NEUROLOGICAL SURGERY

THIRD EDITION

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NEUROLOGICAL SURGERY

A Comprehensive Reference Guide to the Diagnosis and Management of Neurosurgical Problems

THIRD EDITION

Edited by

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Cerebrospinal Fluid Fistulae: Their Management and Repair

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Post-traumatic epilepsy

Post-traumatic epilepsy was first described in 3000 BC by the Egyptians, who may have been copying medical papyri dated much earlier.[30] Seizures were noted to occur contralateral to the site of head injury, an observation repeated by Hippocrates (463–357 BC) 25 centuries later in his work "Injuries of The Head."[13] Hippocrates identified five types of head injuries and outlined operative treatment ("trepanning"). Galen (131–201 AD) quoted Hippocrates and attributed contralateral seizures to "[injury to] the big vein feeding the brain . . ., causing dryness of the other side and convulsions."[3] Ambroise Paré (1510–1590 AD) supported this theory and believed that "injury of one side of the brain causes emptiness and dryness of the other side because Nature violently sends all humors and spirits to help the affected side [and this, in turn, exhausts the other side]." Paré reiterated Hippocrates' warning not to cut the temporal muscle in performing the trepanning procedure for fear of inducing fatal postoperative seizures.[3] Paré's Italian contemporary, Berengario da Carpi, was the first to note that post-traumatic epilepsy can appear years after the precipitating injury.[34] In 1818, Benjamin W. Dudley, a professor of surgery at Transylvania University in Lexington, Kentucky, was the first American surgeon to treat post-traumatic epilepsy with a decompression procedure utilizing the trephine.[10] He reported a series of five successful cases in 1823 in which chronic subdural hematomas were drained.

Types and Significance of Post-Traumatic Epilepsy

Post-traumatic epilepsy is classified into two types: early and late. Early post-traumatic seizures occur within the first week after injury. Late post-traumatic epilepsy includes seizures occurring after the first week. Seizures following injury but secondary to other causes (such as alcohol withdrawal) are excluded. The importance of early epilepsy generally is as a predictor of increased risk for late post-traumatic epilepsy. About 25 per cent of patients with early epilepsy develop late epilepsy.[15] Late epilepsy has considerably greater medical and economic sequelae, which include the psychological consequences of the ever-present anxiety of waiting for the next seizure, side effects of prolonged anticonvulsant medication, and harm from the seizure itself. Late epilepsy hinders the self-sufficiency provided by gainful employment and limits both job opportunities and the ability to retain employment. Based upon epidemiological data, between 8000 and 30,000 persons in the United States will develop early or late epilepsy each year.[15,18] Disability costs for the half of those individuals who cannot return to work have been estimated at $95,000,000.[44]

B. Young

EARLY SEIZURES

The risk of early epilepsy has been shown in large brain injury series to range from 2.5 to 7 per cent.[1,15] Early seizures occurred in 5 per cent of Jennett's unselected series of patients requiring hospitalization.[15] Location, severity, and type of head injury are the best indicators of the risk for developing early seizures. The greatest risk occurs with subdural intracerebral hematomas, which have an associated incidence of 30 to 36 per cent.[16] Patients with epidural hematomas, frontoparietal depressed skull fractures, injuries producing focal neurological signs, and post-traumatic amnesia lasting longer than 24 hours have an incidence of early seizures of 9 to 13 per cent.[6,15,16] Early seizures occur infrequently with severe missile wounds. For example, only 2 to 6 per cent of combat soldiers receiving penetrating missile wounds developed these seizures.[2,29] Fewer than 2 per cent of patients with minor head injuries with no other neurological signs have seizures within the first week of injury.[15]

One third of all early seizures occur within the first hour of injury, one third within the first 24 hours, and one third between the second and seventh days of injury.[15] Rish and Caveness reported that early epilepsy develops most often within the first 5 days following a combat head injury, with the greatest frequency on the first post-injury days.[27] Two thirds of patients with blunt head injuries who have one early seizure will have additional seizures during the first week.[15] Slightly more than half of all early seizures are focal. Penetrating injuries are more likely than blunt injuries to result in focal seizures.

