A. Course Description:
This is an integrated system based course which emphasizes anatomy, physiology, pharmacology, microbiology and pathology of the peripheral nervous system. The course provides integrated knowledge covering the peripheral nervous system including peripheral nerves, nerve plexuses and peripheral nerve branches cranial nerves and special senses. The objectives of this course are achieved via selected lectures, relevant laboratory sessions. To enhance integration of basic and clinical sciences as well as self-directed learning, common clinical disorders related to this system are also explored using case based small group discussions and seminars.

B. General Objectives:
By the end of this course, students are expected to:-
1. Learn the mechanisms of sensing the various environmental stimuli.
2. Analyze the structures conveying information to and from the central nervous system.
3. Understand the biochemical events taking place within this system.
4. Be able to comprehend how drugs modify the functions of this system.
5. Explain the various possibilities where things can go wrong in different parts of the system.
6. Know common infections affecting this system.
7. Be able to explain symptoms, signs, investigations and forms of treatments of nervous system’s anomalies.

Small group discussion Objectives:
1. Present the case in simple and clear way.
2. Point out the relevant information of the various disciplines and elaborate on them.
3. Explain and Discuss symptoms, signs, investigations and forms of treatment using these relevant information. (Cases are attached as an appendix.)

C. Specific Learning Objectives:
The specific objectives of individual lectures are as follows.
It is essential that you are prepared before you listen to the lecture.
The lecture is a meeting to explain some ideas (what is read and not understood) and it is by no means the only source of information or a replacement of the textbook.
<table>
<thead>
<tr>
<th></th>
<th>Introductory case presentation. (All Disciplines)</th>
<th>A case will be presented. Then open discussion of the case and relevant knowledge needed to explain and solve the case will be emphasized.</th>
</tr>
</thead>
</table>
| 2 | Tumor of the Nervous system (pathology) | 1. Classify tumors and describe the general features of primary brain tumors in comparison to other tumors in the body.  
2. Know the pathology and prognosis of the various types of brain tumors.  
3. Describe tumors of the peripheral nerves.  
4. Know the common types of metastatic tumors and their pathologic characteristics. |
| 3 | The Eye and optic nerve. (Anatomy) | 1. Make a list of structures making the eyeball.  
2. Define each part.  
3. Make sure to use essential keywords in your definitions.  
4. Discuss the structure of the coats of the eye.  
5. Describe the anterior modifications of the eye coats.  
6. Describe the contents of the eyeball.  
7. Describe the sensory, sympathetic and parasympathetic nerve supply.  
8. Define the optic nerve.  
9. Follow the optic nerve from the eyeball to its point of entry to the brain. Note important relations.  
10. List the related structures to the eye, eyelids and lacrimal system. |
| 4 | The orbit, orbital contents and cranial nerves III, IV and VI (Anatomy) | 1. Describe the location of the orbit.  
2. Make a list of structures making the orbit starting from orbital margin.  
3. Define each component.  
4. Describe openings into orbital cavity.  
5. Define the orbital fascia.  
6. Describe muscles of the orbit, their cone arrangement, origin, insertion, nerve supply and their function.  
7. Describe the nerves of the orbit, their courses, important relations and their targets.  
8. Describe blood supply and lymph drainage of the orbit. |
| 5 | Neurophysiology of vision, the retina, eye and central visual pathway. (Physiology) | 1. Describe the light refraction by the eye and know the refractive indices of the cornea, lens aqueous humor and vitreous humor.  
2. Define accommodation and know its mechanism of action as well as its importance for near vision.  
3. Define visual acuity and know that the fovea has the highest visual acuity.  
4. Know the types of photoreceptors in the retina.  
5. Understand the mechanism of phototransduction and the ionic basis of receptor potential in rods and cones.  
6. Describe different types of neuronal cells in the retina and their synaptic connections (neural circuit in retina).  
7. Know the functions of bipolar cells, horizontal cells, amacrine cells and their role in processing of visual signal.  
8. Describe the functions of the visual cortex in perception of visual signals.  
9. Review the major relay stations of the visual pathway.  
10. List the major functions of the geniculate nucleus and superior colliculus.  
11. Discuss the role of the visual cortex in perception of vision.  
12. Outline briefly the major pathways of color and black and white vision.  
13. Describe the major types of visual cortex cells and their role in visual perception. |
| 6 | Trigeminal nerve. (Anatomy) | 1. Review the general anatomical features of the face and scalp.  
2. Discuss briefly how the face is developed.  
3. Follow up the course of trigeminal nerve from its point of central connections, exit and down to its target areas.  
4. Describe briefly important cranial reflexes involving the face and trigeminal nerve. |
| 7 | The external and middle ear | 1. Make a list of structures making the external and middle ear.  
2. Define each part – use keywords.  
3. Highlight the structural features of the external auditory meatus.  
4. Describe the shape, position and various boundaries of the middle ear.  
5. Discuss the features of the tympanic membrane.  
6. Describe the ossicles and their muscles.  
7. Describe the auditory tube, its openings and structure.  
8. Have an idea about mastoid air cells and their connection to the middle ear.  
9. Follow up the facial nerve from the brain down to the stylomastoid foramen. (turn page))  
10. Follow up the central connections of the facial nerve.  
11. Note the proximity of the internal carotid artery to the middle ear. |
|---|---|---|
| 8 | The facial nerve VII | 1. Follow up the course of facial nerve from its point of central connections, exit and down to its target areas.  
2. Describe in details important relation along its course.  
3. Discuss the various modalities of its fibers.  
4. Review your knowledge of its target organs. |
| 9 | Inner ear & cranial nerve VIII. | 1. Make a list of parts making the internal ear.  
2. Define each part. Make sure to use keywords.  
3. Note how structures fit each other.  
4. Describe the bony labyrinth.  
5. Explain how the membranous labyrinth fits the bony one.  
6. Describe the hearing receptors.  
7. Describe the balancing receptors.  
8. Follow the course of the VIII nerve down to its point of entry to the brain.  
9. Follow up the central connections of the VIII nerve. – Review the list of structures making the different parts of the ear. |
| 10 | Hearing. | 1. Review the ossicular system of the ear and discuss its role in the conduction of sound waves from the tympanic membrane to the cochlea sound waves.  
2. Outline the properties of traveling waves and describe how, via these waves, particular movement of the footplate of the stapes produce maximal deflection of the basilar membrane at a particular point.  
3. Discuss the functions of the organs of Corti and describe how deformation of the basilar membrane is converted to impulses in auditory fibers.  
