

Surgical Implications of Cerebral Dysgenesis

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ABSTRACT: Cerebral dysgenesis encompasses varied disorders of brain development. Based on the understanding of these conditions provided by histopathologists, embryologists, radiologists and developmental pediatricians, surgeons are able to appropriately assist in the care of these patients. The surgeon can offer assessment of the ventriculomegaly that commonly accompanies cerebral dysgenesis in addition to providing methods to control hydrocephalus, to reconstruct cranial and facial malformations and to remove dysfunctional tissue. For most patients, surgical intervention is only one of the many factors that determine developmental prognosis. Based on the foundation built by other specialists, this review discusses cerebral dysgenesis from the perspective of historical and current surgical interventions.

RÉSUMÉ: Implications chirurgicales de la dysgénésie cérébrale. La dysgénésie cérébrale comprend des désordres variés du développement du cerveau. En se basant sur la compréhension de ces affections fournie par les histopathologistes, les embryologistes, les radiologistes et les pédiatres du développement, le chirurgien est capable de fournir une assistance appropriée aux soins de ces patients. Le chirurgien peut offrir une évaluation de la ventriculomégalie qui accompagne fréquemment la dysgénésie cérébrale, en plus de fournir des méthodes de contrôle de l'hydrocéphalie, de reconstruire les malformations crâniennes et faciales, et de faire l'ablation du tissu dysfonctionnel. Pour la plupart des patients, l'intervention chirurgicale n'est qu'un des multiples facteurs qui déterminent le pronostic développemental. À partir des connaissances accumulées par d'autres spécialistes, cette revue discute de la dysgénésie cérébrale du point de vue des interventions chirurgicales réalisées dans le passé et de celles qui sont faites actuellement.

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SURGICAL IMPLICATIONS OF CEREBRAL DYSGENESIS

Cerebral dysgenesis refers to those malformations that arise as a result of intrinsic and abnormal development affecting the brain. The pathological and radiological morphologists, embryologists, neurologists, and surgeons involved in the assessment and care of these patients, bring unique and often differing perspectives to these malformations. The morphologist views and classifies these conditions based on structural aberrations and the embryologist, on disordered development. The neurologist and surgeon deal with developmental and neurological dysfunction. Amongst these various specialties, there is considerable overlap and sometimes confusion in classification, diagnosis, and clinical implication. Building on the structural alterations seen by pathologist and radiologist, this paper outlines the surgical implications of these malformations and the results of treatment. Conditions due to a breakdown or interference with initially normal development such as hydranencephaly, will not be discussed nor will the neurocutaneous syndromes.

Cerebral dysgenesis encompasses a variety of congenital entities that will be grouped on the basis of the surgeon's role in assessment and treatment (Table 1). These roles include cerebrospinal fluid diversion, cranial reconstruction and lesion excision. Disorders of ventricular morphology, conditions resulting in craniofacial and brain distortion and disorders of neural

development that present with focal neurological dysfunction will be discussed (Table 2).

Abnormalities in ventricular morphology are common accompaniments of disorders of brain development. Treatment decisions require the differentiation of non-progressive ventriculomegaly from disorders of cerebrospinal fluid circulation. If hydrocephalus is present, cerebrospinal fluid diversion can be undertaken. The developmental prognosis of this group of disorders is dependent upon the primary dysgenetic malformation and the hydrocephalus. Craniofacial and brain distortion occur as the result of a variety of processes. This group which includes encephaloceles, requires the surgeon to focus on correction of deformity. Developmental prognosis is defined in large part by the involvement of the brain in the lesion. Dysgenetic conditions that produce focal neurological dysfunction have important implications for the surgeon who is able to offer tissue resection or decompression.

Table 1: Determinants of Neurosurgical Involvement in the Treatment of Cerebral Dysgenesis

1. Is hydrocephalus present and is cerebrospinal fluid diversion required?
2. Is there craniofacial dysmorphism requiring reconstruction?
3. Is there a focal lesion requiring excision?

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DISORDERS OF VENTRICULAR MORPHOLOGY

Abnormal ventricular morphology, is the commonest facet of cerebral dysgenesis with which surgeons deal. Although hydrocephalus has ventriculomegaly as its cardinal morphological feature, it must be differentiated from ventricular enlargement that is not due to disorders of cerebrospinal fluid circulation. Ventriculomegaly can result from one or more of the following mechanisms: a developmental arrest at a fetal stage when the lateral ventricles are normally large, structural alterations in the ventricular wall or hydrocephalus. In the fetus, ventriculomegaly is the commonest and most easily recognized feature of brain maldevelopment.^{1,2} With improved postnatal imaging studies, the etiology of ventricular enlargement can usually be determined allowing proper selection of those patients who have hydrocephalus and who would benefit from ventricular shunting.

Ventriculomegaly Due to Dysgenesis

In these conditions, the ventricular enlargement seen on imaging studies is not due to disorders of cerebrospinal fluid circulation. The surgeon's role is to differentiate these causes of ventricular enlargement from that due to hydrocephalus and thereby avoid inappropriate ventricular shunting.

Megalencephaly

Megalencephaly is common in the paediatric neurosurgical practice because a rapidly increasing head circumference during the first year of life and "large" ventricles on imaging studies prompt referral for assessment (Figure 1). While the ventricular system is larger than normal, it is usually dysmorphic in shape and when viewed relative to the size of the brain, the ventricular volume is in proportion to the brain volume. Rapid head growth in infancy is not associated with disproportionate ventricular enlargement. Such patients may demonstrate either normal or delayed development. A family history of macrocrania may be

present. Head circumference measurements typically plateau and parallel the 98thile during the second year of life. The differential diagnosis includes hydrocephalus and extracerebral fluid collections. Imaging studies allow the differentiation of megalencephaly from macrocrania due to these conditions.³

Shunting is not indicated for rapid head growth and may increase the likelihood of the development of a seizure disorder in these patients.

Periventricular Heterotopias and Other Migration Disorders

Periventricular heterotopias are a reflection of disordered cellular migration occurring during the second trimester when the lateral ventricles are normally large in comparison to the cerebral mantle.² Persistence of this enlargement in conjunction with structural distortion of the ventricular wall by the heterotopia combine to produce the commonly associated ventriculomegaly. Depending on the quality of in vivo neuroimaging, and the nature and magnitude of the migration disorder, many patients with this type of cerebral dysgenesis are thought to have hydrocephalus. However, if one considers the ventricular wall structure in addition to the ventricular size, the true nature of these conditions becomes apparent. When the migration disorder is extensive, such patients should be diagnosed as lissencephaly and pachygyria (Figures 2,3).

Classically, these patients do not demonstrate the progressive macrocrania and ventriculomegaly characteristic of hydrocephalus and therefore are not assessed by surgeons, however with improved postnatal imaging and more widespread assessment of infants and children with developmental delay, such patients do come to attention because of large lateral ventricles. Shunting is only indicated for those few who have in addition, disorders of cerebrospinal fluid circulation.

Table 2: Spectrum of Cerebral Dysgenesis Requiring Neurosurgical Assessment or Intervention.

A. Dysgenesis presenting because of, or associated with, ventriculomegaly	
I.	Hydrocephalus is usually present Dandy Walker Syndrome Aqueductal Stenosis Chiari II Malformation Lhermitte Duclos Disease
II.	Hydrocephalus may not be present Lobar Holoprosencephaly Agenesis of the Corpus Callosum associated with a dorsal sac
III.	Hydrocephalus is not usually present Alobar Holoprosencephaly Megalencephaly Periventricular Heterotopias
B. Dysgenesis presenting because of craniofacial dysmorphism	
I.	Encephalocele Occipital Frontobasal Sphenoidal
II.	Amniotic Band Syndrome
C. Dysgenesis presenting because of focal neurological dysfunction	
I.	Hypothalamic Hamartomata
II.	Cortical Dysplasia
III.	Chiari Malformation

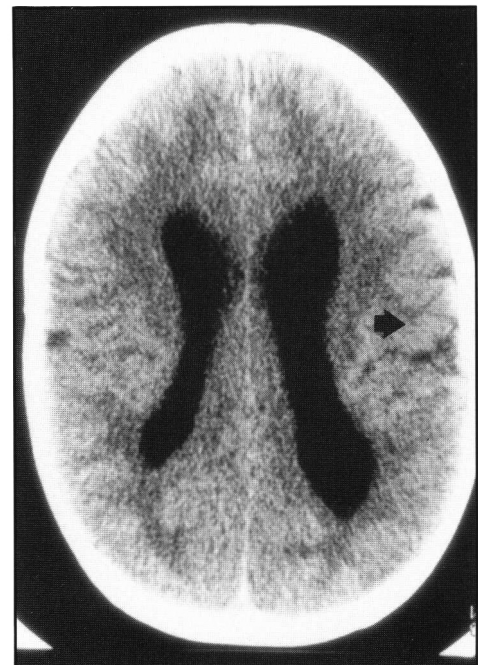


Figure 1 — Megalencephaly. The lateral ventricles are dysmorphic and enlarged. The gyral pattern is simplistic (arrow), suggesting an associated migration abnormality in this patient.

