to have structural abnormalities of the larynx or trachea (such as tracheobronchial narrowing from glycosaminoglycan infiltration in patients with MPS, or tracheomalacia in children with diastrophic dysplasia), then preoperative fiberoptic airway endoscopy by an anesthesiologist or otolaryngologist skilled in the technique is helpful in defining the etiology, site, and extent of airway compromise[31] (fig. 1B). The degree of functional extrathoracic or intrathoracic obstruction can be evaluated by flow-volume loops. Since neck flexion may aggravate the airway obstruction in patients with achondroplasia, metatropic dysplasia, or MPS, these flow-volume loops should be performed in positions of neck flexion and extension.[25-27]

Anesthetic Management

Preoperative sedation should be avoided if the potential for upper airway obstruction exists.[2,8] Atropine or glycopyrrolate should be administered preoperatively if excessive oral and nasal secretions are present, if a difficult airway is anticipated, or if a fiberoptic intubation is planned.[8] Intravenous access should be established before induction in patients in whom airway problems are likely. Both awake intubation and inhalational induction with oxygen and halothane, while spontaneous ventilation is maintained, are relatively safe anesthetic techniques, if difficulty in maintaining a patent airway or in intubating the trachea is anticipated. Muscle relaxants should be avoided until positive-pressure ventilation by mask can be ensured.[7-10] It is important to avoid neck manipulation, particularly positions of neck flexion during laryngoscopy in patients with atlantoaxial instability or foramen magnum stenosis. A subsequent section on the anesthetic management of the dwarf with neurologic complications reviews in detail the appropriate positioning and airway management of patients with cervical cord compression and instability.

Laryngeal exposure may be impossible with a conventional laryngoscope in some dwarfs with very short necks and with a severe pectus carinatum chest deformity (such that the head appears to rest upon the chest) because it is not possible to rotate such a laryngoscope to the midline. A laryngoscope with a very short handle may be useful in these cases. If the glottis cannot be exposed by direct laryngoscopy, then fiberoptic intubation with the patient awake or under general inhalational anesthesia during spontaneous ventilation is indicated. Particular care must be exercised in sedating a patient with upper airway obstruction for an awake endoscopy, in order to avoid pre-

pitating complete airway obstruction.[31] In children reathing spontaneously under general anesthesia, an-sthetic gas and oxygen can be provided through one aris and the bronchoscope and endotracheal tube ma-ipulated through the other, or a mask with an endoscopic ort may be used. A blind nasal intubation technique may e useful in some situations, although it may cause trou-lesome pharyngeal bleeding, especially in patients with 1PS who have enlarged adenoids.[10] Retrograde passage f a guide wire through the cricothyroid membrane is nother option when visualization of the larynx is impos-ible.

Even with a careful inhalational technique, anesthetic nduction in a dwarf with upper airway obstruction and ossibly with concomitant myocardial and pulmonary in-olvement is a high-risk undertaking. Complete upper irway obstruction that cannot be relieved by the usual aw thrust or chin lift maneuver or by an oral or naso-haryngeal airway may develop, particularly in patients vith MPS. Direct traction on the tongue, together with entle neck flexion, can overcome airway obstruction aused by this enlarged organ. If severe upper airway bstruction is anticipated preoperatively, a surgeon or tolaryngologist skilled in emergency tracheostomy hould be requested to be present during induction. Tra-heostomy may be extremely difficult[15] or even impossible without a concomitant thoracotomy in some patients with hort necks and pectus carinatum deformity. A trache-ostomy will not always completely relieve airway obstruc-ion in some patients with advanced MPS because of con-siderable tracheal narrowing distal to the tracheostomy. Preoperative CT or MRI scanning and fiberoptic bron-choscopy will alert the anesthesiologist and otolaryngol-ogist to the site and extent of the tracheobronchial ste-nosis.

PULMONARY DYSFUNCTION

Preoperative Evaluation

A comprehensive history, examination, and appropri-ate testing will aid in determining both the cause and the severity of respiratory dysfunction. Chest dimensions can be compared with accepted standards to quantitate the degree of chest wall hypoplasia. The degree of scoliosis and kyphosis can be determined radiologically.[47] Spirom-etry, blood gas, hematocrit, and serum electrolyte deter-minations, as well as more sophisticated pulmonary func-tion tests, such as diffusion capacity measurements, can help in quantitating the extent of underlying pulmonary involvement. The interpretation of spirometric measure-ment of lung volumes is complicated in dwarfs because there are no reference standards for these measurements in short-trunk dwarfs. Serial measurements, over time, if

available, will provide the most information. Stokes *et al.*[43] have recently published spirometric standards for asymp-tomatic adults with achondroplasia that are based on the sitting rather than the standing heights of the patients. Information about the dimensions of the intrathoracic tracheobronchial tree can be obtained from the chest ra-diograph,[40] thoracic CT scan, or MRI (fig. 1A). The extent of functional intrathoracic obstruction can be diagnosed by inspiratory and expiratory flow-volume loops.

