



# Corpus callosotomy in the treatment of medically intractable secondarily generalized seizures of children

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**C**ORPUS CALLOSOTOMY has been enthusiastically embraced as a palliative treatment for two types of medically intractable seizure disorders: those generalized seizures other than primary epilepsy, which defy localization, and infantile hemiplegia. In the latter disorder, corpus callosotomy is a substitute for hemispherectomy. Both groups of patients usually have early seizure onset of an unremitting nature. The rationale for this procedure in humans began as an empirical observation by Van Wagenen in 1940, was supported by experimental data in animals by Erickson in the same year, and extended in a small series of patients by Bogen during the next twenty years.<sup>1-4</sup>

It would be logical that this procedure could be applied to children, but it was 30 years later before the successful use of corpus callosum section in infancy and childhood was described by Luessenhop, primarily as a substitute for hemispherectomy.<sup>5,6</sup> The rationale included avoiding the long-term risks of hemisphere resection, such as intracranial hemorrhage and hydrocephalus, while maintaining neurologic functions in the affected hemisphere, such as hand coordination and vision. In Luessenhop's group of four children, this was accomplished without apparent neurologic sequelae. In 1971, using microsurgical technique, Wilson revived corpus callosotomy and gradually moved from total commissurotomy to central commissurotomy

(corpus callosum and dorsal hippocampal commissure) as a technique that successfully interrupted secondary seizure generalization and carried a low morbidity and mortality.<sup>4</sup> Since the efficacy of this procedure was re-established, however, there have been only two additional reports detailing results in a small number of children.<sup>7,8</sup> A growing body of literature has described the operation and its effects on a population of primarily young adults and a few children, but no attempt has been made to address the potential risks and benefits that may be peculiar to various stages of the developing child.

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## REVIEW OF GENERAL CALLOSOTOMY LITERATURE

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Series of patients from Yale, Dartmouth, Vancouver, and Minnesota have provided a large enough group of patients of all ages undergoing partial or complete corpus callosotomy and hippocampal commissurotomy to enable us to analyze selection criteria and judge outcome.<sup>9-18</sup> These results can then be compared to the available data on callosotomy in children.

Patient selection criteria were broader at some institutions than at others, but patients were generally selected for intractable secondarily generalized seizures or partial seizures that could not be localized or were localized to unresectable functional regions such as the language cortex. The seizures significantly interfered with daily living, often with recurrent status epilepticus or frequent falls. The surgical procedures performed at these centers reflect the present spectrum of callosot-

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omy. Either the entire callosum was divided during one operation (Minnesota), staged with the posterior half divided first (Dartmouth), or the anterior two thirds sectioned initially (Yale). Both latter institutions completed the section only if seizure control was unsatisfactory. At Vancouver, only anterior two-thirds sectioning was reported. At all centers, total callosotomy or section of the posterior half always included the hippocampal commissure. The anterior commissure, fornices, and massa intermedia were not divided. Overall, however, results are similar at these centers among the various seizure types. Seventy to 80% of patients enjoyed control of secondarily generalized seizures (tonic, atonic, tonic-clonic, and myoclonic). Twenty-five to 50% of the Yale group had control of complex partial seizures after total callosotomy. A few patients were cured, and several (25% in most series) had more intense partial seizures (simple or complex). The increase in partial seizures sometimes elicited fear and led to an unsatisfactory result in retarded patients now conscious of their seizures.<sup>12</sup> Electroencephalographic (EEG) results correlated poorly with clinical outcome although there was a decrease in bisynchrony in most, and occasional ictal lateralization was newly noted postoperatively.

Ventriculitis, meningitis, hydrocephalus, and death have been reported previously as operative complications. These most recent series, however, have noted fewer complications, including postoperative subdural hematoma, isolated venous infarction noted on postoperative computed tomographic scans, and wound infection. Postoperative transient leg weakness occurs frequently and is thought to be secondary to a combination of retraction and callosal section, particularly since this occurs without direct compression of the leg area.

In previous series, neurologic and neuropsychologic deficits have been few. Our most recent series indicates that those deficits due strictly to callosal section can be almost completely predicted by the patient's preoperative behavior, cognitive deficits, and the presence of unilateral lesions resulting in interhemispheric dependence for function.<sup>11</sup> Campbell described four patients with right hemispheric pathology who suffered significant decline in the Wechsler Performance IQ Index after callosotomy.<sup>19</sup> He suggested that the left hemisphere was partially compensating for previous right hemispheric injury, and callosal section "reinstated" this deficit.

