nections). The clinician's access to the diagnostic utility of this finding and its symptomatic implications of residual peripheral vision for motion, hallucinations, dyslexia, and so on is "endangered" by the well-established trend of performing automated perimetry limited to the central visual fields.

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The efficacy of epidural blood patch in spontaneous CSF leaks

Article abstract—Of 25 consecutive patients with spontaneous CSF leaks treated with epidural blood patch (EBP), nine patients (36%) responded well to the first EBP. Of 15 patients who received a second EBP, five became asymptomatic (33%). Of eight patients who received three or more EBP (mean 4), four patients (50%) responded well.

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Epidural blood patch (EBP) has emerged as the most important nonsurgical treatment for spontaneous CSF leaks.[1-3] We have attempted to determine the efficacy of EBP in the treatment of spontaneous CSF leaks. These leaks typically occur at the level of the spine and only rarely occur at the skull base.[2]

Materials and methods. Utilizing our institution's diagnostic indexing system for computer retrieval, we identified 54 patients with symptomatic and documented spontaneous CSF leaks seen from 1986 through 1998. Twenty-nine had EBP as a treatment modality. Follow-up was obtained through review of records, correspondence, and telephone calls. Four patients were eliminated from this study (three because of unavailability of follow-up and one because of leak from cribriform plate). Our study thus consisted of 20 women and five men, all with documented CSF leaks at the spine level. Age ranged from 18 to 62 years (mean 42 years). Follow-up ranged from 3 months to 11 years. All patients had received EBP using 10 to 20 mL (mean 17 mL) of autologous blood.

A logistic regression model was constructed to assess the joint effects of site and number of the EBP application on the odds of a positive response.[4]

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Results. The implemented diagnostic imaging studies are listed in the table. Overall, the level of the leak was determined in 16 patients and the actual site of the leak in nine. All patients had headaches with orthostatic features. Other less common manifestations were nausea and emesis, change in hearing, horizontal diplopia, upper limb pain, photophobia, blurred vision, and face pain. Spinal taps had been performed in 23 patients.

All 25 patients had failed an initial period of conservative, noninvasive management that ranged from 1 week to 3 years (median 1 month) and consisted of one, but often more of the following: bedrest, analgesics, hydration, nonsteroidal drugs, caffeine, steroids, tricyclic antidepressants, and ergot preparations.

With the first epidural blood patch, nine patients (36%) improved (seven became entirely asymptomatic within a few weeks, and two markedly improved but had mild lingering headaches for more than 2 years). One patient who had not responded to the first EBP underwent surgical correction of the leak and became asymptomatic. Fifteen patients who had failed the first EBP underwent a second EBP. Five of these (33%) responded to the second EBP and became asymptomatic. Of the 10 patients who failed the second EBP, two were treated surgically. One became asymptomatic and one, although improved, was still symptomatic but responded to a third EBP. The remaining eight patients had received three or more epidural blood patches (range 3 to 6, mean 4). Four patients (50%) responded well and the remaining four were treated surgically, with complete resolution of symptoms in two.

Overall, 49 EBP had been delivered with complete and durable response in 17. EBP had been given at the level of the leak in 24 instances and at a different level in 13

Table *Diagnostic imaging studies and level and site of spontaneous CSF leaks in 25 patients*

Parameters	No. of patients
Diagnostic study	
Head MRI	24
Spine MRI	12
Myelogram/CTM	16
Radioisotope cisternography	14
Level of the leak determined	16
Cervical	4
Cervicothoracic	2
Thoracic	7
Thoracolumbar	2
Lumbar	1
Actual site of the leak also identified	9
Cervical	3
Thoracic	5
Lumbar	1

CTM = CT myelography.

(typically patients with CSF leak at cervical or thoracic levels who received EBP at lumbar level). In 12 cases, either the exact level of the leak had not been identified or adequate information was not available. A logistic regression model was constructed with a generalized estimating equations approach to account for the correlation between multiple EBP applications on the same subject utilizing an exchangeable correlation structure.[4] The odds ratios were determined comparing the odds of responding to the treatment in a particular group with the odds of the reference category for that group. In general, relative to those patients with the EBP at the same level as the leak (the reference group), those with EBP at a different level tended to do worse, although the difference did not reach significance ($p = 0.07$).

For the first EBP, those who responded had a significantly shorter average duration of symptoms than those who did not respond (median 2 weeks vs 3 months, $p = 0.02$, Wilcoxon's rank sum test), but for the eventual response there was no significant difference in the duration of the symptoms or length of follow-up for the responders vs the nonresponders, either for the first patch or overall.

Discussion. The initial reports on application of EBP in CSF leaks involved epidural injection of only 1 to 3 mL of autologous blood.[5-6] The recommended volume has increased over the years. Although the optimal volume remains controversial, a 20 mL volume EBP has been mostly recommended,[7] commonly referred to as the "target volume." Some have practiced application of even larger volumes.[1] The recommended duration of post-EBP recumbency is about 2 hours.[9]

Despite almost one-half century of experience with application of EBP in CSF leaks, there have been no controlled studies. Utilization of EBP has been based on the clinical observation of its effectiveness.[10] The criticism of lack of control for spontaneous recovery can also be extended to our study; although most of our patients had been referred from other centers, many had received other treatments (including EBP in some) before our evaluation.