Attention should be directed toward eliciting a history of sleep-related breathing disorders such as snoring, ap-nea, cyanosis, restless sleep, chest retraction, paradoxical chest movements, and daytime somnolence. Multichannel polysomnography can be used to confirm these clinical suspicions. The cause of obstructive sleep apnea can fur-ther be determined by fiberoptic visualization of the upper airway by a competent otolaryngologist and by radio-graphic, CT, or MRI evaluation of the upper airway. Central apnea suggests cervicomedullary or cervical cord compression that can be appropriately evaluated with cervical radiographs in flexion and extension,[70] CT my-elography,[81] MRI,[68] and evoked potential monitoring.[34] Apart from the potential risk of hypoxia and hypercarbia in the perioperative period, the most important compli-cation of lung and airway involvement that influences an-esthetic management is the development of pulmonary hypertension. The preoperative evaluation of this com-plication is discussed in the section on cardiovascular dys-function.

Anesthetic Management

Anesthetizing a patient with pulmonary dysfunction, possibly accompanied by airway obstruction, pulmonary hypertension, or right ventricular compromise, presents the anesthesiologist with many challenges. Restrictive lung disease prolongs an inhalation induction that may already be compromised by upper airway obstruction. The low functional residual capacity and high closing volume in patients with restrictive lung disease tends to promote atelectasis and ventilation/perfusion mismatching. Low resting lung volumes reduce pulmonary reserve such that oxygenation may be easily compromised; in these cases high inspired concentrations of oxygen are required to maintain adequate arterial P_{O_2}.[59] This respiratory dys-function mandates the use of pulse oximetry and end-tidal CO_2 monitoring. Arterial cannulation for intra- and postoperative blood gas analyses is recommended for all but the shortest and simplest of surgical procedures in any dwarf with significant respiratory disease. These pa-tients may also require postoperative mechanical venti-lation, which may be prolonged, particularly in patients with severe thoracic dystrophy (*e.g.*, infants with Jeune syndrome).[59]

CARDIOVASCULAR DYSFUNCTION

Preoperative Evaluation

The preoperative evaluation of cardiac dysfunction requires a comprehensive history, examination, chest radiograph, electrocardiography, and, in many cases, echocardiography. The expertise of a cardiologist frequently is needed, and a cardiac catheterization may be required to delineate the hemodynamic significance of valvular dysfunction, the extent of pulmonary hypertension and coronary artery disease, and the specific anatomy of congenital heart disease.

The detailed preoperative evaluation of patients with ischemic and valvular heart disease exceeds the scope of this review and is discussed elsewhere.[115] Pulmonary hypertension, the most common cardiovascular complication of dwarfs, requires careful analysis. The typical signs of established pulmonary hypertension include a prominent parasternal heave, the auscultatory findings of a widely split second heart sound with a loud pulmonary component, a systolic pulmonary ejection murmur, and less frequently, an early diastolic murmur of pulmonary insufficiency. Chest radiography may reveal an enlarged heart with a prominent pulmonary artery segment, and in severe cases, peripheral "pruning" of the pulmonary arterial vasculature. Right ventricular enlargement and hypertrophy can be demonstrated by the electrocardiogram and echocardiogram. A prolonged right ventricular preejection period also may be noted.[116]

Anesthetic Management

The anesthetic management of patients with cardiac ischemia, valvular disease, pulmonary hypertension, and impaired myocardial function must be meticulously planned and executed. Appropriate monitoring includes continuous arterial and right atrial pressure measurement, and in severe cases, pulmonary artery catheterization. Endocarditis prophylaxis is necessary in patients with either congenital cardiac abnormalities or acquired valvular disease. The anesthetic management of dwarfs with pulmonary hypertension must be planned such that anesthetic agents and various other stimuli that aggravate pulmonary arterial vasoconstriction can be avoided, and yet adequate cardiac output and coronary perfusion pressure be maintained.[60,64]

Hypoxic pulmonary vasoconstriction superimposed on preexisting pulmonary hypertension may cause catastrophic reduction in right ventricular function.[117–119] Both hypercarbia and acidosis have similar adverse hemodynamic effects.[120] Respiratory and metabolic alkalosis can reduce pulmonary vascular resistance and pulmonary artery pressure.[120,121] Regardless of the anesthetic agents used, an adequate depth of anesthesia must be maintained to prevent elevations of pulmonary artery pressure, which may develop under light anesthesia.[64]

