

Neurology Differential Diagnosis

Introduction: Hello Clinical Problem Solvers! This is Gurbani Kaur, a medical student, and I am so excited to continue our campaign to end neurophobia with you by sharing our new schema describing a systematic approach to the neurology differential diagnosis or as Dr. Aaron Berkowitz likes to say: the $E = MC^2$ of neurology.

Here, our $E = MC^2$, is DDX for any neurology case should start as a product of the localization and the time course of onset and evolution of the chief concern. With this framework in mind, let's dive into our schema.

Start with localization or figuring out WHERE in the nervous system the problem lies. To do this, we'll need to use clues from the history and physical exam in conjunction with our knowledge of neuro-anatomy. We'll first need to consider if our lesion or lesions are likely affecting the central nervous system or the peripheral nervous system. The central nervous system is comprised of the brain, brainstem, cerebellum, and spinal cord. The PNS is divided into the nerve roots, dorsal root ganglia, plexus, nerves, neuromuscular junction, and muscle itself.

Next, we'll consider the tempo or time course or WHEN the chief concern or associated symptoms have arisen. We'll come to appreciate how the common pathophysiology buckets will naturally follow our temporal buckets of: hyperacute, acute, sub-acute, and chronic. Hyperacute onset will refer to sudden onset over seconds to minutes, and this bucket refers mostly to emergent neurological diseases. A mnemonic I use to remember this category is: remember to VET emergencies first. V for Vascular, E for Electrical and T for Traumatic. Vascular pathophysiology of hyperacute neurological findings includes stroke, hemorrhage and subarachnoid hemorrhage. Electrical pathophysiology includes seizures and migraines. Finally, T refers to traumatic injuries and toxic-metabolic etiologies.

Second, acute onset refers to symptoms emerging and evolving over hours to days and is associated most commonly with infectious and inflammatory causes. For infections, our patient may be experiencing a bacterial or viral infection such as a bacterial meningitis caused by *Neisseria meningitidis* or a viral encephalitis due to herpes simplex virus 1. Remember there are many bacterial etiologies of meningitis and viral etiologies of encephalitis, these are just one example of each. The inflammatory bucket for acute neurologic diseases includes both PNS and CNS inflammatory disorders: In the PNS, Guillain-Barre syndrome (GBS) in which there is inflammation of peripheral nerves causing rapidly evolving weakness and/or sensory changes. In the CNS, optic neuritis and transverse myelitis are examples of inflammatory conditions that can be seen in multiple sclerosis (MS) flares for example.

Third, subacute onset of symptoms occurs over weeks to months. At this tempo we'll find infectious, inflammatory, and neoplastic etiologies of neurological disease. Subacute infections include TB, fungal infections, and neurologic complications of HIV. So these disproportionately affect immunocompromised patients and include central nervous system tuberculosis, and fungal infections such as cryptococcosis. Subacute inflammatory etiologies include CIDP or chronic inflammatory demyelinating polyneuropathy, an inflammatory PNS disorder that is sort of a chronic 'cousin' of Guillain-Barre. Antibody mediated conditions include disease like myasthenia gravis and autoimmune encephalitis. Last but not least for the subacute tempo of neurological disease consider space occupying lesions such as neoplasms—in the nervous system these may be primary or metastatic.

For chronic neurological disease our patient will be reporting symptoms on the time scale of months to years. This should clue us in to thinking mostly about degenerative diseases like Amyotrophic Lateral Sclerosis, ALS, Parkinson's, and Alzheimer's.

Finally note that Toxic and Metabolic causes should be considered in the differential of neurologic disease that arises over ANY tempo, because they can manifest hyperacute, acute, subacute, or in chronic neurological disease depending on the toxin, metabolite, drug and how they impact the nervous system.

In summary, for hyperacute VET vascular, seizure, migraine, and trauma. For acute, focus on infectious and inflammatory etiologies. For subacute: focus on infectious, inflammatory, and neoplasms. Chronic tempo is mostly degenerative neurological disease. Toxic, metabolic, and drug causes must be considered at ANY time scale.

Even though we're introducing the DDx = localization x time course approach for neurology, this approach can be applied to other organ systems, just adjust your localization to outside of the nervous system. For example: with a chief concern of chest pain, first localize to cardiac, pulmonary, esophageal or musculoskeletal and then consider the time course to help generate your DDx for chest pain.

We hope you enjoyed this schema! For practice applying this schema and continuing to work to end your neurophobia check out Neurology VMR featuring Dr. Aaron Berkowitz on Tuesdays ☺