Year 2003 Paper two: Questions supplied by Tricia

Question 90
A 50-year-old woman presents with sudden onset of profound deafness in the left ear. Examination indicates that nerve deafness is more likely than a conduction problem. Other findings include right infero-medial scleritis, bilateral osteoarthritic fingers, blood-stained nasal discharge and obesity.
Which one of the following investigations is most likely to lead to the correct diagnosis?

A. Magnetic resonance imaging (MRI) of the brain  
B. Anti-double-stranded-DNA antibodies assay  
C. Anti-neutrophil cytoplasmic antibody (ANCA) assay  
D. Lumbar puncture  
E. Urinary drug screen

ANATOMY AND PHYSIOLOGY — The ear is divided into three segments:
- The outer ear, comprising the auricle and ear canal
- The middle ear, comprising the tympanic membrane (TM), ossicles, and the middle ear space
- The inner ear, comprising the cochlea, semicircular canals, and internal auditory canals.

Causes of hearing loss

OUTER EAR CAUSES

All hearing loss related to the outer ear is by nature a conductive hearing loss.
- Congenital — The external auditory canal (EAC) develops from the 8th to the 28th week of gestation; problems can occur anytime during this developmental phase.
- Infection blockage of the EAC due to the accumulation of debris, edema, or inflammation. Otitis externa usually develops as a result of local trauma coupled with contamination by bacteria (or occasionally fungi) after swimming, showering, or exposure to hot humid conditions. Significant edema of the EAC occurs; the canal is often also filled with squamous and purulent debris. The most common symptoms are otalgia, pruritus, discharge, and hearing loss.
- Trauma — Penetrating trauma to the external auditory canal or meatus due to a bullet, knife, or fracture may cause mild or profound conductive hearing loss, depending upon the degree of EAC occlusion.
- Tumor — The most common malignant tumor of the EAC is squamous cell carcinoma. This and other tumors of the EAC, such as basal cell carcinoma and melanoma, typically cause conductive hearing loss due to occlusion of the canal.
- Benign bony growths may also occlude the EAC with a resulting conductive hearing loss. The two most common benign growths are exostosis and osteoma.
- Systemic disease — Diabetes mellitus and other immunocompromised states do not in themselves cause hearing loss, but these disorders predispose to developing necrotizing otitis externa, which in turn can cause conductive hearing loss due to occlusion of the EAC.
- Dermatologic — Certain skin diseases, such as psoriasis, may cause scaling and edema of the EAC and meatus.

MIDDLE EAR CAUSES — As with the outer ear, all hearing loss associated with the middle ear is conductive hearing loss.
- Congenital — Atresia or malformation of the ossicular chain can cause conductive hearing loss.
- Eustachian tube dysfunction — Eustachian tube dysfunction can cause perceived hearing loss. Eustachian tube dysfunction occurs commonly in the setting of a viral upper respiratory infection (URI) or sinusitis, and it can also occur with allergies. Any process that causes swelling in the back of the nose around the eustachian tube opening may cause symptoms
- Infection — Otitis media (OM) is a common childhood disorder that also frequently occurs in adults
- Tumors — Malignant tumors such as Langerhans cell histiocytosis (including the Letterer-Siwe variant) or squamous cell carcinoma may cause conductive hearing loss. However, these entities are relatively rare when compared with benign cholesteatoma or otosclerosis.
Cholesteatoma — Cholesteatoma is a growth of desquamated, stratified, squamous epithelium within the middle ear space.

Otosclerosis — Otosclerosis is a bony overgrowth that involves the footplate of the stapes. As the overgrowth develops, the stapes can no longer function as a piston, but rather rocks back and forth and eventually becomes totally fixated. Conduction gradually becomes worse until a maximal conductive hearing loss of 60 dB is reached.

