Specialty Conference

Moderator

THOMAS T. YOSHIKAWA, MD

Discussants

STANLEY J. GOODMAN, MD
THOMAS T. YOSHIKAWA, MD

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Brain Abscess

THOMAS T. YOSHIKAWA, MD:* Treatment of brain abscesses, unlike treatment of most infected purulent material, has failed to achieve the high rate of cure usually resulting from traditional therapy with antibiotics and surgical drainage. Although this infection does involve a vital organ that is not easily accessible, the failure to improve the survival rate in the past two or three decades must be due in part to inadequate recognition and management by practicing physicians. Thus, in this symposium, the clinical recognition and management of brain abscess will be emphasized. Dr. Stanley Goodman will begin the discussion by stressing some key aspects of clinical recognition of brain abscess and the approach to diagnostic evaluation of this disease. I will review the microbial flora of brain abscess and the proper approach to antibiotic therapy. Dr. Goodman will conclude by commenting on the neurosurgical therapy of this disease.

From Divisions of Infectious Diseases and Neurosurgery, and Department of Surgery, University of California, Los Angeles, School of Medicine, Harbor General Hospital, Torrance.

*Fellow, Division of Infectious Diseases, Harbor General Hospital.

Reprint requests to: Division of Infectious Diseases, Department of Medicine, Harbor General Hospital, 1000 West Carson Street, Torrance, CA 90509.

Clinical Diagnosis

STANLEY J. GOODMAN, MD:† It is appropriate that a review of the subject of brain abscess begin with comments on diagnosis. With the development of potent antimicrobial therapy, the mortality rate from brain abscess declined from virtually 100 percent to 40 percent. However, over the past thirty or so years, there has been no further improvement in the mortality rate.[1] Some of the patients who die from brain abscess have overwhelming disease, such as huge necrotic lesions, "malignant" cerebral edema, multiple abscesses, rapid progression of one or more cerebral herniation syndromes, deficiency in host defense mechanisms or severe underlying diseases. Yet there are many patients who die from brain abscess with a clinical course that was "benign" for awhile but ultimately fatal. My contention is that fully one-half of the brain abscess deaths occur in this "benign" and, therefore, potentially salvageable category, and that correctable physician-related problems contribute to the lethality of these otherwise curable lesions. There are several recurring

†Chief, Division of Neurosurgery, Harbor General Hospital; Assistant Professor of Surgery, UCLA School of Medicine.

physician-related problems: (1) when the diagnosis is incorrect or not considered; (2) when inappropriate and highly dangerous diagnostic studies are done; (3) when the diagnosis may have been made but there is tardiness in instituting therapy, overlooking the fact that these lesions may progress with extraordinary speed and (4) when surgical therapy is appropriately instituted but the entire abscess is missed by the exploring needle, or the extent of the loculations is not adequately appreciated. Since the successful management of a patient with a brain abscess often depends on early clinical suspicion, my comments will be directed to the clinical setting that should trigger suspicion.

The "Composite Symptoms" Approach

Any attempt to describe a typical brain abscess patient would not produce a very exact picture. Yet virtually every article dealing with the subject of brain abscess that does describe symptoms and signs simply lists those clinical features encountered, in order of frequency. The symptoms and signs are nonspecific and it is difficult to extract the information needed for increased clinical suspicion. I propose that patients with brain abscesses present basically in one of several recognizable syndromes, and although these syndromes are not specific for abscess alone, they are helpful to keep in mind because these syndromes emphasize the ominous and precarious nature of the intracranial mass dynamics. Before describing these four syndromes, we should review the reasons why brain abscesses present so bewildering an array of symptoms and signs.

Variation in Clinical Symptoms and Signs

The host-organism interaction may be so indolent as to cause a slowly emerging, focal dystrophic calcification within the brain. Conversely, this interaction may be so fulminant as to cause only a small nidus of "infection" but with an enormous surrounding edematous brain tissue response. The edematous brain, confined within the rigid skull, then becomes the lethal component causing increased intracranial pressure, decreased cerebral blood flow and herniation. Or, the host-organism interaction may provoke a thick-walled, collagenous capsule that in itself becomes important because of its tumorous size.

Brain abscesses may be unicentric or multifocal. The vast majority (90 percent) of abscesses resulting from pericranial infection (sinusitis, mastoiditis, otitis media) are unicentric, but many of the hematogenous-borne brain abscesses (for example, those from bacterial endocarditis, pulmonary infection and osteomyelitis) are multifocal, especially in patients with cyanotic congenital heart disease.[2]

Obviously, some clinical symptoms or signs result from the particular location of the abscess or abscesses in the brain. A pontine abscess will cause specific brain stem symptoms and signs, distinguishable from an abscess in the occipital lobe. What is less obvious but of crucial importance in successfully managing these patients is the array of "neighborhood" complications that can arise. The pontine abscess can bulge posteriorly, block the aqueduct of Sylvius acutely at some time, and cause obstructive hydrocephalus requiring urgent surgical venting of the ventricular system. The occipital lobe abscess could rupture, or leak, into the ventricular system, causing life-threatening ventriculitis (or ependymitis) and perhaps necessitating intraventricular chemotherapy or ventricular drainage or more direct and rapid abscess drainage. Or the occipital lobe abscess could involve the transverse sinus, causing a spreading thrombophlebitis and necessitating very attentive treatment of the associated cerebral edema and seizures.

Many other subtleties could be discussed regarding varied pathophysiological features. However, in general, the clinical syndrome will be caused by the forces involved in the host-organism interaction, the number and size and distribution of abscess, the specific brain structures involved and the "neighborhood" anatomy disturbances involving cisterns, ventricles, dural venous sinuses and the like.

Brain Abscess: Four Basic Clinical Syndromes

Since brain abscesses cause damage by altering intracranial mass dynamics or by destroying the brain in a necrotizing fashion, four syndromes have been formulated that depict most of the clinical features of patients with such lesions. A review of charts from 24 patients with proven brain abscess (Table 1) treated in the past ten years at UCLA Medical Center (10 patients), Harbor General Hospital (5 patients) or the Wadsworth Veterans Hospital (9 patients) serves to emphasize four distinct syndromes of brain abscess and to place in clearer perspective problems in disease recognition and in adequate surgical management.

