CNS Infections and Encephalitis

Benjamin M. Greenberg, MD, MHS
Department of Neurology and Neurotherapeutics
Department of Pediatrics
University of Texas Southwestern Medical Center
Children's Health

Disclosures

■ No disclosures specific to the content of this presentation.

Objectives

■ At the conclusion of the talk participants will be able to clinically distinguish between the various types of CNS infections.
■ At the conclusion of the talk participants will be able to recognize the most common pathogens and required treatments for various CNS Infections.
■ At the conclusion of the talk participants will be able to recognize the potential for autoimmune mimics of CNS infections.
Classification of CNS Infections

- Bacterial
- Viral
- Fungal
- Parasitic
- Spirochetes
- Mycobacterial

Anatomy and Clinical Presentation

- Meningitis
  - Pachymeningitis
  - Leptomeningeal meningitis
- Encephalitis
- Myelitis
- Abscesses

Clinical Spectrum of Infections

- Meningitis
  - Inflammation of Leptomeninges
  - Stiff Neck
  - Headache
  - Fever

- Meningencephalitis
  - Meningitis and Parenchymal Inflammation
  - Meningeal and Cerebral Dysfunction

- Encephalitis
  - Parenchymal Inflammation
  - Cerebral Dysfunction
Clinical Spectrum of Infections

- Meningitis
  - Inflammation of Leptomeninges
  - Stiff Neck
  - Headache
  - Fever

- Meningoencephalitis
  - Meningeal and Parenchymal Inflammation
  - Meningeal Irritation and Cerebral Dysfunction

- Encephalitis
  - Parenchymal Inflammation
  - Cerebral Dysfunction

Etiologies of Meningitis

- Meningitis
  - Infectious
  - Neoplastic
  - Toxic/Chemical

Infectious Meningitis
- Bacterial
- Viral
- Mycobacterial
- Spirochete
- Fungal
- Parasitic
### Clinical Findings in Bacterial Meningitis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Percent</th>
<th>Characteristic</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>77</td>
<td>Hemiparesis</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>87</td>
<td>Seizures</td>
<td></td>
</tr>
<tr>
<td>Neck Stiffness</td>
<td>Sx &lt; 24-hours</td>
<td><strong>TRIAD</strong></td>
<td>Otitis Media</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td>Pneumonia</td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>GCS less than 14</td>
<td>Focal Neuro</td>
<td>Avg SBP</td>
</tr>
<tr>
<td>CN Palsy</td>
<td>Avg DBP</td>
<td>Aphasia</td>
<td>Avg Age</td>
</tr>
</tbody>
</table>

Van de Beek, et. al. NEJM 2004
### Clinical Findings in Bacterial Meningitis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Percent</th>
<th>Characteristic</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>77</td>
<td>Hemiparesis</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>87</td>
<td>Seizures</td>
<td></td>
</tr>
<tr>
<td>Neck Stiffness</td>
<td>83</td>
<td>Sx &lt; 24 hours</td>
<td></td>
</tr>
<tr>
<td><strong>TRIAD</strong></td>
<td>44</td>
<td>Otitis Media</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td>Pneumonia</td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td></td>
<td>GCS less than 14</td>
<td></td>
</tr>
<tr>
<td>Focal Neuro</td>
<td></td>
<td>Avg SBP</td>
<td></td>
</tr>
<tr>
<td>CN Palsy</td>
<td></td>
<td>Avg DBP</td>
<td></td>
</tr>
<tr>
<td>Aphasia</td>
<td></td>
<td>Avg Age</td>
<td></td>
</tr>
</tbody>
</table>

Van de Beek, et al. NEJM 2004
Signs of Meningeal Irritation

Kernig's Sign
- Flexing the patient's leg 90 degrees then extending the patient's knee causes pain.

Brudzinski's Neck Sign
- flexion of the patient's neck causes flexion of the patient's hips and knees.

Kernig and Brudzinski are Worthless, Except for USMLE.