Novelly and Lifrak noted that a severe lateralized deficit produced more intrahemispheric recovery and

was not as dependent upon callosal function as mild to moderate deficits.<sup>20</sup> Thus, a patient with unilateral memory problems on carotid amobarbital testing and a history of mild contralateral motor weakness during childhood would have more profound manual dexterity problems contralateral to the old injury following callosal transection. Another interhemispheric compensation has resulted when the speech-dominant hemisphere is contralateral to the hemisphere controlling the dominant hand.<sup>11</sup> Language deficits have consistently followed callosal division in this setting. Postoperative memory impairments have also been documented in callosotomy series; although some have attributed this to attention problems, the predictability of this deficit has been uncertain. Sass analyzed the literature and the Yale series and found 7% to 11% of patients declining in attention, verbal memory, or visual memory.<sup>21</sup> Declines in attention and verbal memory were again associated with mixed language hand dominance or related to the occurrence of more intense partial seizures after surgery. Increased partial seizures have been most frequently described in the setting of multifocal asymmetric bifrontal epilepsy.

The sequelae of language, memory, and attention deficits are the most serious consequences of callosotomy in a patient who has cortical reorganization resulting from injury. These can generally be predicted using carotid amobarbital testing. Patients most likely to suffer more intense focal seizures are also at risk and should be considered for surgery only with caution.

Cortical organization is, obviously, an important issue in the general population that has undergone callosal section. With this background, we now examine theories regarding developmental plasticity and cerebral organization, followed by an analysis of callosal sections in children, allowing us to organize selection criteria at various ages. Early callosal section might be very reasonable if one could prevent excitotoxic injury to viable brain by confining seizure spread, thus allowing a more favorable milieu for cortical reorganization of lost function. On the other hand, if there is evidence that cortical reorganization demands interhemispheric communication across this major commissure, positive reorganization may be dampened by an early section. Is there an optimal time for such surgery? The final question would then be whether callosal section or neocortical resection would be preferred in order to optimize potential cortical reorganization in childhood epilepsies that can be lateralized, such as infantile hemiplegia, forme fruste infantile hemiplegia, and lateralized chronic progressive encephalopathy

(Rasmussen's syndrome).

#### PLASTICITY AND CEREBRAL ORGANIZATION

The phenomenon of functional recovery following a lateralized cerebral lesion has been observed and debated for generations. Jackson described this partial or complete recovery as compensation, since he felt that specific cortical regions had designated functions but that these functions were rerepresented in adjacent or distant sites.<sup>22</sup> Hemispherectomy, which was performed for tumor in a few adult patients, corroborated severe and persistent deficits in visual-spatial function in the nondominant hemispherectomy and similar deficits in language following dominant hemispherectomy. Although, over time, some language ability emerged in these latter patients, the visual-spatial deficits showed no recovery.<sup>23–25</sup> Tachistoscopic testing of callosally sectioned patients has revealed the same lateralized function of the two hemispheres, but only rare reports appear to document the reattainment over time of language capabilities of the nondominant hemisphere following callosotomy.<sup>26</sup> Hemispherectomy in an adult infantile hemiplegic, however, provided evidence for profound compensation in the nonlesioned hemisphere if the insult took place during infancy. In addition, it confirmed experiments indicating a more functional plasticity of reorganization in the developing brain of infants.<sup>27</sup>

Callosotomy likewise is especially well tolerated functionally in the infantile hemiplegic.<sup>27–29</sup> Evidence seems to be accumulating that at birth both hemispheres contain the neuroanatomic and genetic derivatives to acquire the totality of verbal and visual spatial cognitive function.<sup>30</sup> Over time, however, this equipotentiality is lost as functional asymmetry is solidified. The apparent ages at which cerebral reorganization and plasticity are maximum and then begin to diminish seem to closely parallel the onset of language (1 year) and the subsequent acquisition of language skills (1 year to 6 years). Likewise, damage after age 1 of the nondominant hemisphere reveals imperfect transfer of this function to the opposite hemisphere. The compensation seen in infantile hemiplegia would appear to be intrahemispheric or supported by subcortical-environment-hemisphere interaction. Cortical development, therefore, can be divided into four phases: Phase 1: 0 to 1 year; Phase 2: 1 to 6 years; Phase 3: 6 to 12 years; Phase 4: adolescence.