4. Describe the ionic basis of auditory receptors.  
5. Explain how pitch (frequency) and loudness of sound are coded in the auditory pathways.  
6. Discuss the mechanisms that permits sound localization  
7. Describe the function of auditory cortex in hearing perception and sound localization. |
| 11 | Equilibrium. | 1. Explain how hair cells in the semicircular canals detect rotational acceleration.  
2. Explain how hair cells in the utricle and saccule detect linear acceleration  
3. Describe the role of the vestibular system in stabilizing eye movements during acceleration.  
4. Review the major connections of the vestibular system with the brainstem and cerebellum.  
5. List the major sensory input that provides the information, which is synthesized in the brain into the sense of position in space.  
6. Describe the caloric test for evaluation of vestibular functions. |
| 12 | Cranial nerves IX, X. | 1. Follow up its course from its central connections, exit from the brain and down to its target organs.  
2. Make a list of types of nerve modalities conveyed by this nerve.  
3. Review structure of the pharynx tongue and mouth as the target organs.  
4. Follow up its course from its central connections; exit from the brain and down to its target organs.  
5. Make a list of types of nerve modalities it conveys and Review your knowledge of its target organs.  
6. Make note of plexuses it creates in the thorax and abdomen. |
| 13 | Sensory receptors and neural circuits | 1. Define sensory receptors and adequate stimulus.  
2. List different types of receptors and classify them according to modality to which they best respond.  
3. Describe the transduction properties of receptors.  
4. Define receptor potential (generator potential) and know the ionic basis underlying receptor potential and list the properties of receptor potential.  
5. Diagram the electrical response of sensory receptors to graded increase in stimulus strength and describe the relation between receptor potential and the frequency of action potential generated in the sensory nerve that innervate or contain the receptor.  
6. Define receptor adaptation and the mechanism of adaptation in receptors and understand the difference between fast and slowly adapting receptors and know the general functions of each type.  
7. Understand the encoding of modality, intensity, and location of stimulus.  
8. Define labeled line principle, law of projection and law of specific energies.  
9. Define sensory unit and receptive field and describe the effects of there size on acuity of sensations.  
10. List the major types of neuronal circuits involved in the processing of information. |
| 14 | Chemical senses, taste & smell. | 1. Describe the olfactory receptors and the mechanism of their excitation.  
2. Review the anatomy of olfactory pathway.  
3. Describe the primary taste of modalities  
4. Discuss the characteristics of taste buds and distribution in relation to the primary taste modalities  
5. List major substances that produce sweet, sour, bitter and salty taste and comment on their interaction.  
6. Describe taste pathway.  
7. Describe the mechanism of excitation of taste receptors and impulse generation in the primary afferents carrying taste sensation. |
| 15 | Cranial nerves XI, XII. | 1. Follow up its course from its central connections; exit from the brain and down to its target organs.  
- Make a list of types of nerve modalities it conveys.  
- Review your knowledge of its target organs.  
2. Follow up its course from its central connections; exit from the brain and down to its target organs.  
- Make a list of types of nerve modalities it conveys  
- Review your knowledge of its target organs. |
| 16 | Development of head & neck. | 1. Define the following:  
Pharyngeal arches.  
Neural crest cells.  
Pharyngeal grooves.  
Pharyngeal pouches.  
Pharyngeal membranes.  
2. Discuss the changes that will take place on the above structures leading to formation of various organs in the head and neck.  
3. Make a list of these processes involved in the formation of each organ.  
4. Define each process. |
| 17 | Histology of peripheral nervous system. | 1. Review the basic histology of neurons, glial cells and synaptic communications.  
2. Classify nerves.  
3. Describe the structure of peripheral nerves.  
4. Discuss myelination.  
5. Describe the structure of ganglia (sensory and autonomic). |
| 18 | Physiology of peripheral nerves. | 1. List various types of nerve fibers in peripheral nerves and know their function.  
2. Describe and explain the compound action potential and understand its clinical significance  
3. Define latent period and know how to calculate the conduction velocity of peripheral nerves. |
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<th>Page</th>
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| 19   | Local anesthetics. (Pharmacology) | 1. Describe the classification of the local anesthetic  
2. Indicate the pharmacological characteristics of their chemical structures  
3. Describe the mechanism of blockade of the impulse by local anesthetics.  
4. Discuss the relation between pH, pKₐ, and the speed of onset of local anesthesia.  
5. List the factors that determine the susceptibility of nerve fibers to blockade by local anesthetics.  
6. List the major toxic effects of the local anesthetics.  
7. Explain use-of dependent blockade by local anesthetics. |
| 20   | Spinal nerves, cervical plexus & nerves of the neck. (Anatomy) | 1. Describe how spinal nerves are formed.  
2. Make a list of contributing roots to cervical plexus.  
3. Discuss the general arrangement.  
4. Describe the location of this plexus.  
5. Make a list of the out coming nerves.  
6. Follow the branches to their target organs.  
7. Point out the point where the major cutaneous nerves emerge.  
8. Make a list of the cutaneous nerve.  
9. Follow the cutaneous branches to their destinations. |
| 21   | Demyelinating diseases. (Pathology) | 1. Know the various causes and types of peripheral neuropathies  
2. Know about various axonal degeneration and injures  
3. Know the general features of demyelinating diseases, with special emphasis on Multiple Sclerosis, its clinical & morphological characteristics. |
| 22   | Degenerative diseases. (Pathology) | 1. Know the general features of degenerative diseases & dementias, with special emphasis on Alzheimer’s disease, its clinical & morphological findings.  
2. Know briefly about Parkinson’s Disease, Huntington's disease and amyotrophic lateral sclerosis |
| 23   | Brachial plexus (Anatomy) | 1. Make a list of contributing spinal nerves.  
2. Discuss the general arrangement of this plexus.  
3. Locate the plexus in the axilla and note important relations to blood vessels.  
4. Make a list of local branches with short notes on its target organs. |
| 24   | Nerves of the upper limb. (Anatomy) | 1. Make a list of the terminal main branches of brachial plexus.  
2. Follow up each branch down to its target organs (myotomes and Dermatomes). |
| 25   | Lumbosacral plexus & nerves of the lower limb. (Anatomy) | 1. Make a list of contributing spinal nerves to the lumbar plexus.  
2. Discuss the arrangement of the plexus.  
3. Describe the location of this plexus and its relation to the psoas muscle.  
4. List the terminal branches and follow up each branch to its final destination.  
5. Make a list of contributing spinal nerves to the sacral plexus.  