Patients who develop early post-traumatic epilepsy have been observed to have a high risk of late seizures, which ranges from 25 per cent in some large series to 50 per cent in a series of combat soldiers during the Vietnam war.[15,31] Even patients with mild injuries who have early epilepsy have a 25 per cent chance of developing late seizures. Patients with mild head injury without early seizures have less than a 2 per cent risk for subsequent epilepsy.[15] The frequency and type of early seizures do not affect the incidence of late epilepsy. A generalized seizure that occurs immediately following head injury in childhood does not appear to place the child at increased risk for either early or late seizures.[15]

Complications of early post-traumatic seizures can be life-threatening. Status epilepticus ocurs in 11 per cent of all patients and in 22 per cent of children younger than 5 years of age.[14] Poorly controlled seizures have been reported to be the sole cause of death following a mild head injury.[28] Early seizures that alter consciousness make assessment of the patient's neurological condition difficult. Costly diagnostic tests may be needed to rule out a brain lesion as a cause of a deteriorating level of consciousness.

Since about half of post-traumatic seizures occur within 6 hours of injury, no practical regimen exists for preventing this proportion of early seizures. Furthermore, no clinical investigation has indicated that early post-traumatic seizures can be significantly decreased by the administration of prophylactic anticonvulsants. In Young and associates' study of prophylaxis for early post-traumatic seizures, more than 78 per cent of the treated patients had therapeutic plasma levels of phenytoin throughout the first week following head injury. There was no significant difference in seizure incidence, however, between the treated and the untreated groups.[46] If the prevention of early seizures is the sole goal, based on the results of these studies it is recommended that phenytoin be used only after an early seizure has occurred. When phenytoin has been administered to prevent recurrent early post-traumatic seizures, the drug is continued for 1 year in an attempt to prevent the ocurrence of late seizures in this high-risk group. If no late seizure occurs during the first year, the medication can be discontinued. If the patient has a single seizure during the first year following injury, phenytoin is recommended for a year after the seizure. If multiple seizures have occurred, the patient will require medication for a more prolonged period.

LATE SEIZURES

Late epilepsy occurred in 5 per cent of Jennett's series of unselected patients with head injury who required hospitalization.[15] Annegers and co-workers noted the incidence of late seizures to be 7.1 per cent in patients with head injury during the first year following the injury.[1] Nearly half of all patients with subdural or intracerebral hematomas develop late post-traumatic epilepsy; those with epi-

dural hematomas have a risk of about 20 per cent.[15] Patients with depressed skull fractures who also have dural lacerations, focal neurological signs, post-traumatic amnesia lasting longer than 24 hours, or early seizures may have an incidence of late seizures of up to 60 per cent.[15] Without these factors, the incidence is less than 10 per cent.[15] Extensive focal damage, prolonged coma, and injuries in the motor strip are risk factors for late seizures in patients with penetrating wounds.[6,15]

Some evidence has accumulated that these reported incidence figures for late post-traumatic epilepsy may be excessive. Using actuarial percentages, McQueen and associates' 1983 study showed an incidence of injury-induced seizures of only 7 per cent at the end of 1 year and 10 per cent at the end of 2 years.[19] Even excluding patients with early seizures, the patients included in this study are those found by Jennett to have the greatest likelihood of developing post-traumatic epilepsy. In the 1983 study of Young and colleagues, the minimal criterion for entry into the series was a patient estimated to have at least 15 per cent or greater probability (based on Jennett's work) of developing post-traumatic seizures following a brain injury.[47] Most patients had a much higher predicted rate of developing seizures. Only 10.8 per cent of the control patients and 12.4 per cent of the treated group developed seizures during an 18-month follow-up.

Korean War and World War II soldiers who sustained closed head injuries with loss of consciousness lasting up to 6 hours had seizure incidences of 11.9 per cent and 17.5 per cent, respectively.[6,7] Those with more severe injuries with focal brain damage and prolonged loss of consciousness had seizure incidences of 26.6 per cent and 25 per cent, respectively.[6,7] In both these series reported by Caveness and co-workers in 1961 and 1962, cases of early and late seizures were analyzed together. Patients with depressed skull fractures were included in both studies.