#### CORTICAL DEVELOPMENT

##### Phase 1: 0 to 1 year

In the search for a neuroanatomical substrate for hemispheric equipotentiality, investigators have demonstrated a steady increase in synaptic density from birth through 24 months.<sup>31</sup> This density then declines, reaching the adult quantity of about 60% of maximum during adolescence. Those synaptic contacts form in specific regions from which they are eliminated concurrently with functional differentiation. Goldman-Rakic has noted that the maximum synaptic excess in humans at around 8 months correlates with the first utterance of words and the parallel improvement on a delayed response task thought to represent intentionality in the developing child.<sup>32</sup> Performance on the delayed response task strikingly improves as the process of synaptic elimination begins.

A hypothesis can be developed, therefore, that the period of synaptogenesis, which increases to the age of 8 to 12 months and is equally rapid in all cortical areas, is the period before functional differentiation begins. Prior to a human utterance of a first word, there is optimum bihemispheric equipotentiality; this diminishes moderately, declining more rapidly after age 6.

##### Phase 2: 1 to 6 years (fundamental acquisition)

The end of this equipotentiality is signalled by the first word and is the period of maximum possible plasticity and reorganization of any cortical lesion. Once language begins, synaptic elimination in specific cortical regions of the dominant hemisphere may block the equipotential accrual of language in the nondominant hemisphere. Although some components of language may be assumed by the nondominant cortices, particularly from ages 1 to 6 years, it is never as completely transferred after age 1. Additionally, after age 1, there seems to be a hierarchy of plasticity that is poorly understood but favors more complete transference of language first, manual dexterity second, and visual-spatial function third.<sup>11,32–35</sup> The transference of other cognitive properties is not clear. Thus, as represented by comparing neonatal infantile hemiplegia to later childhood hemispheric injury, the capacity of one hemisphere to acquire totally the abilities of the other ends when language develops.

##### Phase 3: 6 to 12 years (organization and learning)

Lateralization of language seems to be well established by the age of 6 years. After this critical time, the same lesion, which in a neonatal dominant hemisphere

would provoke complete transfer of language, may now result in segregated speech. We have noted expressive speech and writing in the nondominant hemisphere, although the lexicon remains within the dominant hemisphere. When this is accompanied by incomplete transfer of handedness demanding support from both hemispheres, language is impaired following callosotomy.

Abundant evidence exists that recovery from acquired smaller lesions after the acquisition of language (age 6) depends more on interhemispheric cooperation than on intrahemispheric reorganization. This hypothesis has been alluded to earlier when investigators discovered that callosotomy in patients with hemispheric lesions (particularly nondominant lesions) incurred between ages 6 and 12 "reinstated a functional visual-spatial deficit." What cannot be determined from the literature at the present time is whether callosotomy at this period of development, i.e., after language acquisition and before functional reorganization reaches its lowest plateau during adolescence, will prevent optimal cortical reorganization by preventing interhemispheric communication. Since callosotomy reinstates functional deficits that were compensated by interhemispheric interaction, callosal section might prevent this compensation in the first place.

Theoretically, during the period of rapid learning from the age of 6 to adolescence (around 12 years of age), synapses are being eliminated and patterns of function through cortical organization are solidified. In a child with epilepsy and a cortical lesion, callosal communication may be important in optimizing function. A callosal section during this phase of development could disrupt this interhemispheric assistance and thus decrease the child's ultimate neurologic and cognitive potential. On the other hand, callosal division might stimulate more intrahemispheric reorganization to support the same function that would previously have utilized callosal interaction.

#### REVIEW OF CALLOSOTOMY IN CHILDREN

Our survey of the literature on callosal section in children is limited to patients 16 years of age and below. Arbitrarily, we have divided this review into the three developmental phases discussed above, plus the adolescent years when the brain most resembles that of the young adult in terms of synaptic density, learning, and potential for cortical reorganization. Patients in these successive phases may respond differently to

callosal section. During each of these phases, the normal brain is developing more stable asymmetry and enjoys less functional plasticity. Superimposed on the seizure population is the initial injury that may be focal or diffuse and demands optimal adaptive reorganization. While this adaptation is occurring, the patient's epilepsy, depending on frequency and severity, is potentially disrupting attempts at reorganization. In addition, anticonvulsant drugs must be considered since they may partially control seizures but may also have side effects of sedation and behavior change, which may alter the environmental interaction necessary for proper development and learning.

Table 1 includes a portion of children who have undergone callosal section worldwide.

