PANEL DISCUSSION

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Question: Do you think IQ should be used as a criterion in evaluating children and adolescents for epilepsy surgery?

Dr. Wyllie: Mental retardation of a moderate or severe degree makes us worry about diffuse brain disease, and perhaps a slightly worse outcome after epilepsy surgery of all types, as Dr. Spencer mentioned. With all types of epilepsy surgery, however, we have to keep in mind a specific goal for improved lifestyle that we think could be realistically accomplished by improvement of the seizures after surgery. This is somewhat different for high-functioning children with temporal lobe epilepsy compared to moderately or severely retarded children with corpus callosotomy. But, in either case, we have to have some realistic expectation that lifestyle would be improved. Sometimes mental retardation is a factor in our assessment, but if the EEG evidence and all the other clinical and radiographic evidence suggest that there is a single resectable focus, and if the child meets the other criteria for this type of epilepsy surgery, then my personal feeling is that mental retardation should not be a contraindication.

Dr. Andermann: There were many centers which would not consider surgery for a retarded child. Dr. Rasmussen's dictum was that it was always easier to look after somebody who was retarded but had no seizures rather than to look after somebody who was retarded and had seizures as well; thus retardation is not a criterion of exclusion for us.

Question: What is a staged procedure for callosotomy? If a good result is seen with the first stage, do you automatically do the second, or do you wait to see what happens?

Dr. Spencer: At our center we have the most experience with young adults, but our approach with children is much the same. We begin by trying to localize; if localization is not possible and we have an idea that the patient's hemispheric disease is more anterior, we begin with an anterior two-thirds callosotomy. It is designed to come to the mid-portion of the hippocampal commissure. Our results would indicate that after that, about 50% of our patients have satisfactory control of their secondary generalization; in other words, they have met the goals that we set for them. We go to the second stage, usually around 6 months later, if the patient continues to generalize and if he has not suffered a cognitive deficit or neurologic problem. We follow this procedure in about half the patients.

Question: Is it beneficial to perform a callosotomy in a patient with the Lennox-Gastaut syndrome?

Dr. Spencer: Many of the patients we see who are the most severely retarded probably have that syndrome. The Lennox-Gastaut syndrome, however, is certainly not a contraindication to callosotomy, though it is sometimes difficult to determine this from the literature.

Dr. Andermann: We recently looked at a series of more than 60 patients who had a callosotomy done by Dr. André Olivier. They fell into four major groups: those with sizable lateralized abnormality and secondary generalized epilepsy who were not resection candidates; those with very specific syndromes; those who had frontal or bifrontal abnormalities; and those, 14 in number, with the Lennox-Gastaut syndrome. The results in the last group were the same compared with the other three groups.

Some of Dr. Henri Gastaut's patients were treated surgically by Dr. Bouvier, who visited there; he operated, on three patients with secondary generalization

and two with Lennox-Gastaut syndrome. In that small series, the patients with Lennox-Gastaut syndrome did not do as well as the others. In our facility, however, the results were quite comparable, the benefit of surgery being largely in abolition or reduction of tonic drop attacks, which are so disabling.

Question: Why should removal of the insular cortex be associated with hemiparesis?

Dr. Andermann: Removal of the insula is likely to result in additional deficit due to interference with penetrating blood vessels. Dr. Rasmussen has always taken care to point this out. Some surgeons, however, remove the insula apparently without producing additional deficit.

It is very likely that sparing the insula may also be related to the persistence of auras following temporal removal; thus, persistent auras may originate in the insula. We have clearly seen this in one patient in whom all cortex except the insula was removed when she had an anatomically subtotal functionally complete hemispherectomy. After the operation, medication was reduced fairly quickly; and the girl developed her usual auras, which disappeared when the medication was reincreased. She had ictal discharges correlating with the auras and these could only originate in the insular cortex unless they were generated in subcortical structures.

Dr. Lüders: I still have some difficulties with leaving the insula in these cases. I understand it in cases in which a temporal lobe resection is carried out, which extends close to the insula and could produce damage to the vascular supply in the remaining cortex. But in the particular case of a hemispherectomy in which you remove essentially the whole cortex, I do not know why you would want to save the insula, unless you are concerned with subcortical vascular supply.

Dr. Andermann: Such patients never have a complete hemiplegia. They can usually walk, move the arm and sometimes the hand. With practice, however, the hand becomes a little less spastic and more functional. They can always be made worse by interference with the blood supply to deeper structures.

