Neurological Diagnostic Tests and Procedures

U.S. DEPARTMENT OF HEALTHAND HUMAN SERVICES National Institutes of Health

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Diagnostic tests and procedures are vital tools that help physicians confirm or rule out a neurological disorder or other medical condition. A century ago, the only way to make a definite diagnosis for many neurological disorders was to perform an autopsy after someone had died. Today, new instruments and techniques allow scientists to assess the living brain and monitor nervous system activity as it occurs. Doctors now have powerful and accurate tools to better diagnose disease and to test how well a particular therapy may be working.

Perhaps the most significant changes during the past 10 years have occurred in genetic testing and diagnostic imaging. Much has been learned from sequencing the human genome (the complete set of a person's genes) and developing new technologies that detect genetic mutations. Improved imaging techniques provide highresolution images that allow physicians to view the structure of the brain. Specialized imaging methods can visualize changes in brain activity or the amounts of particular brain chemicals. Scientists continue to improve these methods to provide more detailed diagnostic information.

Researchers and physicians use a variety of diagnostic imaging techniques and chemical and metabolic tests to detect, manage, and treat neurological disease. Many tests can be performed in a physician's office or at an outpatient testing facility, with little if any risk to the person. Some procedures are performed in specialized settings to determine particular disorders or abnormalities. Depending on the type of test, results may be immediate or may take time to process.

What is a neurological examination?

A neurological examination assesses motor and sensory skills, hearing and speech, vision, coordination, and balance. It may also test mental status, mood, and behavior. The examination uses tools such as a tuning fork, flashlight, reflex hammer, and a tool for examining the eye. The results of the neurological examination and the person's history are used to determine a list of possibilities, known as the differential diagnosis, that help determine which additional diagnostic tests and procedures are needed.

What are some of the more common screening tests?

aboratory tests of blood, urine, or other body fluids may help doctors diagnose disease, understand disease severity, and monitor levels of therapeutic drugs. Certain tests, ordered by the physician as part of a regular check-up, provide general information, while others are used to identify specific health concerns. For example, blood tests can provide evidence for infections, toxins, clotting disorders, or antibodies that signal the presence of an autoimmune disease. Genetic testing of DNA extracted from cells in the blood or saliva can be used to diagnose hereditary disorders. Analysis of the fluid that surrounds the brain and spinal cord can detect meningitis, encephalitis, acute and chronic inflammation, viral infections, multiple sclerosis, and certain neurodegenerative disorders. Chemical and metabolic testing of the blood can indicate some muscle disorders, protein or fat-related disorders that affect the brain and inborn errors of metabolism. Blood tests can monitor levels of therapeutic drugs used to treat epilepsy and other neurological disorders. Analyzing urine samples can reveal toxins, abnormal metabolic substances, proteins that cause disease, or signs of certain infections.

Genetic testing of people with a family history of a neurological disease can determine if they are carrying one of the genes known to cause the disorder. Genetic counseling may help people understand the purpose of the tests and what the results could mean. Genetic testing that is used for diagnosis or treatment should be done in a laboratory that has been certified for clinical testing. Clinical testing can look for mutations in specific genes or in certain regions of several genes. This testing may use a panel of genes for a specific type of disease (for example, infant-onset epilepsy) or a test known as whole exome sequencing. Exomes are the parts of the genome formed by exons, which code for proteins. Exome sequencing may take several months to analyze. Clinicians and researchers also sequence whole exomes or whole genomes to discover new genes that cause neurological disorders. These genes may eventually be used for clinical testing in more focused panels.

Prenatal genetic testing can identify many neurological disorders and genetic abnormalities in utero (while the child is inside the mother's womb).