6. Discuss the arrangement of this plexus.  
7. Describe the location of this plexus.  
8. List its terminal branches and follow up each branch to its target organs.  
9. Make a list of nerves of the lower limb including the Gluteal region.  
10. Follow up each nerve down to its target joints(cont) myotomes and dermatomes. |
| 26   | Spinal cord reflexes. (Physiology) | 1. Describe the components that make up the reflex arc, the neural substrate for reflex responses.  
2. The general properties of reflexes will be also analyzed.  
3. Distinguish between and compare monosynaptic and polysynaptic reflexes. using stretch and withdrawal reflexes as examples.  
4. Give examples of stretch reflexes, including those that are frequently tested clinically.  
5. Describe the muscle spindles and analyze their function, with particular attention to how they operate as part of a feedback system to maintain muscle length.  
6. Define reciprocal innervations, inverse stretch reflex, clonus, and lengthening reaction.  
7. Describe superficial reflexes and autonomic reflexes. Define spinal shock, and explain the initial and long-term changes in reflexes that follow transaction of the spinal cord. |
<table>
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<tr>
<th>27</th>
<th>Prions</th>
<th>Historical background, basic structure, classification of diseases involved, epidemiology, pathogenesis and pathology, laboratory diagnosis, treatment and prevention.</th>
</tr>
</thead>
</table>
| 28 | Sympathetic nervous system. | 1. Review the subdivisions of the nervous system.  
2. Review the general arrangement and compare the sympathetic and parasympathetic parts.  
3. Describe the following plans  
   - Para vertebral ganglia.  
   - Prevertebral ganglia.  
   - Parasympathetic ganglia.  
   - Splanchnic nerves.  
   - Autonomic plexuses.  
4. Map out the various plexuses in head and neck, thorax, abdomen and pelvis.  
5. Make a list of the components of the system.  
6. Review the basic structure of sympathetic trunk.  
7. Describe the source of sympathetic system in the neck and make a list of target organs.  
8. Describe the Para vertebral sympathetic ganglia in the abdomen, their locations and target organs.  
9. Discuss the relation of this system to the adrenal medulla.  
10. Discuss the sympathetic innervation of blood vessels. |
| 29 | Parasympathetic nervous system. | 1. Make a list of the components of the system.  
2. Make a list of cranial nerves having parasympathetic activity.  
3. Describe the parasympathetic ganglia in the head and neck, their locations and target organs.  
4. Describe the sacral parasympathetic out flow.  
5. Make a list of its target organs. |
| 30 | Functions of the Autonomic nervous system and central regulation of viscera. | 1. Review the functions of the ANS and the response of effector organs on the neurotransmitters releases by the two divisions.  
2. Understand the concept that ANS is a reflex based control system and emphasize the general feature of autonomic neuronal reflexes.  
3. Describe autonomic reflexes integrated at the level of spinal cord and brain stem  
4. Describe central regulation of autonomic output and the role of nucleus of the solitary tract, limbic system and hypothalamus in the control of autonomic functions.  
5. List the major functions of the hypothalamus including body rhythm, temperature regulation, and appetite control and water intake. |
| 31 | Directly acting cholinergic agonists | 1. Review the steps involved in the synthesis, storage, release and the termination of action of acetylcholine  
2. Mention examples on inhibitors of acetylcholine synthesis, storage, and release.  
3. List the locations and types of acetylcholine receptors in various organ systems.  
4. Describe the effects of acetylcholine on major organ systems.  
5. Correlate the pharmacokinetic properties of various choline esters and cholinomimetic alkaloids with their chemical properties.  
6. List the major clinical indications and adverse effects of cholinomimetic agonists. |
| 32 | Indirectly acting cholinergic agonists | 1. Describe the distribution and function of cholinesterase  
2. Provide a classification and examples on drugs that inhibit cholinesterase  
3. Describe the pharmacodynamic differences between direct and indirect-acting cholinomimetic agents.  
4. List the major signs and symptoms of organophosphate insecticide poisoning.  
5. Describe the treatment modalities of organophosphate poisoning. |
<table>
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<tr>
<th>Page</th>
<th>Subject</th>
<th>Content</th>
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<tbody>
<tr>
<td>33</td>
<td>Group B streptococci, Listeria &amp; mycobacterium Leprae, Clostridium tetani &amp; Clostridium Botulism.</td>
<td>Understand the characteristics, laboratory diagnosis and management of mycobacterium leprae, group B streptococcus and listeria. – Understand the bacteriological aspects, laboratory diagnosis, management and prevention of Clostridium Tetani and Botulism.</td>
</tr>
</tbody>
</table>
| 34   | Cholinergic antagonists | 1. Describe the effects of cholinergic antagonists on various organ systems.  
2. List the major clinical indications of muscarinic antagonists.  
3. List the major adverse effects of antimuscarinic agents.  
4. Describe the signs, symptoms and treatment of atropine poising. |
| 35   | Adrenergic agonists. | A.  
1. Review the steps involved in the synthesis, storage, release and the termination of action of epinephrine and nor epinephrine  
2. List examples on the inhibitors of norepinephrine synthesis, storage, release and re-uptake.  
3. List tissues that contain significant numbers α₁ or α₂ adrenergic receptors.  
4. Describe the major systemic effects of a pure alpha agonist.  
5. Indicate the major clinical applications and major adverse effect of α-receptor agonists.  
B.  
1. List tissues that contain significant numbers of β₁ or β₂ receptors.  
2. Describe the major organ system effects of a pure beta agonist, and a mixed alpha and beta agonist.  
3. List the major clinical applications and adverse effect of β-receptor agonists (turn page).  
4. Indicate the pharmacodynamic differences between direct and indirect acting sympathomimetic amines. |
| 36   | Rabies and arboviruses | Rabies, Arboviruses: Classification, basic structural, morphological and physical properties, epidemiology, pathogenesis, clinical presentation, laboratory diagnosis, treatment, and prevention. |
| 37   | Adrenergic antagonists I | 1. Indicate the differences between selective and nonselective α-receptor antagonists.  
2. List the main indications and the major adverse effects of α-receptors antagonists  
3. Provide a classification for α-receptor antagonists. |
| 38   | Adrenergic antagonists II | 1. Compare the pharmacokinetics of various β-receptor antagonists  
2. Describe the main indications and major adverse effects of β receptors antagonists  
3. Describe the main drug-drug interactions of α and β receptors antagonists. |
| 39   | Enteroviruses. | Enteroviruses : Polio viruses, coxsaki viruses, echo viruses, basic structural, morphological and physical properties, epidemiology, pathogenesis, clinical presentation, laboratory diagnosis, treatment, and prevention. |
| 40   | Ticks | 1. Definition of Ticks  
2. Morphology.  
3. Life cycle.  
4. Pathogenesis and clinical disease.  
5. Clinical manifestations.  
6. Laboratory diagnosis.  
7. Treatment.  
**Laboratory Sessions.**