Caveness and others have reported that after late post-traumatic seizures have become established, the frequency of occurrence seldom varies. Three frequency patterns were noted in his 10-year follow-up of Korean War veterans with combat head injuries: fewer than 4 seizures, between 4 and 30 seizures, and more than 30 seizures.[5] Each category accounted for approximately one third of the patients. Patients who had frequent late seizures were more likely to have persistent epilepsy.

Several formulas for predicting the likelihood of post-traumatic epilepsy for an individual patient have been devised. Weiss and associates have shown that if the first 3 post-injury years are seizure-free, there is a 95 per cent probability that epilepsy will not develop.[37] The addition of electroencephalography data does not contribute to the accuracy of prediction.[17]

Possible Mechanisms for Development of Epileptogenic Focus

The pathophysiological mechanisms of post-traumatic epilepsy have never been elucidated. Penfield and Erickson have called the first 8 weeks following head trauma "a silent period of strange ripening" during which the potential for late seizures develops.[21] The brain injury presumably initiates a series of biochemical, electrical, and structural changes that lead to the development of the epileptiform focus.[24] Decreased inhibitory controlling mechanisms, chronic ischemia, mechanical distortion of dendrites, blood-brain barrier defects, altered buffering action of glial cells, kindling, and hereditary factors are all potential explanations that need further study.[12] Wyler and Ray and Westrum and associates have described this epileptogenic focus as consisting of normal neurons, abnormal or "pacemaker" neurons, and transitional neurons.[38,44] If abnormal neurons recruit enough of the transitional and normal neurons to fire abnormally, the loss of inhibitory mechanisms within dendrites in the epileptogenic focus may permit abnormal firing and seizure ocurrence.

According to Wilkins and Rengachary, operative specimens removed to control post-traumatic epilepsy show neuronal and oligodendroglial loss, gliosis, and hemosiderosis. The epileptogenic focus is adjacent to the injury site.[39] The hyperirritable epileptogenic focus may be caused by mechanical stress, long-standing localized ischemia.[14] Tower demonstrated that an epileptogenic focus has biochemical defects in acetylcholine, glutamic acid, and potassium metabolism.[35] Schmidt and co-workers attributed the burst of autonomous electrical activity in the epileptogenic

focus to a dendritic depolarization and the difference in potential between the cell body and the dendritic network.[32] Westrum and associates proposed that the decreased synaptic endings or dendrites within the epileptogenic focus permit postsynaptic hypersensitivity.[38] Gliotic changes may also impair the glial control of acid-base balance and allow an excessive excitability of adjacent neurons.[22]

Willmore and associates' work suggests that hemorrhage and the deposition of iron salts may induce the changes leading to the development of the epileptogenic focus.[41] Willmore and Triggs have observed that corticosteroids prevented peroxidation and iron-induced seizures.[38,41] Phenytoin did not prevent lipid peroxidation but did prevent seizures by its anticonvulsant action. These investigators questioned whether phenytoin's prophylactic effect in the cobalt model may be due to the chemical action of cobalt upon neurons rather than the actual prevention of development of the epileptogenic focus set in motion by injured neurons. In this model, pretreatment with an antioxidant such as tocopherol prevents lipid peroxidation. These investigators suggested that treatment aimed at prevention of lipid peroxidation may be an effective route to true prophylaxis.

Prophylaxis and Treatment of Late Post-Traumatic Epilepsy

Many laboratory investigations, including primate models, suggest that prophylactic administration of a variety of drugs tends to lessen the incidence of post-traumatic epilepsy. However, none of these experimental models truly duplicates the traumatic epileptogenic lesion in humans. Prophylaxis must be distinguished from treatment or suppression of an established epileptogenic focus. Successful prophylaxis implies that the anticonvulsant regimen prevented the development of the epileptogenic focus. Administration of the prophylactic agent can then cease after 2 or 3 months without significant risk of seizure occurrence. By contrast, successful treatment suppresses the developed epileptogenic focus so that a seizure does not occur. Seizures are likely if the anticonvulsant drug is withdrawn.

