Fellowship Core Curriculum in Neuroinfectious Disease

Clinical evaluation:
All trainees will have completed a neurology residency and hence would be expected to be able to obtain a complete history and conduct a thorough neurological examination. However, the diseases encountered in the subspecialty of Neuroinfectious diseases and neuroimmunology require special emphasis on certain elements of the neurological assessment.

- History should include a detailed systemic history, travel history, social and family history.
- General physical examination should include examination of the skin, lymph nodes, chest and abdomen.
- Neurological exam should include fundoscopy, extra ocular movements, assessment of gait and spasticity. The trainees should know how to use various neurological assessment scales developed for these diseases, including the EDSS, HIV Dementia scale, the Memorial Sloan Kettering scale (for HIV dementia), and MMSE. They should understand the pros and cons of these scales.

Pathological manifestations:
- Gross and microscopic pathology of acute viral meningoencephalitis, brain abscess, HIV encephalitis and CNS opportunistic infections associated with AIDS, chronic bacterial or fungal meningitis, Multiple Sclerosis and its variants, and various forms of CNS vasculitis.
- Develop an understanding of the various pathological and staining techniques including tissue processing for diagnosis of these diseases.
- Learn to make and interpret both cryostat and fixed tissue sections.
- Learn how to handle pathological specimens and autopsy tissue from patients with transmissible diseases.
- Learn techniques for inactivation of infectious agents, such as prions, viruses, and other microbial agents.

Diagnostic evaluations:
Radiology:
- CT scan,
- MRI findings of various CNS infections and immune disorders, to include findings in FLAIR, diffusion weighted and ADC images, and post-contrast scans.
- Use of SPECT and PET scanning.
- Develop an understanding of the basic principles behind each of the imaging techniques.

Neurophysiology:
- EEG criteria for CJD, SSPE, and evolution over the disease course.
- Use of evoked potentials in the evaluation of neuroimmune conditions.

Cerebrospinal fluid: Expertise in performing LPs is usually accomplished during neurology residency. The fellowship training program would reinforce the technique and apply it to special circumstances when there is concern for particularly high risk transmissible diseases (e.g. prions, HIV)
- Should develop expertise in performing LPs in sitting and lateral decubitus positions.
- In accordance with AAN guidelines, should learn to use atraumatic needles and know the indications, contraindications of doing a spinal tap.
- Learn how to do LPs in patients with transmissible diseases.
- Know the potential complications from the procedure and how to manage the complications.
- Know the CSF findings in each of the neuro-infectious and neuroimmune diseases.
- Use of PCR, its sensitivity and specificity for diagnosis of microbial infections.
• Understand the composition, formation and fluid dynamics of the CSF.

**Microbiology:** Develop a working knowledge of various methods of detecting CNS microbial infections including use of:
  • antibody titers,
  • culture and staining,
  • molecular biological techniques,
  • the morphological characteristics of the infectious agents.

**Integration and Presentation of Findings**
1. Integration of collateral history into the clinical assessment.
2. Development of a differential diagnosis pertinent to the neuro-immune or neuroinfectious disorder.
3. Formulation of a diagnosis based on findings from the clinical and laboratory assessment.
4. Development of treatment plan for the neuro-immune or neuroinfectious disorder.
5. Presentation, both verbally and in writing, of clinical impressions and recommendations derived from the comprehensive clinical assessment to:
   a. The patient and his or her family
   b. Other health care professionals
   c. Other private or public agencies providing services to the patient.

**Treatment strategies:**

**Immunomodulatory drugs:** Have a thorough knowledge of current and emerging immunomodulatory drugs used to treat CNS autoimmune diseases. This should include their mechanisms of action, their pharmacology, modes of administration, indications and contraindications and potential side effects and management of the complications. Drugs in this category may include, corticosteroids, beta interferon, glatiramer acetate, natlizumab, plasmapheresis, mitoxantrone, B cell antagonists such as rituximab, T cell antagonists such as cellcept, daclizumab, other chemotherapeutic drugs such as cyclophosphamide and other immunomodulatory drugs such as IVIG. It is being increasingly recognized that patients on these therapies may be a risk for developing CNS opportunistic infections. Hence knowledge of the evolving guidelines for monitoring for such infections and appropriate management of these complications is essential.