**Instructions:**

It is important that you get prepared for your lab sessions by:
1. Studying your reading material.
2. Have a preliminary idea by having a look at your atlas.
3. Prepare a list of structure you need to identify, Micro and Macro.
4. Then you come to the lab (with atlases and books if you wish) to develop your skills of comparison, identification and observing how things fit on each other.
5. Instructors will facilitate your learning.

<table>
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<tr>
<th>No.</th>
<th>Title</th>
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<tbody>
<tr>
<td>1</td>
<td>Morphology of the Orbit, Eye and Ear Face &amp; Neck <em>(Anatomy 1)</em></td>
<td>Recognize individual structures. Observe how they fit on each other. Compare &amp; contrast between your understanding, your atlas and the real thing you see in the lab.</td>
</tr>
<tr>
<td>2</td>
<td>Neck <em>(Anatomy 2)</em></td>
<td>Recognize individual structures. Observe how they fit on each other. Compare &amp; contrast between your understanding, your atlas and the real thing you see in the lab.</td>
</tr>
<tr>
<td>3</td>
<td>Brachial plexus and Nerves of the upper limb. Lumbo-sacral plexus and nerves of the lower limb. <em>(Anatomy 3)</em></td>
<td>Recognize individual structures. Observe how they fit on each other. Compare &amp; contrast between your understanding, your atlas and the real thing you see in the lab.</td>
</tr>
<tr>
<td>4</td>
<td>Pathology 1.</td>
<td>Students are expected to study computerized images of gross &amp; microscopic findings of: CNS tumors I</td>
</tr>
<tr>
<td>5</td>
<td>Pathology 2.</td>
<td>Students are expected to study computerized images of gross &amp; microscopic findings of: 1. Tumors II 2. Gross &amp; microscopic findings in Multiple Sclerosis, Parkinson’s disease and Alzheimer’s disease and other degenerative diseases</td>
</tr>
<tr>
<td>6</td>
<td>Physiology 1.</td>
<td>Students are expected to do experiments demonstrating the following tests: 1. Visual acuity test, Snellen, Charts. 2. Color vision test using Ishihara charts. 3. Confrontational perimetry and mapping of blind spot. 4. Use of ophthalmoscope and examination of the retina.</td>
</tr>
<tr>
<td>7</td>
<td>Physiology 2.</td>
<td>Students are expected to perform auditory tests, including Rennn’s and Webber’s tests. Demonstrating physiology of balance and equilibrium using Barny chair.</td>
</tr>
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E. Assessment:

<table>
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<tr>
<td>First Exam</td>
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<td>MCQ</td>
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<tr>
<td>Practical Exam</td>
<td>Identifying structures or tissues of pictures.</td>
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<tr>
<td>Small group Discussion</td>
<td>2%</td>
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<tr>
<td>Final Exam</td>
<td>40%</td>
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</table>

IV  
Recommended reading material:  
References:

Anatomy:
5. www.medicalstudent.com or search the web for any subject of your preference.

Pathology:
3. Supplementary handouts.

Physiology:

Pharmacology:

Microbiology:
- Medical Microbiology. By John C Sherris. Third edition

D. Summary of teaching activities of the module.

<table>
<thead>
<tr>
<th></th>
<th>Lectures</th>
<th>LABS</th>
<th>Small group discussions</th>
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<tbody>
<tr>
<td>Introduction</td>
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<td>15</td>
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<tr>
<td>Anatomy</td>
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### Neurosciences II
#### 2010
#### Timetable

### Week – 1

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<tr>
<td>11:15 – 12</td>
<td></td>
<td>Case Presentation Scie – Hall 11:15</td>
<td>Eye &amp; Optic nerve (Anatomy)</td>
<td>Neurophysiology of vision, the eye, retina and central visual pathway. (Physiology)</td>
<td>facial nerve. (Anatomy)</td>
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<td>12:15 -1:0</td>
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<td>Tumors of the nervous system (Pathology)</td>
<td>The Orbit, Cranial nerves III, IV and VI (Anatomy)</td>
<td>Trigeminal nerve, V (Anatomy)</td>
<td>Inner ear and cranial nerve VIII (Anatomy)</td>
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<td>1:15 – 2</td>
<td>M 382</td>
<td></td>
<td>The external and middle ear (Anatomy)</td>
<td>M 362</td>
<td>Hearing. (Physiology)</td>
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### Week - 2

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<td>Equilibrium. (Physiology)</td>
<td>Sensory receptors (Physiology)</td>
<td>Development of head and neck. (Anatomy)</td>
<td>Physiology of peripheral nerves (Physiology)</td>
<td>Demyelinating diseases. (Pathology)</td>
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<td>Cranial nerves IX, and X. (Anatomy)</td>
<td>Chemical senses, taste and smell. (Physiology)</td>
<td>Histology of peripheral nerves. (Anatomy)</td>
<td>Local anesthetics. (Pharmacology)</td>
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Case Study of Peripheral Neuropathy for small group discussion sessions.
Please read the case very carefully.
Every word and idea is subjected for criticism.
Prepare your questions and comments for discussion in your small group.

A 57-year-old woman was seen in the neurology clinic of this hospital because of longtime numbness and weakness in her feet and legs. When she was in her early 30s, numbness developed over the anterior surfaces of her shins and ankles. In her early to mid-40s, she became unsteady when using the stairs or walking in the dark. She noticed weakness in her feet. She had no dorsiflexion of her toes, and they tended to catch on carpets or on thresholds. Her feet occasionally ached, and she believed that her arches had become higher. Dysesthetic sensations developed in her feet, which she said felt “cold and wet.” The father of the patient had had high-arched feet, and poor balance. The patient had five siblings; two brothers had polyneuropathy, one of whom had high-arched feet and hammertoes. The patient had three children.

The patient had hammertoes but not high-arched feet. No hypertrophic nerves were palpable. On neurological examination she was alert and cooperative. She had a head tremor. She walked with forearm crutches. She was unable to walk on her toes or heels. Romberg’s sign was present. Strength in her arms and proximal legs was normal. Strength in the dorsiflexor, invertor, and evertor muscles in the feet was 2/5 bilaterally. Plantar flexor strength was 4/5. Deep-tendon reflexes were absent except for triceps jerks. Sensory examination revealed reduced sensation to light touch in the feet up to the proximal legs and to pinprick to the middle of the legs. Position sense and vibration sensation were absent at the toes and reduced at the ankles. Coordination was normal.

Laboratory studies at that time, including routine blood chemical studies, a complete blood count, liver-function tests, a lipid profile, serum protein electrophoresis, antinuclear antibody and rapid plasma reagin tests, erythrocyte sedimentation rate, and levels of vitamin B12, folate, and thyrotropin were normal. The creatine kinase level was reported to be slightly high.

Electromyography at that time showed absent sural and superficial peroneal sensory responses. Median, ulnar, and radial sensory potentials were slightly small with mildly prolonged latencies.