Tympanic membrane perforation — Conductive hearing loss due to TM perforation is common. The degree of conductive hearing loss depends upon the size and location of the perforation. Small perforations and those located in the anterior/inferior quadrant cause the least amount of conductive hearing loss; near total or posterior/superior quadrant perforations have a much higher chance of causing significant hearing loss. TM perforations can be caused by many events, including blast injury, barotrauma, foreign body trauma, temporal bone fractures, ear infections, self-inflicted trauma from a Q-tip or other object, or the hole may persist after myringotomy or after tubes fall out. After an acute perforation, the ear needs to be examined under the microscope to ensure that skin is not trapped on the undersurface of the TM, since trapped skin could lead to cholesteatoma formation. Documentation of a patient's auditory status also is mandatory for any newly diagnosed perforation. Most acute TM perforations heal on their own or with the aid of a paper or biogenic film patch. Occasionally surgical correction is required, usually with a temporalis muscle fascia graft. Repair of the perforation often corrects the conductive hearing loss.

Vascular — Glomus tympanicum or glomus jugulare tumors are benign paragangliomas that arise either from the promenatory of the middle ear or the adventitia of the dome of the jugular bulb. As they grow they tend to fill the middle ear, with resultant conductive hearing loss. They also erode bone as they enlarge, especially inferiorly, causing damage to cranial nerves. In addition, glomus tumors may impede upon the ossicular chain and TM, thereby decreasing motility of either or both structures.

INNER EAR CAUSES — Disorders of the inner ear normally cause a sensorineural hearing loss. The etiology may be associated with the cochlea, eighth nerve, internal auditory canal, or brain.

Congenital or hereditary — Congenital hearing loss will be defined as any hearing loss that occurs at or shortly after birth that may be due to either a hereditary or non-hereditary cause. Non-hereditary etiologies involve an insult to the developing cochlea, including viral infections such as cytomegalovirus (CMV), hepatitis, rubella, toxoplasmosis, HIV, and syphilis. Some medications also may have a teratogenic affect on the developing ear of the fetus, including recreational drugs, alcohol, quinine, and retinoic acid.

Presbycusis — Presbycusis is the sensorineural hearing loss that is associated with aging. Multiple factors influence the rate at which hearing loss occurs, including a lifetime of noise exposure, genetics, medications, and infections.

Infection — The most common infection of the inner ear in adults is viral cochleitis; in young children it is meningitis. Meningitis can access the cochlea by way of CSF-perilymph fluid connection and cause a profound sensorineural hearing loss by destroying the inner ear hair cells. **Lumbar puncture more likely in children**
- Viral cochleitis usually manifests as a sudden sensorineural hearing loss; vertigo, facial paralysis, or pain occur rarely.

Meniere's disease — Patients with Meniere's disease complain of episodic spells of vertigo that last for hours, associated with aural fullness, tinnitus, and sensorineural hearing loss. Occasionally the auditory system is affected in what is commonly called cochlear Meniere's or cochlear hydrops; in these cases the patient experiences episodic hearing loss that recovers within a 12- to 24-hour period, usually with associated aural fullness and tinnitus. The spells of hearing loss may occur on a daily, weekly, or monthly basis. The hearing loss is almost always low frequency. Over time and with repeated attacks, the hearing deficit can become permanent and may even eventually involve all frequencies

Noise exposure — Everyday noise exposure, compounded over time, has an impact upon our ability to hear and ultimately on the degree of the presbycusis that develops. Constant exposure to loud noises can cause high frequency sensorineural hearing loss.