- The mother's blood can be screened for abnormalities that suggest a risk for a genetic disorder. Cell-free DNA from the mother's blood can also be used to look for Down syndrome and some chromosomal disorders.
- Doctors may also use a type of blood test called a triple screen in order to identify some genetic disorders, including trisomies (disorders such as Down syndrome in which the fetus has an extra chromosome) in an unborn baby. A blood sample is taken from a pregnant woman and tested for three substances: alpha-fetoprotein, human chorionic gonadotropin, and estriol. The test is performed between the 15th and 20th week of pregnancy. It usually takes several days to receive results from a triple screen. Abnormal results of a triple screen may indicate a possible problem such as spina bifida (the incomplete development of the brain, spinal cord, or the cord's protective coverings) or a chromosome abnormality. However, the test has many false positive results, so additional testing is needed to confirm if there is a problem.
- *Amniocentesis* is usually done at 14-16 weeks of pregnancy. It tests a sample of the amniotic fluid in the womb for genetic defects (the cells found in the fluid and the fetus have the same DNA). Under local anesthesia, a thin needle is inserted through the woman's abdomen and into the womb. About 20 milliliters of fluid (roughly 4 teaspoons) is withdrawn and sent

to a lab for evaluation. Test results often take 1-2 weeks.

• *Chorionic villus sampling* is performed by removing and testing a very small sample of the placenta during early pregnancy. The sample, which contains the same DNA as the fetus, is removed by catheter or fine needle inserted through the cervix or by a fine needle inserted through the abdomen. Results are usually available within 2 weeks.

Brain scans include several types of imaging techniques used to diagnose tumors, blood vessel malformations, stroke, injuries, abnormal brain development, and hemorrhage in the brain. Types of brain scans include computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and single proton emission (SPECT) scans.

• Computed tomography (CT scan) uses X-rays to produce two-dimensional images of organs, bones, and tissues. A CT scan can aid in proper diagnosis by showing the area of the brain that is affected. CT scans can be used to quickly detect hemorrhage in the brain and to determine if someone who has had a stroke can safely receive intravenous treatment to dissolve clots. CT scans also may be used to detect bone and vascular irregularities, brain tumors and cysts, brain damage from head injury, hydrocephalus, brain damage causing epilepsy, and encephalitis, among other disorders. A contrast dye may be injected into the bloodstream to highlight the different tissues in the brain. A CT of the spine can be used to show herniated discs, spine fractures, or spinal stenosis (narrowing of the spinal canal).

CT scanning takes about 20 minutes and is usually done at an outpatient imaging center or in a hospital. The person lies on a special table that slides into a narrow, doughnut-shaped chamber. A sound system built into the chamber allows the person to communicate with the physician or technician. X-rays (ionizing radiation) are passed through the body at various angles and are detected by a computerized scanner. The data is processed and displayed as crosssectional images, or "slices," of the internal structure of the body or organ. Occasionally a light sedative may be given if the person is unable to lie still and pillows may be used to support and stabilize the head and body.

If a contrast dye is injected into a vein, the individual being scanned may feel a warm or cool sensation as the dye circulates through the bloodstream or may experience a slight metallic taste. CT scans are particularly useful in people who are unable to undergo MRI. Because CT uses X-rays, pregnant women should avoid the test because of potential harm to the fetus.

• *Magnetic resonance imaging* (MRI) uses computer-generated radio waves and a powerful magnetic field to produce detailed images of body tissues. Using different sequences of magnetic pulses, MRI can show anatomical images of the brain or spinal cord, measure blood flow, or reveal deposits of minerals such as iron. MRI is used to diagnose stroke, traumatic brain injury, brain and spinal cord tumors, inflammation, infection, vascular irregularities, brain damage associated with epilepsy, abnormally developed brain regions, and some neurodegenerative disorders. MRI is also used to diagnose and monitor disorders such as multiple sclerosis. A contrast dye may be injected into the vein to enhance visibility of certain areas or tissues.