Leaks resulting from spinal taps (typically done with small needles) respond better to EBP than those resulting from inadvertent dural puncture from epidural needles or the spontaneous type, which may result from leaking meningeal diverticula or dural defects confirming the importance of anatomy of the leak. Also important is the durability of response. Although over 90% of post–dural puncture headaches respond initially to an EBP, a durable response is noted in only 61 to 75%.[8]

An *early effect* from EBP may take place within minutes and is likely related to the displacement of dura toward the cord and cauda equina, decreasing the volume of the "container," therefore compensating for some of the depleted volume of CSF. A *latent effect* results from sealing of the leak. The interval between the two effects varies considerably. Sometimes the interval may be so short that the two effects may fuse, accounting for patients who obtain immediate and persistent relief from EBP. Sometimes the interval may be more prolonged, accounting for those who obtain early relief but the effect wears off either partially or completely, and then after a period of delay patients begin to improve. Sometimes the latent effect may never appear or may occur only partially. In these cases, the dural leak has either completely failed to seal or has sealed only partially and inadequately.

Our data confirm that the results of EBP in spontaneous CSF leaks are not as dramatic as those reported from diagnostic lumbar punctures or even from inadvertent dural punctures. However, EBP is considered the treatment of choice in those patients who have failed the initial noninvasive treatments. Failure to respond to one EBP does not guarantee failure of subsequent EBP.

Epidural blood patch given at the level of the leak is somewhat more effective than given at a distant site. In CSF leaks with firmly established diagnosis, it would seem reasonable to proceed with at least one lumbar EBP. If unsuccessful, further investigation could localize the site or at least the level of the leak for a possible targeted EBP. These studies might also show single or multiple meningeal diverticula, more than one site of CSF leak, or dural defects with high-flow leaks accounting for some of the failures. The investigations could also help with selection of the patients who might be reasonable surgical candidates.

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Apolipoprotein E and age at onset of Alzheimer's disease in African American patients

Article abstract—The authors examined whether the *APOE*-ϵ4 allele is associated with an earlier age at onset of AD in 71 African American patients with probable AD. The authors found a linear dose effect in which each copy of the ϵ4 allele was associated with a 3.6-year earlier onset of AD, indicating a dose-dependent relationship between *APOE*-ϵ4 and age at onset of AD in African Americans.

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The *APOE*-ϵ4 allele is associated with both an increased risk of developing AD and an earlier age at onset.[1-2] However, most research has been conducted in Caucasian patients, with less known about its effects in African Americans. Whereas APOE-ϵ4 is a risk factor for AD in African Americans,[3] studies suggest a weaker association than in Caucasians, as well as a genetic influence restricted to homozygotes (two ϵ4 alleles) rather than heterozygotes (one ϵ4 allele).[4-6]

We examined whether the ϵ4 allele is associated with an earlier age at onset in African American patients with probable AD. Duara et al.[7] examined risk factors for age at onset of possible and probable AD in African American, Hispanic, and Ashkenazi Jewish patients. They observed a lower mean age at onset in their entire sample as the number of ϵ4 alleles increased. However, the investigators did not specifically determine the relationship in the African American patients because of the small sample size (n = 19). The meta-analytic investigation of Caucasians, Hispanics, and African Americans by Farrer et al.[4] excluded the last group when examining the risk for AD in relation to the patient's age and ϵ4 status because of the wide variability in the odds ratios among the African American studies.

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Methods. Our sample consisted of 71 African American patients with probable AD[8] who were participants in the Emory–Morehouse AD Center. Patients were consecutively recruited between 1994 and 2000. To be included in this study, they had to have all pertinent genotype, demographic, age at onset, and family history data. Seven additional patients with AD were excluded because of missing information. As part of their registry enrollment, patients underwent extensive evaluations to exclude alternative etiologies of dementia. Neuropsychological evaluations routinely incorporated the Mattis Dementia Rating Scale, Clock Drawing, and the Consortium to Establish a Registry for AD Neuropsychological Assessment Battery, which includes the Mini-Mental State Examination. In cases where a patient was too demented to receive the standard procedures, the Severe Impairment Battery was administered. Diagnoses were made based on consensual agreement of physicians and neuropsychologists. Although there was neuropathologic confirmation of AD in only one patient in this series, our overall diagnostic accuracy for clinically defined probable AD was 97% in a separate group of 37 registry patients who had undergone autopsy. Three of these 37 patients were African American, but did not have either *APOE* genotyping or age at onset data, and were not included in this study.

Age at onset of symptoms was determined from an interview with a knowledgeable significant other(s). Most informants were children of the patients (50%), followed by spouses (19%), others (15%; e.g., caretakers), grandchildren (9%), and siblings (7%). There were no differences in the relationship of the informant to the patient as a function of the number of alleles (χ^2, $p = 0.49$). *APOE* genotyping was performed on blood samples using PCR, followed by digestion of the PCR product with *Hha*I and visualization of the resulting bands by polyacrylamide gel electrophoresis.[9] Clinicians were unaware of the genotype results both when the age at onset was determined and when the

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