Peroneal and tibial motor responses were very small, and conduction velocities were slowed. Median and ulnar motor responses were of normal amplitude, but conduction velocities were mildly slow. Needle examination showed fibrillation potentials in the left extensor hallucis longus and medial gastrocnemius. No fibrillation potentials were seen in the tibialis anterior, vastus, lateralis, or muscles in the arms.
Below are three mini problems. Study these problems carefully at the beginning of the module, keep them in your mind and during the lectures follow up the information that will solve the problems.

Mini problem 1:
A 42-year-old construction worker comes to the emergency department because of severe low back pain that began after lifting a heavy object at work 2 days ago. Since awakening this morning he has had numbness in his buttocks and the soles of both feet. He has not urinated for 6 hours, and bladder catheterization leads to the drainage of 400 mL of urine. Examination shows severe pain on straight leg raising bilaterally to 20 degrees. Strength is normal except for 3/5 weakness in plantar flexion bilaterally. There is diminished pin sensation in the soles of his feet. Ankle reflexes are absent, and plantar responses are flexor.

Mini problem 2: A 29-year-old, right handed, East Indian woman presented with worsening numbness and tingling in both hands.
The patient's symptoms began about 2 years before hospital admission, when she noted discoloration of the skin on her feet. She first noticed the rash on the top medial aspect of her left foot. A few months later, she saw a similar discoloration on the top of her right foot. She was not aware of any numbness in that region and did not pay further attention to this.
Toward the beginning of her pregnancy in 1998, she became aware of tingling sensations in the fingertips of her left hand. After her pregnancy, however, these symptoms resolved. From the end of December 1999 to the beginning of January 2000, she began to experience more frequent tingling sensations in the index and middle fingers of her left hand. This gradually progressed to include all the digits of the left hand.

During this time, she also noticed a blister on her left index finger and the left middle finger, but she assumed this was the result of a burn she might have sustained, unawares, while cooking or ironing. She also noticed that she was dropping objects held in the left hand.

At this time, she sought medical attention from her internist who thought this could be arthritis and who prescribed celecoxib.

The patient traveled to India on January 26, 2000. This was the first visit to India she had made in 12 years. The tingling sensation in her left hand had become continuous and now she began to feel more numbness as well. She saw a dermatologist and a neurologist in India who examined her and the discolored patches on her feet and found them to be numb.

She underwent a skin biopsy to look for evidence of vascular or infectious changes. She was told that the skin biopsy was negative, but was prescribed antibiotics for a presumed bacterial infection.

Within days after starting the antibiotics, she began experiencing severe pain, primarily in the left shoulder and extending to the entire left arm. She also experienced further discoloration and rash on multiple areas on her body, including patches on her right foot extending to the right ankle, the left foot now extending more medially, the right side of her face, and several areas on her back. She was unaware that these areas were particularly numb.

Along with the worsening pain, she also developed numbness her right hand, more medially side (the little finger and the ring finger). During this time, she also developed daily fevers to 100-101° F (38.3-38.8° C) and felt extremely tired with very poor appetite, losing 15-16 lbs. during this time.

These symptoms continued for approximately 6 weeks, until her return to the United States on March 30. Since then, her fever has subsided and the pain is virtually gone in her shoulder region. Even the skin rashes have subsided with the corticosteroid cream given by her dermatologist in the United States.

Mini problem 3:
A 44-year-old, right-handed black woman presents with right-sided facial droop after noting left-sided facial droop 1 month earlier. The left facial droop is still resolving.
The patient has been aware of a right facial droop for the past 3 days and reports having had a mild left-sided facial droop last month, which was diagnosed as idiopathic Bell's palsy. She denies headache, focal weakness, paresthesias, or vertigo, but complains of right foot pain and right knee pain, both worsened by weight bearing for the past 2 months. Her joints feel stiff in the morning, and she noted a fever when she took her temperature at home. She has taken ibuprofen, which led to some improvement.
She reports increased fatigue, but denies weight loss or night sweats. Most recently, she has noticed feeling nauseated, and everything she eats tastes like butter. She also states that things “sound louder” in the right ear.

Past Medical History: No medical or significant childhood illnesses

Medications: Ibuprofen 600 mg as needed

Physical Examination

General exam is normal.

Neurological exam:
Mental status was intact.
Cranial nerves: Pupils equally round and reactive to light; visual fields full; visual acuity normal; extraocular muscles intact; right facial droop including forehead; decreased nasolabial fold on the right side; facial sensation intact; mild left-facial droop; corneal reflexes intact; dulled taste sensation on right side of tongue; hearing intact bilaterally; palate symmetric; shoulder shrug symmetric; tongue midline
Motor: 5/5 throughout, normal tone and bulk, no drift
Sensation: pinprick and vibration intact throughout
Coordination: Finger-to-nose and heel-to-shin intact
Reflexes: 2+ and symmetric
Plantar reflex: downgoing bilaterally
Gait: normal, no ataxia

Suggested reading material for small group discussion case.
What is peripheral neuropathy?
How are the peripheral neuropathies classified?
What are the symptoms of peripheral nerve damage?
What causes peripheral neuropathy?
How is peripheral neuropathy diagnosed?
What treatments are available?
What research is being done?
Where can I get more information?

Peripheral neuropathy describes damage to the peripheral nervous system, the vast communications network that transmits information from the brain and spinal cord (the central nervous system) to every other part of the body. Peripheral nerves also send sensory information back to the brain and spinal cord, such as a message that the feet are cold or a finger is burned. Damage to the peripheral nervous system interferes with these vital connections. Like static on a telephone line, peripheral neuropathy distorts and sometimes interrupts messages between the brain and the rest of the body.

Because every peripheral nerve has a highly specialized function in a specific part of the body, a wide array of symptoms can occur when nerves are damaged. Some people may experience temporary numbness, tingling, and prickling sensations (paresthesia), sensitivity to touch, or muscle weakness. Others may suffer more extreme symptoms, including burning pain (especially at night), muscle wasting, paralysis, or organ or gland dysfunction. People may become unable to digest food easily, maintain safe levels of blood pressure, sweat normally, or experience normal sexual function. In the most extreme cases, breathing may become difficult or organ failure may occur.

Some forms of neuropathy involve damage to only one nerve and are called mononeuropathies. More often though, multiple nerves affecting all limbs are affected-called mononeuropathies. Occasionally, two or more isolated nerves in separate areas of the body are affected-called mononeuritis multiplex.

In acute neuropathies, such as Guillain-Barré syndrome, symptoms appear suddenly, progress rapidly, and resolve slowly as damaged nerves heal. In chronic forms, symptoms begin subtly and progress slowly. Some people may have periods of relief followed by relapse. Others may reach a plateau stage where symptoms stay the same for many months or years. Some chronic neuropathies worsen over time, but very few forms prove fatal unless complicated by other diseases. Occasionally the neuropathy is a symptom of another disorder.