TABLE 1.—*Data on Patients with Brain Abscess Classified by Four Types of Clinical Syndromes*

Patient	Age (years)	Abscess Location	Initial Suspected Diagnosis	Outcome	Cause of Death	Worsened by LP?	Origin of Infection, Predisposing Factor, Underlying Disease	Organism from Abscess	Antibiotic Therapy	Surgical Therapy
TYPE I: RAPID FOCAL MASS EXPANSION										
1	10	Brain stem	Brain abscess	Died	Inc. abscess drainage	No	Cyanotic congenital heart disease	Peptostreptococcus	Multiple	Suboccipital craniectomy; aspiration*
2	35	Right frontal	Brain abscess	Survived; residual seizures	..	No	Putrid pneumonia	Bacteroides	Penicillin	Burr hole; aspiration*; catheter in place
3	47	Left temporo-parietal	Metastatic Ca	Survived; residual dysphasia	..	Probably	Bronchiectasis; pneumonia	Fusobacterium fusiforme	Chloramphenicol, Lincomycin	Burr hole; aspiration*
4	59	Right frontal left parietal	Metastatic Ca	Died; CNS function improving	G.I. bleeding	No	Bronchitis, empyema	Anaerobic streptococci	Penicillin	Burr hole; aspiration; right frontal and left parietal craniotomy; excision
5	1½	Right fronto-parietal	Brain abscess	Survived; no residual	..	No	Cyanotic congenital heart disease	Bacteroides fragilis Anaerobic streptococci	Methicillin, Chloramphenicol	Burr hole; aspiration
6	26	Right thalamus	Intracerebral hematoma	Died	Sepsis w/bleeding into abscess cavity	Possibly	Pneumonia; cirrhosis; steroid therapy; ?DIC	"Hemophilus-like" organism	Penicillin, Cephalothin	Stereotaxic biopsy; aspiration*
7	45	Left temporal	Brain abscess	Survived; no residual	..	No	Chronic otitis media	Paracolon species	Multiple	Burr hole; aspiration*; catheter in place
8	34	Right temporal	Brain abscess	Survived; no residual	..	No	Chronic otitis media	Anaerobes not fully characterized	Penicillin	Burr hole; aspiration
9	6	Right temporal parietal	Brain abscess	Died	Cerebral edema	Probably	Cyanotic congenital heart disease	Sterile culture	Chloramphenicol, Cephalothin	Burr hole; drainage
10	35	Left parietal	Glioma vs. hematoma	Survived; no residual	..	Yes, major herniation	None found	Microaerophilic streptococci	Penicillin, Chloramphenicol	Craniotomy; drainage; re-aspiration
TYPE II: INTRACRANIAL HYPERTENSION										
11	47	Right frontal	Meningitis	Survived; severe neurological deficit	..	Possibly	Post-op craniotomy	Sterile culture; CSF with Gram (+) cocci on smear	Methicillin, Penicillin, Gentamicin	Burr hole; drainage
12	33	Left temporal	CNS disease of unknown etiology	Died	Rapid herniation 6 hours post admission	LP not done	Severe chronic gingival infections	Culture report lost	None. Died before Rx started	None. Advanced too rapidly; Angiogram—"carotid-stop"
13	38	Left occipital	?Migraine ?glioma ?meningitis	Died	Herniation 2° LP and missed abscess	Yes, major herniation	None found	E. coli	Multiple	Burr hole; aspiration
14	20	Left frontal	Brain abscess	Survived; no residual	..	LP not done	Prior gun shot wound to head	Hemophilus sp.	Ampicillin, Cephalothin	Burr hole; drainage; craniotomy with total excision
15	34	Right frontal	Brain abscess	Survived; no residual	..	LP not done	Pansinusitis	Microaerophilic streptococci	Penicillin	Burr hole; aspiration; frontal sinus drainage
16	39	Right cerebellar hemisphere	Brain abscess	Survived; no residual	..	No	Chronic mastoiditis	Proteus sp.	Ampicillin, Chloramphenicol	Burr hole; drainage
17	21	Left temporal	Brain abscess	Survived; no residual	..	No	Chronic mastoiditis	Proteus sp.	Ampicillin, Chloramphenicol, Methicillin	Burr hole; drainage
18	15	Right occipital	Brain abscess	Survived; no residual	..	No	SBE; rheumatic mitral stenosis	Staphylococcus aureus	Nafcillin, Dicloxacillin	Craniectomy; catheter drainage*
TYPE III: DIFFUSE DESTRUCTION										
19	34	Diffuse left hemisphere	Brain abscess	Died	Sepsis; cerebritis	No	SLE; septic arthritis; sepsis; steroids	Culture sterile; Gram (−) rod on smear in brain, blood, joint	Cephalothin	Stereotaxic biopsy; minimal fluid; no drainage
20	48	Diffuse bilateral	Brain abscess	Died	Diffuse cerebritis	No	Not found	Nocardia sp.	Multiple	Burr hole; aspiration
21	54	Diffuse, brain and meninges	Brain abscess	Died	Diffuse cerebritis	No	Not found	Actinomyces sp.	Penicillin, Chloramphenicol	None. Clinically and angiographically failed to "localize" lesion
TYPE IV: FOCAL NEUROLOGICAL DEFICIT										
22	61	Right occipital	Glioma vs. meningioma	Survived; no residual	..	Yes	Acute diverticulitis with prolonged fever	Beta streptococci	Penicillin	Burr hole; aspiration*; craniotomy with total excision
23	43	Left parasagittal parietal	Meningioma	Survived; no residual	..	No	Not found	Cryptococcal granuloma	Amphotericin B	Craniotomy with total excision
24	38	Left parietal	Glioma vs. meningioma	Survived; residual seizure	..	No	Old skull fracture; bone fragment in abscess	Staphylococcus aureus	Penicillin, Methicillin	Craniotomy with total excision

*Antibiotic irrigation into abscess cavity either at time of surgery and/or postoperatively.

Abbreviations LP = lumbar puncture Inc = incomplete CNS = central nervous system Ca = carcinoma DIC = disseminated intravascular coagulation CSF = cerebrospinal fluid SBE = subacute bacterial endocarditis SLE = systemic lupus erythematosus

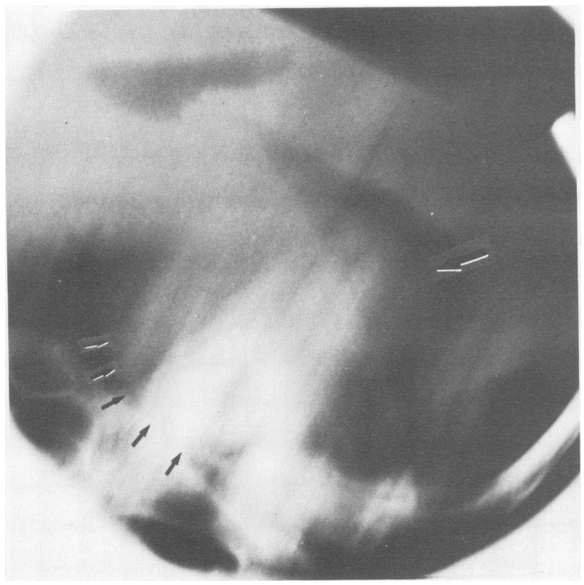

Figure 1.—Midline lateral tomographic view during pneumoencephalogram. Small arrows outline anterior border of pons against the clivus. Large arrow points to posterior aspect of abscess bulging into fourth ventricle.