**Antimicrobials:** Know how to treat with and monitor patients on antiretroviral drugs, particularly those that penetrate the CNS and those that may cause neurologic side effects. Know how to use anti-herpes virus drugs, how to monitor and treat patients for resistance to acyclovir and other antivirals. Know how to treat bacterial and fungal infections of the CNS including syphilis, Lyme disease, tuberculosis, cysticercosis and toxoplasmosis. Trainees should know the pharmacodynamics of agents with respect to the blood-brain barrier, and the potential neurotoxicities and systemic side effects of these anti-infective agents.

**Symptomatic:** This should include treatment of neuropathic pain, such as painful peripheral neuropathies and trigeminal neuralgia; antispastic agents, anticonvulsants, chronic fatigue, spastic bladder and urinary retention and sexual dysfunction.

**Indications for surgical intervention:** baclofen pump, brain biopsy, surgical drainage of brain abscess.

**Infusion center:** Learn how to manage an infusion clinic and how to administer and monitor patients on immunomodulatory and antimicrobial drugs that require infusions.
  • Patient and family education
  • Use of and referral to other health professionals such as rehabilitation services, urologist, neuroophthalmologist, neuropsychologist.
Reporting requirements:
Know the reporting requirements of neurologic infections, including the urgency of reporting. Should also know how to access state and national public health agencies.

Didactic course:
Twenty hours of a didactic course that covers all aspects of Neuroinfectious and neuroimmune disorders is an essential requirement. However, this requirement may be fulfilled by any one or a combination of the following: classroom lectures, journal clubs, web based courses, or courses at the AAN in the related subspecialty.

Neuroinfectious and neuroimmune disorders:
Fellows in this training program are expected to develop in-depth knowledge regarding the neuropsychiatric and neurobehavioral consequences of many neurological and psychiatric conditions. All fellows are expected to bring to subspecialty training the level of knowledge and clinical competence required by the ACGME-RRC in Neurology.

Due to the limited duration of training in this fellowship, and the fact that some infections and immune disorders are prevalent in different geographical regions around the world, some trainees may not have direct patient interactions with all the diseases that fall under this subspeciality. The elements of the Core Curriculum described above are designed to ensure that Fellows develop the knowledge base and clinical skills required to understand, evaluate, and treat patients with neuroinfectious and neuroimmune disorders. In the service of preparing Fellows to provide care for persons with neuroinfectious and neuroimmune disorders they are expected to both complement and supplement “bedside-learning” through guided self-directed learning activities and/or didactic experiences. Guided self-directed learning activities may include reading relevant textbooks, peer-reviewed articles, or other materials recommended by training program faculty. Didactic experiences may include seminars or other course work provided by the training program itself or by other programs either within or affiliated with the institution in which the fellowship training occurs. Additionally, Fellows should be encouraged to attend local or national conferences relevant to this aspect of training in neuroinfectious and neuroimmune disorders. Through these means, it is expected that the fellow will develop an advanced level of knowledge regarding the neuroinfectious and neuroimmune disorders including their epidemiology, neurogenetics, putative neurological substrates, and typical neuropathological features of the conditions listed below, where such are known.