Ventriculomegaly Due to Hydrocephalus

This group of conditions includes many of the classical malformations that present with hydrocephalus and require surgical intervention for the control of disordered cerebrospinal fluid circulation. From the surgeon's perspective, decision making hinges on confirmation of the diagnosis, appropriate choice of procedure and timing of operation(s).

Progressive and disproportionate ventricular and cranial enlargement must be demonstrated or inferred to make the diagnosis of hydrocephalus in these conditions. Using this criterion, differentiation from other causes of ventriculomegaly is possible and inappropriate shunting is avoided.

Obstruction of the Cerebral Aqueduct

Aqueductal obstruction is the commonest cause of isolated congenital hydrocephalus. Surgical involvement is usually required for cerebrospinal fluid diversion. Russel has classified congenital aqueductal obstruction on the basis of observed pathology into stenosis, forking or atresia and membrane formation.⁴ These histological patterns do not differentiate intrinsically abnormal development from the effects of secondary insults on the immature brain, as similar appearances can occur as a result of either mechanism.⁵

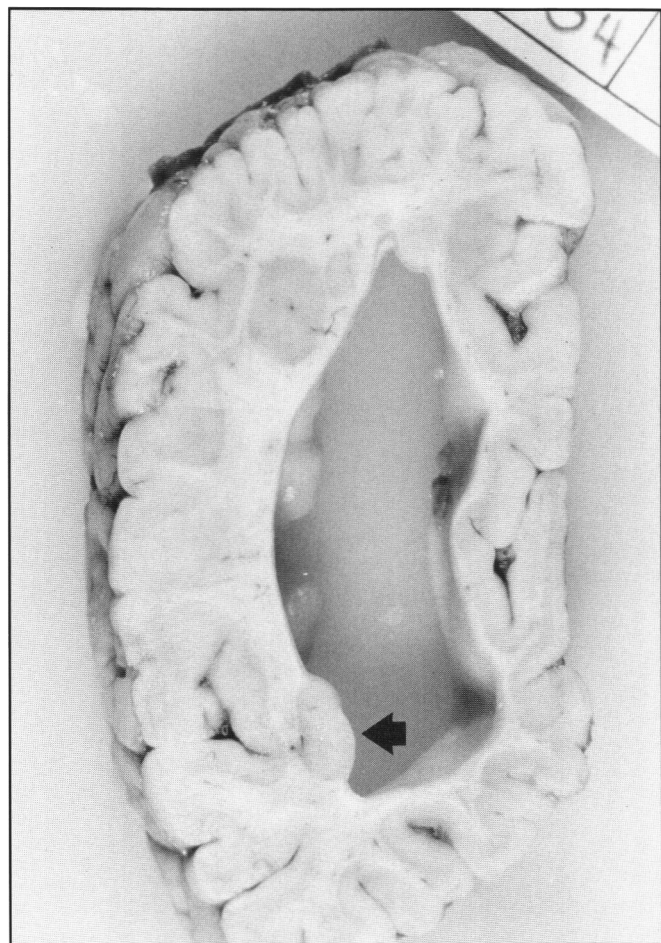


Figure 2 — Periventricular heterotopia in the centrum and projecting into the body of the lateral ventricle associated with ventriculomegaly (arrow)

In the pre-shunt era, because choroid plexectomy and third ventriculostomy were the mainstays of treatment, a variety of studies, particularly ventriculography, were undertaken to establish aqueductal patency. In aqueductal obstruction, a ventriculostomy to bypass the obstruction was created from the third ventricle to the subarachnoid space. The first successful shunts (ventriculocisternal shunts) done for the treatment of hydrocephalus were done in patients with aqueductal stenosis.⁶

Currently, the availability of ventricular shunts has, in many North American institutions, allowed the replacement of surgical third ventriculostomy with ventricular shunting and has eliminated the need to establish aqueductal patency with pre-operative ventriculography. Percutaneous or stereotaxic third ventriculostomy remain popular in Europe.^{7,8} Percutaneous cannulation of the aqueduct has been attempted but can result in damage to the periaqueductal grey and reticular formation and is therefore not widely accepted.⁹ Current neuroradiographic imaging allows the demonstration of aqueductal patency using flow sensitive magnetic resonance sequences.¹⁰ Magnetic resonance imaging also allows the recognition of those cases of aqueductal obstruction caused by distortion of the tectum and aqueduct by encysted quadrigeminal cisterns or periaqueductal gliomas. In these situations, the treatment is directed to the offending lesion (Figure 4).¹¹

Sex-linked familial or autosomal recessive cases of "aqueductal stenosis", associated with adducted and flexed thumbs, have been described¹² and were thought to be ideal candidates for in utero shunting because early detection is possible.¹³ Our experience with four such families has shown that these patients rarely demonstrate progressive ventriculomegaly. The ventricular enlargement is usually due to migration abnormalities and not hydrocephalus. The ventricles are dysmorphic in appearance.



Figure 3 — Ventriculomegaly associated with pachygyria. In the absence of hydrocephalus, shunting is not indicated.

None of the patients in our series have had isolated aqueductal obstruction. Significant developmental delay is not uncommon in this condition.

Agenesis of the Corpus Callosum Associated with Hydrocephalus

When massive ventriculomegaly, with craniomegaly is diagnosed in utero, agenesis of the corpus callosum is a common accompaniment.¹ The third ventricle is expanded upward between the fornices, Probst's bundles and leaves of the septum pellucidum forming the dorsal sac. This expansion within the interhemispheric fissure, between the occipital and parietal lobes, displaces the falx and results in the ultrasonographic appearance of asymmetrical ventricular enlargement in the fetus. Interhemispheric arachnoid cyst(s) may also be present. Ventricular asymmetry is the only clue that suggests this diagnosis in the fetus. In our experience the massive hydrocephalus at the time of detection obscures this and other cerebral abnor-

malities, specifically holoprosencephaly and migration defects (Figure 5).

From the surgeon's perspective, the compartmentalization of cerebrospinal fluid containing spaces in the face of hydrocephalus can pose a problem if not recognized. Preoperative knowledge of ventricle-dorsal sac communication is required for effective shunt placement (Figure 6). Developmental prognosis is dependent on the extent of hydrocephalus and the associated anomalies.²⁵ In our experience, all of these patients have shown severe developmental delay.

Lobar Holoprosencephaly Associated with Hydrocephalus

The holoprosencephalies are developmental disorders of the forebrain and have been classified by DeMeyer into alobar, semilobar and lobar varieties depending on the pattern of the malformation.²⁶ The intracranial anatomy of the alobar variety is easy to recognize in utero and may be associated with mid-face clefting. These patients do not usually have hydrocephalus and are not therefore a concern for the surgeon. The lobar variety is associated with hydrocephalus and poses a problem in the differential diagnosis and prognosis of fetal ventriculomegaly. In the absence of facial malformations, this diagnosis is usually

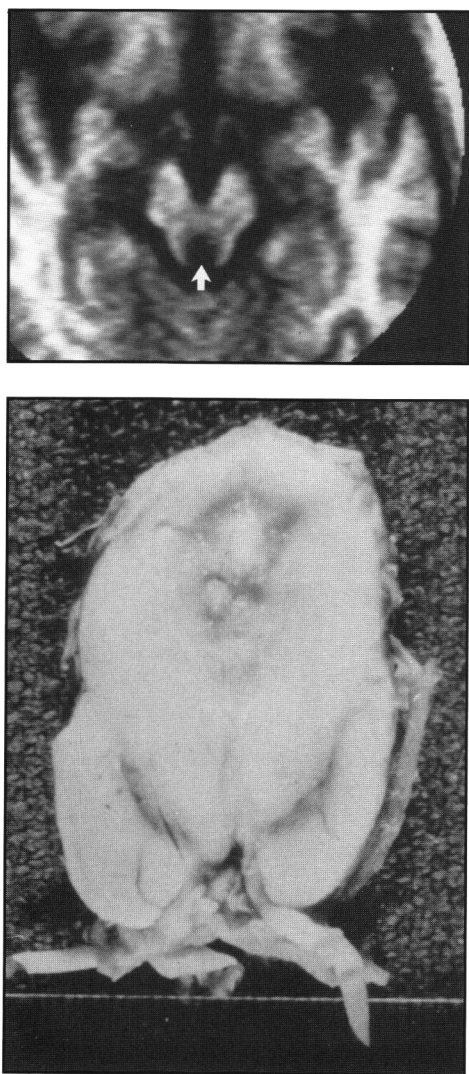


Figure 4 — Top. Periaqueductal low density on computed tomography (arrow). Bottom. Midbrain specimen showing aqueductal obstruction due to astrocytoma.