These four syndromes undoubtedly do not depict all varieties of brain abscess presentation, but abstracting syndromes from clinical data may help physicians recognize disease processes earlier.

Type I abscess presentation (rapid focal mass expansion). Ten patients presented with the symptoms and signs of a rapidly progressive localized intracranial mass lesion. The rapidity of the neurologic progression was usually days to weeks, but in two instances the progression was over hours. Therefore, in terms of the temporal profile, these lesions behaved like malignant astrocytomas, metastatic neoplastic tumors or even spontaneous intracerebral hematomas. Localization to the correct lobe of the cerebral hemispheres, cerebellum or brain stem in the posterior fossa on clinical criteria alone was possible and usually accurate.

In this group, a correct clinical diagnosis was made early in six of the ten patients because of associated known facts (three children with cyanotic congenital heart disease, two adults with chronic otitis media and purulent drainage and one adult with recent cavitating bacterial pneumonia). Despite the fact that these patients presented with a rapidly expanding mass syndrome, there was at least one lumbar puncture (LP) done on each patient in this group: one patient had a major uncal herniation syndrome 40 minutes after the first LP; one patient had accelerated neurological deterioration over three days coinciding with three daily LP's and one patient's hemiparesis worsened about three hours after an LP. Three patients died from complications related to the abscess.

One death occurred, in a ten-year-old with a brain stem abscess. This lesion was correctly diagnosed clinically, was subsequently localized with both pneumoencephalography and cerebral angiography (Figure 1) and was partially drained following surgical exploration of the posterior fossa (Figure 2). The patient showed significant and sustained neurologic improvement for two weeks, then rapidly deteriorated over a 24-hour period and died while plans were being made to return her to the operating room. On autopsy, large loculations of abscess more rostral in the brain stem that had not been drained by the first procedure were observed (Figure 3). Another example of a Type I lesion is described in the following case.

REPORT OF A CASE

A 35-year-old man, a heavy smoker, was admitted to hospital because of a three-week cough productive of thick, foul-smelling sputum and chest wall pain. Lobar and hilar infiltrates were seen on chest x-ray films. Soon after admission, a right hemiparesis, progressive dysphasia and right homonymous hemianopsia rapidly developed and, eventually, there were seizures and papilledema. The clinical suspicion was that the patient had a malignant pulmonary lesion with secondary pulmonary infection and brain metastasis. A positive brain scan and a cerebral angiogram showing a large avascular lesion were interpreted as supporting the original clinical diagnosis. Finally, after repeat cytological examinations of sputa failed to show malignant cells, and after bronchoscopic biopsy yielded only "inflammatory changes," burr hole exploration and abscess aspiration were done. Preoperatively, the patient was given penicillin G intravenously, 20 million units a day, and this was continued following operation. This patient had deteriorated during a period of three consecutive LP's. The patient made a good recovery except for mild dysphasia.

Type II abscess presentation (intracranial hypertension). Eight patients presented with symptoms and signs predominantly of neurological deterioration associated with intracranial hypertension. These patients complained of headache, nau-

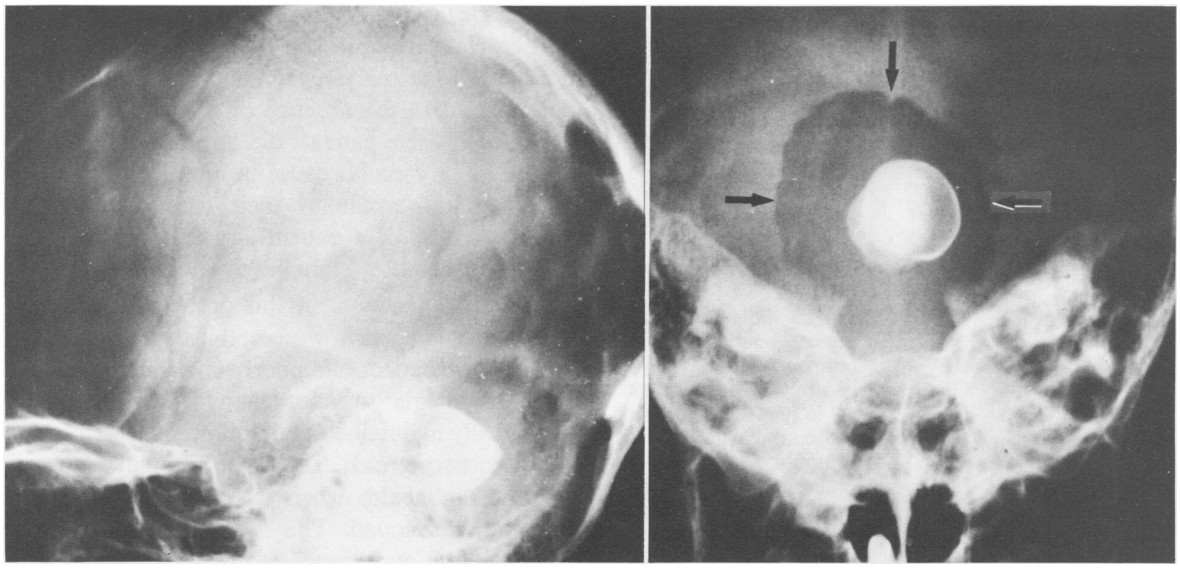

Figure 2.—Left, lateral plain skull x-ray film. Contrast material has been absorbed by cells lining the abscess cavity, therefore, contrast material outlines the size and shape of the abscess cavity on plain x-ray film. **Right,** Towne view plain x-ray film. Arrows point to margins of bone opening (suboccipital craniectomy) used for direct approach to abscess cavity in brain stem.

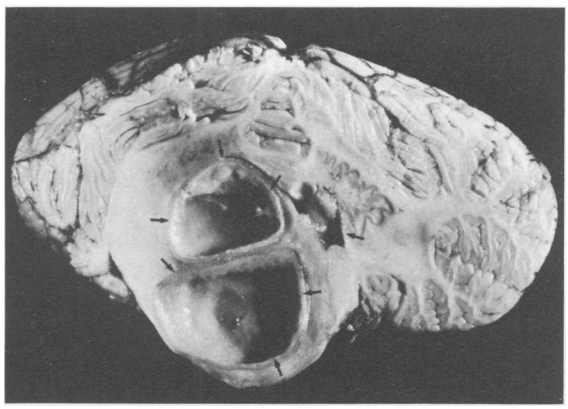

Figure 3.—Brain specimen obtained at autopsy. View of multiloculated abscess within the upper brain stem. Arrows point to thick-walled collagenous capsule surrounding contiguous abscess cavities.

sea, vomiting, obtundation, memory loss or some other defect in mental function and personality change. Papilledema was a commonly encountered sign. Some of these patients indeed had varying degrees of localizing or lateralizing neurologic deficits but their major clinical syndrome was that of increased intracranial pressure.