In 1972, Popek reported that only 1.1 per cent of patients receiving both phenytoin and phenobarbital had late seizures, compared with 25 per cent of patients in the control group.[23] Wohns and Wyler concluded from their 1979 retrospective nonrandomized study of 62 patients with severe head injury that prophylactically administered phenytoin reduced the incidence of post-traumatic seizures.[43] Similarly, results of a nonrandomized trial by Young and associates suggested that phenytoin reduces the incidence of late post-traumatic seizures.[49] The conclusions of this study were based on comparisons with other large clinical series published before 1979 rather than on randomized groups. In 1981, Zervit and Musil reported the long-term follow-up to Popek's study in which 87 per cent of the 73 patients were followed for more than 5 years and 37 per cent for more than 10 years. In this study, the phenytoin dosage was 160 to 240 mg per day and the phenobarbital dosage was 30 to 60 mg per day. Of the treated group, 2.1 per cent had had post-traumatic seizures; of the control group, 25 per cent had had seizures.[51] This study was not randomized, placebo-controlled, or double-blind.

A study of 1030 patients with head injuries received during the Vietnam War showed that 84 per cent of the men received anticonvulsants within 24 hours of injury, 75 per cent of whom received 300 to 400 mg per day of phenytoin, 20 per cent of whom received phenytoin and phenobarbital (96 mg per day), and 3 per cent of whom received phenobarbital alone.[5] A review of the patients' records showed that 453 patients had continued taking anticonvulsant medication throughout the post-injury period for intervals of 3 months to 9 years. In 524 patients the medication was interrupted at varying periods after injury, and 53 men had no anticonvulsant medication prescribed. The study demonstrated no benefit of continuous therapy compared with interrupted therapy, or with patients receiving no treatment.

In 1983, Young and co-workers reported a randomized, placebo-controlled, double-blind trial of phenytoin as a prophylactic agent for late seizures.[47] The study comprised 179 patients who were followed for 18 months. Therapeutic drug levels (10 to 20 μg per ml) were difficult to sustain for the entire 18 months; patient compliance dropped to about 25 per cent at 6 months. There was no significant difference in the percentage of patients having late seizures in the treated and placebo groups. Young and associates found that a

plasma concentration of 12 μg per ml was a clear breakpoint above which no patient experienced a late seizure. This suggests that higher therapeutic doses of phenytoin may lessen the occurrence of post-traumatic seizures. The study could not conclude that higher phenytoin plasma concentrations and higher compliance rates would not have significantly decreased the occurrence of late epilepsy by causing a suppressive effect on the already developed epileptogenic focus. The risk of late epilepsy in this series was similar to the risk reported by Annegers and co-workers in their retrospective study of a civilian population considered by the authors as untreated.[1] Late seizures occurred in 7.1 per cent of their patients within the first year following severe head injury; during the first year of Young and associates' series, 10.9 per cent of patients had at least one seizure.

Young's findings are supported by two other studies. McQueen and colleagues' 1983 clinical trial of phenytoin for prophylaxis of injury-induced seizures demonstrated no difference in the incidence of seizures between 84 treated patients and 80 controls.[19] In Salazar and associates' 1985 study of 421 Vietnam War veterans, 53 per cent had sustained at least one post-traumatic seizure during the first 15 years following injury. Despite 85 per cent of these patients having received anticonvulsant therapy for 1 year or more following the penetrating injury, the incidence of seizures in these patients did not differ from that reported in earlier wars.[31] Salazar and associates concluded that anticonvulsant therapy did not significantly prevent the onset of post-traumatic epilepsy. Three clinical trials of phenytoin or phenobarbital or both are currently being supported by the National Institutes of Health to test Young's findings.

If the decision is made to administer anticonvulsants, the rationale based on current evidence should be to prevent the occurrence of seizures by suppression of the epileptogenic focus, not prophylaxis. Treatment should therefore be continued for at least 1 to 2 years, when the risk of post-traumatic epilepsy is highest. Since the efficacy of prophylaxis for post-traumatic epilepsy is unproved, only those patients with the highest risk should be treated. The author's current practice is not to administer prophylactic anticonvulsants but instead to institute treatment only after a late seizure occurs. Phenytoin is the drug of choice to begin treatment.