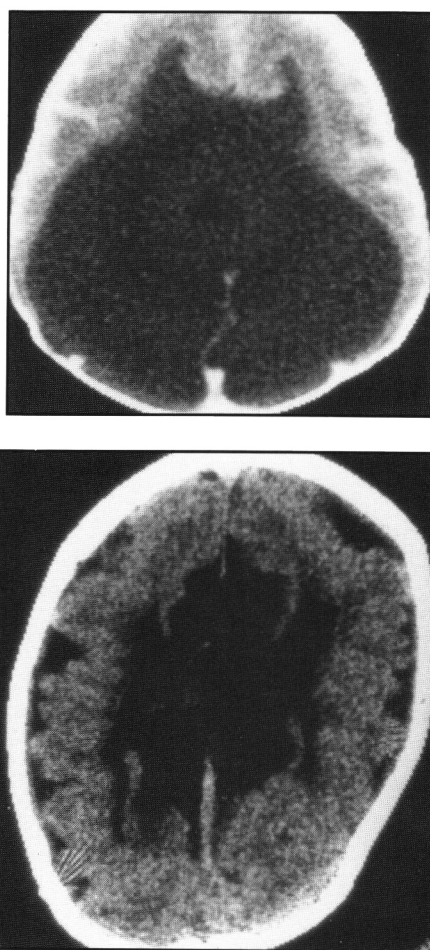


Figure 5 — Top. Agenesis of the corpus callosum with massive hydrocephalus and interhemispheric cyst. Bottom. Following shunting, the associated migration abnormality as reflected by the gyral pattern, is more obvious.

not made in the fetus. On postnatal studies, the cerebral hemispheres are seen to be partially separated by an interhemispheric fissure. This fissure is deepest in the occipital region and has cortex at its depth bridging between the two hemispheres. The temporal horns are separated. The falx is hypoplastic particularly anteriorly. Facial and chromosomal anomalies are not common in the variety (Figure 7, 8).

Surgical treatment can address the hydrocephalus but the developmental prognosis is a reflection of the brain malformation.

Dandy-Walker Malformation

The Dandy-Walker malformation is a developmental abnormality of the roof of fourth ventricle associated with varying degrees of hypoplasia or aplasia of the cerebellar vermis and the medial aspects of the cerebellar hemispheres, cystic dilation of

the fourth ventricle and an enlarged posterior fossa with upward displacement of the tentorium, transverse sinuses and torcula herophili.¹⁴⁻¹⁶ Atresia of the foramina of Luschka and Magendie may or may not be present.¹⁷ Cystic expansion of the fourth ventricle enlarges the posterior fossa, prevents the normal descent of the tentorium and results in the persistence of a high parietal location of the transverse sinuses (Figure 9). Hydrocephalus and other neuroanatomical abnormalities are commonly associated.

From the perspective of the surgeon, hydrocephalus, the cystic 4th ventricle and their intercommunication and the associated cerebral anomalies must be considered when planning cerebrospinal fluid diversion and judging prognosis. Magnetic resonance imaging in the sagittal plane has greatly improved our understanding of this anatomical arrangement.¹⁸

Hydrocephalus, the surgical focus in this condition, is seen in the majority of patients with the Dandy-Walker malformation.^{19,20} Treatment has taken the form of craniotomy and resection of the cyst wall and/or cerebrospinal fluid shunting. The former procedure was designed to restore normal cerebrospinal fluid flow out of the fourth ventricle and the latter to divert cerebrospinal fluid from the lateral ventricle, or the cyst or both.

The cyst wall is a translucent membrane separate from the posterior fossa dura attaching the calamus scriptorius inferiorly with the residual vermis superiorly and the mesial aspects of the



Figure 6 — Top. Sagittal MRI. Agenesis of corpus callosum and interhemispheric cyst. Bottom. Coronal MRI. Interhemispheric cyst exerting mass effect, lateral ventricles are not enlarged. Communication of intracranial cerebrospinal fluid spaces can be demonstrated on MR and assists in determining the appropriate location for shunt placement.

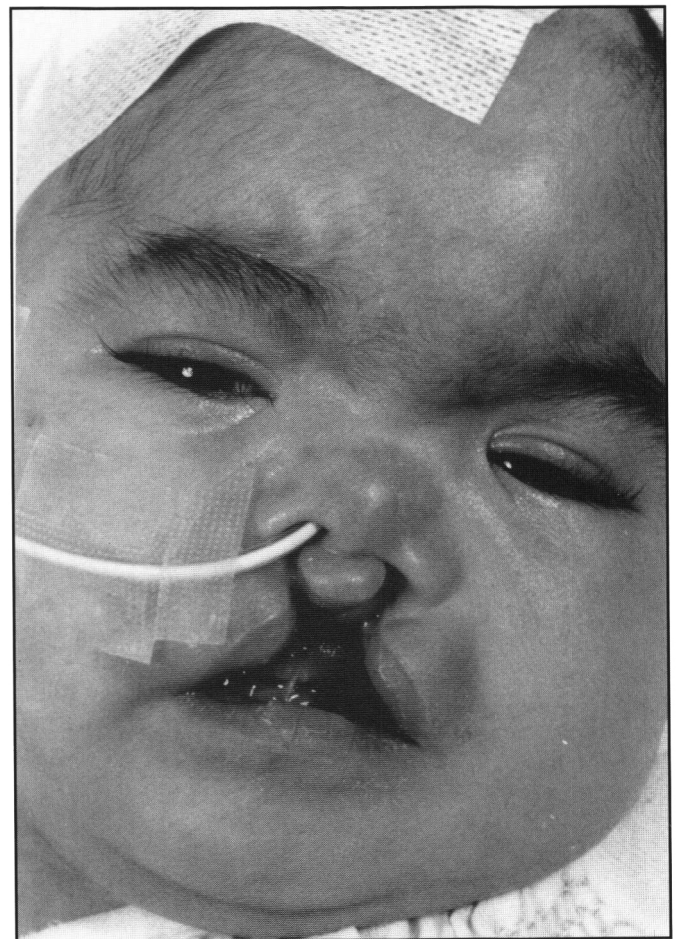


Figure 7 — Cleft lip and palate in lobar holoprosencephaly.

hemispheres laterally. The cyst typically extends down into the upper cervical canal. The wall is composed of an outer arachnoidal and inner ependymal lining with an intervening layer, if present, composed of dysplastic cerebellar vermal tissue, glia and nerve fibers. Posterior fossa structures are affected by the

mass and pressure effects of the cystic expansion of the fourth ventricle. The emboliform, globose and fastigial nuclei may be atrophied or absent. The dentate nucleus is usually preserved.¹⁷ The medial accessory olivary nuclei may show cellular depletion and heterotopias may be seen in the inferior olive.²⁴

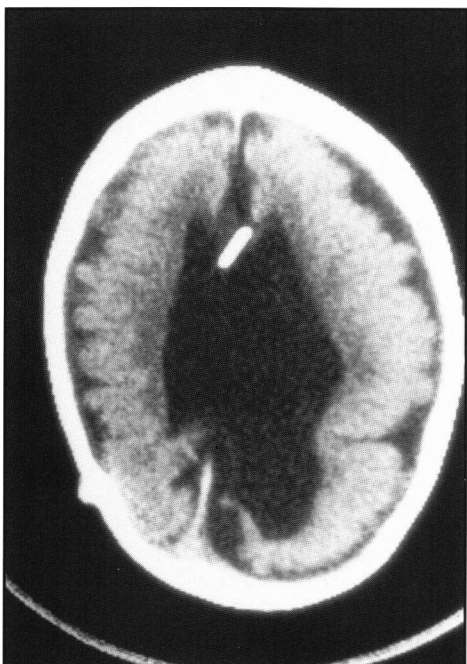
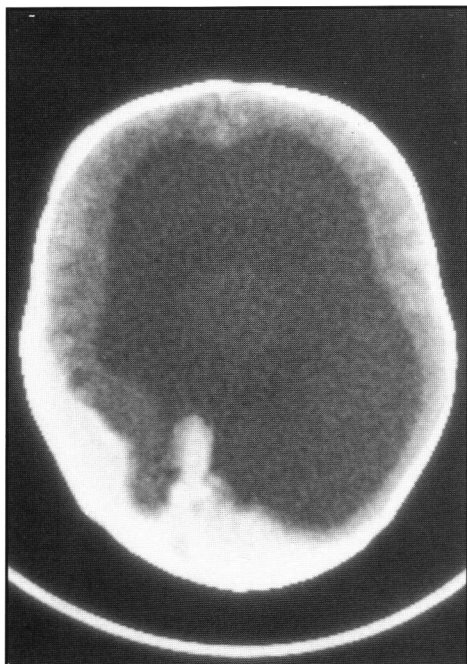


Figure 8 — Top. Neonatal CT demonstrating hypoplastic falx and massive hydrocephalus characteristic of lobar holoprosencephaly. The subdural hematoma is secondary to cephalocentesis performed to allow delivery. Bottom. Following placement of a VP shunt, the holovertricle and the rudimentary gyri are seen.