Keep in mind from my earlier comments that the increased intracranial pressure can result from many mechanisms: the lesion may be located so far frontally or occipitally that lateralizing internal capsule dysfunction is relatively insignificant as the abscess enlarges greatly; there may be multiple lesions; there may be widespread cerebritis; there may be a component of associated hydrocephalus; and thrombophlebitis of dural venous sinuses and cortical veins may be present.

In this group, an early correct diagnosis was made clinically in five of the eight patients because of associated known facts (two adults with chronically draining mastoiditis, one teenager with rheumatic mitral stenosis and infective endocarditis, one adult with frontal sinusitis and focal fluctuance and one adult who had received a gunshot wound in that area of the brain six years earlier). The other three patients were first considered to have glioma, mental deterioration of unknown cause, and meningitis. A lumbar puncture was done on five patients: one patient had an uncal herniation syndrome within two hours of the LP; and one patient's level of consciousness declined considerably over 24 hours following an LP.

There were two deaths in this group. One patient died from overwhelming mass effects. The patient with an uncal herniation following LP was the other patient in this group to die. He had at first improved, the lesion had been localized angiographically, but two attempts at burr hole aspiration had yielded only a small amount of purulent material (about 1 ml) plus clear ventricular fluid. Multiple complications then occurred (stress ulcers, metastatic renal and abdominal abscesses and intraperitoneal bleeding) and the patient died. At autopsy, an untreated 4 by 5 cm occipital lobe abscess was found with nearby needle tracks enter-

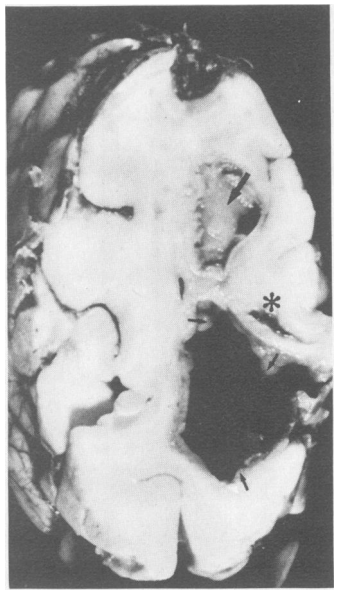

Figure 4.—Brain specimen obtained at autopsy. View of left occipital pole. The large arrow points to the abscess. Small arrows indicate inflammatory ependymal changes within the ventricle. The asterisk (*) is just above one of the cannula tracts. Cannula apparently entered the posterior horn of lateral ventricle but not the abscess.

ing the lateral ventricle (Figure 4). The abscess itself was in communication with the ventricular system and there was suppurative ependymitis. An example of a Type II lesion is illustrated in the following case.

REPORT OF A CASE

A 34-year-old man was admitted to hospital with a history of having "sinusitis" three months earlier, followed by progressive headache and more recently, confusion for two weeks before admission. On examination, a low grade fever (38°C, 100.4°F) and focal fluctuance and tenderness over the right forehead were noted. Only two abnormalities were found on neurologic examination: the patient was confused and there were two diopter papilledema. Plain x-ray studies showed frontal sinusitis and osteomyelitis. Cerebral angiography showed a right frontal avascular mass lesion. At surgical operation, a temporal burr hole was placed, the abscess aspirated and the frontal osteomyelitis was debrided. A catheter was left in the abscess cavity and intermittent irrigations and aspirations were done for six days. Penicillin G, 20 million units a day, was administered intravenously and continued for four weeks. The patient made a complete neurological recovery.

Type III abscess presentation (diffuse destruction). Three patients presented with the symptoms and signs of a diffuse, rapidly progressive, destructive brain process. The clinical progression evolved over days. The "destructive" component refers to the fact that these patients deteriorated neurologically out of proportion to their estimated intracranial pressure: two patients had no papilledema and one had only mild papilledema. They deteriorated in the absence of a brain herniation syndrome. These patients did not have any known reason for a vascular cause of their syndrome but the temporal profile of their deterioration was similar to that of a patient sustaining showers of multifocal cerebral emboli.

The three patients in this group all died and the correct diagnosis was established in each instance. One patient had poorly controlled systemic lupus erythematosus for many years and was chronically maintained on immunosuppressive levels of corticosteroids. The other two patients were in excellent health when overwhelming systemic infection developed. The duration of the illness from the first appearance of neurologic abnormalities to death was eight, ten and 24 days. Each patient had one lumbar puncture performed. There was no obvious deleterious effect of the LP but the patients had advanced neurologic deficits at the time of the study. An example of a Type III lesion is provided in the following case.

REPORT OF A CASE

A 54-year-old man was healthy and working as a landscape gardener when he developed multiple, painful pustules on his finger tips six weeks before admission. Similar painful lesions developed on his toes and then his calf ten days before admission. Profound anorexia developed. On admission, he appeared cachectic, febrile (38.4°C, 101.2°F) with multiple fluctuant lesions, both subcutaneous and intramuscular over his body. Mental activity appeared to have slowed and a mild left hemiparesis was noted. Extensive incisions and drainage were done on the peripheral abscesses; the material was foul-smelling and eventually Actinomyces was cultured. Despite vigorous local wound care and massive antibiotic therapy including penicillin and chloramphenicol, he steadily deteriorated neurologically. Over the next seven days, he became comatose with only lower brain stem function preserved. Results of LP showed nine leukocytes per cu mm (three neutrophils and six lymphocytes) and negative culture. Brain scan was diffusely abnormal over the right hemisphere and bilateral carotid angiography showed some vascular spasm with no localized mass lesion. The patient died ten days after the onset of his hemiparesis. At autopsy, numerous cerebral and meningeal abscesses were seen of

varying size and age, with widespread edema surrounding the lesions. There was no evidence of infective endocarditis.

Type IV abscess presentation (focal neurologic deficit). Three patients presented with the symptoms and signs of focal neurologic deficit. The temporal profile was that of a very slowly expanding lesion. In each case, the major clinical diagnosis was that of a meningioma and in two patients the differential diagnosis included a slowly growing benign glioma. The diagnosis of meningioma (versus glioma) was believed to be correct even after cerebral angiographic studies. In one patient there was transiently exacerbated left hemiparesis following a pneumoencephalogram. In the other two patients there were no detectable consequences of lumbar puncture. In another patient, a diagnosis of abscess was not considered despite the history of an earlier compound, comminuted skull fracture overlying the angiographically demonstrated mass. However, the fracture had occurred 14 years earlier. At operation, a bone fragment was found within one of four contiguous but loculated abscess cavities. An example of a Type IV lesion is provided in the following case.