In the most common forms of polyneuropathy, the nerve fibers (individual cells that make up the nerve) most distant from the brain and the spinal cord malfunction first. Pain and other symptoms may appear over a period of days, weeks, or years. Muscle weakness is the most common symptom of motor nerve damage. Other symptoms may include painful cramps and fasciculations (uncontrolled muscle twitching visible under the skin), muscle loss, bone degeneration, and changes in
the skin, hair, and nails. These more general degenerative changes also can result from sensory or autonomic nerve fiber loss.

Sensory nerve damage causes a more complex range of symptoms because sensory nerves have a wider, more highly specialized range of functions. Larger sensory fibers enclosed in myelin (a fatty protein that coats and insulates many nerves) register vibration, light touch, and position sense. Damage to large sensory fibers lessens the ability to feel vibrations and touch, resulting in a general sense of numbness, especially in the hands and feet. People may feel as if they are wearing gloves and stockings even when they are not. Many patients cannot recognize by touch alone the shapes of small objects or distinguish between different shapes. This damage to sensory fibers may contribute to the loss of reflexes (as can motor nerve damage). Loss of position sense often makes people unable to coordinate complex movements like walking or fastening buttons, or to maintain their balance when their eyes are shut. Neuropathic pain is difficult to control and can seriously affect emotional well-being and overall quality of life. Neuropathic pain is often worse at night, seriously disrupting sleep and adding to the emotional burden of sensory nerve damage.

Smaller sensory fibers without myelin sheaths transmit pain and temperature sensations. Damage to these fibers can interfere with the ability to feel pain or changes in temperature. People may fail to sense that they have been injured from a cut or that a wound is becoming infected. Others may not detect pains that warn of impending heart attack or other acute conditions. (Loss of pain sensation is a particularly serious problem for people with diabetes, contributing to the high rate of lower limb amputations among this population.) Pain receptors in the skin can also become oversensitized, so that people may feel severe pain (allodynia) from stimuli that are normally painless (for example, some may experience pain from bed sheets draped lightly over the body).

Symptoms of autonomic nerve damage are diverse and depend upon which organs or glands are affected. Autonomic nerve dysfunction can become life threatening and may require emergency medical care in cases when breathing becomes impaired or when the heart begins beating irregularly. Common symptoms of autonomic nerve damage include an inability to sweat normally, which may lead to heat intolerance; a loss of bladder control, which may cause infection or incontinence; and an inability to control muscles that expand or contract blood vessels to maintain safe blood pressure levels. A loss of control over blood pressure can cause dizziness, lightheadedness, or even fainting when a person moves suddenly from a seated to a standing position (a condition known as postural or orthostatic hypotension).

Gastrointestinal symptoms frequently accompany autonomic neuropathy. Nerves controlling intestinal muscle contractions often malfunction, leading to diarrhea, constipation, or incontinence. Many people also have problems eating or swallowing if certain autonomic nerves are affected.

**What causes peripheral neuropathy?**

Peripheral neuropathy may be either inherited or acquired. Causes of acquired peripheral neuropathy include physical injury (trauma) to a nerve, tumors, toxins, autoimmune responses, nutritional deficiencies, alcoholism, and vascular and metabolic disorders. Acquired peripheral neuropathies are grouped into three broad categories: those caused by systemic disease, those caused by trauma from external agents, and those caused by infections or autoimmune disorders affecting nerve tissue. One example of an acquired peripheral neuropathy is trigeminal neuralgia (also known as tic douloureux), in which damage to the trigeminal nerve (the large nerve of the head and face) causes episodic attacks of excruciating, lightning-like pain on one side of the face. In some cases, the cause is an earlier viral infection, pressure on the nerve from a tumor or swollen blood vessel, or, infrequently, multiple sclerosis. In many cases, however, a specific cause cannot be identified. Doctors usually refer to neuropathies with no known cause as idiopathic neuropathies.

Physical injury (trauma) is the most common cause of injury to a nerve. Injury or sudden trauma, such as from automobile accidents, falls, and sports-related activities, can cause nerves to be partially or completely severed, crushed, compressed, or stretched, sometimes so forcefully that they are partially or completely detached from the spinal cord. Less dramatic traumas also can cause serious nerve damage. Broken or dislocated bones can exert damaging pressure on neighboring nerves, and slipped disks between vertebrae can compress nerve fibers where they emerge from the spinal cord. Systemic diseases — disorders that affect the entire body — often cause peripheral neuropathy. These disorders may include: Metabolic and endocrine disorders. Nerve tissues are highly vulnerable to damage from diseases that impair the body's ability to transform nutrients into energy, process waste products, or manufacture the substances that make up living tissue. Diabetes mellitus, characterized by chronically high blood glucose levels, is a leading cause of peripheral neuropathy in the United States. About 60 percent to 70 percent of people with diabetes have mild to severe forms of nervous system damage. Kidney disorders can lead to abnormally high amounts of toxic substances in the blood that can severely damage nerve tissue. A majority of patients who require dialysis because of kidney failure develop polyneuropathy. Some liver diseases also lead to neuropathies as a result of chemical imbalances.

Hormonal imbalances can disturb normal metabolic processes and cause neuropathies. For example, an underproduction of thyroid hormones slows metabolism, leading to fluid retention and swollen tissues that can exert pressure on peripheral nerves. Overproduction of growth hormone can lead to acromegaly, a condition characterized by the abnormal enlargement of many parts of the skeleton, including the joints. Nerves running through these affected joints often become entrapped.
Vitamin deficiencies and alcoholism can cause widespread damage to nerve tissue. Vitamins E, B1, B6, B12, and niacin are essential to healthy nerve function. Thiamine deficiency, in particular, is common among people with alcoholism because they often also have poor dietary habits. Thiamine deficiency can cause a painful neuropathy of the extremities. Some researchers believe that excessive alcohol consumption may, in itself, contribute directly to nerve damage, a condition referred to as alcoholic neuropathy.

Vascular damage and blood diseases can decrease oxygen supply to the peripheral nerves and quickly lead to serious damage to or death of nerve tissues, much as a sudden lack of oxygen to the brain can cause a stroke. Diabetes frequently leads to blood vessel constriction. Various forms of vasculitis (blood vessel inflammation) frequently cause vessel walls to harden, thicken, and develop scar tissue, decreasing their diameter and impeding blood flow. This category of nerve damage, in which isolated nerves in different areas are damaged, is called mononeuropathy multiplex or multifocal mononeuropathy.