Inner ear barotrauma — Barotrauma occurs when a patient is exposed to a sudden, large change in ambient pressure, often during diving or flying. Middle ear pressure becomes more positive with respect to ambient pressure during ascent until the eustachian tube is forced open. On descent, ambient
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pressure exceeds middle ear pressure until swallowing opens the eustachian tube. Inner ear barotrauma is a fairly uncommon injury but should be excluded in all cases of middle ear barotrauma

- Trauma — Penetrating trauma typically causes sensorineural or mixed hearing loss. These injuries are usually due to gunshot wounds that upon impact cause significant temporal bone fractures.
- Tumors — Most tumors of the inner ear are benign, although malignant tumors such as squamous cell carcinoma, sarcomas, and adenoid carcinoma rarely occur with bony involvement. Benign bony tumors including fibrous dysplasia and Paget's disease are also rare. The most common tumor that causes sensorineural hearing loss is an acoustic neuroma. This is a benign tumor that usually originates from the vestibular portion of the eighth cranial nerve. The most common complaint is an asymmetric or unilateral sensorineural hearing loss, which occurs in 90 percent of all patients. Other symptoms include unilateral tinnitus, disequilibrium, dizziness, lipomas, or headaches. Additional findings may include facial hyperesthesias or facial muscular twitching.  **Ix = MRI**

- Endocrine/systemic/metabolic — Various metabolic abnormalities have been known to either cause or be associated with sensorineural hearing loss.
  - diabetic vasculopathy can cause cochlear ischemia.
  - anaemia or a white blood cell dyscrasia may lead to sensorineural hearing loss by an unknown mechanism that may involve decreased oxygenation, microblockage of vessels, or infection.
  - hyper or hypothyroidism.

- Autoimmune hearing loss — Autoimmune hearing loss was first described in 1979 [56]. It is usually bilateral, asymmetric, sensorineural hearing loss that is either fluctuating or progressive in nature. The autoimmune inner ear disease may be limited just to the ear, or it may be part of an overall systemic problem such as
  - Wegener's granulomatosis,  **Ix ANCA**
  - Cogan's syndrome,
  - rheumatoid arthritis,
  - systemic lupus erythematosus,  **Ix double stranded DNA but ANA more sensitive**
  - polyarteritis nodosa,
  - or relapsing polychondritis.
    - A number of studies are consistent with autoimmune hearing loss, including an elevated erythrocyte sedimentation rate (ESR), antinuclear antibody (ANA), rheumatoid factor (RF). One of the more useful tests is the detection of a cochlear autoantibody, a 68 kilodalton protein.
    - Autoimmune hearing loss is typically first treated with high-dose corticosteroids (60 to 80 mg prednisone) every morning for two to three weeks. This often results in significant recovery of hearing.

- Iatrogenic — Iatrogenic inner ear injuries may occur during surgical procedures such as tympanomastoidectomy or stapedectomy, following radiation therapy, either for intracranial or nasopharyngeal tumors, or they may be medication related.

- A number of ototoxic medications can cause sensorineural hearing loss: All aminoglycosides are ototoxic. Some are more vestibulotoxic than cochleotoxic. The relative order of cochleotoxicity is gentamicin>tobramycin>amikacin>neomycin. Other antibiotics that can cause ototoxicity include erythromycin, vancomycin, and tetracycline. These drugs have a more pronounced ototoxic effect in patients who are renally impaired. Many chemotherapeutic agents are known to cause hearing loss. The most common are 5-fluorouracil (5-FU), bleomycin, and nitrogen mustard. The worst ototoxicity occurs with cisplatin.
  - The hearing loss caused by antibiotic or chemotherapeutic agents usually begins at high frequencies; with continued medication use, the hearing loss will become more pronounced and may even continue to worsen for a time after the drug is discontinued. Any sensorineural hearing loss associated with these drugs is permanent.
  - Aspirin or other salicylates can also cause hearing loss, but this is reversible with discontinuation of the drug. The etiology is believed to be enzymatic inhibition; thus, very high doses (6 to 8 grams/day) are required to cause ototoxicity.
  - Antimalarial medications such as quinine and chloroquine may also cause sensorineural hearing loss and tinnitus but, similar to salicylates, these effects are usually reversible. This is also true for high-dose nonsteroidal antiinflammatory agents. Loop diuretics are an additional cause of temporary hearing loss and tinnitus.
Ototopical medications — Several ototopical drops have the potential to cause ototoxicity. These include the aminoglycoside ear drops Tobradex and Garamicin, and Cortisporin (since it contains neomycin).