REPORT OF A CASE

A 61-year-old man complained of visual disturbances for about two months. The only abnormality on examination was a complete left homonymous hemianopsia. Approximately two weeks before the onset of visual symptoms, the patient had an episode of diverticulitis with fever. Although he first became afebrile after treatment with antibiotics, there were several periods of recurrent febrile episodes requiring additional courses of antibiotic therapy. Angiography and pneumoencephalography showed a right occipital and posterior temporal mass. Needle biopsy through a burr hole led to the correct diagnosis of brain abscess and the initial therapy was direct aspiration and intravenously administered penicillin. Two weeks later, the abscess was totally excised. The patient then recovered gradually but had a sustained homonymous hemianopsia.

Recapitulation and Formulation of Diagnostic Evaluation

I have emphasized that the patient with a brain abscess does not present with a problem of the diagnostic work-up of a brain abscess. These patients present with clinical problems predominantly caused by major alterations of intracranial mass dynamics. Perhaps in one-half of all such cases there is antecedent history or physical signs that lead to a realistic consideration of the possibility of a brain abscess. Usually "brain abscess" at best is included in a working differential diagnosis after a careful history and physical examination.

Since brain abscesses most often cause intracranial hypertension and brain shifts (incipient herniations), it is axiomatic that the entire patient work-up and therapy be planned with this in mind. Several key points should be emphasized.

A lumbar puncture is extremely hazardous and does not yield critical information. A brain abscess uncommonly presents as "meningitis," so theoretically LP's should be quite uncommon in these patients. However, clinical surveys repeatedly show frequent LP catastrophes in brain abscess patients.[1,3,4] Even when the LP is done with a relatively small-bore needle and only 1 to 3 ml of CSF is intentionally withdrawn, the recently needled dura-arachnoid opening may persist because of the increased intracranial pressure and a slow unseen CSF leak may continue into deep paraspinous musculature. Thus, the major herniation following LP may occur minutes to hours after the procedure.

In the infrequent patient in whom meningitis was suspected but only normal CSF was found (or CSF changes were inadequate to correlate with symptoms and signs), the physician should be especially alert for any subsequent neurologic changes. (The rare abscess leaking into ventricle or subarachnoid space will obviously still remain a consultant's challenge.) Therefore, even with suspected "intracranial infection" there should not be a conditioned reflex to perform an LP. An LP is urgently needed in a patient with meningitis but is hazardous in a patient with brain abscess (and in subdural empyema).

Those maneuvers that cause hypercarbia or potential hypoxia (sedating patients for headache or too much premedication for diagnostic studies) are hazardous to the brain because of deleterious effects on cerebral blood flow. Any Valsalva maneuver is hazardous because of decreased venous drainage and subsequently increased intracranial pressure. Valsalva can occur with a sedated (or neurologically obtunded) patient developing obstructed breathing or with inattention to straining caused by constipated stool. Excessive intravenous hydration can abruptly worsen the associated cerebral edema.

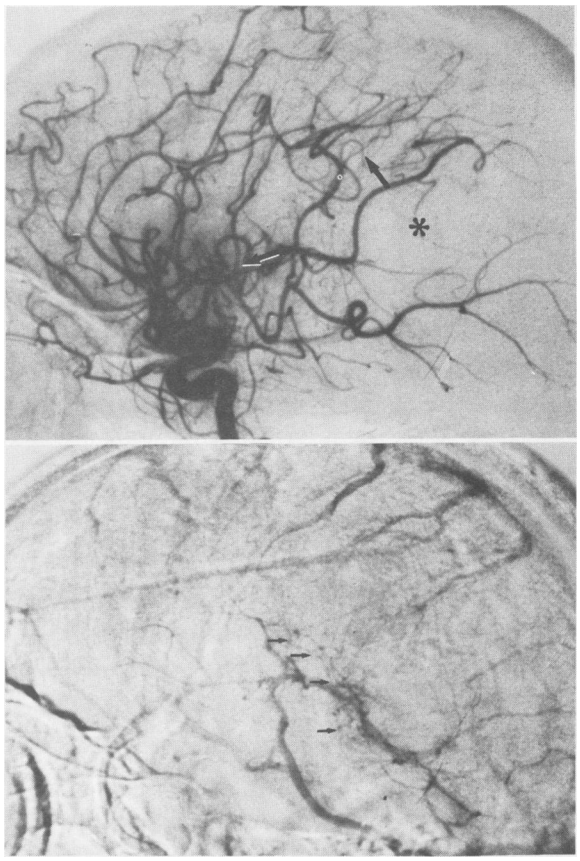

Figure 5.—Upper, lateral view, arterial phase of a selective internal carotid angiogram. Asterisk (*) is in the center of an avascular mass. The upper large arrow indicates displacement forward of parietal lobe vessels. Lower arrow indicates temporal lobe effect in that the middle cerebral artery is displaced forward. **Lower,** lateral view, venous phase of same study depicted in upper frame. Arrows point to abnormal subependymal and deep white matter veins. Neuroradiological impression was a large occipital lobe mass, "probably a primary glioma."

In summary, the diagnostic evaluation must begin with disease recognition and must continue with the patient's safety assured by an understanding of those maneuvers constituting a grave danger to the intracranial hypertension. If the patient's clinical course is not rapidly worsening, brain scan and electroencephalogram are two safe studies that may often provide useful information. Cerebral angiography must be done at some point for a more precise understanding of the lesion (Figure 5).

If the patient's clinical condition is precarious, angiography should be the first diagnostic procedure to be done when the diagnosis of brain abscess is considered. Depending on the clinical symptoms and signs, the angiographic study may have to be performed through both internal carotid arteries as well as through the vertebral system. Therefore, at all three hospitals reviewed for this symposium, the route of choice for cerebral angiography has been transfemoral for the past ten years. Once the angiographic catheter has been passed into the thoracic aorta, it can be successfully guided into the orifices of any major cerebral artery. (The specific and nonspecific findings on EEG, brain scan and cerebral angiography will not be discussed. This subject is not as important as improving disease recognition and suspicion.)

Microbial Flora

THOMAS T. YOSHIKAWA, MD: The microbial flora of brain abscess has been traditionally reported as involving a variety of organisms with a predominance of aerobic streptococci and coagulase-positive staphylococci. However, with the recent development of more sophisticated anaerobic bacteriological techniques, the role of anaerobes in brain abscess has become increasingly important. Before discussing in detail the specific microbial flora isolated from brain abscesses, a review should be made of the various factors which may be relevant in determining the types of microorganisms often recovered from this infection.