Connective tissue disorders and chronic inflammation can cause direct and indirect nerve damage. When the multiple layers of protective tissue surrounding nerves become inflamed, the inflammation can spread directly into nerve fibers. Chronic inflammation also leads to the progressive destruction of connective tissue, making nerve fibers more vulnerable to compression injuries and infections. Joints can become inflamed and swollen and entrap nerves, causing pain.

Cancers and benign tumors can infiltrate or exert damaging pressure on nerve fibers. Tumors also can arise directly from nerve tissue cells. Widespread polyneuropathy is often associated with the neurofibromatoses, genetic diseases in which multiple benign tumors grow on nerve tissue. Neuromas, benign masses of overgrown nerve tissue that can develop after any penetrating injury that severs nerve fibers, generate very intense pain signals and sometimes engulf neighboring nerves, leading to further damage and even greater pain. Neuroma formation can be one element of a more widespread neuropathic pain condition called complex regional pain syndrome or reflex sympathetic dystrophy syndrome, which can be caused by traumatic injuries or surgical trauma. Paraneoplastic syndromes, a group of rare degenerative disorders that are triggered by a person's immune system response to a cancerous tumor, also can indirectly cause widespread nerve damage.

Repetitive stress frequently leads to entrapment neuropathies, a special category of compression injury. Cumulative damage can result from repetitive, forceful, awkward activities that require flexing of any group of joints for prolonged periods. The resulting irritation may cause ligaments, tendons, and muscles to become inflamed and swollen, constricting the narrow passageways through which some nerves pass. These injuries become more frequent during pregnancy, probably because weight gain and fluid retention also constrict nerve passageways.

Toxins can also cause peripheral nerve damage. People who are exposed to heavy metals (arsenic, lead, mercury, thallium), industrial drugs, or environmental toxins frequently develop neuropathy. Certain anticancer drugs, anticonvulsants, antiviral agents, and antibiotics have side effects that can include peripheral nerve damage, thus limiting their long-term use.

Infections and autoimmune disorders can cause peripheral neuropathy. Viruses and bacteria that can attack nerve tissues include herpes varicella-zoster (shingles), Epstein-Barr virus, cytomegalovirus, and herpes simplex-members of the large family of human herpes viruses. These viruses severely damage sensory nerves, causing attacks of sharp, lightning-like pain. Postherpetic neuralgia often occurs after an attack of shingles and can be particularly painful.

The human immunodeficiency virus (HIV), which causes AIDS, also causes extensive damage to the central and peripheral nervous systems. The virus can cause several different forms of neuropathy, each strongly associated with a specific stage of active immunodeficiency disease. A rapidly progressive, painful polyneuropathy affecting the feet and hands is often the first clinically apparent sign of HIV infection.

Lyme disease, diphtheria, and leprosy are bacterial diseases characterized by extensive peripheral nerve damage. Diphtheria and leprosy are now rare in the United States, but Lyme disease is on the rise. It can cause a wide range of neuropathic disorders, including a rapidly developing, painful polyneuropathy, often within a few weeks after initial infection by a tick bite.

Viral and bacterial infections can also cause indirect nerve damage by provoking conditions referred to as autoimmune disorders, in which specialized cells and antibodies of the immune system attack the body's own tissues. These attacks typically cause destruction of the nerve's myelin sheath or axon (the long fiber that extends out from the main nerve cell body).

Some neuropathies are caused by inflammation resulting from immune system activities rather than from direct damage by infectious organisms. Inflammatory neuropathies can develop quickly or slowly, and chronic forms can exhibit a pattern of alternating remission and relapse. Acute inflammatory demyelinating neuropathy, better known as Guillain-Barré syndrome, can damage motor, sensory, and autonomic nerve fibers. Most people recover from this syndrome although severe cases can be life threatening. Chronic inflammatory demyelinating polyneuropathy (CIDP),
generally less dangerous, usually damages sensory and motor nerves, leaving autonomic nerves intact. Multifocal motor neuropathy is a form of inflammatory neuropathy that affects motor nerves exclusively; it may be chronic or acute.

Inherited forms of peripheral neuropathy are caused by inborn mistakes in the genetic code or by new genetic mutations. Some genetic errors lead to mild neuropathies with symptoms that begin in early adulthood and result in little, if any, significant impairment. More severe hereditary neuropathies often appear in infancy or childhood.

The most common inherited neuropathies are a group of disorders collectively referred to as Charcot-Marie-Tooth disease. These neuropathies result from flaws in genes responsible for manufacturing neurons or the myelin sheath. Hallmarks of typical Charcot-Marie-Tooth disease include extreme weakening and wasting of muscles in the lower legs and feet, gait abnormalities, loss of tendon reflexes, and numbness in the lower limbs.

**How is peripheral neuropathy diagnosed?**

Diagnosing peripheral neuropathy is often difficult because the symptoms are highly variable. A thorough neurological examination is usually required and involves taking an extensive patient history (including the patient’s symptoms, work environment, social habits, exposure to any toxins, history of alcoholism, risk of HIV or other infectious disease, and family history of neurological disease), performing tests that may identify the cause of the neuropathic disorder, and conducting tests to determine the extent and type of nerve damage.

A general physical examination and related tests may reveal the presence of a systemic disease causing nerve damage. Blood tests can detect diabetes, vitamin deficiencies, liver or kidney dysfunction, other metabolic disorders, and signs of abnormal immune system activity. An examination of cerebrospinal fluid that surrounds the brain and spinal cord can reveal abnormal antibodies associated with neuropathy. More specialized tests may reveal other blood or cardiovascular diseases, connective tissue disorders, or malignancies. Tests of muscle strength, as well as evidence of cramps or fasciculations, indicate motor fiber involvement. Evaluation of a patient’s ability to register vibration, light touch, body position, and pain reveals sensory nerve damage and may indicate whether small or large sensory nerve fibers are affected.

Based on the results of the neurological exam, physical exam, patient history, and any previous screening or testing, additional testing may be ordered to help determine the nature and extent of the neuropathy.

Computed tomography, or CT scan, is a noninvasive, painless process used to produce rapid, clear two-dimensional images of organs, bones, and tissues. X-rays are passed through the body at various angles and are detected by a computerized scanner. The data is processed and displayed as cross-sectional images, or "slices," of the internal structure of the body or organ. Neurological CT scans can detect bone and vascular irregularities, certain brain tumors and cysts, herniated disks, encephalitis, spinal stenosis (narrowing of the spinal canal), and other disorders.

Magnetic resonance imaging (MRI) can examine muscle quality and size, detect any fatty replacement of muscle tissue, and determine whether a nerve fiber has sustained compression damage. The MRI equipment creates a strong magnetic field around the body. Radio waves are then passed through the body to trigger a resonance signal that can be detected at different angles within the body. A computer processes this resonance into either a three-dimensional picture or a two-dimensional "slice" of the scanned area.