<table>
<thead>
<tr>
<th>Sign</th>
<th>No. of patients</th>
<th>With meningitis</th>
<th>Without meningitis</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kernig</td>
<td></td>
<td>13</td>
<td>16</td>
<td>29</td>
</tr>
<tr>
<td>Present</td>
<td>3</td>
<td>9</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>60</td>
<td>163</td>
<td>223</td>
<td></td>
</tr>
<tr>
<td>Brudzinski</td>
<td></td>
<td>12</td>
<td>13</td>
<td>25</td>
</tr>
<tr>
<td>Present</td>
<td>3</td>
<td>9</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>60</td>
<td>162</td>
<td>222</td>
<td></td>
</tr>
<tr>
<td>Nuchal rigidity</td>
<td></td>
<td>21</td>
<td>18</td>
<td>39</td>
</tr>
<tr>
<td>Present</td>
<td>21</td>
<td>18</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>96</td>
<td>148</td>
<td>244</td>
<td></td>
</tr>
</tbody>
</table>

Diagnostic Accuracy of Signs of Meningitis • CID 2002:35

How Do You Establish a Diagnosis of Meningitis

- Clinical History
- CSF
The Inherent Dilemma in Caring for Patients with Suspected Bacterial Meningitis

Diagnostic Testing  Therapeutic Interventions

The Need for Empiric Treatment

Acute Bacterial Meningitis CSF Findings

Reproduced from Table 58.3 in Mechanisms of Microbial Disease, 2nd edition, Schaechter, Medoff and Eisenstein, 1993.
Time to CSF Sterilization Post Antibiotics

Testing
- CSF Testing
- Microbiology

Treating
- Time to Antibiotics
- Avoiding Complications
To CT or Not To CT, That is the Question…..

- Why is this such a big issue?
  - Time to antibiotics is significantly associated with mortality
  - CSF profiles change with antibiotics
    - Loss of gram stain and culture within hours of antibiotic treatment
    - CSF maintains cell counts and protein for 24-48 hours
      - Differential and Glucose are first measures to change
  - Multiple reports (mainly in pediatrics literature) place the risk of herniation in patients with purulent meningitis at 4-6% (adult rates are significantly lower)
    - Of note, the CT scan was often "normal" in the cases that herniated!

A 6 year old boy is brought in to the emergency room by his parents with 3 hours of fever, headache, nausea, vomiting, lethargy and rash. On exam he is altered, somnolent with nuchal rigidity and no localizing signs on physical exam. Your next step should be
  a) CT scan of the head
  b) Lumbar puncture
  c) Blood cultures
  d) Antibiotics
  e) Steroids followed by antibiotics.

Acute Bacterial Meningitis

Practice Guidelines for the Management of Bacterial Meningitis

IDSA Guidelines

Practice Guidelines for Bacterial Meningitis • CID 2008; 37 (Suppl 3)
Acute Bacterial Meningitis

The Roid Controversy

Mortality Rates with Steroids
Hearing Loss

Acute Complications of Bacterial Meningitis
- Edema and herniation
- Hydrocephalus
- SIADH or CSW
- Sepsis
- Multiorgan failure

Sequelae of Bacterial Meningitis
- Mortality rates approaching 35% in some studies
- More than 50% of survivors have neuropsychological changes
A 20 year old pregnant woman, who owns a dog kennel and whom just returned from Malaysia presents to the emergency department in August with 3 days of headache, nausea, photophobia and neck stiffness. She has had fevers up to 102. GCS is 15. Neurologic exam is normal. CSF WBC is 250, 70% Lymphs, Glucose 60, Protein 100. The most likely diagnosis is

a. Listeria meningitis
b. Pneumococcal meningitis
c. Enteroviral meningitis
d. Rabies
e. Nipah virus

Acute Viral Meningitis
- Characterized by headache, mild meningismus, fever, and occasionally altered mental status
- Self limited, supportive care only
- Etiologies:
  - Non-polio Enteroviruses (85%)
    - Echovirus
    - Coxsackievirus
  - Arboviruses (5%)
    - Eastern Equine Encephalitis
    - Western Equine Encephalitis
    - St. Louis Encephalitis
  - Herpes family viruses (4%)
    - HSV-2