These children were selected only from reports that listed age at sectioning and afforded some detail regarding preoperative cognitive status, seizure type, and outcome.<sup>1,3-10,13,17,36</sup> Thirty-eight children were thus available, and 36 could be more carefully analyzed (see following Tables). Most children had more than one seizure type, but at least one type (and usually more) involved frequent daily or weekly secondary generalization, and many seizure types were so rapidly generalized that falling and injury were common. Very few children had normal intelligence, and many were severely retarded.

The procedures ranged from total commissurotomy (earlier series)—including the corpus callosum (CC), hippocampal commissure (HC), anterior commissure (AC), one fornix (F), and massa intermedia (MI)—to only anterior CC section. Most recent surgical procedures have been termed central commissurotomy (C Comm), which includes the entire CC plus the underlying dorsal HC. This is performed as a single or staged procedure, as has been noted in Table 1.

Table 1 also lists the major neurologic diagnosis of each child and, when known, the potential cause of each seizure disorder. In terms of seizure etiology, five children suffered neonatal infantile hemiplegia, seven developed infection (either meningitis or encephalitis), two had febrile seizures, 11 had a diffuse neonatal insult such as hypoxia or ischemia; two were felt to have chronic progressive encephalopathy (Rasmussen's syndrome); in five the insult was unknown but diffuse.

Outcome can be difficult to assess. It must be stressed that corpus callosotomy is palliative. The object of surgery is unlike temporal lobectomy or cortical excision, in both of which the goal is cure. Very rarely, all seizures may cease following callosotomy; but the main purpose is to stop secondary generalization or reduce it

**TABLE 1**  
CORPUS CALLOSOTOMY IN CHILDREN. LITERATURE REVIEW AND AVAILABLE STATISTICS

\* Age at operation

† Information not sufficient to include in statistical results

Abbreviations:

Seizure types: GTC – Generalized tonic-clonic; P – Partial;  
AKN – Akinetic; ABS – Absence; MYO – Myoclonic;  
EPC – Epilepsia partialis continua; TC – Tonic-clonic;  
CPS – Complex partial; ATN – Atonic; GT – Generalized tonic

Cognitive testing: MA – Mental age;

Procedures: CC – Corpus callosum;  
AC – Anterior commissure; HC – Hippocampal commissure;  
F – One fornix; MI – Massa intermedia

Unsatisfactory – U

| Source                               | Age* | Sex | Diagnosis & neurologic deficit                                                                                | Preoperative cognitive testing              | Seizure type                          | Procedure            | Outcome                                                                                                            |
|--------------------------------------|------|-----|---------------------------------------------------------------------------------------------------------------|---------------------------------------------|---------------------------------------|----------------------|--------------------------------------------------------------------------------------------------------------------|
| Van Wagenen <sup>1</sup><br>1940     | 0    | M   | L hemiparesis<br>Onset seizure age 18 mo                                                                      | NA                                          | GTC status                            | CC body              | GTC – ↓ 99%                                                                                                        |
|                                      | 16   | F   | Neonatal seizure<br>Onset age 5 with head injury                                                              | Normal development then decreased intellect | GTC                                   | CC body + genu       | ? # GTC persisting <u>U</u>                                                                                        |
|                                      | 14   | M   | Viral infection<br>L hemiplegia<br>1st seizure at age 8                                                       | Retarded                                    | GTC                                   | CC<br>F<br>HC        | GTC – ↓ 90%                                                                                                        |
| Bogen <sup>3,4</sup><br>1962<br>1965 | 14   | M   | Maternal toxemia<br>Febrile seizures                                                                          |                                             |                                       | CC<br>AC<br>HC<br>MI | Hemiparesis leg > arm<br>Seizures reduced                                                                          |
|                                      | 13   | M   | Birth injury                                                                                                  |                                             | GTC<br>P                              | CC<br>AC<br>HC<br>MI | GTC – good<br>P Motor – continued                                                                                  |
|                                      | 13   | M   | Cyanotic at birth                                                                                             |                                             | GTC<br>P                              | CC<br>AC<br>HC<br>MI | ? Better †                                                                                                         |
| Gessenhop <sup>6</sup>               | 3    | M   | Perinatal hypoxia<br>Hypoglycemia<br>Hypokalemia<br>Seizures<br>1st seizure at 2 yrs;<br>gradual L hemiplegia | MA – 4 yr                                   | GTC<br>MYO<br>20/day                  | CC<br>AC<br>F        | All seizures ↓ 99%                                                                                                 |
|                                      | 3    | M   | 1st seizure at 2 days<br>L hemiplegia                                                                         | NA                                          | GTC<br>80–100/day<br>Begin L or R arm | CC<br>AC<br>F        | GTC – ↓ 99%                                                                                                        |
|                                      | 7    | F   | Febrile seizure 4½ yr;<br>EPC 4½<br>Stupor – 6<br>L hemiplegia – 7<br>Biopsy: Neuronal degeneration           | NA                                          | EPC<br>AKN                            | CC<br>AC<br>F        | Only partial tongue seizures<br>Improved paresis & consciousness<br>Improved cognition                             |
|                                      | 4 Mo |     | GTC at 5 days<br>Begin on L                                                                                   | NA<br>Retarded                              | Blinking<br>Q 30 min<br>TC – L        | CC<br>AC             | Unchanged<br><u>U</u>                                                                                              |
| Amacher <sup>7</sup><br>1976         | 14   | M   | Infantile hemiplegia<br>Field cut                                                                             | IQ – 95                                     | GTC<br>GTC<br>P<br>AKN                | CC<br>AC<br>HC       | Transient memory loss<br>(Short term)<br>GTC – ↓ 100%<br>P ↓ 75%<br>Reduced anti-convulsants<br>Improved cognition |