Electromyography (EMG) involves inserting a fine needle into a muscle to compare the amount of electrical activity present when muscles are at rest and when they contract. EMG tests can help differentiate between muscle and nerve disorders.

Nerve conduction velocity (NCV) tests can precisely measure the degree of damage in larger nerve fibers, revealing whether symptoms are being caused by degeneration of the myelin sheath or the axon. During this test, a probe electrically stimulates a nerve fiber, which responds by generating its own electrical impulse. An electrode placed further along the nerve’s pathway measures the speed of impulse transmission along the axon. Slow transmission rates and impulse blockage tend to indicate damage to the myelin sheath, while a reduction in the strength of impulses is a sign of axonal degeneration.

Nerve biopsy involves removing and examining a sample of nerve tissue, most often from the lower leg. Although this test can provide valuable information about the degree of nerve damage, it is an invasive procedure that is difficult to perform and may itself cause neuropathic side effects. Many experts do not believe that a biopsy is always needed for diagnosis.

Skin biopsy is a test in which doctors remove a thin skin sample and examine nerve fiber endings. This test offers some unique advantages over NCV tests and nerve biopsy. Unlike NCV, it can reveal damage present in smaller fibers; in contrast to conventional nerve biopsy, skin biopsy is less invasive, has fewer side effects, and is easier to perform.

**What treatments are available?**
No medical treatments now exist that can cure inherited peripheral neuropathy. However, there are therapies for many other forms. Any underlying condition is treated first, followed by symptomatic treatment. Peripheral nerves have the ability to regenerate, as long as the nerve cell itself has not been killed. Symptoms often can be controlled, and eliminating the causes of specific forms of neuropathy often can prevent new damage.

In general, adopting healthy habits—such as maintaining optimal weight, avoiding exposure to toxins, following a physician-supervised exercise program, eating a balanced diet, correcting vitamin deficiencies, and limiting or avoiding alcohol consumption—can reduce the physical and emotional effects of peripheral neuropathy. Active and passive forms of exercise can reduce cramps, improve muscle strength, and prevent muscle wasting in paralyzed limbs. Various dietary strategies can improve gastrointestinal symptoms. Timely treatment of injury can help prevent permanent damage. Quitting smoking is particularly important because smoking constricts the blood vessels that supply nutrients to the peripheral nerves and can worsen neuropathic symptoms. Self-care skills such as meticulous foot care and careful wound treatment in people with diabetes and others who have an impaired ability to feel pain can alleviate symptoms and improve quality of life. Such changes often create conditions that encourage nerve regeneration.

Systemic diseases frequently require more complex treatments. Strict control of blood glucose levels has been shown to reduce neuropathic symptoms and help people with diabetic neuropathy avoid further nerve damage. Inflammatory and autoimmune conditions leading to neuropathy can be controlled in several ways. Immunosuppressive drugs such as prednisone, cyclosporine, or azathioprine may be beneficial. Plasmapheresis—a procedure in which blood is removed, cleansed of immune system cells and antibodies, and then returned to the body—can limit inflammation or suppress immune system activity. High doses of immunoglobulins, proteins that function as antibodies, also can suppress abnormal immune system activity.

Neuropathic pain is often difficult to control. Mild pain may sometimes be alleviated by analgesics sold over the counter. Several classes of drugs have recently proved helpful to many patients suffering from more severe forms of chronic neuropathic pain. These include mexiletine, a drug developed to correct irregular heart rhythms (sometimes associated with severe side effects); several antiepileptic drugs, including gabapentin, phenytoin, and carbamazepine; and some classes of antidepressants, including tricyclics such as amitriptyline. Injections of local anesthetics such as lidocaine or ical patches containing lidocaine may relieve more intractable pain. In the most severe cases, doctors can surgically destroy nerves; however, the results are often temporary and the procedure can lead to complications.

Mechanical aids can help reduce pain and lessen the impact of physical disability. Hand or foot braces can compensate for muscle weakness or alleviate nerve compression. Orthopedic shoes can improve gait disturbances and help prevent foot injuries in people with a loss of pain sensation. If breathing becomes severely impaired, mechanical ventilation can provide essential life support.

Surgical intervention often can provide immediate relief from mononeuropathies caused by compression or entrapment injuries. Repair of a slipped disk can reduce pressure on nerves where they emerge from the spinal cord; the removal of benign or malignant tumors can also alleviate damaging pressure on nerves. Nerve entrapment often can be corrected by the surgical release of ligaments or tendons.

What research is being done?

The National Institute of Neurological Disorders and Stroke (NINDS), a component of the Federal government's National Institutes of Health (NIH) within the U.S. Department of Health and Human Services, has primary responsibility for research on peripheral neuropathy. Current research projects funded by the NINDS involve investigations of genetic factors associated with hereditary neuropathies, studies of biological mechanisms involved in diabetes-associated neuropathies, efforts to gain greater understanding of how the immune system contributes to peripheral nerve damage, and efforts to develop new therapies for neuropathic symptoms.

Because specific genetic defects have been identified for only a fraction of the known hereditary neuropathies, the Institute sponsors studies to identify other genetic defects that may cause these conditions. Presymptomatic diagnosis may lead to therapies for preventing nerve damage before it occurs, and gene replacement therapies could be developed to prevent or reduce cumulative nerve damage.

Several NINDS-funded studies are investigating some of the possible biological mechanisms responsible for the many forms of neuropathy, including the autonomic neuropathies that affect people with diabetes. The Institute also is funding studies to measure the frequency and progression rates of diabetic neuropathies, examine the effects of these disorders on quality of life, and identify factors that may put certain individuals at greater risk for developing diabetes-associated neuropathies.

Scientists have found that the destructive effects of abnormal immune system activity cause many neuropathies for which a cause could not previously be identified. However, the exact biological mechanisms that lead to this nerve
damage are not yet well understood. Many NINDS-sponsored studies are studying inflammatory neuropathies, both in research animals and in humans, to clarify these mechanisms so that therapeutic interventions can be developed.

Neuropathic pain is a primary target of NINDS-sponsored studies aimed at developing more effective therapies for symptoms of peripheral neuropathy. Some scientists hope to identify substances that will block the brain chemicals that generate pain signals, while others are investigating the pathways by which pain signals reach the brain.

Studies of neurotrophic factors represent one of the most promising areas of research aimed at finding new, more effective treatments for peripheral neuropathies. These substances, produced naturally by the body, protect neurons from injury and encourage their survival. Neurotrophic factors also help maintain normal function in mature nerve cells, and some stimulate axon regeneration. Several NINDS-sponsored studies seek to learn more about the effects of these powerful chemicals on the peripheral nervous system and may eventually lead to treatments that can reverse nerve damage and cure peripheral nerve disorders.