- Neurogenic — Several neurologic disorders may cause sensorineural hearing loss:
  - Cerebrovascular accident or transient ischemic attack.
  - Arnold-Chiari malformations may stretch the auditory vestibular nerve, thereby causing hearing loss and/or vestibular complaints.
  - Multiple sclerosis is another disease that can initially present as a sudden sensorineural hearing loss and/or vertigo.

A. Magnetic resonance imaging (MRI) of the brain

? acoustic neuroma – clinical picture not consistent with acoustic neuroma presentation

CLINICAL PRESENTATION — Symptoms associated with acoustic neuroma are due to cranial nerve involvement, cerebellar compression, and tumor progression. In a series of 1000 acoustic neuromas treated at a single institution, the acoustic nerve was involved in almost all cases, followed by the vestibular, trigeminal, and facial nerves.

Cochlear nerve — Symptomatic cochlear nerve involvement occurred in 95 percent of patients. The two major symptoms were hearing loss and tinnitus.

Vestibular nerve — Involvement of the vestibular nerve occurred in 61 percent of patients. Affected patients frequently acknowledged having unsteadiness while walking, which was typically mild to moderate in nature and frequently fluctuated in severity. True spinning vertigo was uncommon because these slow growing tumors cause gradual rather than acute asymmetries in vestibular function. In this setting, the central vestibular system can often compensate for the gradual loss of input from one side.

Trigeminal nerve — Trigeminal nerve disturbances occurred in 17 percent of patients. The most common symptoms were facial numbness (paresthesia), hypesthesia, and pain. The average duration of symptoms was 1.3 years; the symptoms usually occurred after hearing loss had been present for more than two years and vestibular symptoms for more than one year.

Facial nerve — The facial nerve was involved in 6 percent of patients. The primary symptoms were facial paresis and, less often, taste disturbances.

Tumor progression — Other presenting signs are the result of tumor progression, leading to pressure on adjacent posterior fossa structures. Very large tumors can press on the cerebellum or brainstem and result in ataxia. Brainstem compression, cerebellar tonsil herniation, hydrocephalus and death can occur in untreated cases. The functions of the lower cranial nerves (nerves IX, X, and XI), such as speaking and swallowing, can also become impaired, leading to dysarthria, dysphagia, aspiration, and hoarseness.

DIAGNOSIS — The diagnosis of acoustic neuroma is made by the demonstration of asymmetric sensorineural hearing loss or other cranial nerve deficits followed by imaging with MRI or CT scan. Acoustic neuroma accounts for 80 to 90 percent of posterior fossa lesions. Meningioma accounts for 4 to 10 percent; the remainder are accounted for by facial nerve schwannomas, gliomas, cholesterol cysts, cholesteatomas, hemangiomas, aneurysms, arachnoid cysts, lipomas, and metastatic tumor.

B. Anti-double-stranded-DNA antibodies assay

? SLE

The diagnosis of SLE is straightforward in a patient who presents with several compatible clinical features and has supportive laboratory studies. A good example is a young woman who presents with complaints of fatigue, arthralgia, and pleuritic chest pain, who is found to have hypertension, a malar rash, a pleural friction rub,
several tender and swollen joints, and mild peripheral edema. Laboratory testing may reveal leukopenia, anemia, an elevated serum creatinine, hypoalbuminemia, proteinuria, an active cellular urinary sediment, hypocomplementemia, a positive Coombs test, and positive tests for antinuclear antibodies, including those to double stranded DNA and the Smith antigen.