TABLE 1 (continued)

| Source                        | Age* | Sex | Diagnosis & neurologic deficit                                              | Preoperative cognitive testing | Seizure type                                     | Procedure           | Outcome                                                                                                                            |
|-------------------------------|------|-----|-----------------------------------------------------------------------------|--------------------------------|--------------------------------------------------|---------------------|------------------------------------------------------------------------------------------------------------------------------------|
| Geoffroy <sup>8</sup><br>1983 | 16   | M   | Encephalitis<br>Atrophic<br>R brain                                         | IQ - 6                         | GTC<br>AKN<br>P                                  | CC<br>AC<br>HC      | GTC - ↓ 100%<br>AKN - ↓ 50%<br>P - ↓ 50%<br>Transient memory loss                                                                  |
|                               | 16   | M   | Encephalitis                                                                | IQ - 70                        | GTC<br>AKN                                       | ⅓ CC<br>AC          | GTC - ↓ 90%<br>AKN - ↓ 100%                                                                                                        |
|                               | 16   | F   | Familial retardation<br>Onset 8 mo                                          | MA - 4 yr                      | ABS<br>MYO<br>GTC                                | F<br>CC<br>HC       | Transient L hemiparesis<br>Ab - ↓ 90%<br>Myo - ↓ 90%<br>CTC - ↓ 90%<br>No functional improvement<br>MA - 4 yr<br>Institutionalized |
|                               | 13   | F   | Premature<br>Retarded<br>Onset 7 mo                                         | MA - 15 mo                     | GTC                                              | CC<br>HC            | U<br>MA - 20 mo<br>GTC - ↓ 96%                                                                                                     |
|                               | 10   | F   | Retarded<br>Onset 3 yr                                                      | MA - 22 mo                     | GTC<br>MYO<br>AKN                                | CC<br>HC            | P - Motor remained<br>MA - 22 mo<br>Functionally improved                                                                          |
|                               | 7    | M   | Hydrocephalus<br>Shunted<br>Onset 5 yr                                      | MA - 5.6 yr                    | AKN                                              | CC<br>HC            | MA - 5.6<br>AKN - ↓ 100%<br>P - Motor<br>Remarkable improvement                                                                    |
|                               | 5    | F   | Cytomegalo virus<br>infection<br>Onset 8 mo                                 | MA - 12 mo<br>Retarded         | AKN<br>ABS                                       | CC<br>HC            | MA - 12<br>No improvement                                                                                                          |
|                               | 6    | M   | Prenatal chronic<br>encephalopathy<br>Onset 2 mo                            | MA - 8 mo                      | GTC<br>AKN                                       | CC<br>HC            | MA - 12<br>GTC - ↓ 100%<br>AKN - ↓ 70%<br>Notable improvement                                                                      |
|                               | 16   | F   | Chronic neonatal<br>encephalopathy<br>1st seizure age 7                     | MA - 6.6                       | GTC                                              | CC<br>HC            | MA - 6.6<br>GTC - ↓ 98%<br>P remain; memory & motor<br>improvement notable                                                         |
|                               | 10   | M   | Chronic neonatal<br>encephalopathy;<br>1st seizure age 1                    | MA - 9                         | GTC                                              | CC<br>HC            | MA - 15<br>GTC - ↓ 100%<br>P - ↓ 84%<br>Notable improvement                                                                        |
| Harbaugh <sup>9</sup><br>1983 | 7    | F   | Hydrocephalus<br>VP shunt<br>1st seizure age 3                              | IQ - 70                        | AKN<br>Q - 5 min<br>Occasional<br>GTC<br>absence | CC<br>HC            | IQ - 70<br>No seizures<br>Memory better<br>Remarkable improvement                                                                  |
|                               | 9    | NA  | Meningitis<br>Hydrocephalus<br>L hemiplegia<br>Shunt<br>Dilated R ventricle | IQ - 74                        | GTC<br>ATN                                       | CC<br>AC<br>HC<br>F | GTC = ↓ 99%<br>ATN<br>Excellent result                                                                                             |
|                               | 16   | NA  | Normal radiology                                                            | IQ - 81                        | GTC<br>P                                         | CC<br>AC<br>HC<br>F | Seizures ↓ 50%<br>Good result                                                                                                      |
|                               | 15   | NA  | Dilated R ventricle<br>Normal neurological<br>L hemiparesis                 | IQ - 82                        | GTC<br>P<br>ATN<br>CPS                           | CC<br>HC            | Seizures ↓ >50%<br>Good result                                                                                                     |
|                               | 15   | NA  | Normal radiology<br>L hand apraxia<br>Aseptic meningitis                    | IQ - 89                        | GTC<br>ATN                                       | CC<br>HC            | Seizures ↓ >50%<br>Good result                                                                                                     |
|                               | 16   | NA  | Normal neurological &<br>radiology                                          | IQ - 80                        | GPS<br>GTC                                       | CC<br>HC            | GTC = ↓ 99%<br>CPS<br>Excellent result                                                                                             |