Nitrous oxide should probably be avoided in patients with pulmonary hypertension, since studies suggest that it increases pulmonary vascular resistance.[122,123] Similarly, enflurane has been associated with a modest increase in pulmonary artery pressure[124]; it is prudent to avoid the use of this agent in patients with pulmonary hypertension. Halothane[125] and isoflurane[126,128] may reduce pulmonary artery pressure and are therefore the inhalational agents of choice for these patients. Narcotics in high doses have little effect on the pulmonary circulation. In patients with right ventricular failure they are the preferred anesthetic agents[129,131] since, unlike the inhalational agents, they do not depress myocardial function. Ketamine is useful in children with pulmonary hypertension or poor myocardial function.[132,133] The safe use of ketamine in adults with pulmonary hypertension has not been established. In some studies of adults, an increase in pulmonary vascular resistance has been documented.[134] Although the results of laboratory studies are conflicting,[135,136] barbiturates do not appear to have a substantial selective effect on the pulmonary circulation.[60]

In addition to avoiding hypoxia, acidosis, and anesthetic agents that aggravate pulmonary hypertension, the anesthesiologist must choose the anesthetic to maintain adequate cardiac output and coronary perfusion. When right ventricular function is compromised by increased right ventricular afterload, anesthetic agents with negative inotropic actions, such as halothane, are contraindicated, and either narcotics or ketamine (in children) should be chosen.

NEUROLOGIC DYSFUNCTION

Preoperative Evaluation

The neurologic manifestations of cervicomedullary compression are varied and may be suggested by a thorough history and physical examination. These manifestations include not only the typical findings of an upper motor neuron lesion, such as weakness, hyperreflexia, clonus, abnormal plantar responses, but also a spectrum of less well-appreciated, nonspecific respiratory symptoms and signs that are noteworthy in children and infants.[25,34] In children, apnea of central origin resulting from direct compression of the medulla and upper cervical spinal cord is a characteristic, relatively recently recognized symptom.[34] Other nonspecific presentations, such as hypoxia without appreciated respiratory problems, respiratory distress, recurrent cyanotic spells,[34,36,37] and even sudden infant death,[36,39] are recognized as manifestations of cervicomedullary compression in infants and young children. The classic signs and symptoms of upper motor neuron

lesions may be difficult to elicit or may even be absent in infants and young children.[34]

Odontoid hypoplasia *per se* does not necessarily imply atlantoaxial instability and cord compression. In dwarfs with cervical spine involvement, lateral radiographs of the cervical spine should be performed in positions of active, not passive, neck flexion and extension, to determine whether instability is present.[70] With full neck flexion, the atlantoodontoid interval increases, and the spinal canal diameter decreases. When these dimensions are exaggerated with flexion, cord compression is likely to be present.[70] In addition, in this group of patients, not only odontoid dysplasia but also other cervical abnormalities, which may extend from the skull to the third cervical vertebra, may also be responsible for cervical instability and cord compression[70] (fig. 6). Further CT, CT myelographic, or MRI examinations should be performed if clinical or roentgenographic findings are suggestive of spinal instability and cord compression (figs. 5 and 6).

Short-latency somatosensory evoked potentials monitoring is a useful noninvasive means of evaluating cord compression in dwarfs. The monitoring of evoked potentials is particularly useful in children to demonstrate cord compression before significant and perhaps irreversible clinical impairment develops.[34,137,138]