Dr. Spencer: I wonder if this is not caused by some additional extrapyramidal control. There may be damage to the underlying extrapyramidal system, and not just the insula. These patients obviously have good proximal control of the hemiparetic side of their bodies. It is either that this motor function is transferred to the opposite side so there is ipsilateral control, or there is additional extrapyramidal control.

Question: Does Dr. Lüders require two seizure recordings of the patient if he has one seizure type or two types, one being the aura of the other?

Dr. Lüders: If I understand the question correctly, it refers to patients who have two types of seizures in which one is evolving into the other. Both types of seizures have essentially identical localization value, if you are certain that one is evolving into the other and therefore that the second one is due to spreading of the epileptiform discharge.

What is important to consider in such a situation (for example, a complex partial seizure evolving into a generalized tonic-clonic seizure) is that the complex partial seizure that is followed by a generalized seizure frequently is an abbreviated version of the initial focal seizure when it occurs in isolation (not followed by a generalized seizure). In many cases this is less useful than the isolated focal seizure, which evolves more slowly and therefore allows more time for looking at its origin.

Question: Excitotoxicity is cited as a reason for surgery. What is the clinical evidence for this?

Dr. Spencer: I think the question refers to whether there is any evidence in humans that the excitatory neurotransmitters cause ongoing injury or destruction to cells. We do not have good pathologic evidence for that. What we have is circumstantial evidence of knowing a bit more about neurotransmitters and about how destructive they are to their brethren, and good evidence of at least cognitive and neuropsychological decreases over time in patients with ongoing seizures and who have otherwise no underlying destructive pathology.

Question: Do psychomotor seizures in infants less than 1 year old correlate with the EEG?

Dr. Wyllie: This is an area where we do not have much data yet; as we all continue to work in this field, we will know more about it. In my own experience, we have noted rather difficult-to-define paroxysmal slowing in the temporal region in such very young children during clinical seizures. Because their background EEGs have more slow activity in them as resting background, it can sometimes be difficult to pick this up. But in the cases where we have made that diagnosis, there has been a definite paroxysmal aspect to the slowing that went along with the clinical changes which we saw on videotape; and we feel this indicates that psychomotor seizures in infants, as in older children, do correlate with EEG changes.

One special difficulty is that oftentimes these infants with partial seizures do not have well-defined interictal epileptiform abnormalities, which can sometimes be so much more helpful in localization than the actual seizures. By the time one can record a seizure, there has often been recruitment of larger areas. The specific localization that we get from interictal epileptiform abnormalities in older children is sometimes denied us in the youngest patients.

Question: In infants, is unresponsiveness instead of unconsciousness enough to justify the diagnosis of complex partial seizures, as was suggested by Yamamoto et al in 1987?

Dr. Wyllie: Unresponsiveness is about all we have to work with in children of this age group. However, unresponsiveness does not necessarily indicate altered consciousness, and may be due to other phenomena, such as preoccupation with ictal sensory or motor symptoms. In older patients, unresponsiveness may be due to aphasia, apraxia, or severe dysarthria. For these reasons, officially, by the current International Classification of seizures, unresponsiveness does not qualify to diagnose partial seizures as complex. Amnesia is required, but obviously amnesia is not something that can be assessed in infants. We are left, therefore, with unresponsiveness; and that is a somewhat difficult clinical feature to assess in babies. We need to reconsider the clinical usefulness of the present classification system in assessing our youngest children.

Question: What is the evidence that extra-spike mapping produces better results than the 10/20 system in localization for surgery?

Dr. Lüders: I showed some anecdotal evidence in my talk, and a paper has been published recently by Morris et al, comparing the amount of additional information one can get from closely-spaced scalp electrodes. This work shows very clearly that significant additional precision in localization of epileptiform activity can be achieved by using these extra electrodes.

The most striking example of an extra electrode that allows better localization of epileptiform activity is the sphenoidal electrode. The sphenoidal electrode allows one to differentiate very clearly whether a discharge has a predominantly mesiotemporal origin or originates mainly from the convexity of the temporal lobe. That single electrode can be used to subdivide patients with complex partial seizures from temporal lobe origin into those with a mesiotemporal focus, and those who have an origin from the lateral convexity. That division is extremely important from the point of view of prognosis. The patient who has a mesiotemporal focus has an extremely good chance of remaining seizure-free after surgery. In those who have the focus in the convexity, the chances of a successful surgery are significantly smaller.

Question: At what age is myelinization of the corpus callosum complete?

Dr. Spencer: As far as I know, myelinization is complete in the first year. But that is not the reason there is no callosal interdependence during that first year.