Acute Viral Encephalitis

<table>
<thead>
<tr>
<th>CSF Findings</th>
<th>Normal</th>
<th>Acute bacterial meningitis</th>
<th>Viral meningitis</th>
<th>TBC meningitis</th>
<th>HSV enceph.</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBCs (no./μl)</td>
<td>0-6</td>
<td>&gt;1000</td>
<td>100-1000</td>
<td>&gt;100000</td>
<td>&lt;100</td>
</tr>
<tr>
<td>% Neutrophils</td>
<td>0</td>
<td>&gt;50</td>
<td>&lt;10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total lymphocytes (no./μl)</td>
<td>0-2</td>
<td>&gt;10</td>
<td>&lt;10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>40-80</td>
<td>&lt;30</td>
<td>&lt; or = 40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein (mg/dl)</td>
<td>20-50</td>
<td>&gt;100</td>
<td>50-100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Reproduced from Table 58.3 in Mechanisms of Microbial Disease, 2nd edition, Schaechter, Medoff and Eisenstein, 1993.
Discerning Bacterial and Viral Meningitis

- Classically, CSF findings are helpful, but there can be overlap and several concerning possibilities
  - 'Partially treated' bacterial meningitis
  - Medico-legal issues – treating patients until cultures negative for 48 hours.
- Other possible markers
  - CSF IL-6, CSF IL-1beta, CSF lactic acid has > 90% sensitivity and specificity for discriminating bacterial and 'aseptic' meningitis.

Klimo, et. al., 2003

Other Causes of Meningitis

- Tuberculous Meningitis
  - Insidious onset
  - Headache, nausea, photophobia, fever
  - Causes a basilar meningitis
    - Secondary angiitis possible
  - Complications
    - Hydrocephalus
    - Stroke (obliterative endarteritis)
TB Meningitis
CSF Findings

<table>
<thead>
<tr>
<th></th>
<th>No infection</th>
<th>Acute bacterial meningitis</th>
<th>Viral meningitis</th>
<th>TB meningitis</th>
<th>HSV enceph.</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBCs (no./μl)</td>
<td>0-6</td>
<td>&gt;1000</td>
<td>100-500</td>
<td>50-500</td>
<td></td>
</tr>
<tr>
<td>% Neutrophils</td>
<td>0</td>
<td>&gt;50</td>
<td>&lt;10</td>
<td>&lt;50</td>
<td></td>
</tr>
<tr>
<td>RBCs (no./μl)</td>
<td>0-2</td>
<td>0-10</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>40-80</td>
<td>&lt;30</td>
<td>&lt; or = 40</td>
<td>&lt;40</td>
<td></td>
</tr>
<tr>
<td>Protein (mg/dl)</td>
<td>20-50</td>
<td>&gt;100</td>
<td>50-100</td>
<td>&gt;100</td>
<td></td>
</tr>
</tbody>
</table>

Reproduced from Table 58.3 in *Mechanisms of Microbial Disease, 2nd edition*, Schaechter, Medoff and Eisenstein, 1993.

Tuberculous Meningitis

- **Treatment**
  - Four drug TB therapy (INH, rifampin, pyrazinamide, ethambutal)
  - Consider moxifloxacin
  - Steroids can be used if focal edema is severe
  - Ventriculostomy for hydrocephalus
  - Surgical decompression of spinal lesions is often necessary
Fungal Meningoencephalitis

- More common in immunocompromised
- Common organisms
  - Cryptococcus neoformans
  - Coccidioides immitis
  - Candida albicans
  - Mucor
  - Aspergillus fumigatus
  - Histoplasma capsulatum
  - Blastomyces dermatitidis

Cryptococcus Meningoencephalitis

- Most common fungal infection of the CNS
  - Typically in immunocompromised host
  - Inhalation of spores from soil and pigeon excrement
  - Position head- and- shoulders ICP, and trunkal nerve palsies are common presentations
  - Can have a very bland presentation
  - CNS involves white and grey matter, with lymphocytic pleocytosis and elevated protein
  - India ink can be helpful with demonstrating organisms in CSF
  - Cryptococcal antigen is highly sensitive and specific
  - Hydrocephalus: chronic meningitis affecting basal leptomeninges may obstruct outflow of cerebrospinal fluid from the foramina of Luschka and Magendie, giving rise to hydrocephalus
- Antimicrobial treatment
  - Amphotericin B
  - Flucytosine
  - Fluconazole consolidation therapy