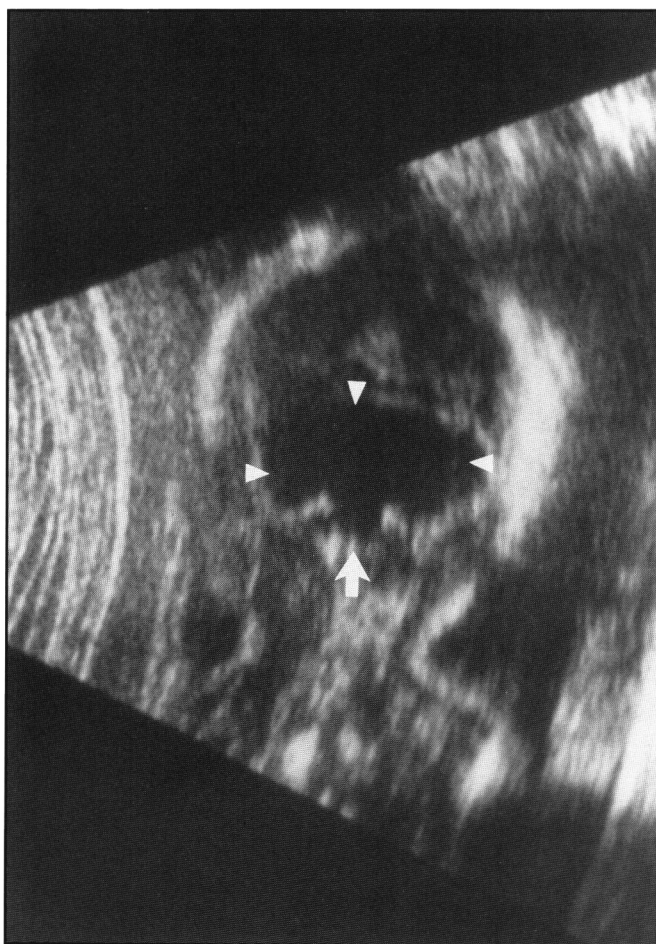
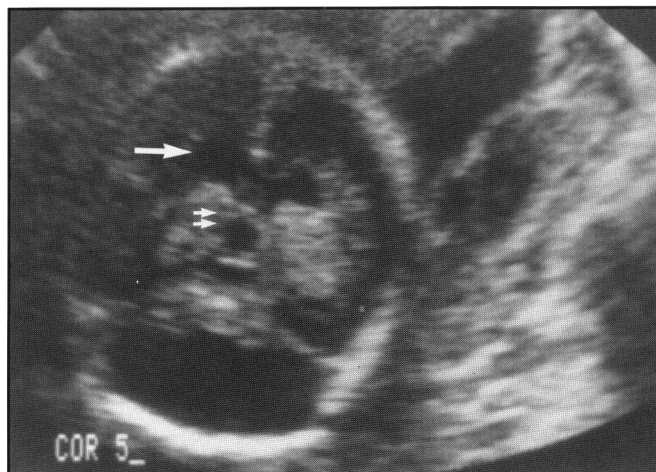


Figure 9 — Top. In utero posterior view of Dandy-Walker cyst showing extension through the foramen magnum (arrows). Bottom. Transverse image of fetus showing mild dilation of lateral (arrow) and third ventricles (double arrow) in addition to the posterior fossa cyst.

Other anomalies are seen in 40-70% of patients.^{19,20} These include 30% with agenesis of corpus callosum, heterotopic glia in the subarachnoid space around the brain stem, heterotopic cerebellar cortex, agenesis of anterior commissure, and cingulate gyrus, occipital encephalocele, infundibular hamartomas and brain stem lipomas.

Direct surgical resection of the cyst wall was the method of choice for the treatment of this condition prior to the availability of modern ventricular shunts.^{16,21,22}

Resection of the wall and marsupialization of the cyst into the cervical subarachnoid space is easily performed but produced inconsistent relief of hydrocephalus. Obliteration of the cerebellopontine angle cisterns due to lateral and anterior displacement of the lateral cerebellar hemispheres anterior to the brain stem and obliteration of the quadrigeminal cistern because of the superior displacement of the culmen through the tentorial notch preclude the establishment of cerebrospinal fluid flow via these routes. As a result, cerebrospinal fluid flow is impeded between the infratentorial and supratentorial compartments.

The aqueduct of Sylvius is patent in 87% of reported cases,¹⁷ although it can be blocked for anatomical or functional reasons. Prior to treatment, aqueduct occlusion may be present on a congenital basis because of associated stenosis or forking or occur secondary to compression of the quadrigeminal plate by upward herniation of the superior vermis or the cyst. This anatomical arrangement sets the stage for the isolation of supra- and infratentorial cerebrospinal fluid compartments. Direct fourth ventriculostomy may only drain the fourth ventricular cyst and not the lateral and third ventricles. Functional obstruction can also occur following shunting of either a lateral ventricle or the posterior fossa cyst.

Due to these anatomical factors, surgical cyst wall excision has been successful in a minority of patients.^{19,22,23} Currently, the role of fourth ventriculostomy is limited to those older patients with minimal or no hydrocephalus who present because of the posterior fossa mass effects of the cyst.²²

Previously a procedure reserved for a failed fourth ventriculostomy, cerebrospinal fluid shunting is now the preferred method of initial treatment for patients with Dandy-Walker Syndrome and hydrocephalus. Controversy exists as to whether a lateral or 4th ventricular shunt or both should be placed initially. The demonstration of a patent aqueduct prior to shunting does not guarantee that a single shunt will drain the entire ventricular system. Entrapment of the 4th ventricular cyst following ventricular shunting can result in acute brain stem compression.²³ Similarly, a 4th ventricular shunt may fail to drain the lateral ventricles. As a result, balanced control with simultaneous lateral and 4th ventricular shunts has been recommended.^{19,23}

Regardless of the ordering of shunt placement, the high location of the transverse sinuses must be remembered when placing the lateral ventricular catheter by the parieto-occipital approach, lest the surgeon enter the sinus inadvertently.

The results of treatment in the Dandy-Walker syndrome are dependent upon control of hydrocephalus and the impact of associated anomalies on neurological function. The prognosis for older children and adults is better than for infants as these patients have fewer associated cerebral and brain stem anomalies. While control of hydrocephalus is the most important determinant of intellectual prognosis, agenesis of corpus callosum and cortical dysgenesis may be associated with developmental

retardation independent of successful shunting.¹⁹ In Raimondi's series only 20% had an intelligent quotient over 80 and 50% had gross motor disability.²³

Chiari Type II Malformation

Cleland in 1883 described the elongation of the vermis of the cerebellum lying dorsal to a prolongation of the fourth ventricle in a child with myelodysplasia and hydrocephalus.²⁷ Associated with this was beaking of tectum and a membrane in the region of the median aperture of the 4th ventricle.

Chiari in 1891 and 1896 described four types of hindbrain anomalies.^{28,29} The type II anomaly consists of impaction of the inferior vermis plus cerebellar tonsils, elongation of the fourth ventricle and choroid plexus and caudal displacement of the dorsal part of the medulla through the foramen magnum into the upper cervical canal. A dorsal prominence containing the cuneate and gracile nuclei, is seen below the vermal herniation and compresses the upper cervical cord. The upper cervical roots ascend to their exit foramina and there may be an associated syringohydromyelia. Postnatal magnetic resonance imaging has clarified our understanding of this malformation in life.^{30,31}

Of those fetuses with ventriculomegaly in the Western Canadian series, the commonest associated anomaly was a myelomeningocele.¹ While it is possible to diagnose this condition on the basis of hydrocephalus and the back lesion, the Chiari malformation provides the earliest fetal ultrasonographic sign.³² The malpositioned cerebellar vermis and medulla within the cervical spinal canal result in the absence of the cisternal magna on 1st trimester ultrasound studies. The implications of this finding relate to family counselling and pregnancy termination options.