Anesthetic Management

Care is necessary during induction of anesthesia and laryngoscopy to avoid positions of extreme flexion or extension, which can aggravate cord compression in patients with foramen magnum stenosis and cervical instability.[74,75] Improper positioning of the head, neck, and shoulders during prolonged surgery in the supine position is particularly harmful and may lead to catastrophic intraoperative cord ischemia.[74,75] In the patient with Morquio syndrome and atlantoaxial instability, if the shoulders, neck, and occiput rest on the same plane while the patient is lying in the supine position, the skull and atlas will be
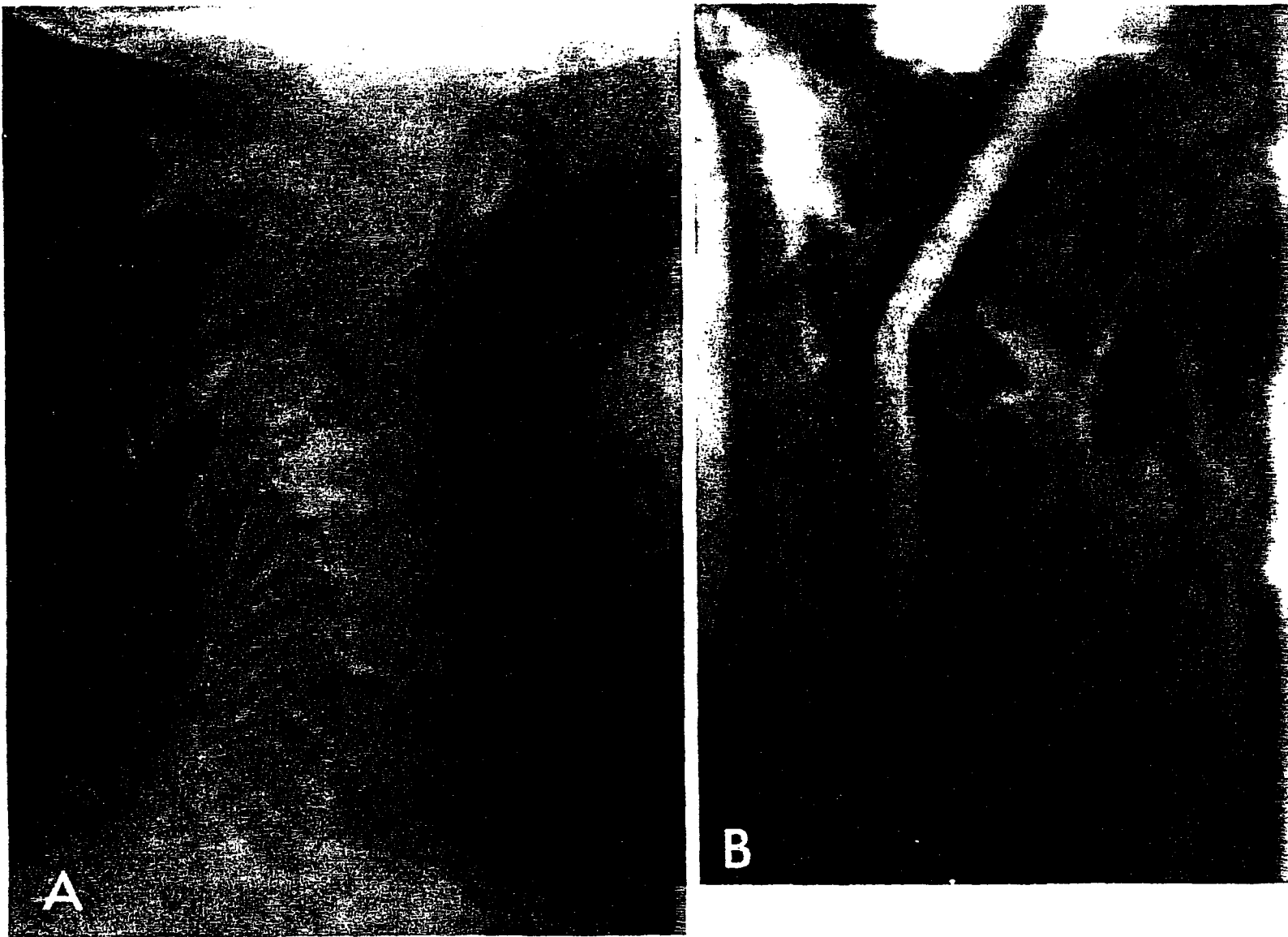

FIG. 6. Four-year-old child with diastrophic dysplasia and cervical kyphosis. (*A*) Lateral cervical radiograph demonstrates anterior subluxation of C2 and C3, a typical finding in this dysplasia. (*B*) Cervical magnetic resonance image demonstrates the "bowstringing" of the spinal cord on the prominence of the posteriorly displaced hypoplastic C3 vertebra.

displaced anteriorly on the axis, compressing the cord. The same position in the patient with diastrophic dysplasia and cervical kyphosis can cause bowstringing of the cord within the spinal canal and result in ischemic myelopathy. The large occipital bossing of the achondroplast results in anterior displacement of the head when the patient lies supine on a flat surface, such that the prominent posterior margin of the foramen magnum may indent the cervicomedullary junction. These complications can be prevented by placing a folded towel behind the shoulders, elevating them with respect to the occiput and restoring a neutral neck alignment. Cervical stabilizing devices such as a halo cast or a Milwaukee brace should be applied prior to anesthesia, for cervical fusion, to avoid cervical subluxation and dislocation.[139]

In some patients whose necks are appropriately immobilized, laryngoscopy is impossible, particularly if other anomalies, such as a short neck, large tongue, or pectus carinatum co-exist. In such cases, fiberoptic intubation may be necessary. If spinal cord compression is associated with paresis and muscle wasting, succinylcholine is contraindicated, since this drug can cause life-threatening hyperkalemia in the presence of peripheral denervation.[140] Autonomic hyperreflexia is also a potential problem with cervical cord compression and myelopathy.