Clinical Spectrum of Infections

- Meningitis
  - Inflammation of leptomeninges
  - Stiff neck
  - High-grade fever
- Meningoencephalitis
  - Meningeal and parenchymal inflammation
  - Meningeal irritation and cerebral dysfunction
- Encephalitis
  - Parenchymal inflammation
  - Cerebral dysfunction
**Clinical Spectrum of Infections**

- **Meningitis**
  - Inflammation of Leptomeninges
  - Stiff Neck
  - Headache
  - Fever

- **Meningoencephalitis**
  - Meningeal and Parenchymal Inflammation
  - Meningeal Irritation and Cerebral Dysfunction

- **Encephalitis**
  - Parenchymal Inflammation
  - Cerebral Dysfunction

---

**ENCEPHALITIS**

**Encephalitis = Inflammation of the Brain**

*Clinically there is cerebral dysfunction and inflammation is evident by testing.*
Encephalitis

- Inflammation of the brain parenchyma
  - Confusion, delirium, focal neurologic deficits, seizures and coma
- Infectious Etiologies (sporadic versus epidemic)
  - Arboviruses
    - St. Louis encephalitis, eastern/western equine encephalitis, West Nile virus
  - Enteroviruses
    - Cytomegalovirus, Epstein Barr virus, varicella-zoster virus
  - Herpes Simplex Virus (typically HSV1)

TB Meningitis

CSF Findings

<table>
<thead>
<tr>
<th>WBCs (no./μl)</th>
<th>No infaction</th>
<th>Acute bacterial meningitis</th>
<th>Viral meningitis</th>
<th>TB meningitis</th>
<th>Herp enceph.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-6</td>
<td>&gt;1500</td>
<td>100-500</td>
<td>50-1000</td>
<td>0-1000</td>
</tr>
<tr>
<td>Neutrophils</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>&gt;50</td>
<td>&lt;10</td>
<td>&lt;50</td>
<td>&lt;50</td>
</tr>
<tr>
<td>Red blood cells (no./μl)</td>
<td>0-2</td>
<td>0-10</td>
<td>0.2</td>
<td>0.2</td>
<td>10-500</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>40-80</td>
<td>&lt;30</td>
<td>&lt; or = 40</td>
<td>&lt;40</td>
<td>&gt;30</td>
</tr>
<tr>
<td>Protein (mg/dl)</td>
<td>20-50</td>
<td>&gt;100</td>
<td>50-100</td>
<td>&gt;100</td>
<td>&gt;75</td>
</tr>
</tbody>
</table>

*Reproduced from Table 58.3 in Mechanisms of Microbial Disease, 2nd edition. Erskine & Moellering, 1996.

Typical case………………

23 year old male from the East Texas is transferred to Parkland MICU at 1 am after a 3 day hospitalization. He presented with fever and mental status changes. Lumbar puncture revealed 125 lymphocytes, no red blood cells, normal glucose and protein of 85. The patient deteriorated during the hospitalization, becoming obtunded, developing difficult to control seizures and ultimately requiring intubation.
What to do

- The HSV PCR comes back negative…

Encephalitis

- Infectious
- Immune Mediated
- Post Infectious/Autoimmune
- Toxic

Infectious Causes

- Viral
- Bacterial
- Fungal
- Rickettsial
- Mycobacterial
- Parasitic
Causes of Viral Encephalitis

- Herpes Simplex Virus (HSV-1, HSV-2)
- Varicella-Zoster Virus
- Cytomegalovirus
- Epstein-Barr Virus
- Human Herpes Virus 6 (HHV6)
- Adenovirus
- Influenza
- Enteroviruses
- Measles, Mumps Rubella
- Rabies
- Arboviruses
  - West Nile, St. Louis, Eastern Equine, Western Equine, Venezuelan Equine, Japanese B, Tick born
- Bunyavirus
- LaCrosse
- Reoviruses
  - Colorado Tick Fever

Herpes Simplex Encephalitis

- Herpes simplex virus type 1
  - Most commonly in children and young adults
  - Presents with alterations in mood, memory, and behavior, seizures common in subacute course
- Pathology
  - Encephalitis involves inferior and medial regions of temporal lobes and lateral gyrus of frontal lobes
  - Necrotizing and often hemorrhagic
  - Cowdry intranuclear viral inclusion bodies
- Treatment: IV Acyclovir must be started as soon as diagnosis is suspected