Four determinants appear to be most important in the ultimate microbial flora of brain abscess:

1. The primary source of infection or predisposing factors to brain abscess.
2. The age of the patient.
3. The patient's basic underlying disease or immune status.
4. Previous use of antibiotics.

Primary source of infection or predisposing factors

Ear, mastoid and sinus infections. Chronic otitis media or mastoiditis along with paranasal sinusitis are among the most common sources of infections preceding the development of brain abscess. The pathogenesis of brain abscess from these infected sites is usually by direct extension from the primary infected site to the brain or by retrograde thrombophlebitis via various venous channels connecting either the ear structures or sinuses to cerebral cortex.[5] Although data obtained by careful anaerobic isolation techniques on the microbial flora of chronic ear infection are not available, by inference, it would be anticipated that anaerobic bacteria may play a more significant role in chronic ear infections. One-half of Heineman and

Braude's[6] cases of anaerobic brain abscess were associated with ear infections and in each instance anaerobes were isolated from the abscess fluid. Data from patients with chronic sinusitis has been more readily available.

A recent study of 83 patients with paranasal sinus infections[7] showed anaerobes to be present in 52 percent of the cases while aerobes were present in 43 percent with mixed infections commonly found. Of the 28 specimens (30 percent of cases) with heavy growth of organisms, 23 were due to anaerobes alone and only three due to aerobes alone while in two instances, mixed anaerobic and aerobic flora were found. The predominant anaerobes were streptococci (anaerobic or microaerophilic). However, Bacteroides species were recovered in nine instances as a pure heavy growth, four being Bacteroides fragilis. Although not recovered in heavy growth, Staphylococcus aureus and Streptococcus viridans were the most common aerobes isolated.

Metastatic. Hematogenous or metastatic spread of infection from distant foci has been, in many reported series, the most common cause of brain abscess. Lower respiratory tract infection, especially chronic empyema, lung abscess and bronchiectasis, is commonly found. Organisms frequently associated with these infections have been anaerobic and microaerophilic streptococci, Fusobacterium, staphylococci, Klebsiella, pneumococci and occasionally Actinomyces and Nocardia. Other peripheral infections associated with brain abscess have been cellulitis, postoperative intra-abdominal and wound infections, osteomyelitis and pelvic inflammatory disease. Additionally, it should be remembered that infective endocarditis is not an uncommon cause of brain abscess. In fact, it is only after the diagnosis of a brain abscess is made that some cases of endocarditis are suspected. With infective endocarditis, the cerebral abscesses tend to be multiple, are usually relatively small in size and often associated with a mild to moderate degree of leptomeningitis. The presence of a coagulase-positive staphylococcal brain abscess or meningitis in the absence of cranial injury or infected peripheral foci should make one strongly suspect infective endocarditis, especially if the patient is young and has a history of drug abuse.

Cranial trauma or surgery. Direct head trauma or penetrating wounds to the skull can lead to brain abscess either by direct implantation of micro-organisms into cerebral tissue or by extension of secondarily infected scalp, bone flap or cranial osteomyelitis. Similarly, surgical craniotomy can lead to brain abscess. The most common bacteria associated with these injuries is Staphylococcus aureus. Occasionally aerobic Gram-negative bacilli, especially Pseudomonas aerúginosa, can be found in these infections.

Congenital heart disease with right-to-left shunt. Cyanotic heart disease is a frequent cause of brain abscess. The postulate is that the usual "normal" bacteremia one encounters daily is generally, in part, filtered out of the circulation by the lungs. However, with a right-to-left shunt, bacteremia bypasses the lung and can reach peripheral sites, including the brain. The microbial flora will depend on the type of peripheral infection and bacteremia involved. The brain may be prone to infection in these patients because of polycythemia and resultant intravascular thrombosis and infarction. The thrombosis may be from peripheral vein clots reaching the cerebral circulation as a paradoxical embolus, or from *in situ* thrombosis or embolism from cardiac chambers.[8]

Age of patient. The age of the patient is a determining factor largely in the pediatric group. Neonatal infections are generally due to Gram-negative bacilli and Staphylococcus aureus. Children up to the age of ten years will often become infected with Hemophilus influenza, commonly in the upper respiratory tract, ears and sinuses. At the other end of the age spectrum, older patients may be more prone to Gram-negative and staphylococcal infections, perhaps due to frequent hospital admissions with greater risk to hospital-acquired infections or associated underlying disease.

Underlying disease or immune status. Certain disease states are commonly associated with particular types of infecting organisms. A few examples would be sickle cell disease with Salmonella or pneumococci; alcoholic liver disease with pneumococci, Klebsiella or E. coli; prosthesis (heart valves, ventriculo-jugular shunts and the like) with coagulase-negative or -positive staphylococci; heroin addiction with Staphylococcus aureus, Candida or Gram-negative bacilli, especially Pseudomonas; and burn patients with infections due to Pseudomonas aeruginosa. Additionally, patients with lymphoma, leukemia or cancer or abnormal immune defense mechanisms secondary to drug therapy (steroids, anti-neoplastic agents) can develop brain abscess due to unusual micro-organisms.

In a recent report by Chernik et al[9] describing central nervous system infections in cancer patients, 39 patients had brain abscess; almost one-half of these were due to Gram-negative bacilli and one-third were caused by fungi (Aspergillus, Mucor, Candida and Nocardia). Two patients had brain abscess due to Toxoplasma gondii.

Previous use of antibiotics. Not uncommonly, patients are often given antibiotics for various types of infections before the clinical onset of brain abscess. Under these conditions, it is predictably more difficult to anticipate the type of microbial flora that might be found at the time brain abscess is diagnosed. The usual aerobic and anaerobic flora of the primary disease or predisposing factors to brain abscess may be replaced by other less commonly found microorganisms. This frequently occurs in the hospital patient receiving antibiotics where the usual mouth and respiratory tract microbial flora is replaced by Gram-negative bacilli or staphylococci.

Despite the emphasis on the four major determinants of the microbial flora of brain abscess, most centers reporting their experiences with this disease have consistently demonstrated the streptococci and staphylococci as the most common pathogens. However, the majority of these reports failed to utilize careful anaerobic isolation techniques to identify the bacteriology of brain abscess.

Heineman and Braude[6] provided a major breakthrough in this regard by carefully studying 18 cases of brain abscess not associated with cranial trauma or congenital heart disease. Using careful aerobic and anaerobic techniques, they demonstrated some interesting data. Aerobic cultures yielded organisms in only six instances with 12 patients having "sterile" brain abscess cultures. However, anaerobic cultures were sterile in only three instances. Anaerobic or microaerophilic streptococci comprised the majority of total isolates but Bacteroides were recovered in seven instances, three due to Bacteroides fragilis.