Anesthetizing a dwarf with raised ICP who, in addition, has the potential for upper airway obstruction, presents an enormous challenge for the anesthesiologist. An inhalation induction with a spontaneously breathing patient and a halogenated agent may be associated with hypercarbia and a consequent increase in ICP. An intravenous induction can result in unconsciousness and apnea in the patient who cannot be ventilated or intubated—a potential catastrophe if the patient has raised ICP. Balancing these conflicting requirements necessitates a case-by-case, careful determination of anesthetic priorities.

Suboccipital craniectomy for the relief of foramen magnum stenosis in patients with achondroplasia is often done with the patient in the sitting position. The expected complications associated with surgery in this position, such as air embolism, have been reported in these patients.[20] Other major intraoperative neurologic complications of this procedure include C1-level spinal cord infarction and brachial plexus palsies.[20] The intraoperative monitoring of somatosensory evoked potentials may help in the early detection of cord compression and ischemia, whether from foramen magnum stenosis, odontoid dysplasia, or spinal stenosis.[138,141]

THERMAL REGULATION DYSFUNCTION

The hyperthermia that occasionally develops in patients with OI is not usually associated with the clinical features of malignant hyperthermia and should not be diagnosed

as such.[90–92,142] Therapy should consist of measures to provide external cooling. Sodium dantrolene administration is not indicated.

Although most of these hyperthermic episodes are not indicative of true malignant hyperthermia, a few cases with clinical features typical of true malignant hyperthermia have been described in patients with OI.[93,143] In these patients, the diagnosis of malignant hyperthermia was not confirmed, however, by the caffeine contracture test. Anesthetic agents that precipitate malignant hyperthermia need not necessarily be avoided in patients with OI or in other dwarfs unless malignant hyperthermia is clinically suspected because of possible prior adverse anesthetic events in the patient or a family member.

COAGULATION DYSFUNCTION

The multifactorial nature of the hemostatic defects of patients with OI, the only one of the chondrodystrophies with an associated coagulopathy, has been reviewed above. Preoperative evaluation should include a test of bleeding time.[95] Platelets and fresh frozen plasma should be available in case clinical bleeding becomes a problem.[95]

The Future

DWARFISM AND RESEARCH

Dramatic technologic advances in molecular biology are beginning to define the underlying molecular and genetic abnormalities in some of the osteochondrodystrophies. Mutations that result in defects of cartilage components, such as collagen, or defects of the regulatory mechanisms of chondrogenesis are believed to cause this heterogeneous group of diseases.

Identification of the responsible type I collagen mutations have been detected in fibroblasts of some OI patients.[144] More recently, a single exon deletion has been demonstrated in the structure of the type II collagen gene in a large family with spondyloepiphyseal dysplasia.[145] Research, in the near future, will likely define gene defects in other chondrodystrophies as well.[146] This essential first step must be taken before the development of specific therapeutic gene manipulation can begin.

FUTURE CLINICAL GOALS AND PROGRESS

In addition to genetic advances, new surgical procedures to alter the phenotypes of some dwarfs have been developed. Although some of these modalities present medical, moral, and ethical dilemmas, it is likely that their application will become more widespread.[147,148]

Limb-lengthening orthopedic procedures, using a dynamic axial external fixation system to produce slow distraction of the callus (callostosis) or epiphysis (chondro-

diastasis) after corticotomy, have achieved a normal trunk-to-lower-limb ratio in patients with achondroplasia.[148-151] Such procedures, however, are sometimes complicated by the development of contractures, fractures, and nonunion. Healing, sometimes painful, is protracted, averaging 10 months per limb. After leg-lengthening, these patients remain disproportionate because of short arms. Even if these are also lengthened, other problems associated with achondroplasia, such as upper airway abnormalities and spinal cord compression, persist and may still require therapy.

Recently, bone marrow transplantation has been performed in patients with MPS IH,[152] MPS II,[153] and MPS VI in an attempt to replace the deficient lysosomal enzymes by providing a source of normal cells containing normal genes. This procedure has been associated with a reduction in glycosaminoglycan accumulation in liver, spleen, skin, cornea, and upper airway structures.[152] Although less dramatic, neurologic improvement also has occurred in some patients.[154] Glycosaminoglycan deposition in cartilage is not lessened, and bone changes in the MPS appear resistant to bone marrow transplantation.[152] These studies are in their infancy and longer follow-up periods are necessary to evaluate their outcome.