ARA criteria for diagnosis of systemic lupus erythematosus

Using the analogy of the ARA criteria for the diagnosis of rheumatoid arthritis, we have suggested that patients be classified as follows:

- Classical SLE — many criteria
- Definite SLE — 4 or more criteria
- Probable SLE — 3 criteria
- Possible SLE — 2 criteria

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Malar rash</td>
<td>Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds</td>
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<tr>
<td>Discoid rash</td>
<td>Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions</td>
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<td>Photosensitivity</td>
<td>Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation</td>
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<td>Oral ulcers</td>
<td>Oral or nasopharyngeal ulceration, usually painless, observed by a physician</td>
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<tr>
<td>Arthritis</td>
<td>Nonerosive arthritis involving 2 or more peripheral joints, characterized by tenderness, swelling, or effusion</td>
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<tr>
<td>Serositis</td>
<td>Pleuritis - convincing history of pleuritic pain or rub heard by a physician or evidence of pleural effusion OR Pericarditis - documented by EKG, rub or evidence of pericardial effusion</td>
</tr>
<tr>
<td>Renal disorder</td>
<td>Persistent proteinuria greater than 0.5 grams per day or greater than 3+ if quantitation not performed OR Cellular casts - may be red cell, hemoglobin, granular, tubular, or mixed</td>
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<tr>
<td>Neurologic disorder</td>
<td>Seizures OR psychosis - in the absence of offending drugs or known metabolic derangements (uremia, ketoacidosis, or electrolyte imbalance)</td>
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<tr>
<td>Hematologic disorder</td>
<td>Hemolytic anemia - with reticulocytosis OR Leukopenia - less than 4,000/mm3 total on two or more occasions OR Lymphopenia - less than 1,500/mm3 on two or more occasions OR Thrombocytopenia - less than 100,000/mm3 in the absence of offending drugs</td>
</tr>
<tr>
<td>Immunologic disorders</td>
<td>Positive antiphospholipid antibody OR Anti-DNA - antibody to native DNA in abnormal titer OR Anti-Sm - presence of antibody to Sm nuclear antigen OR False positive serologic test for syphilis known to be positive for at least six months and confirmed by Treponema pallidum immobilization or fluorescent treponemal antibody absorption test</td>
</tr>
<tr>
<td>Antinuclear antibody</td>
<td>An abnormal titer of antinuclear antibody by immunofluorescence or an equivalent assay at any point in time and in the absence of drugs known to be associated with &quot;drug-induced lupus&quot; syndrome</td>
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</tbody>
</table>
Autoantibodies — The ANA test is the best diagnostic test for SLE and should be performed whenever SLE is suspected. The ANA is positive in significant titer (usually 1:160 or higher) in virtually all patients with SLE. Depending upon the titer of the ANA the false positive rate varies from approximately 30 percent to as little as 3 percent (for ANA titers of 1:40 and 1:320, respectively) among healthy controls. Since diseases other than SLE are associated with positive ANA test results, the predictive value of a positive test depends upon the control population. If patients with other rheumatic and collagen vascular diseases are used, a positive ANA has only a 20 to 35 percent predictive value for SLE. However, the negative predictive value, that is the probability of having SLE if the ANA test is negative, is less than 0.14 percent.

dsDNA and Sm antibodies — There are two autoantibodies that are highly specific for SLE: anti-double-stranded DNA (dsDNA) antibodies; and anti-Sm antibodies. Their sensitivity is much lower at about 75 and 25 percent, respectively. One study, for example, evaluated seven commercial ELISA assays for anti-dsDNA antibodies; the following results were obtained:
Sensitivity — 66 to 95 percent
Specificity — 75 to 100 percent
Predictive value — 89 to 100 percent

C. Anti-neutrophil cytoplasmic antibody (ANCA) assay

Wegener's granulomatosis

Clinical manifestations and diagnosis of Wegener's granulomatosis and microscopic polyangiitis

Wegener's granulomatosis is a systemic vasculitis of the medium and small arteries, as well as the venules, arterioles, and occasionally large arteries. "Classic" Wegener's granulomatosis is a form of systemic vasculitis that primarily involves the upper and lower respiratory tracts and the kidneys.