Since then, other reports have reaffirmed the role of anaerobes in brain abscess.[10,11] Thus, the so-called "sterile" cultures reported in brain abscess may indeed be in part due to the failure of recovering anaerobes. Anaerobes are fastidious microorganisms which survive only under conditions of low oxidation-reduction potential (oxygen-free environment). The collection of the brain abscess material in oxygen-free transport containers is extremely important. Failure to adhere to this practice will result in poor yield of anaerobes regardless of whatever sophisticated anaerobic culture method is used. Although there are some differences in the type of anaerobic culture techniques used by various centers, the Infectious Disease Research Laboratory at Harbor General Hospital has adopted the Virginia Polytechnic Institute method.[12] Details of this method are beyond the scope of our discussion. However, it is hoped that most hospital clinical microbiology laboratories will eventually use some acceptable form of anaerobic bacteriological technique. The clinical relevance of anaerobes in brain abscess will be discussed further under antibiotic therapy.

Antibiotic Therapy

Once the diagnosis of brain abscess has been established clinically, systemic antibiotic therapy should be administered before surgical drainage unless surgical operation is contemplated in the immediate future. Although several reports have presumed that the "sterile" cultures obtained from brain abscesses may have been due to prior antibiotic therapy, there have been no conclusive data to confirm this. Indeed, a recent careful study of six consecutive patients with brain abscesses treated with systemic antibiotics showed that organisms could be recovered from brain abscesses aspirated in all patients.[13] This occurred despite therapeutic concentrations of antibiotics in five of the six brain abscess aspirates. Again, the "sterile" cultures reported by other investigators may be related to the failure of isolating anaerobic bacteria. The importance of initiating systemic antimicrobial therapy early is two-fold. First, the associated cerebritis with brain abscess can only be effectively managed by antibiotic therapy. Second, local tissue contamination and possible bacteremia during surgical operation may be minimized with preoperative chemotherapy.

In determining the appropriate antibiotic before surgical drainage, the physician should be aware of the four determinants previously discussed and select the drug according to the microorganism most likely to be found. Generally speaking, most brain abscesses will have organisms sensitive to penicillin. In the absence of clinical clues as to the most likely infecting agent, penicillin G would be the drug of choice and should be administered intravenously in four to six divided doses totalling twenty million units a day. If staphylococcus is suspected, a penicillinase resistant penicillin, such as methicillin, should be added. If the patient has a

definite penicillin allergy chloramphenicol should be substituted for penicillin in a dose of 4 grams a day administered intravenously. The cephalosporins, especially cephalothin (Keflin®) and clindamycin (Cleocin®) do not cross the blood-brain barrier very well and, therefore, are not recommended.

The single most important diagnostic tool available in making a decision concerning antibiotic therapy is the Gram stain. At the time of surgical drainage of the brain abscess, the abscess fluid must be Gram stained. The presence of thin nonpleomorphic Gram-negative bacilli suggests Bacteroides, and the possibility of B. fragilis cannot be excluded. This latter organism is resistant to penicillin[14] and over one-half of the strains are not susceptible to tetracycline.[15] Chloramphenicol would be the drug of choice in the initial therapy before sensitivity data are available in this situation. Organisms which are Gram-positive branching rods might suggest Actinomyces or Nocardia, the latter often being weakly acid-fast and requiring sulfonamide therapy while the former would be best treated with penicillin. Large Gram-positive cocci most often are staphylococci and methicillin, or nafcillin would be indicated. Therefore, the Gram stain is extremely helpful in determining initial antibiotic therapy before culture results. Once the culture data are available, necessary adjustments in chemotherapy can be made. Brain abscess fluid must be cultured aerobically and anaerobically. Again, transport of the material in oxygen-free containers is extremely important. Cultures for fungi should also be obtained.

Despite the importance of antibiotic therapy, it should be emphasized that a cure for brain abscess (like any other abscess) can only be achieved by concomitant adequate surgical drainage. This therapeutic aspect will be discussed by Dr. Goodman. Additionally, it should be remembered that the primary foci of infection must also be adequately treated (such as drainage of infected sinuses, mastoidectomy, drainage of empyema and removal of infected prosthetic devices). One last comment on therapy pertains to the intracavitary local instillation of antibiotics. Mechanical irrigation undoubtedly aids in removing necrotic and infected material, but the direct bactericidal effect of local antibiotics remains to be proven.

Surgical Therapy

DR GOODMAN: There are two surgical approaches available in treating brain abscess: drainage or excision. Each approach has a number of variations. In addition, there are several adjunctive measures that can be used to supplement surgical therapy. Finally, important clinical determinants of surgical therapy are the status of the patient and the manner in which the diagnosis of brain abscess was made (for example, was the diagnosis made preoperatively or was the diagnosis made unexpectedly in the operating room?).

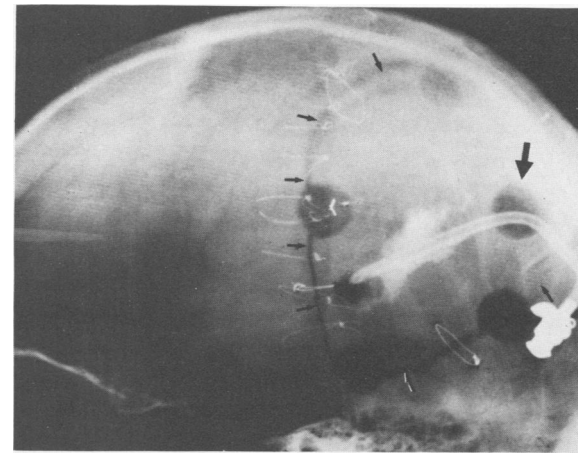

Figure 6.—Immediate post-operative skull x-ray film showing strategic placement of a burr hole in patient depicted in Figure 5. Small arrows outline craniotomy used to approach occipital mass. Wire skin sutures are still in place. After the abscess was encountered, the bone flap was secured to the skull and a burr hole was centrally placed (large arrow) as close as possible to abscess. A catheter can be seen passing through burr hole into abscess cavity. Contrast material can be seen in cavity.