From a historical perspective, the Chiari malformation and its associated hydrocephalus are of great surgical importance as these conditions were the impetus for the development of valve regulated ventricular shunts by Nulsen and Spitz and by Holter for his own child in 1952.^{33,34} This work provided the foundation for the current treatment of hydrocephalus.

From the perspective of surgical intervention, closure of the spinal deformity and cerebrospinal fluid diversion are the commonest procedures required in these patients. Hydrocephalus is due to several factors including aqueductal obstruction, blockage of the foramen of Magendie by fibrogial tissue and obliteration of the cisterna magna by the displaced brainstem and vermis.

Numerous other cerebral anomalies occur in patients with Chiari Type II malformation. Beaking of the tectum, due to fusion of the inferior colliculi, large massa intermedia, microgyria, and polymicrogyria. In general, developmental prognosis is a reflection of control of the hydrocephalus.³⁵

Approximately 10% of infants with myelomeningocele develop symptoms of brain stem dysfunction. This usually takes the form of inspiratory stidor, secondary to bilateral abductor vocal cord paralysis, dysphagia with regurgitation and aspiration, and episodic apnea with or without circulatory collapse. It would appear from clinical observations that patients exhibit varying degrees of symptomatology with some having stidor alone, while others have stidor and apnea and others stidor, apnea and circulatory impairment. In general, patients do not progress from one form to another although respiratory rhythm disturbances may be difficult to diagnose early in life.³⁶ Apnea in our experience has been a life threatening complication.

There are several factors that may be involved in the pathogenesis of these symptoms. Clinical observations suggest that the most important is hydrocephalus either untreated or due to shunt obstruction. Further caudal displacement of brain stem structures caused by the increased intracranial pressure may put additional traction upon the vagus nerves resulting in their dysfunction. This is likely true in those patients who have stridor only, as the majority with stridor will have it resolve following control of their hydrocephalus.³⁶ When symptomatology implicates medullary dysfunction additional factors must be considered. Progressive medullary ischemia secondary to basilar arachnoiditis, possibly due to amniotic fluid contamination of fetal cerebrospinal fluid^{36,37} and medullary hemorrhage have been reported.^{38,39} Primary dysgenesis or absence of cranial nerve nuclei 9 through 12 have been reported as has subependymal gliosis, destruction of glossopharyngeal and vagal nuclei, specifically the nucleus ambiguus.³⁶

Surgeons agree that treatment of bulbar symptoms in myelomeningocele patients begins with adequate ventricular shunting. The role of surgical decompression of the impacted malformation by cervical laminectomy is controversial.⁴⁰⁻⁴³ In patients treated at the BC Children's Hospital, stridor has been reversed by ventricular shunting and cervical decompression. Episodic apnea if present has not responded to decompression and appropriate shunting. Supportative measures including tracheostomy and gastrostomy are usually required when symptoms are severe.

Lhermitte-Duclos Disease (Granular Cell Hypertrophy of the Cerebellum, Diffuse Hypertrophy of the Cerebellar Cortex)

Described initially in 1920, Lhermitte-Duclos disease is a cerebellar malformation that presents in early adult life with macrocrania and symptoms of subacute or acute increased

intracranial pressure due to hydrocephalus.⁴⁴ The cerebellum (unilaterally or bilaterally) is enlarged and compresses the fourth ventricle causing hydrocephalus. Males predominate in this condition (Figure 10).⁴⁵

The cerebellum shows thickened folia and radial and parallel myelinated fibers in the outer layer of the cortex. The inner cortical layer composed of abnormal neurons which may be either Purkinje or granule cells.⁴⁶ The white matter is reduced or absent (Figure 11).

Obstructive hydrocephalus is managed with ventricular shunting and differentiation from tumor by biopsy. Resection of the cerebellar mass may be palliative.

CEREBRAL DYSGENESIS PRESENTING AS CRANIOFACIAL AND BRAIN DISTORTION

This category of disorders encompasses both malformations and secondary disruptions as occur in encephaloceles and deformations and cerebral dysgenesis as occur in the amniotic band syndrome. Disorders of cerebrospinal fluid circulation and brain maldevelopment play major roles in the prognosis of these patients, surgeons are primarily involved in the reconstruction of major craniofacial malformations.

Encephalocele

Encephalocele refers to a protrusion of the intracranial contents beyond the confines of the skull. This general term encompasses meningocele where the protrusion is composed only of meninges, encephalomeningocele in which the protrusion contains meninges and cerebral tissue and hydroencephalomeningocele in which a portion of the ventricular system has also herniated. The skull defect through which the herniation occurs is termed cranium bifidum. These lesions are variable in their

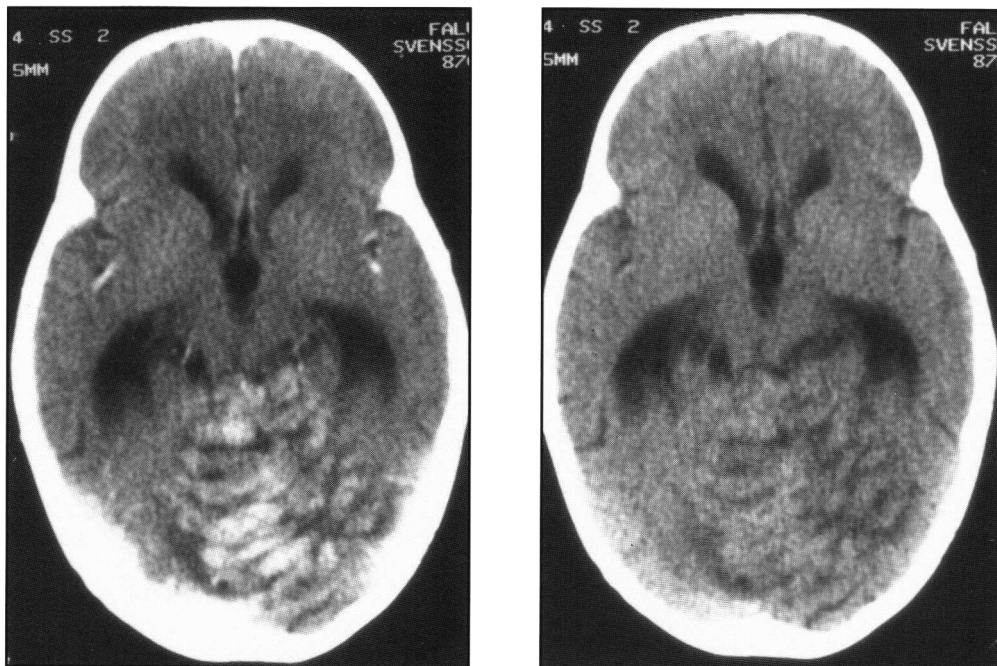


Figure 10 — Computed tomogram without (left) and with (right) intravenous contrast from a patient with Lhermitte-Duclos disease. Enlarged cerebellar folia, distortion of the quadrigeminal cistern and moderate hydrocephalus are present.

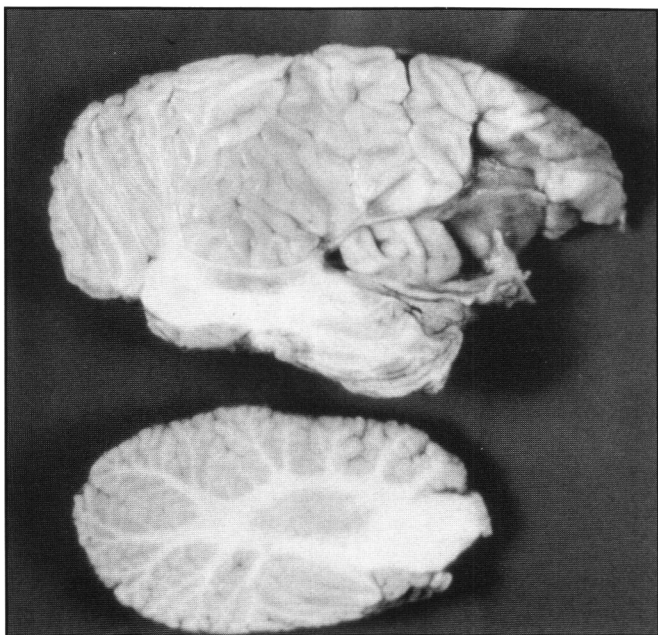


Figure 11 — Top. Superior view of the tentorial hiatus showing the greatly expanded right cerebellar hemisphere (arrow) and pontine distortion (double arrow) due to Lhermitte-Duclos disease. Bottom. Sagittal section of right (above) and left cerebellar hemispheres (below) of the same patient.

location and content as well as their associated lesions and malformations. The role of surgery in the treatment of encephaloceles depends on these factors and varies from no intervention to excision.