A "limited" form, with clinical findings isolated to the upper respiratory tract or the lungs, occurs in approximately one-fourth of cases. Although many of these patients (up to 80 percent) may eventually develop glomerulonephritis, there are incompletely understood phenotypic differences in Wegener's granulomatosis. Specifically, patients with limited disease are younger at disease onset, and more likely to be women.

Renal involvement is manifested by acute renal failure with red cells, red cell and other casts, and proteinuria. Patients with microscopic polyangiitis have a renal lesion that is essentially indistinguishable from that of patients with classic Wegener's granulomatosis. The principal difference is the absence of granulomatous inflammation in the former disease, although the clinical manifestations of these disorders overlap substantially. In distinguishing these two conditions, some experts consider the presence of any significant upper respiratory tract involvement to be indicative of Wegener's granulomatosis. Patients presenting with only pauci-immune glomerulonephritis in the absence of other organ system involvement are generally classified as "renal-limited" vasculitis or idiopathic necrotizing glomerulonephritis.

OTHER DISEASE MANIFESTATIONS — In addition to renal and pulmonary involvement, other organ systems that may become involved include:

- Upper and lower airways, including the subglottic region or trachea
- Joints (myalgias, arthralgias, arthritis)
- Eyes (conjunctivitis, corneal ulceration, episcleritis/scleritis, optic neuropathy, nasolacrimal duct obstruction, proptosis, diplopia, retinal vasculitis, and uveitis)
- Skin (vesicular, palpable purpuric, ulcerative, and hemorrhagic lesions)
- Nervous system (mononeuritis multiplex, cranial nerve abnormalities, central nervous system mass lesions, external ophthalmoplegia, hearing loss)
- Less commonly, the gastrointestinal tract, heart (pericarditis, myocarditis, conduction system abnormalities), lower genitourinary tract (including the prostate), parotid glands, thyroid, liver, or breast
- Patients with Wegener's granulomatosis also appear to have a high incidence of venous thrombosis
PRESENTING SYMPTOMS AND FINDINGS — The most common presenting symptoms include persistent rhinorrhea, purulent/bloody nasal discharge, oral and/or nasal ulcers, polyarthritis, myalgias, or sinus pain. Less common symptoms of upper airway involvement are hoarseness, stridor, earache, both conductive and sensorineural hearing loss, or otorrhea.

Other frequent early complaints relate to the lower respiratory tract and include cough, dyspnea, hemoptysis (due to an alveolar capillaritis, necrotic lesions, or endobronchial disease), and pleuritic pain.

Nonspecific complaints of fever, night sweats, anorexia, weight loss, and malaise may accompany upper or lower airway disease. In addition, signs and symptoms related to involvement of other organ systems may also be observed. These include ocular inflammation, nasal congestion, joint tenderness and or effusion, and rash. Skin lesions include palpable purpura, ulcers, vesicles, papules, and subcutaneous nodules. Diarrhea associated with colorectal ulceration may also occur [19]. Central diabetes insipidus has also been described.

Renal involvement is another common component of Wegener's granulomatosis and microscopic polyangiitis.

Routine laboratory tests — Routine laboratory tests are generally nonspecific in Wegener's granulomatosis. Common abnormalities include leukocytosis, thrombocytosis (>400,000/mm3), marked elevation of the erythrocyte sedimentation rate, and normochromic, normocytic anemia [1].

Antineutrophil cytoplasmic antibodies — The diagnosis of Wegener's granulomatosis is suggested from the clinical and laboratory findings and from the presence of circulating antineutrophil cytoplasmic antibodies (ANCA).

Approximately 90 percent of patients with active, generalized Wegener's granulomatosis are ANCA-positive.

D. Lumbar puncture
? meningitis – no other infective features, or heamorrhage – headache better presenting feature

E. Urinary drug screen
Antibiotics are the major ototoxic agents – chronic may be previous exposure