PHENYTOIN ADMINISTRATION

Phenytoin's mode of action is most likely due to a frequency-dependent blockade of the Na^+ action potential. This action, by means of a variety of mechanisms, interrupts the positive feedback mechanisms essential in the development of seizures.[45] Phenytoin's pharmacokinetic properties, which follow Michaelis-Menton kinetics, require frequent blood assays to assure continuous therapeutic blood levels.

The difficulties in obtaining a high rate of compliance in order to keep drug plasma levels in the high therapeutic range for a prolonged period of time have been well documented. In McQueen and associates' study, not more than half the patients entering the trial persisted on drug treatment for a full year.[19] Only 48 per cent of the patients in the drug group achieved plasma concentrations greater than 40 μmol per liter on at least one occasion. One third had phenytoin concentrations of 20 to 39 μmol per liter, while 12 per cent were in the range of 10 to 19 μmol per liter and 4 per cent never achieved concentrations of more than 9 μmol per liter. In Young and associates' series, half the patients had known blood levels of phenytoin at 6 months, and only 50 per cent of these had levels between 10 and 20 μg per ml.[47] This represents only one fourth of the initial patients given phenytoin.

Measurement of both total and unbound plasma phenytoin concentrations may be important to determine accurate dosing. The portion of phenytoin unbound to plasma proteins is the pharmacologically active component. Ninety per cent of phenytoin is bound to albumin and about 10 per cent is unbound. During the acute phase response to head injury, plasma albumin concentrations are diminished. Bauer and co-workers found that total phenytoin concentrations were lower in patients with head injury than in patients with epilepsy who were given similar doses of phenytoin, although there was no difference in unbound concentrations in the two groups.[4] Total phenytoin concentrations may not accurately reflect the unbound concentration of phenytoin. Even though the total phenytoin plasma concentration may be below the therapeutic range, the unbound level may be within the normal range of 1 to 2 μg per ml. Therefore, using the total plasma concentration to determine dosing adjustments may lead

to unnecessary dosage increases that may increase the risk of toxicity.

Two types of adverse effects are caused by phenytoin: reversible dose-dependent central nervous system effects and hypersensitivity effects. The most common of the hypersensitivity reactions is a morbilliform rash. One fifth of the patients in Rapp and associates' study developed this complication.[25] Other dose-related adverse effects include gingival hypertrophy, hypertrichosis, leukopenia, thrombocytopenia, pancytopenia, and aplastic anemia. Reversible dose-dependent central nervous system effects include nystagmus, ataxia, and stupor and are related to blood levels above the upper limits of the therapeutic range (10 to 20 μg per ml).[43,45]