Encephaloceles show a marked anatomical and geographic variability with those occurring in the occipital area being more common in the Western hemisphere and those involving the cranial base more common in the Eastern hemisphere.⁴⁷⁻⁴⁹ The anatomical location determines the content of the lesion, and this, the operative indications and the type of operation(s). Prognosis is determined by the content of the lesion, its associated and secondary anomalies and any systemic abnormalities.

Occipital Encephalocele

Occipital encephaloceles may take the form of any of the pathological lesions defined above. Most lesions present as a pedunculated mass protruding through a circular defect located at or below the external occipital protuberance. The encephalocele sac is usually covered by normal skin, or by rudimentary skin without secondary appendages. Hemangiomatous discoloration and hypertrichosis at the base of the mass can be present. The cutaneous covering, usually intact but may be secondarily ulcerated, removes the need for immediate operation. This allows time for a full assessment of the infant's central nervous system for other anomalies (Figure 12).

Large occipital encephaloceles contain herniated parts of an occipital lobe and or cerebellum. The lateral ventricle with its choroid may extend into the lesion. The neural tissue is hypoplastic or dysplastic and structurally disorganized. Despite this, the encephalocele content may show electrical activity as measured by electroencephalographic or evoked potentials.⁵⁰ Lesions that contain brain stem structures can result in alteration or failure of vital signs when manipulated.⁵¹

Arterial and venous factors need to be considered in determining whether an occipital mass contains functional tissue and whether it can be excised or should be preserved. Arterial supply derived from the posterior circulation may be supplemented in large lesions, with contributions from all three cerebral arteries. If the content of the encephalocele is to be preserved, this supply must be left intact. The tentorium is hypoplastic and extends from the petrous portions of the temporal bone to the margins of the defect. As it splits around the defect, the contained torcula and the occipital sinuses may also be split and therefore lie in the dura at the base of the encephalocele neck. The transverse sinuses are rarely found within the sac being either absent or running above the defect. Infarction is not uncommon in these lesions and can be on the basis of arterial and or venous compromise.

Extensive herniation of posterior fossa structures occurs in the occipitocervical variety of encephalocele. This lesion presents as a sessile midline, skin covered mass in the occipital and posterior cervical regions. The squamous portion of the occipital bone is cleft in the midline and may be continuous with a cervical spina bifida. The brain stem may be cleft in the midline and displaced posteriorly into the sac.⁵¹ The cerebellar hemispheres can be displaced anteriorly in front of the brainstem. Such patients do not benefit from attempted excision of the mass.

Hydrocephalus may be present in utero, usually on the basis of aqueduct or basal subarachnoid space obliteration although the intrauterine diagnosis of an encephalocele is usually made on the basis of the visualized lesion.²

Other cerebral anomalies are usually present and may be due to distortion produced by the lesion as well as damage to the content of the mass. Atropic or absent optic nerves and damage to the corpora quadrigemina can be present. Dysgenesis of brain stem tracts and nuclei depends on the involvement of the cerebellum, cortex and brainstem. The inferior olive is most frequently involved, as are the spinocerebellar tracts, red nucleus, the dentatorubral tract and the dentatothalamic tract. Corpus callosum is usually normal while the anterior commissure, septum pellucidum and fornix may be deficient.^{49,51} The Chiari malformation is rare; the Dandy-Walker malformation has been reported.

A variety of systemic abnormalities have been reported in association with occipital encephaloceles and these may impact on operative decisions. These include, polydactyly, trisomy,¹³⁻¹⁵ micrognathia, cleft palate, subglottic stenosis, and congenital heart defects. Meckel's syndrome⁵³ has in addition to the occipital encephalocele, polydactyly and polycystic kidneys which eventually lead to fatal renal failure. Occipital meningoceles or meningoencephaloceles are seen in conjunction with Joubert's Syndrome.⁵⁴

The applicability of surgery (either excision or cranial reconstruction) in the treatment of occipital encephaloceles depends almost entirely on the neural elements within the mass. The content of the lesion can be assessed using computed tomography (Figure 12), magnetic resonance imaging and electrophysiological studies.

The goals of operation are to preserve function, remove the mass, and to provide a water tight dural closure of the lesion. Most pedunculated lesions can be excised. Attention should be paid to venous structures at the base of the stalk, and therefore the stalk is amputated superficial to the cerebral dura. If the lesion is known to contain functional tissue, this should be preserved by enlarging the bony and dural opening and reconstructing the dura, calvarium and skin cover. The sessile occipitocervical variety that contains the brain stem is not a surgical lesion. Shunting for hydrocephalus may be necessary.

The prognosis for normal development in these patients is dependent upon the content of the excised lesion and ranges from a good prognosis if the lesion is a meningocele⁴⁸ to a fatal outcome if it contains brain stem structures.

Interparietal Encephalocele

Located anterior to the posterior fontanelle on the midline or in a paramedian location, these lesions may simply contain heterotopic glial elements separated from the intracranial content by intact meninges or may be encephalomeningoceles (Figure 13). The former can be excised with good prognosis and the latter is similar to the occipital variety in terms of outcome. Meningocele do occur and can be excised.

Frontoethmoidal (Sincipital) Encephalocele

Frontoethmoidal encephaloceles have a different set of surgical problems than do the occipital variety.⁵⁵ These lesions are usually encephalomeningoceles and present as a orbital-facial mass. They all have a skull defect at the foramen cecum through which they enter the face or orbit. These lesions are classified on the basis of the location of the external opening.

From a surgical perspective, these lesions require an intracranial operation⁵⁶ for proper repair, and may require additional craniofacial reconstruction to repair facial deformities and to restore binocular vision. In most cases, the content of the encephalocele is not critical for life or function.

The frontonasal encephalocele presents externally between the frontal and nasal bones and is usually a meningocele. The nasoethmoidal variety presents in the midline between the nasal bone above and the depressed nasal cartilage below. Hypertelorism is usual. The naso-orbital type presents through the medial orbital wall anteriorly.

The nasoethmoidal and naso-orbital varieties are encephalomeningoceles containing mesial frontal lobe and olfactory apparatus. If large, the third ventricle, anterior cerebral artery and optic nerves may be within the encephalocele. In the most severe forms, the sac may contain both frontal lobes and falx. Holoprosencephaly, elongation of quadrigeminal plate, angulation of aqueduct and hydrocephalus may be seen.

To repair these encephaloceles, an intracranial approach must be used. The frontal lobe tissue can be sacrificed or reduced into the cranium and the internal opening at the level of the foramen cecum grafted. Initial operative planning should also include consideration of the need for later craniofacial reconstruction.

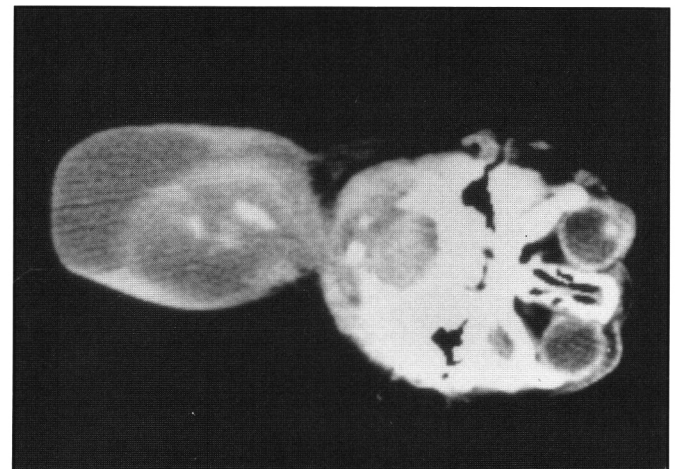


Figure 12 — Left. Infant with massive occipital encephalocele. Right. Computed tomogram confirming this to be a hydroencephalomeningocele.