Question: What are the indications for the carotid amobarbital, or Wada, test? What is its value?

Dr. Spencer: A brief digression on the carotid amobarbital, or Wada, test might be useful. The first prototype Wada test was performed some years ago by Dr. Gardner, in Cleveland, before Wada described it in Montreal. Dr. Gardner injected lidocaine into the brain to inactivate language, and to prove that he was operating on the language-dominant hemisphere.

All of us who do much epilepsy surgery both praise and condemn the Wada test in the same breath. We say it is crude, and we do not know precisely what areas of the brain are being made dysfunctional; therefore, how can we make important decisions based upon it? At the same time, we do continue to make decisions on the basis of the test. It is valuable depending on what we ask it in each of the age groups.

In the young adult, and the adolescent, with whom good memory testing can be carried out, it is important to attempt to lateralize memory function and to determine the reproducibility of good memory function in each hemisphere. In retarded patients who may be undergoing an invasive procedure, many of the questions that we ask in this context are crucially important. If the patient is at the age (between 6 and 12) of becoming functionally asymmetric, we want to know if a surgical decision will confront the problem of mixed dominance and callosal interdependence. We need to know on which side of the brain language resides—at that time, in that patient. In young people, the aim of the test is primarily to lateralize speech.

Dr. Lüders: We have, as you know, a number of questions regarding the clinical usefulness of the Wada test. They can be summarized in the following three points. First, in what cases does the Wada test actually provide additional, clinically-useful information re-

garding lateralization of language? Right-handed patients almost invariably are left hemisphere dominant. The few exceptions to the Wada test and the results of cortical stimulation frequently provide discrepant data.

A second problem refers to the Wada test as a tool to assess memory. As is well known, memory functions are related to the hippocampus. But, only part of the hippocampus is supplied by the anterior circulation. In most cases, a significant portion of the hippocampus, particularly the posterior portion, is supplied by the posterior circulation. Therefore, what are we actually testing when during the Wada test we inject only the anterior circulation? How can one test the memory function of the remaining hemisphere, if with the injection we only inactivate part of the hippocampus?

Another aspect refers to the reproducibility of the Wada test. In a study by Dinner et al, we noted that in a good percentage of the cases in which the Wada test was repeated (cases in which a first Wada test had shown a presumable memory deficit on one side), the results of a second Wada test were different. That is, the hemisphere which initially had performed poorly now showed results that would be considered within normal limits.

Dr. Wyllie: Dr. Lüders referred to a recent review we made at the Cleveland Clinic of our own series of 130 Wada tests. It was found that very few right-handed patients had unsuspected right hemisphere dominance for speech. In addition, when Wada test results were then compared with results of cortical electrical stimulation with language mapping, it was found that sometimes the two techniques did not agree. The question arises as to which technique is giving the correct picture, and there is certainly some concern that the Wada might be at fault.

Question: Is there a correlation between outcome after temporal lobectomy and the underlying pathology?

Dr. Wyllie: Certainly, many centers have reported that when pathology is present after operation, such findings tend to explain the status of patients who do less than well. In our own series and at some other centers where similar techniques have been used, it has been difficult to assess that kind of information because of the way we do our resections. We do not usually get *en bloc* removal of the mesiotemporal structures. However, I have always had difficulty with the concept of correlation between pathology and outcome, because it is based on information that is unavailable until you have done the surgery. It is difficult to use that criterion when your patients are undergoing triage beforehand. I think other information comes into play in the triage procedure and is more important in terms of decision making—information such as MR and CT findings, physical examination findings, history of a certain type of insult, such as encephalitis, and so forth.

Question: Is unilateral anterotemporal lobectomy appropriate if bilateral mesial origins of seizure are noted, but one side is the origin of approximately 80% to 90% of the seizures?

Dr. Wyllie: That is the subject of much controversy, with many people asking the same question. It is generally agreed among all concerned that, if interictal abnormalities are present on both sides, but seizures all come from one side, it is worthwhile to resect the side where the seizures are actually originating. Results in such patients appear to be nearly as good as in patients whose epileptiform abnormalities are all on one side. That group is clear-cut and enjoys fairly uniform agreement. When many seizures are recorded from each side, and there is clearly a high degree of epileptogenicity on both sides of the brain, most people feel pretty comfortable with discouraging epilepsy surgery.