TABLE 1 (continued)

| Source                                                      | Age* | Sex | Diagnosis & neurologic deficit                                           | Preoperative cognitive testing  | Seizure type                                           | Procedure                      | Outcome                                                                                   |
|-------------------------------------------------------------|------|-----|--------------------------------------------------------------------------|---------------------------------|--------------------------------------------------------|--------------------------------|-------------------------------------------------------------------------------------------|
| Gates <sup>18</sup><br>1984<br>Purves <sup>10</sup><br>1988 | 16   | NA  | R frontal porencephaly<br>L hemiparesis                                  | IQ – 71                         | ATN<br>ABS<br>P                                        | CC<br>HC<br>Staged<br>CC<br>HC | All seizures ↓ >50%<br>Good result                                                        |
|                                                             | 15   | M   | Tumor                                                                    |                                 |                                                        | CC<br>HC                       | †                                                                                         |
|                                                             | 13   | M   | Perinatal<br>R porencephaly<br>L hemiplegia<br>Onset seizure age 10      | IQ – 83                         | CPS<br>L Focal<br>Motor<br>Multifocal                  | ANT ⅓<br>CC<br>AC              | All seizures ↓ 80%<br>Excellent                                                           |
| Spencer <sup>13</sup><br>1988                               | 13   | F   | Bilateral atrophy<br>perinatal<br>Onset age 3<br>Mild L incoordination   | IQ – 40                         | Nocturnal GTC<br>Sexual<br>automatism                  | ANT ⅓<br>CC<br>AC              | All seizures ↓ 80%;<br>Moderate to good<br>outcome                                        |
|                                                             | 15   | M   | Chronic encephalitis<br>Onset age 5<br>L hemiparesis                     | VIQ – 55<br>PIQ – 49            | P – 500/mo<br>CPS – 20/mo<br>GTC – 10/mo               | Staged<br>CC<br>HC             | All seizures ↓ 99%<br>Excellent result<br>VIQ – 65<br>PIQ – 55                            |
|                                                             | 12   | M   | L frontal lesion<br>Onset age 1<br>R frontal seizures                    | Retarded<br>Behavior<br>problem | P – 20/mo<br>CPS – 20/mo<br>GTC – 8/mo<br>Falls – 5/mo | Staged<br>CC<br>HC             | P – 10/mo<br>CPS – 10/mo<br>GTC – 2/mo<br>Fall-0/mo                                       |
|                                                             | 15   | F   | Chronic encephalitis<br>Onset age 6<br>R hemisphere dominant<br>R handed | VIQ – 82<br>PIQ – 86            | CPS – 200/mo<br>GTC – 30/mo                            | CC<br>HC                       | Fair result to poor <u>U</u><br>CPS – 50/mo<br>GTC – 0/mo                                 |
|                                                             | 5    | M   | L hemiparesis                                                            | Retarded                        | P – 200/mo<br>CPS – 100/mo<br>GTC – 30/mo              | CC<br>HC                       | Poor result<br>Language problems<br>postop <u>U</u><br>Unchanged<br>P & CPS<br>100% ↓ GTC |
| Murro <sup>36</sup><br>1988                                 | 6    | F   | L hemisphere atrophy on<br>CT<br>R hemiparesis<br>Onset age 3            | Retarded                        | GTC<br>ATN<br>500/mo                                   | ANT CC                         | Not satisfactory <u>U</u><br>GTC ↓ 99%<br>ATN ↓ 100%                                      |
|                                                             | 16   | F   | Asphyxia<br>Onset < 1 yr                                                 | Retarded                        | GTC 4/mo<br>CPS                                        | ANT CC                         | Unchanged<br><u>U</u>                                                                     |
|                                                             | 14   | M   | Onset age 3<br>Normal CT                                                 | Retarded                        | GTC<br>GT<br>62/mo                                     | ANT CC                         | Unchanged<br><u>U</u>                                                                     |