Appendix. Dwarfs: The Anesthetic Implications of the Osteochondrodysplasias

Disorder and Clinical Feature[5,22,24,44,45,155]		Anesthetic Implications	
Achondroplasia			
Presenting age:	At birth	Airway:	Narrow nasal passages and nasopharynx; visualization of larynx usually uncomplicated
Craniofacial:	Megelencephaly, frontal bossing, depressed nasal bridge, maxillary hypoplasia	Cervical spine:	Occipitalization of Cl
Stature:	Rhizomelic short stature	Pulmonary:	Mild restrictive lung disease from rib hypoplasia and thoracic lordosis; central and obstructive sleep apnea
Deformities:	Lumbar hyperlordosis and thoraco-lumbar kyphosis, limited elbow extension	Cardiac:	Cor pulmonale from restrictive lung disease and apnea
Respiratory:	Thoracic dystrophy	Neurologic:	Hydrocephalus with elevated intracranial pressure; cervicomedullary compression from foramen magnum stenosis; thoracolumbar and generalized spinal stenosis
Neurologic:	Hypotonia, hydrocephaly, foramen magnum stenosis		
Adult height:	Usually less than 1.3 m		
Diastrophic dysplasia			
Presenting age:	At birth	Airway:	Micrognathia and cleft palate; normal facies; upper airway obstruction from laryngomalacia or laryngotracheal stenosis
Craniofacial:	Normal appearance; aural chondritis "cauliflower ear", cleft palate, micrognathia, laryngomalacia	Cervical spine:	Normal odontoid process; cervical kyphosis with occasional subluxation at C2-C3
Stature:	Rhizomelic short stature	Pulmonary:	Restrictive lung disease from severe kyphoscoliosis and thoracic dystrophy
Deformities:	Talipes equinovarus; dislocations, contractures, and limited movement of hips, knees, elbows; "hitch-hikers thumb"; kyphoscoliosis, odontoid hypoplasia		
Adult height:	0.8-1.4 m		
Metatropic dysplasia			
Presenting age:	At birth	Airway:	Short neck with limited range of movement
Craniofacial:	Normal appearance	Cervical spine:	Odontoid hypoplasia and atlanto-axial instability
Stature:	At birth, long, narrow trunk and chest with rhizomelic limb shortening; progressive kyphoscoliosis, pectus carinatum and short trunk dwarfism with increasing age	Pulmonary:	Severe restrictive lung disease from rib hypoplasia and thoracic dystrophy and severe progressive kyphoscoliosis
Deformities:	Kyphoscoliosis, pectus carinatum, widening of metaphyses, bulbous enlargement of joints, flexion contractures of hips, knees, elbows, taillike appendage over sacrum, odontoid hypoplasia		
Adult height:	Usually less than 1.2 m		
Chondrodysplasia punctata			
Presenting age:	Heterogeneous group of bone dysplasias: severe forms present at birth; milder forms present in later childhood	Airway:	Micrognathia, short neck, laryngomalacia, and tracheomalacia with upper airway obstruction and stippled calcification of laryngeal cartilages
Craniofacial:	Frontal bossing, depressed nasal bridge, micrognathia, cataracts	Cervical spine:	Odontoid hypoplasia or agenesis with atlanto-axial instability in Conradi-Hunermann type
Stature:	Rhizomelic short stature	Cardiac:	ASD, VSD, and PDA