Drainage of the abscess means drainage of necrotic and purulent material externally. A burr hole is strategically placed which provides: (1) the shortest distance between dura and the depth of abscess; (2) a safe trajectory between dura and abscess that does not traverse crucial structures whether neural (for example, motor cortex), vascular, or ventricular and (3) a route not passing through infected bone, paranasal sinuses, or other skull infection. If the first burr hole does not satisfy all these requirements, a second is placed (Figure 6). Through the burr hole a catheter can be placed, providing a route for aspiration and irrigation. Or, the burr hole can be used intermittently for brief, repetitive reintroduction of an aspirating or irrigating cannula. Cannula placement can be done by experienced "dead reckoning" or with fluoroscopic aid, or with full stereotaxic support equipment. Often a catheter is used for three to five days and thereafter the abscess is aspirated as needed with a cannula. Drainage

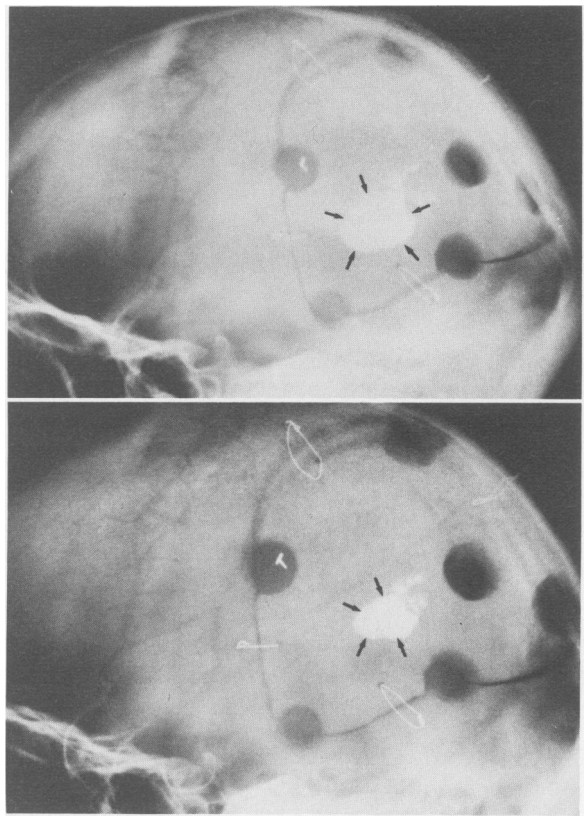

Figure 7.—Upper, abscess cavity outlined by a radiopaque marker approximately 12 days following surgery. Notice the more spherical distribution of the marker compared to Figure 6, and the two irregular posteriorly pointing extensions of the cavity. **Lower,** same patient six months following surgery. The general shape of the abscess cavity has remained unchanged but there has been substantial reduction in the volume of the cavity.

requires that there be a precise understanding of the abscess size and shape so that the most basic judgment can be made daily (such as is the abscess getting bigger or smaller?). Air can be injected into the cavity so that it can be visualized on plain x-ray films. Microbarium sulfate can be injected, and *if* it becomes evenly distributed in the cavity, and *if* it is taken up by the glial lining cells, a convenient radiopaque marker may be visualized (Figure 7). Finally, angiographic, pneumoencephalographic or ventriculographic techniques can be used to delineate the abscess size.

Drainage techniques are simple. The burr hole can be placed with just local anesthesia, and repetitive manipulation of the abscess cavity thereafter is a ward procedure. The major disadvantage is that daughter abscesses may be undetected and untreated. The condition of a patient could precipitously worsen from a daughter abscess spatially related to the main abscess but unrelieved by the percutaneous techniques directed to the main abscess. Intracavitary air or microbarium sulfate may simply lull the physician into assuming gains are being made while daughter abscesses are worsening. Considerable skill and clinical acumen are needed in correlating the clinical course with the neuroanatomic geometric problem.

Excision, or "radical extirpation" refers to complete surgical removal of the abscess. To the extent that there is an organized capsule there will be a readily identifiable brain-abscess interface permitting abscess removal with a minimum of damage to surrounding brain. Radical extirpation removes all daughter abscesses and, therefore, provides the lowest abscess recurrence rate. However, not all lesions can be treated this way. The abscess might be too hazardously deep (thalamic or brain stem) or the abscess might not be sufficiently localized and walled off. (A late complication of brain abscess is seizures. This complication is unaltered by radical extirpation.) Radical extirpation is often done as a secondary procedure after initial abscess drainage, with the initial procedure yielding benefits of organism identification, optimal chemotherapy, decreased mass size and neurologic improvement.

Adjunctive measures are used, as needed, to supplement surgical therapy when the intracranial mass effects and the degree of intracranial hypertension is life-threatening. A detailed discussion of these techniques is beyond the scope of this conference. The techniques that can be marshalled include controlled hyperventilation, acute or semichronic dehydration, steroid administration, hypothermia, "external" (skull) or "internal" (brain) decompression and ventricular drainage.

The clinical setting in which the diagnosis is made is probably the most important determinant of the surgical therapy employed. Patients presenting with Types I, II and III syndromes have rapidly progressive lesions, have ominous, decompensated intracranial mass dynamics and probably have less mature abscess capsules. These patients are most appropriately treated by abscess drainage techniques. Patients presenting with a Type IV syndrome could have primary radical extirpation of a favorable superficial lesion, but since the diagnosis was probably unanticipated, a period of abscess drainage would allow optimal chemotherapy to be started before abscess excision. We prefer, whenever possible and clinically reasonable, to first drain the abscess and then employ

a secondary procedure and radically extirpate the remaining abscess several days or weeks later.

Regardless of the modes of therapy or types of antibiotic used, the prognosis of patients with brain abscess is directly related to the neurological status of the patient when therapy is begun.[4] The major challenge in treating patients with brain abscess is physician education so that the clinical suspicion occurs earlier, patient evaluation is expedited quickly and safely, and antibiotic and surgical therapy are begun relatively early in the unfolding sequence of pathophysiological events.

Trade and Generic Names of Drugs

Cleocin®	clindamycin
Chloromycetin®	chloramphenicol
Keflin®	cephalothin
Garamycin®	gentamicin
Staphicillin®	methicillin
Lincocin®	lincomycin
Unipen®	nafcillin
Dynapen®, Pathocil®, Veracillin®	dicloxacillin
Fungizone®	amphotericin B
Polycillin®, Omnipen®, Totacillin®, Amcill®, Penbritin®, Principen®	ampicillin
Penicillin G	penicillin G

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Informed Consent in California

IF YOU'RE GOING TO GIVE medical therapy that amounts to anything, you'd better briefly but clearly mention the problems to the patient. For example, let's suppose that you have a glaucoma patient come in for the first time. You would, I think, say to him that the medical therapy of glaucoma does involve certain risks and certain problems . . . and obviously mention the effect of the drug on his vision and the possibility of allergies. Then note in your chart: "The medical therapy of glaucoma, including risks and alternatives, was discussed." And date it and sign it. It is important to know that juries believe almost everything that is written in a chart and almost nothing that is not written in a chart. So keep that clearly in mind . . .

—JEROME W. BETTMAN, MD, *Stanford, CA*
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