Neuromyelitis Optica

Neuroimmune disorders
- Multiple sclerosis
  - Relapsing remitting
  - Primary progressive
  - Secondary progressive
  - Progressive relapsing
- Multiple sclerosis variants
  - Marburg’s variant
  - Schilder’s disease
  - Balo’s concentric sclerosis
- Acute disseminated encephalomyelitis
  - Hemorrhagic leukoencephalitis
- Idiopathic Transverse Myelitis
- Optic Neuritis
- Neuromyelitis Optica
• Neurosarcoïdosis
• Neurological manifestations of rheumatological diseases
  o Sjogren’s
  o Systemic lupus erythematosus
  o Behcet’s
  o Rheumatoid arthritis
  o Wegener’s granulomatosis
  o Other CNS vasculitis

Neuro-infectious diseases
• Meningitis
• Bacterial Meningitis
  o Meningococcal Meningitis
  o Pneumococcal Meningitis
  o Haemophilus Meningitis
  o Staphylococcal Meningitis
  o Listeria Meningitis
  o Tuberculous Meningitis
  o Gram negative bacteria
• Aseptic Meningitis
• Chronic Meningitis
• Fungal Meningitis
• Cerebral Abscess
• Spinal Epidural Abscess
• Subdural Empyema
• Neurological Sequelae of Infectious Endocarditis
• HIV-associated Conditions:
  o Aseptic Meningitis
  o Acute/Chronic Inflammatory Demyelinating Polyneuropathy
  o Distal Painful Sensorimotor Polyneuropathy
  o Multiple Mononeuropathies
  o Myopathies
  o Vacuolar Myelopathy
  o HIV associated neurocognitive disorder (HAND)
  o CNS-immune reconstitution syndromes
• HIV-associated Opportunistic Infections:
  o CNS Cryptococcosis
  o CNS Lymphoma
  o CNS Toxoplasmosis
  o Cytomegalovirus Encephalitis and radiculopathy
  o Varicella zoster virus
  o Progressive multifocal leukoencephalopathy
  o Immune reconstitution inflammatory syndrome
• Human T cell leukemia virus I and II
• Herpes Simplex Encephalitis
• West Nile Encephalitis
• Subacute Sclerosing Panencephalitis
• Other Viral Encephalitides
• Poliomyelitis
• Rabies
• Varicella Zoster
• Dengue
• Leprosy
• Lyme neuroborreliosis
• Neurosyphilis
• Amoebiasis
• Rocky Mountain Spotted Fever
• Prion-Related Diseases
• Neurocysticercosis
• Cerebral malaria

Supplementary Curricular Content
Training programs may elect to facilitate the Fellow’s development of special expertise and/or clinical competence in additional areas in neuroinfectious and neuroimmune disorders. Emphasis on these supplementary areas should not detract from the emphasis needed to master all of the elements of the Core Curriculum. Possible supplementary curricular content may include:
1. dysmyelinating disorders
2. neurogenetics
3. neuroophthalmology
4. neuro-urology
5. neuro-rehabilitation
6. cognitive rehabilitation
7. neuro-radiology
8. epidemiology, public health
9. virology, microbiology, molecular biology
10. neuropathology
11. nerve and muscle infections and immunological disorders, such as leprosy, myositis, Guillain-Barre, myasthenia gravis

Suggested Reading:
CNS Infections
5. Practice Guidelines for the Management of Bacterial Meningitis: Clinical Infectious Diseases 2004; 39:1267–84

NeuroAIDS

## Multiple Sclerosis

1. Neuroimmunology (Contemporary Neurology Series) by Patricia K. Coyle; 375 pages Publisher: Oxford University Press (December 30, 2006).

### Practice Parameters

Each of the titles below are hyperlinked to their respective webpage. Alternatively they may be accessed through www.aan.com

<table>
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<tr>
<th>Date</th>
<th>Title</th>
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<tbody>
<tr>
<td>Nov 2003</td>
<td>The Use of Mitoxantrone (Novantrone) for the Treatment of Multiple Sclerosis Note: Current guideline.</td>
</tr>
<tr>
<td>Dec 2002</td>
<td>Immunization and Multiple Sclerosis: A Summary of Published Evidence and Recommendations Note: Current guideline.</td>
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### Transverse Myelitis/NMO

Cerebrospinal Fluid

Neuropathology
4. Select chapters from Greenfield's Neuropathology (2 Volume Set) by David I. Graham and Peter L. Lantos.