Appendix, *continued*

Disorder and Clinical Feature[5,22,24,44,45,155]	Anesthetic Implications
Spondyloepiphyseal dysplasia tarda Presenting age: Late childhood Craniofacial: Normal Stature: Short trunk, short stature with normal limb length Deformities: Scoliosis, short neck	Airway: Short neck Cervical spine: Normal
Camptomelic dysplasia Presenting age: At birth Craniofacial: Micrognathia, cleft palate Stature: Short-limbed, short stature Deformities: Bowed limbs, short-rib thoracic dysplasia	Airway: Micrognathia, cleft palate Pulmonary: Restrictive lung disease from thoracic dystrophy and kyphoscoliosis; tracheobronchomalacia with intrathoracic airway obstruction
Metaphyseal chondrodysplasias (types: Jansen, Schmidt, McKusick, Spahr, Shwachman) Presenting age: Varied, usually early childhood Craniofacial: Normal except for micrognathia in Jansen type Stature: Heterogeneous group of bone dysplasias; rhizomelic short stature Deformities: Wide flared epiphyses with bowing of legs Other anomalies: Immune deficiency in McKusick type (cartilage–hair hypoplasia), hypercalcemia in Jansen type, neutropenia and pancreatic insufficiency in Schwachman variant	Airway: Micrognathia and cervical kyphoscoliosis in Jansen type
Spondylometaphyseal dysplasia (type: Kozlowski) Presenting age: Infancy to childhood Craniofacial: Normal Stature: Short trunk dwarfism Deformities: Progressive kyphoscoliosis, pectus carinatum, coxa vara, odontoid hypoplasia Other anomalies: None Adult height:: Usually less than 1.3 m	Airway: Short neck Cervical spine: Odontoid hypoplasia with atlanto-axial instability Pulmonary: Restrictive lung disease from kyphoscoliosis
Pseudoachondroplasia Presenting age: Early childhood Craniofacial: Normal Stature:: Rhizomelic, short stature, similar to achondroplasia but with normal craniofacial structure Deformities: Lumbar hyperlordosis, genus valgum, genu varum, scoliosis Other anomalies: None Adult height: Usually less than 1.3 m	Airway:: Normal Cervical spine: Normal
Osteogenesis imperfecta (OI) Heterogeneous group of heritable disorders of connective tissue characterized primarily at osteoporosis and bone fragility with repeated fractures, skeletal deformities. There are four distinctive genetic and clinical types of OI (OI types I–IV). Presenting age: Varied (birth to childhood) Craniofacial: Varied (normal to large head with small triangular face Stature: Varied (short limb and trunk secondary to repeated fractures Deformities: Limb deformities, cervical thoracic and lumbar scoliosis secondary to malunion of recurrent fractures Other anomalies: Joint laxity, dentinogenesis imperfecta, altered temperature regulation, bleeding diathesis	Airway: Laryngeal position may be distorted by cervical upper thoracic scoliosis and pectus carinatum Cervical spine: May have cervical scoliosis Pulmonary: Restrictive lung disease from kyphoscoliosis Heart: Cor pulmonale from kyphoscoliosis; aortic root dilatation, aortic regurgitation, and mitral valve prolapse in OI type I Hematologic: Bleeding diathesis from qualitative platelet abnormality Systemic: Hypermetabolic state with hyperthermia (not malignant hyperthermia) may develop during surgery and anesthesia Skeletal: Beware of causing fractures during positioning for anesthetic and surgical manipulations

Appendix, *continued*

Disorder and Clinical Feature[5,22,24,44,45,155]	Anesthetic Implications
Deformities: Limb assymmetry; finger, toe anomalies; vertebral anomalies and scoliosis; odontoid hypoplasia	
Cardiac: Congenital heart disease (VSD, ASD, PDA)	
Other Anomalies: Stippled calcification of growth plates and periarticular cartilages; Icthyosis and thickening of skin	
Pseudometatrophic dysplasia (Kneist syndrome)	
Presenting age: At birth	Airway: Cleft palate occasionally
Craniofacial: Hypertelorism, depressed nasal bridge, prominent eyes, cleft palate	Cervical spine: Odontoid hypoplasia with atlanto-axial instability
Stature: Short trunk, short limbs	
Deformities: Scoliosis, fusiform swelling of joints from metaphyseal and epiphyseal enlargement, joint contractures, odontoid hypoplasia	
Other anomalies: Deafness, myopia, retinal detachment	
Adult height: Usually less than 1.4 m	
Mesomelic dysplasia	
Presenting age: Heterogenous group of several variants; Langer and Robinow variants present at birth; other variants present later in childhood	Airway: Micrognathia in the Langer and Robinow mesomelic dysplasias
Craniofacial: Hypertelorism, flat facies; micrognathia in Langer type	Cardiac: Atrial septal defects in Robinow dysplasia
Stature: Mesomelic upper and lower limb shortening	
Short rib polydactyly syndromes	
• Chondro-ectodermal dysplasia (Ellis–van Creveld syndrome)	
Presenting age: At birth	Airway: Cleft lip and palate, micrognathia occasionally
Craniofacial: Usually normal; may have micrognathia, cleft lip and palate	Cervical spine: Normal
Stature: Mesomelic and acromelic limb shortening	Pulmonary: Respiratory distress and pulmonary failure from restrictive lung disease and pulmonary hypoplasia; bronchial cartilage hypoplasia with tension lobar emphysema possible in chondroectodermal dysplasia
Deformities: Postaxial polydactyly	
Respiratory: Short-rib thoracic dysplasia	
Cardiac: Congential heart disease (ASD, VSD, single atrium)	Cardiac: Cor pulmonale from restrictive lung disease; ASD, VSD, and single atrium defect in chondroectodermal dysplasia
Other anomalies: Ectodermal abnormalities with dysplastic hair, nails, teeth	
Adult height: Usually less than 1.35 m	
• Asphyxiating thoracic dystrophy (Jeune syndrome)	
Presenting age: At birth	Airway: Normal
Craniofacial: Normal	Cervical spine: Normal
Stature: Short stature, mesomelic and acromelic limb shortening	Pulmonary: Respiratory distress and pulmonary failure from restrictive lung disease and pulmonary hypoplasia
Deformities: None except for long, narrow chest; postaxial polydactyly	Cardiac: Cor pulmonale from restrictive lung disease
Respiratory: Short-rib thoracic dysplasia	Kidney: Renal failure
Renal: Interstitial renal fibrosis and polycystic changes; renal failure	
Spondyloepiphyseal dysplasia congenita	
Presenting age: At birth	Airway: Cleft palate occasionally; short neck with limited neck flexion; occasionally laryngotracheal stenosis
Craniofacial: Normal	
Stature: Short trunk and rhizomelic, short stature	Cervical spine: Odontoid hypoplasia with atlantoaxial instability
Deformities: Progressive kyphoscoliosis and pectus carinatum, genu valgum, talipes equino varus, coxa vara, odontoid hypoplasia	Pulmonary: Restrictive lung disease secondary to progressive kyphoscoliosis.
Other anomalies: Myopia, retinal detachment, deafness, cleft palate	
Adult height: Usually less than 1.3 m	