Cranial Base Encephaloceles

Encephaloceles of the cranial base are the most problematic of encephaloceles for a surgeon. They pose difficulty in diagnosis because of the lack of external evidence of the lesion. Presenting because airway obstruction by a nasal or nasopharyngeal mass, they may be misinterpreted as a nasal polyp.⁵⁷ These lesions may contain critical neural elements that can not be sacrificed. Cerebrospinal fluid leakage, meningitis and hypertelorism are rare. Transethmoidal encephaloceles present in the nose through an opening in the cribriform plate. Sphenothmoidal encephaloceles present between the ethmoid and sphenoid bones while the transphenoidal encephalocele herniates directly through the sella and sphenoid sinus.

These encephaloceles contain gyrus rectus and/or hypothalamic structures and may be associated with cleft palate, eye abnormalities, microphthalmia, colobomata, and optic atrophy.

Prior to surgical repair, the anatomy of the lesion requires complete definition. This includes computed tomography and magnetic resonance scanning (Figure 14). Angiography may be required. Surgical repair, if feasible entails an intradural exploration, sacrifice or reduction of the content and dural closure.

AMNIOTIC BAND SYNDROME

Amniotic band syndrome presenting in the newborn may not be a life threatening malformation. It results from fibrous bands of amniotic origin impinging on and deforming the fetus. Approximately one-third of affected patients will have craniofacial involvement; typically cleft lip and palate, scalp defects or encephaloceles. Although not strictly a dysgenetic syndrome, brain distortion and abnormal cerebral development is common in the severely affected child. Holoprosencephaly, hydrocephalus and craniosynostosis can be associated (Figure 15).

The surgeon's role in the care of these patients is determined by the craniofacial deformity and its potential for repair and the presence of hydrocephalus.⁵⁸



Figure 13 — Interparietal encephaloceles. In this patient ultrasound demonstrated a communication with otherwise normal intracranial structures. The differential diagnosis includes aplasia cutis congenita.

CEREBRAL DYSGENESIS PRESENTING WITH FOCAL NEUROLOGICAL DYSFUNCTION

A variety of dysgenetic conditions present in the pediatric age group with seizures or other patterns of focal neurological dysfunction. They do not show overt fetal or neonatal dysmorphism. These lesions include hamartomata and focal areas of cerebral dysplasia. Surgical implications relate to the correct identification of the lesion and its removal. Abnormalities of cerebrospinal fluid circulation are not part of these disorders.

Hypothalamic Hamartoma and Precocious Puberty

Hamartomas of the hypothalamus present with precocious puberty and or seizures, usually in males less than three years of

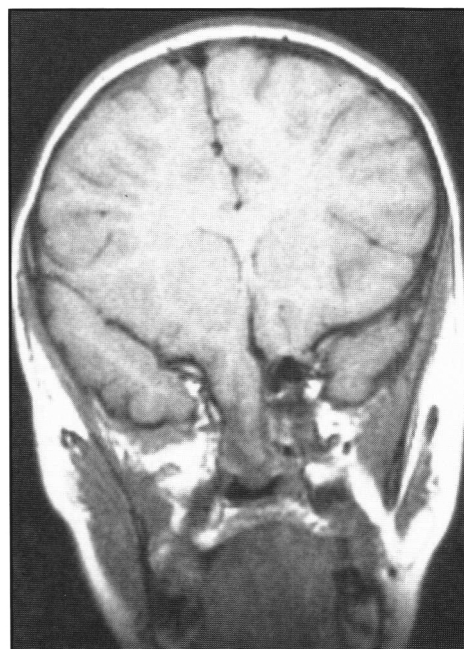
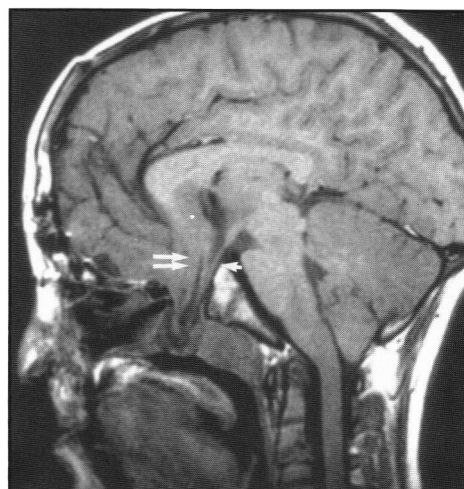


Figure 14 — Top. Parasagittal MRI of sphenoidal encephalocele. The lesion contains the infundibulum (arrow), pituitary gland and mesial frontal lobe (double arrow). Bottom. Coronal MRI of the same patient demonstrating the herniation of the gyrus rectus.

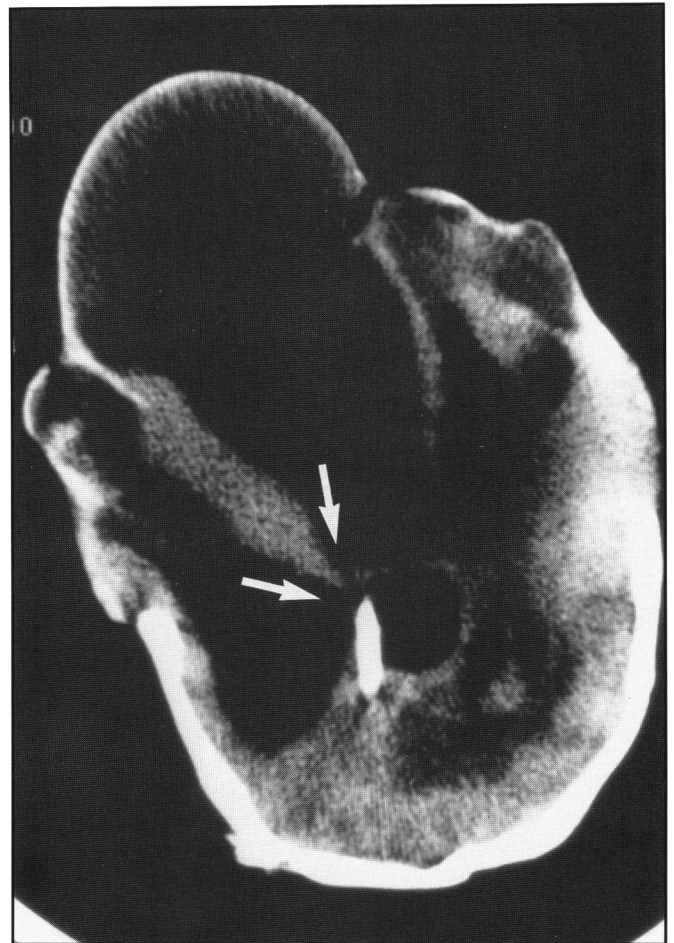
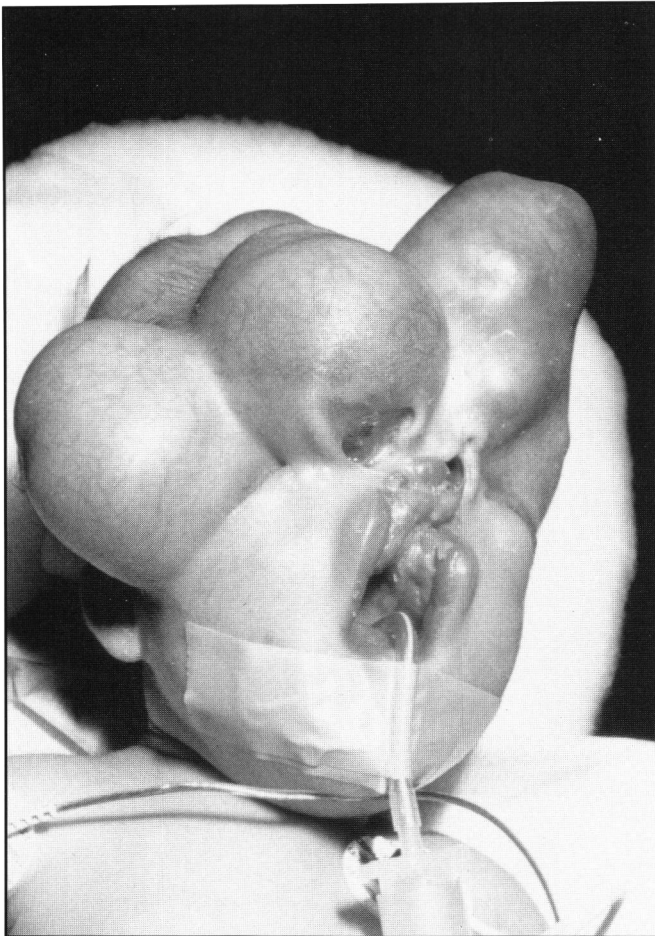


Figure 15 — Left. Cerebral encephaloceles, cleft lip, palate and bifid nose in patient with Amniotic Band syndrome. Right. Pre cranial reconstruction CT scan showing hydrocephalus, and right hemisphere clefting (arrow).

age. These lesions are small and therefore cerebrospinal fluid obstruction and increased intracranial pressure is rare. They may be sessile or pedunculated in the suprasellar or interpeduncular cistern. They may be attached to the tuber cinereum and mammillary bodies.⁵⁹ Composed of neurons, glia and myelinated nerve fibers, these hamartomata may show immunoperoxidase staining for a variety of hormones and releasing factors. Both magnetic resonance and positive contrast computed tomography can demonstrate these lesions.^{60,61}

Surgical resection of all or part of the lesion can lead to regression in the precocious puberty.