<table>
<thead>
<tr>
<th>Pretest Probability of HSV Enceph.</th>
<th>Posttest Prob. If CSF PCR +</th>
<th>Posttest Prob. If CSF PCR -</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low 5%</td>
<td>83.5%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Medium 35%</td>
<td>98%</td>
<td>2%</td>
</tr>
<tr>
<td>High 60%</td>
<td>99%</td>
<td>6%</td>
</tr>
</tbody>
</table>

*DeBiasi and Tyler 2004*
Immune Mediated Encephalitis

- ADEM
- Limbic Encephalitis
- Hashimoto Encephalopathy

Anti-NMDAR Ab

Anti-GAD Ab

Anti-VGKC Ab

Hashimoto Encephalopathy

Anti-NMDA Receptor Ab Mediated Encephalitis

- Can present with behavior changes, catatonia, coma, seizures and/or movement disorders
- One review of 577 patients had 212 under the age of 18 (36.7%)
- Treatment is with high dose corticosteroids, plasmaexchange, cyclophosphamide and/or rituximab


West Nile Virus

- Arbovirus in flavivirus family (Japanese encephalitis, St. Louis Encephalitis, yellow fever, dengue)
- Positive sense RNA virus
- Arbovirus
- First detected in the United States in 1999 in New York City.
  - Until that time, naturally acquired WNV had not been reported in the Western hemisphere.
  - Over 7 years the virus spread across the United States
  - In 2002 and 2003 WNV was responsible for the largest arboviral encephalitis outbreak in U.S. history.
  - 2-7% fatality rate (among CNS infections 12-15%, with 38% fatality in older patients).

2012 WNV Season
Epidemiology of WNV

- Almost all human infections are caused by the bite of an infected mosquito.
- Unique to WNV is its ability to infect a variety of mosquito species.
- Small numbers of cases have resulted from blood transfusions, organ transplants, maternal-fetal or maternal-child transmission.
- Since 2003 the number of transfusion related cases have dropped thanks to screening of donor units in pooled nucleic acid testing.

Epidemiology of WNV

- In the United States most cases occur between June and November (seasonal mosquito cycles)
- Wild birds are the natural reservoir, with Corvid species being the most important hosts.

Clinical Features of WNV

- Asymptomatic: 80%
- WNV Fever: 20%
- Meningitis
- Encephalitis
- Acute Flaccid Paralysis: Less Than 1%

Host Factors
West Nile Virus Fever

- Acute flu-like illness characterized by
  - Fatigue > 95%
  - Fever > 80%
  - Myalgia/weakness > 60%
  - Headache > 70%
  - Some patients may have GI symptoms, arthralgias, rash (macropapular rash often associated with dysesthesias), lymphadenopathy.
- Symptoms may persist for weeks to months.

WNV Meningitis

- In general, this meningitis appears similar to other viral meningitis with fever, headache and nuchal rigidity.
  - Neck pain, nausea, chills, myalgias in 60-80%
  - Back pain in 40%
- Relatively unique features include tremor (postural or kinetic) in up to 80% patients and myoclonus in up to 20%
  - Other causes of viral meningitis rarely cause hyperkinetic movement disorders, so these should be a red flag for WNV.
- Cranial nerve abnormalities are frequently observed in meningitis, but can occur late in the course.

WNV Encephalitis

- Almost always a meningoencephalitis
- Frequency of cases increases with age (median age 70). Very rare in children, unless immunocompromised.
- Patients experience
  - Fever 90-100%
  - Headache 50-100%
  - Altered mental status 50-100%
  - Movement disorders (tremor, myoclonus, parkinsonism) in up to 75%
  - Similar to other flavivirus encephalitides (i.e. JEV)
WNV Acute Flaccid Paralysis

- Patients present with acute rapidly progressive asymmetric flaccid paralysis with absent or decreased reflexes.
  - Close to 90% of patients nadir in under 24 hours!!!!
- Most commonly occurs in patients with meningoencephalitis, but can occur in isolation
- NOT GUILLAIN-BARRE
  - More like a true poliomyelitis with anterior horn cell dysfunction
  - NCS/EMG show dropped amplitudes, preserved conduction velocities and ultimately denervation patterns
- Patients describe aching pain in weak limbs, but sensory loss is rare.
  - Quadraparesis in 60%, monoparesis in 25%, mechanical ventilation in 35-55%