by 90%, thereby protecting more normal cortex from excitotoxic injury, decreasing falls and reducing anti-convulsants. It is also hoped that behavior and cognition may improve, learning be optimized, and some independence achieved. Each investigator has had these general goals in mind. An evaluation of the cases shows that palliation without detrimental effect occurred (satisfactory result), or it did not occur (unsatisfactory result), or palliation was overbalanced by a detrimental effect of callosotomy (unsatisfactory result). Table 1 and subsequent tables have, therefore, listed the outcomes as either satisfactory or unsatisfac-

tory. "Satisfactory" is further defined as 90% control of generalized seizures and/or 50% control of seizures, with worthwhile improvement of psychosocial function or cognition. "Unsatisfactory" indicates that seizures were unchanged, or frequent incapacitating focal seizures appeared or there was unacceptable worsening of the neurologic examination, behavior, or cognitive abilities.

Table 2 divides the children into developmental phases according to age and notes the outcome by phase.

The total number of children is too small to note

**TABLE 2**  
OUTCOME ACCORDING TO AGE

| Age (years) | Satisfactory | Unsatisfactory | Total | % Satisfactory |
|-------------|--------------|----------------|-------|----------------|
| <1          |              | 1              | 1     | 0              |
| 1-6         | 4            | 2              | 6     | 67             |
| 7-12        | 7            | 1              | 8     | 88             |
| 13-16       | 16           | 5              | 21    | 76             |
| TOTAL       | 27           | 9              | 36    | 75             |

**TABLE 3**  
OUTCOME ACCORDING TO DEGREE OF MENTAL RETARDATION

| Retardation | Satisfactory | Unsatisfactory | Total | % Satisfactory |
|-------------|--------------|----------------|-------|----------------|
| Severe      | 4            | 8              | 12    | 33             |
| Not severe  | 23           | 1              | 24    | 96             |
| TOTAL       | 27           | 9              | 36    | 75             |

more than trends among groups, but the overall outcome of 75% satisfactory results is fairly evenly distributed among the last three phases. It is impossible to say anything about infants under 1 year since only one case is represented. It is interesting to note that this satisfactory outcome lies in the middle of the range observed for worthwhile outcome in the overall population of all ages.

Since, in most cases, callosotomy appears to fulfill its promise of palliation, can we sort out the best and worst candidates?

One observation that we have made in the general population of callosally sectioned individuals appears even more striking in children. Of the nine unsatisfactory results, eight were categorized as severely mentally retarded. Although few patients undergoing this procedure have normal IQs, there is a range of intelligence.

Table 3 categorizes the 27 children who were felt to be retarded by IQ or mental age into severe and not severe groups.