Treatment of that middle group, however, with some seizures from each side, is controversial. My personal feeling is that it is worthwhile giving the patient a chance to have lobectomy if there are two clinically different seizure types, if one seizure type is clearly more frequent (80% or more), and if the more frequent seizure type consistently arises on EEG from one side. These findings would suggest that the patient has at least a reasonable chance for significant clinical improvement after temporal lobectomy. However, this is a group that certainly needs to be followed closely and studied further so that we can get more definite conclusions.

Dr. Andermann: Patients who have two different complex partial seizure patterns, one from each side, are extraordinarily rare. Many patients who have been studied with depth electrodes have the same pattern arising on both sides, even though one side is presumably the one which is clinically significant.

Patients occasionally have a fairly equal number of seizures originating from both sides. Judging from EEG evidence of damage and from neurophysiological studies, it is sometimes possible to say that one side is worse than the other. If the clinical situation is really desperate, it may be possible to operate on patients of this type. Often for reasons of memory dysfunction, the hippocampus cannot be removed. They constitute a

small fraction of the patients studied with bitemporal depth electrodes. These people generally do fairly well since the seizures are often stopped or at least considerably reduced. In such patients, one worries more about postoperative behavior and possibilities of rehabilitation than about the seizures themselves.

I would like to add support to Dr. Lüder's point about the usefulness of recording separately and at different times. Under conditions of status epilepticus or very frequent minor temporal attacks, the other side will frequently begin to show seizures as well and that may become confusing. Seizures which occur on both sides at the time when you record a burst of many small attacks are very different in their significance from seizures which are recorded individually.

Question: What is currently thought about the etiology of the Rasmussen syndrome? What treatment is currently recommended for patients of this type?

Dr. Andermann: The cause of the Rasmussen syndrome is still not known. Most people think that it is a slow viral disorder, but no virus has ever been identified. Patients practically always develop a fixed neurologic deficit, hemiplegia, hemianopsia, and retardation. Contralateral involvement is extremely rare, if it occurs at all. Because of the severity of the disorder, many clinicians have felt that a trial of antiviral agents would be justified, despite the fact that no virus has ever been found. Many young people who have the syndrome are now undergoing trials of this type. Steroids in high doses combined with immunosuppressants are currently tried.

The question arises whether confirmation of the diagnosis by cerebral biopsy is always required. It is quite clear that in a number of children, a biopsy is not needed to confirm the diagnosis of chronic encephalitis. In such children, you can confidently wait until the hemiparesis is severe enough to justify a physiologically complete subanatomically partial modified hemispherectomy. This should be carried out only when no useful finger movements remain. In other cases, when one cannot make a clear clinical diagnosis, what Dr. Rasmussen used to call a "king-sized" biopsy enables you to make a tissue diagnosis and at the same time remove the most epileptogenic, accessible area. The mini series of patients with chronic encephalitis now numbers 48 patients who are the subject of a multidisciplinary study that will be summarized in a monograph.

Question: At what age should one consider early surgical intervention for a child with severe intractable seizures who functions at close to grade level but whose seizures are uncontrolled by medications?

Dr. Wyllie: If the criteria we have considered are rigorously fulfilled, and if the school-age child satisfies all those criteria—i.e., has clearly diagnosed localization-related epilepsy and electrographic evidence of a single resectable focus, is definitely debilitated to the extent of having to take medications which have some cognitive effects, however subtle, at the dosages required, and is subjected to the psychosocial difficulties of having repeated attacks of loss of consciousness—then I would say that it is probably time to consider surgery seriously.

Consequently, I personally do not think in terms of a specific age cutoff. At present, an early referral time is still considered to be 7 to 10 years of age. That age may be lowered as we become increasingly aware of how to choose these candidates.

Question: What are the criteria for selection of a child for callosotomy? Would most children with unresectable extratemporal foci be candidates for callosotomy?

Dr. Spencer: The criteria are much the same as for the general population. One should look for resectability, if at all possible. An unresectable focus may be one that lies in cortex in which there is still language or visual-spatial function. For instance, in an infantile hemiplegia, in which the patient has good finger function or other function you want to preserve, then a callosotomy may be considered. However, you first have to fulfill the criteria of unresectability, and then all the other criteria for medical intractability, and secondary generalization causing dysfunction of the child's life.

In regard to a question about pathology of the temporal lobe, I would stress that it is extremely important to look for pathology. In our hands, the correlation has been very good between the pathology of the mesial structures and the outcome of the patient. If one knows that the temporal lobe which has been removed is normal, then it provides a rationale for looking at patients who may fail temporal lobectomy, and may suggest how to change the way we evaluate patients of this type.