Appendix, *continued*

Disorder and Clinical Feature[5,22,24,44,45,155]	Anesthetic Implications
Mucopolysaccharidoses Heterogeneous group of inherited metabolic diseases characterized by deficiency of one or more of ten lysosomal degradative enzymes. There are seven distinct clinical syndromes, only three of which result in dwarfing syndromes. MPS 1-H (Hurler syndrome) is described in detail as a prototype.	The anesthetic implications of the MPS are widespread because of the multisystem involvement of these diseases. The brunt of the disease may, however, be borne by different organ systems in the different MPS.
• Hurler syndrome (MPS 1-H) Presenting age: First few years of life Craniofacial: Coarse facies, frontal bossing, depressed nasal bridge, hypoplastic nasopharynx, persistent nasal discharge, cloudy corneas, hydrocephalus Stature: Marked short stature Deformities: Scoliosis, lumbar gibbus, coxa valga, odontoid hypoplasia; joint stiffness and contractures Neurologic: Severe mental retardation	Airway: Upper airway obstruction from macroglossia; narrowed nasopharynx, nasopharyngeal secretions; infiltration of adenoids, tonsils, larynx and upper airway mucosa with glycosaminoglycan; tracheobronchial stenosis from glycosaminoglycan infiltration and intrathoracic obstruction; short neck with resultant cephalad placement of larynx; temporomandibular joint stiffness Cervical spine: Short neck; odontoid hypoplasia Pulmonary: Restrictive lung disease from kyphoscoliosis and lumbar gibbus formation; obstructive sleep apnea Cardiac: Ischemic and valvular heart disease with aortic and mitral stenosis and regurgitation; myocardial infiltration with cardiomyopathy; cor pulmonale from restrictive lung disease Neurologic: Hydrocephalus with raised intracranial pressure; cervico-medullary junction compression from "napkin ring" thickening of meninges; atlantoaxial instability uncommon Abdomen: Massive hepatosplenomegaly—consider "full stomach"
• Hunter Syndrome (MPS II) There are two forms of MPS II. MPS II A is as severe as MPS 1H; MPS II B is much less severe and without mental retardation	Anesthetic implications of MPA II A and B and MPS 1H/1S are similar to those of Hurler syndrome.
• Hunter-Scheie syndrome (MPS IH/IS) Similar to MPS I-H but with milder somatic involvement and normal intelligence	
• Morquio syndrome (MPS IV) Presenting age: Infancy Craniofacial: Prominent maxilla; no coarse facial features Stature: Short trunk, short stature Deformities: Scoliosis, pectus carinatum, genu valgum, joint laxity, odontoid hypoplasia, cervical compression Respiratory: Restrictive disease and intrathoracic obstruction from tracheobronchial stenosis Cardiac: Aortic regurgitation Neurologic: Normal intelligence; neurologic deficits secondary to cord compression	Airway: Upper airway obstruction from macroglossia and infiltration of upper airway structures with glycosaminoglycans; nasopharyngeal obstruction; tracheobronchial stenosis and intrathoracic airway obstruction; short neck Cervical spine: Short neck; odontoid hypoplasia Pulmonary: Restrictive lung disease from kyphoscoliosis; obstructive sleep apnea; intrathoracic airway obstruction Neurologic: Normal intelligence; odontoid dysplasia and atlantoaxial instability Cardiac: Aortic valve insufficiency

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