CSF and Neuroimaging

- Cell counts range from 20-300, but counts over 2000 have been reported
  - Mean counts in meningitis/encephalitis are about 200
    - Differential is variable with either a lymphocytic or PMN predominance (half of cases will have >200% PMNs)
    - PMNs persisting beyond 48 hr in viral meningitis or encephalitis is unusual and may be suggestive of WNV
    - Lymphocytes may be read out as 'reactive' or 'mollaret'.
- CSF protein is usually elevated and glucose is usually normal.
- MRIs are abnormal in approximately 1/3 cases
  - T2 signal change in deep gray structures
  - DWI bright/ADC dark changes in same areas can be seen
    - MRI can have prognostic value – normal>DWI>T2

Diagnostic Serology

- Diagnosis of both neurological and non-neurological WNV is serologically based.
- Serum PCR tests are used in blood bank screening, but clinically are not useful
  - CSF PCR testing can be used in immunocompromised patient who may fail to mount an immune response
  - CSF PCR is diagnostic of acute CNS infection, but only 70% positive
Diagnostic Serology Pearls

- IgM titers can remain positive for quite some time post infection
  - 75% of patients can have IgM 12 months post infection
  - 35% can be persistently positive 12 months post encephalitis with 20% positive at 16 months
- CSF IgM can be positive in 33% of patients at 6 months
- Serial IgG titers may be needed for diagnosis
- Positive IgM CSF with negative IgG in CSF or serum suggests acute infection
- Positive IgG with negative IgM suggests prior infection.
- ELISAs can cross react to SLE infection and in patients who have had JEV vaccination

California Encephalitis Project

- 1998-2005 (1570 Patients)
- Self reporting of cases of encephalitis
  - Immunocompetent
  - > 6 months of age
  - Altered mental status
  - fever/CSF pleocytosis/seizure/focal finding/EEG abnormality/Imaging abnormality consistent with encephalitis
- Every patient had a standard battery of tests

<table>
<thead>
<tr>
<th>Table 1: Summary of characteristics of all patients in the California Encephalitis Project, 1998–2005.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>Immunocompetent</td>
</tr>
<tr>
<td>Age, median (range)</td>
</tr>
<tr>
<td>Race</td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Cases</td>
</tr>
<tr>
<td>Resistant symptoms</td>
</tr>
<tr>
<td>Gastrointestinal symptoms</td>
</tr>
<tr>
<td>Fever</td>
</tr>
<tr>
<td>Seizure</td>
</tr>
<tr>
<td>Coma</td>
</tr>
<tr>
<td>Death</td>
</tr>
<tr>
<td>Index ± cases of hospitalization</td>
</tr>
<tr>
<td>Index ± cases of hospitalization</td>
</tr>
<tr>
<td>Laboratory</td>
</tr>
<tr>
<td>CSF white cell, median (range)</td>
</tr>
<tr>
<td>CSF protein level, median (range)</td>
</tr>
<tr>
<td>CSF glucose level, median (range)</td>
</tr>
<tr>
<td>CSF lymphocyte count, median (range)</td>
</tr>
</tbody>
</table>
California Encephalitis Project

248 Infectious (16%)
- 170 viral
  - 45 EBV
  - 40 HSV-1
  - 23 VZV
  - 78 non-viral
- 122 Noninfectious (8%)
  - 52 Autoimmune/vasculitis
  - 33 Neoplastic
  - 7 Metabolic
  - 30 ‘other’

13% with ‘Possible Diagnosis’
63% Undiagnosed

*JID, 2008, 198(11):1685-91
Technology has improved, diagnosis hasn’t.

Empiric Management of Encephalitis

Encephalitis

Infectious  Autoimmune

Clinical Approach to CNS Infections Conclusions

- Localize first – this is key to determining microbiology
- Differentiate primary meningeal from cerebral infections
- Recognize emergencies and empiric therapy approaches
- Use history and paraclinical data to help narrow the underlying pathogen
- Be aware of non-infectious CNS conditions that can mimic viral encephalitis