References

1. Annegers, J. F., Grabow, J. D., Groover, R. V., Laws, E. R., Jr., Elveback, L. R., and Kurland, L. T.: Seizures after head trauma: A population study. Neurology (New York), *30*:683–689, 1980.
2. Ascroft, P. B.: Traumatic epilepsy after gunshot wounds of the head. Br. Med. J., *1*:739–744, 1941.
3. Bakay L.: The Early History of Craniotomy from Antiquity to the Napoleonic Era. Springfield, Ill., Charles C Thomas. 1985, pp. 25–26, 71.
4. Bauer, L. A., Edwards W. A. D., Dellinger E. P., Raisys V. A., and Brennan C.: Importance of unbound phenytoin serum levels in head trauma patients. J. Trauma, *23*:1058–1060, 1983.
5. Caveness, W. F.: Epilepsy, a product of trauma in our time. Epilepsia, *17*:207–215, 1976.
6. Caveness, W. F., and Liss, H. R.: Incidence of posttraumatic epilepsy. Epilepsia, *2*:123–129, 1961.
7. Caveness, W. F., Walker, A. E., and Ascroft, P. B.: Incidence of post-traumatic epilepsy in Korean veterans as compared with those from World War I and World War II. J. Neurosurg., *19*:122–129, 1962.
8. Caveness, W. F., Meirowsky, A. M., Rish, B. L., Mohr, J. P., Kistler, J. P., Dillon, J. D., and Weiss, G. H.: The nature of posttraumatic epilepsy. J. Neurosurg., *50*:545, 553, 1979.
9. Corkin, S., Sullivan, E. V., and Carr, F. A.: Prognostic factors for life expectancy after penetrating head injury. Arch. Neurol., *41*:975–977, 1984.
10. Cutter, I. S.: Benjamin Dudley and the surgical relief of traumatic epilepsy. Intl. Abst. Surg., *50*:189–194, 1930.
11. Deutschman, C. S., and Haines, S. J.: Anticonvulsant prophylaxis in neurological surgery. Neurosurgery, *17*:510–517, 1985.
12. Goldensohn, E. S., and Ward, A. A., Jr.: Pathogenesis of epileptic seizures. *In* Tower, D. B., ed.: The Nervous System. Vol. 2: The Clinical Neurosciences. New York, Raven Press, 1975, pp. 249–260.
13. Hippocrates: The Genuine Works of Hippocrates. Translated from the Greek by Adams, F. London, Sydenham Society, 1849.
14. Jasper, H. H.: Physiopathological mechanisms of post-traumatic epilepsy. Epilepsia, *11*:73–80, 1970.
15. Jennett, B.: Epilepsy after Non-missile Head Injuries, 2nd Ed. Chicago, Year Book Medical Publishers, 1975.
16. Jennett, B.: Epilepsy and acute traumatic intracranial hematoma. J. Neurol. Neurosurg. Psychiatry, *38*:378–381, 1974.
17. Jennett, B., and van de Sande, J.: EEG prediction of post-traumatic epilepsy, *38*:378–381, 1974.
18. Kalsbeck, W. D., McLaurin, R. L., Harris, B. S. H., and Miller, J. D.: The national head and spinal cord injury survey: Major findings. J. Neurosurg., *53*:S19–S31 (Suppl.), 1980.
19. McQueen, J. K. Blackwood, D. H. R., Harris, P., Kalbag, R. M., and Johnson A. L.: Low risk of late post-traumatic seizures following severe head injury: Implications for clinical trials of prophylaxis. J. Neurol. Neurosurg. Psychiatry, *46*:899–904, 1983.
20. Meirowsky, A. M.: Notes on posttraumatic epilepsy in missile wounds of the brain. Milit. Med., *147*:632–634, 1982.
21. Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localization. Springifield, Ill., Charles C Thomas, 1941, pp. 3–7.
22. Pollen, D. A., and Trachtenberg, M. C.: Neuroglia: Gliosis and focal epilepsy. Science, *167*:1252–1253, 1970.
23. Popek, K.: Preventive treatment of post-traumatic epilepsy following severe brain injury. Czech. Neurol., *35*:169–174, 1972.
24. Potter, J. M.: The personal factor in maturation of epileptogenic brain scars: Review and hypothesis. J. Neurol. Neurosurg. Psychiatry, *41*:265–271, 1978.
25. Rapp, R. P., Norton, J. A., Young, B., and Tibbs, P. A.: Cutaneous reactions in head-injured patients receiving phenytoin for seizure prophylaxis. Neurosurgery, *13*:272–275, 1983.
26. Rasmussen, T.: Surgical therapy of posttraumatic epilepsy. *In* Walker, A. E., Caveness, W. F., and Critchley, M., eds.: The Late Effects of Head Injury. Springfield, Ill., Charles C Thomas, 1969, pp. 277–305.
27. Rish, B. L., and Caveness, W. F.: Relation of prophylactic medication to the occurrence of early seizures following craniocerebral trauma. J. Neurosurg., *38*:155–158, 1973.
28. Rose, J., Valtonen, S., and Jennett, B.: Avoidable factors contributing to death after head injury. Br. Med. J., *2*:615–618, 1977.
29. Russell, W. R., and Whitty, C. W. N.: Studies in traumatic epilepsy: I. Factors influencing the incidence of epilepsy after brain wounds. J. Neurol. Neurosurg. Psychiatry, *20*:293–301, 1957.
30. Sachs, E.: The History and Development of Neurological Surgery. New York, Paul B. Hoeber (Harper & Bros.), 1952, pp. 25–43.
31. Salazar, A. M., Jabbari, B., Vance, S. C., Grafman, J., Amin, D., and Dillon, J. D.: Epilepsy after penetrating head injury. Part I. Clinical correlates: A report of the Vietnam Head Injury Study. Neurology, *35*:1406–1414, 1985.
32. Schmidt, R. P., Thomas, L. B., and Ward, A. A., Jr.: The hyperexcitable neurone: Micro-electrode studies of chronic epileptic foci in the monkey. J. Neurophysiol., *22*:285–296, 1959.
33. Servit, Z., and Musil, F.: Prophylactic treatment of posttraumatic epilepsy: Results of a long-term follow-up in Czechoslovakia. Epilepsia, *22*:315–320, 1981.
34. Temkin, O.: The Falling Sickness; A History of Epilepsy from the Greeks to the Beginnings of Modern