It is noteworthy that only one unsatisfactory result was not severely retarded. This does not mean, however, that the severely retarded child should be rejected, since palliation will be possible in one third of this group and, generally, these are the most desperate victims of epilepsy for whom all other alternatives have been exhausted. If we then reject severe mental retardation as an absolute contraindication to surgery but list all the cognitive variations under headings of diffuse injury vs focal injury, we can see (Table 4) that all

**TABLE 4**  
OUTCOME IN DIFFUSE v FOCAL CEREBRAL INJURY

| Age at operation (years) | Satisfactory | Unsatisfactory | Total | % Satisfactory |
|--------------------------|--------------|----------------|-------|----------------|
| Diffuse injury           |              |                |       |                |
| <1                       | 0            | 1              | 1     | 0              |
| 1-6                      | 1            | 2              | 3     | 33             |
| 7-12                     | 4            | 1              | 5     | 80             |
| 13-16                    | 9            | 5              | 14    | 64             |
| TOTAL                    | 14           | 9              | 23    | 61             |
| Focal injury             |              |                |       |                |
| 1-6                      | 3            | 0              | 3     | 100            |
| 7-12                     | 3            | 0              | 3     | 100            |
| 13-16                    | 6            | 0              | 6     | 100            |
| TOTAL                    | 12           | 0              | 12    | 100            |

patients with focal (or unilateral hemispheric) damage had satisfactory outcomes, while only three-fifths of those with diffuse injury were helped.

The literature does not support increased cognitive or neurologic problems associated with any of the developmental phases. There were clear examples of language impairments following callosotomy in patients with mixed dominance. This complication, which is predicted by our theory of incomplete transfer and callosal dependence, is seen when injury occurs or seizures begin in the critical developmental phase between the ages of 6 and 12 years. However, except for this one pattern, surgery during this period does not appear more disruptive. Occurrence of this complication in children as well as adults makes it imperative to perform a carotid amobarbital test in children whenever feasible. The more intense focal seizures (MIFS) reported in the general callosotomy population were also seen in children. They were not enumerated in the collective literature, but they may be more frequent in children than in adults. Certainly, MIFS are not tolerated as well by children, often eliciting fear since the child now is conscious of his partial seizures. Asymmetrical bifrontal EEG foci are sometimes associated with this outcome and should always be considered when weighing risks and benefits for an individual patient.

As noted in Table 4, the best results are seen in focal hemispheric disease. Even the best result is still palliative, however, since focal seizures most often remain and anticonvulsant medications are still necessary. If the seizure source can be localized and cortical excision performed, this is preferable. Even though callosal section is a viable alternative to hemispherectomy,

subtotal hemispherectomy and disconnection can be performed safely today, affording a chance for cure. Callosotomy in this group should probably be reserved for patients with incomplete hemispherical loss (forme fruste infantile hemiplegia)—individuals, for instance, who have unilateral paresis but a functional hand, intact stereognosis and intact visual fields. Careful consideration should still be given to invasive monitoring and, particularly in this group, a carotid amobarbital test is necessary.

It appears, therefore, that despite our theoretical consensus regarding disconnecting developing hemispheres, the established efficacy of callosal section can be extended to children, and the deficits be no greater in any phase of development than in adults. The indications are most favorable in those children with secondarily generalized seizures since these seizure types uniformly diminish between 80% and 100% in frequency. Complex partial seizures are variable in response, and partial seizures may either improve, remain the same, or worsen. Our recommendations are to be cautious when callosal section is considered for severely retarded patients with neonatal diffuse injuries. They are the least promising candidates, although some may be helped. When a patient with focal hemispheric disease is evaluated, local resection should always be considered first; but if this is not possible, children of this type are the best candidates for callosal section.

Occasionally, lateralization to a frontal lobe or frontoparietal region is suspected but cannot be confirmed by imaging, EEG, examination, or even invasive testing. In this instance, anterior two-thirds callosal section may succeed in lateralizing the focus and allowing more definitive study and excision as a second stage.

With the generally good results reported for callosotomy, it might seem reasonable to encourage callosal section in the younger age groups (under 6 years) in an

attempt to diminish excitotoxic injury and to preserve as much functional cortex as possible. The caveat here stems from the small number of children reported in the literature who are under 6 and have undergone callosotomy. We were able to find only seven, four of whom had satisfactory outcomes. In this age group, the persistent question will continue to be how much cognitive development, particularly with a compromised central nervous system, depends upon the corpus callosum and interhemispheric communication. Our stance must be that the severity of the seizure disorder takes precedence and that a child in this age group who fulfills the general criteria for section should be offered the operation. As far as we know, acquisition of cognitive processes might even be facilitated by callosotomy. It will be of utmost importance to follow these children over a long period of time.

Finally, the operation to be recommended is clearly a staged central commissurotomy sparing the anterior commissure and fornix. Staging the procedure diminishes the postoperative acute disconnection syndrome and provides the opportunity to control the seizure disorder while maintaining some callosal connectivity.

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