Cortical Dysplasia

Cortical dysplasia is a term introduced by Taylor et al 1971 to describe the histological features seen in cortical specimens resected for the treatment of epilepsy (Figure 16).⁶² This lesion has abnormal appearing neurons in an abnormal arrangement. Cellular atypia is present and differentiates dysplasias from migration disorders.

Cortical dysplasias commonly present with seizures, and focal abnormalities on EEG. These can have their onset at any age. Developmental delay may be present.⁶³ Areas of cortical dysplasia may become the site of dysembryoplastic tumors.⁶⁴

The gyri can be variable in appearance ranging from normal to expanded. They may show normal or rubbery consistency and

either normal or indistinct grey-white matter demarcation. Abnormal lamination beneath the normal molecular layer with large neurons containing tigroid nissel substance associated with large bizarre multinucleated glial cells are typical (Figure 17).

Surgical resection of the dysplastic cortex has proven useful in the control of focal seizures in these patients.

Chungani et al using positron emission tomography scanning have shown that 40% of patients with cryptogenic infantile spasms have cortical dysplasia. Surgical resection can provide some patients with seizure control.⁶⁵

Hemimegalencephaly

Hemimegalencephaly is similar to cortical dysplasia in its pathology and symptomatology. Presenting with refractory seizures in infancy, hemimegalencephaly is characterized by macrocrania, hemiparesis, hemianopia, psychomotor retardation and in infancy, high output cardiac failure.^{66,67} The involved hemisphere is enlarged and may show an agyric or pachygyric pattern (Figure 18). It is typically firm and vascular. The grey-white matter demarcation can be normal or blurred and the cortex shows loss of lamination and leptomeningeal heterotopias. The neurons are enlarged and show bizarre multipolar and distorted morphology. They may be multinucleated. Giant astrocytes, reactive astrocytes, Rosenthal fibers, heterotopic GM are present within the hemisphere. Secondary anomalies of ipsilateral

basal ganglia, thalamus and brainstem are seen. Of importance, less obvious polymicrogyria and heterotopic neurons on the "normal" side may be present.

Hemispherectomy for seizure control poses a surgical challenge because of the size, firmness and vascularity of the hemisphere.⁶⁸

Meningoangiomas without Neurofibromatosis

Meningoangiomas without neurofibromatosis is uncommon. This dysplasia is characterized by a localized proliferation of fibrous tissue in the arachnoid associated with perivascular fibrous tissue infiltration in the cortex. Seizures are the commonest presenting manifestation.⁶⁹

At operation, these lesions show normal to thickened and opaque meninges with calcification. Either single or multiple

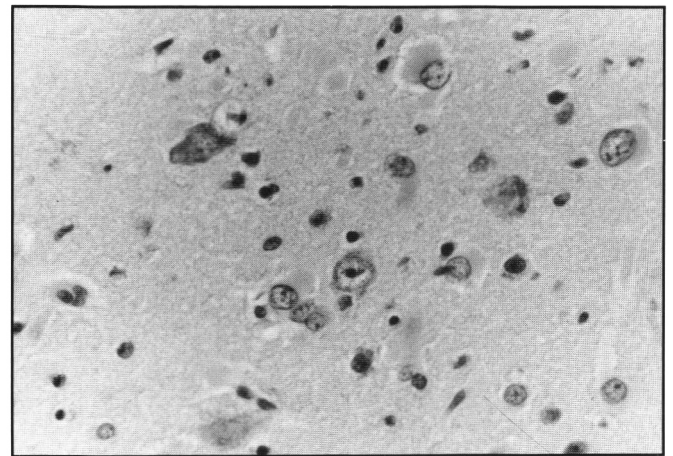


Figure 17 — Surgical specimen from patient in figure 16 showing abnormal neurons and astrocytes.

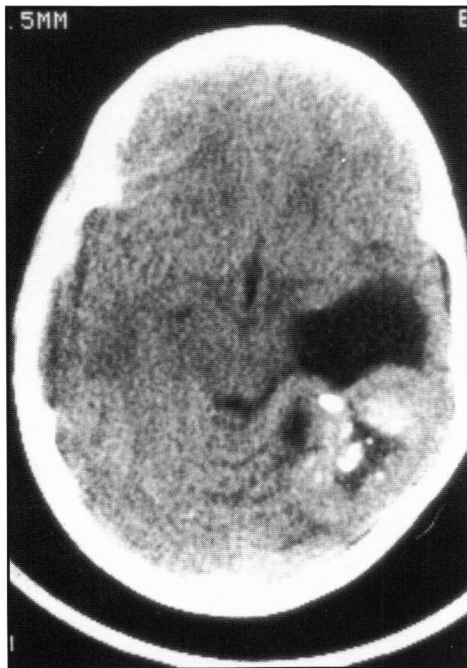


Figure 16 — Top. Computed Tomogram showing the dysmorphic posterior temporal lobe with areas of calcification. The gyral morphology and the lack of mass effect differentiates this lesion from tumor. Bottom. MRI demonstrates the grey matter dysplasia more clearly.



Figure 18 — Top. Computed tomogram of patient with hemimegalencephaly. Bottom. Gross specimen shows the difference in the size of the hemispheres and lateral ventricles.

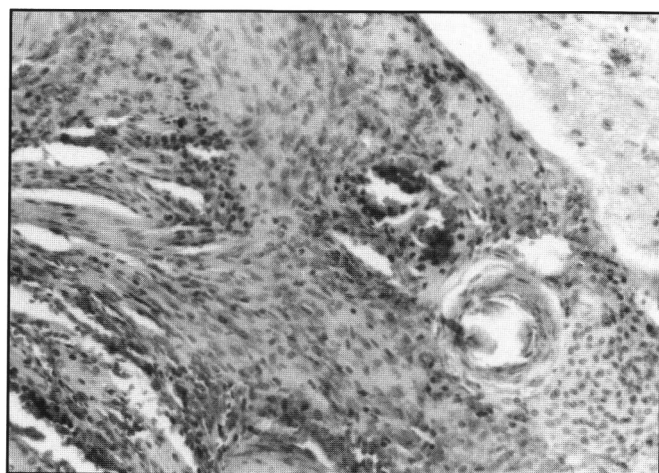
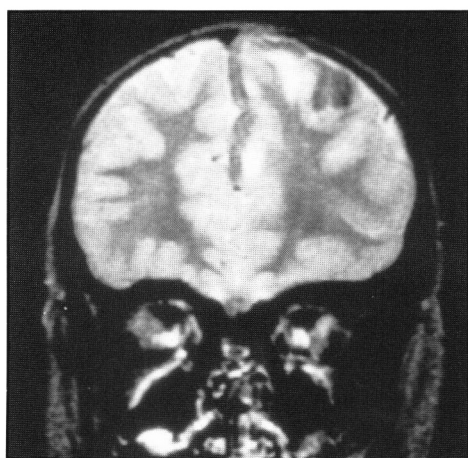


Figure 19 — Top. Coronal MRI showing cortical lesion in patient with focal seizures and meningoangiomas without neurofibromatosis (arrows). Bottom. Fibrous tissue proliferation in the subarachnoid and Virchow Robin spaces.

sharply demarcated areas of involvement can be present. Arachnoidal proliferation is associated with, perivascular layering of spindle shaped fibrocytes, calcification, bone and or fibrocartilage formation. Neurofibrillary tangles along with abnormal neuronal orientation and lamination are seen (Figure 17).

Surgical resection for seizure control may be of benefit for those with localized areas of involvement.

SUMMARY

Cerebral dysgenesis encompasses many varied disorders of brain development. Based on the understanding of these conditions derived from the studies of histopathologists, embryologists, radiologists and developmental pediatricians, surgeons are better able to appropriately assist in the care of these patients. These malformations may require procedures to control disorders of cerebrospinal fluid circulation, reconstruct cranial and facial malformations and remove dysfunctional tissue. For most patients, surgical intervention is only one of many factors that determine developmental prognosis.

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