Neurology. Baltimore, Johns Hopkins Press, 1945, pp. 186–187.
35. Tower, D. B.: Neurochemistry of Epilepsy: Seizure Mechanisms and Their Management. Springfield, Ill., Charles C Thomas, 1960.
36. Tower, D. B., and Elliott, K. A. C.: Activity of acetylcholine system in human epileptogenic focus. J. Appl. Physiol., *4*:669–676, 1952.
37. Weiss, G. H., Salazar, A. M., Vance, S. C., Grafman, J. H., and Jabbari, B.: Predicting posttraumatic epilepsy in penetrating head injury. Arch. Neurol., *43*:771–773, 1986.
38. Westrum, L. E., White, L. E., and Ward, A. A., Jr.: Morphology of the experimental epileptic focus. J. Neurosurg., *21*:1033–1046, 1964.
39. Wilkins, R. H., and Rengachary, S. S.: Neurosurgery. New York, McGraw-Hill Book Co., 1985, pp. 689–690.
40. Willmore, L. J., and Rubin, J. J.: The effect of tocopherol and dimethyl sulfoxide on focal edema and lipid peroxidation induced by isocortical injection of ferrous chloride. Brain Res. *296*:389–392, 1984.
41. Willmore, L. J., Sypert, G. W., and Munson, J. B.: Recurrent seizures induced by cortical iron injection: A model of posttraumatic epilepsy. Ann. Neurol., *4*:329–336, 1978.
42. Willmore, L. J., and Triggs, W. J.: Effects of phenytoin and corticosteroids on seizures and lipid peroxidation in experimental posttraumatic epilepsy. J. Neurosurg., *60*:467–472, 1984.
43. Wohns, R. N. W., and Wyler, A. R.: Prophylactic phenytoin in severe head injuries. J. Neurosurg., *51*:507–509, 1979.
44. Wyler, A. R., and Ray, M. W.: Anticonvulsant prophylaxis against posttraumatic seizures. Contemp. Neurosurg. *7*(8):1–6, 1985.
45. Yaari, Y., Selzer, M. E., and Pincus, J. H.: Phenytoin: Mechanisms of its anticonvulsant action. Ann. Neurol., *20*:171–184, 1986.
46. Young, A. B., Rapp, R. P., Norton, J. A., Haack, D., Tibbs, P. A., and Bean, J. R.: Failure of prophylactically administered phenytoin to prevent early post-traumatic seizures. J. Neurosurg., *58*:231–235, 1983.
47. Young, A. B., Rapp, R. P., Norton, J. A., Haack, D., Tibbs, P. A., and Bean, J. R.: Failure of prophylactically administered phenytoin to prevent late post-traumatic seizures. J. Neurosurg., *58*:236–241, 1983.
49. Young, A. B., Rapp, R. P., Norton, J. A., Haack, D., and Walsh, J. W.: Failure of prophylactically administered phenytoin to prevent post-traumatic seizures in children. Child's Brain, *10*:185–192, 1983.
49. Young, A. B., Rapp, R. P., Brooks, W. H., Maddaus, W., and Norton, J. A.: Posttraumatic epilepsy prophylaxis. Epilepsia, *20*:671–681, 1979.
50. Young, A. B. and Rapp, R. P.: Post-traumatic epilepsy; treatment and prophylaxis. *In* Brock, M., ed.: Modern Neurosurgery, Vol. II (in press).
51. Zervit, Z., and Musil, F.: Prophylactic treatment of posttraumatic epilepsy: Results of a long-term follow-up in Czechoslovakia. Epilepsia, *22*:315–320, 1981.