An MRI scanner consists of a tube surrounded by a very large cylindrical magnet. These scanners create a magnetic field around the body that's strong enough to temporarily realign water molecules in the tissues. Radio waves are then passed through the body to detect the shifting of molecules back to a random alignment. A computer then reconstructs a three-dimensional picture or a two-dimensional "slice" of the tissue being scanned. MRI can distinguish between bone, soft tissues, and fluid-filled spaces because of differences in water content and tissue properties. The individual lies on a special table that slides into the tube and will be asked to remove jewelry, eyeglasses, removable dental work, clothing with metal, and other items that might interfere with the magnetic imaging. The person may hear grating or knocking noises when the magnetic field direction is flipped. Earphones or earplugs can help block out the sounds. For brain MRI scans, a detector is placed over the head.

Due to the incredibly strong magnetic field generated by an MRI, people with implanted medical devices such as a pacemaker or infusion device generally should not have MRIs. In certain circumstances facilities may have equipment to temporarily stop and reset the implanted device's programming in order to allow MRI. Unlike CT scanning, MRI does not use ionizing radiation to produce images. The test is painless and risk-free, although people who are obese or claustrophobic may find it somewhat uncomfortable. Depending on the part(s) of the body to be scanned, MRI can take up to an hour to complete. Some centers use open MRI machines that do not completely surround the person being tested and are less confining. However, open MRI does not currently provide the same picture quality as standard MRI and some tests may not be available using this equipment.

Because people must remain still during the MRI, children may need to be sedated in order to be scanned. If intravenous contrast is required, people may first need a blood test to check kidney function because the contrast agent, called gadolinium, can increase the risk of a rare disease in people with advanced kidney disease.

A fetal MRI may be ordered when prenatal ultrasound reveals a possible problem with a fetus. Fetal MRI is considered safe for the baby because it does not require radiation or contrast dye.

Functional MRI (fMRI) uses the blood's magnetic properties to produce real-time images of blood flow to particular areas of the brain. fMRI can pinpoint areas of the brain that become active and show how long they stay active. This imaging process may be used to localize brain regions for language, motor function, or sensation prior to surgery for epilepsy. Researchers use fMRI to study head injury and degenerative disorders such as Alzheimer's disease.

- Positron emission tomography (PET) scans provide two- and three-dimensional pictures of brain activity by measuring radioactive isotopes that are injected into the bloodstream. PET scans of the brain are used to detect or highlight tumors and diseased tissue, show blood flow, and measure cellular and/or tissue metabolism. PET scans can be used to evaluate people who have epilepsy or certain memory disorders, and to show brain changes following injury. PET may be ordered as a follow-up to a CT or MRI scan to give the physician a greater understanding of specific areas of the brain that may be involved with problems. PET scans are performed by skilled technicians at highly sophisticated medical facilities in a hospital or at an outpatient testing facility. A low-level radioactive isotope, also called a tracer, is injected into the bloodstream and the tracer's uptake in the brain is measured. The person lies still while overhead sensors detect gamma rays in the body's tissues. A computer processes the information and displays it on a video monitor or on film. Using different compounds, more than one brain function can be traced simultaneously. PET is painless and uses small amounts of radioactivity. The length of test time depends on the part of the body to be scanned.
- Single photon emission computed tomography (SPECT) is a nuclear imaging test that can be used to evaluate certain brain functions. As with a PET scan, a radioactive isotope, or tracer, is injected intravenously into the body. A SPECT scan may be ordered as a follow-up to an MRI to diagnose tumors, infections, brain regions involved in seizures, degenerative spine disease, and stress fractures.

A dopamine transporter imaging with singlephoton emission computed tomography (DaT-SPECT) scan can be used to help diagnose Parkinson disease. During a SPECT scan, the person lies on a table while a gamma camera rotates around the head and records where the radioisotope has traveled. That information is converted by computer into cross-sectional slices that are stacked to produce a detailed three-dimensional image of tracer within the brain. The test is performed at either an outpatient imaging center or a hospital.

What are additional tests used to diagnose neurological disorders?

The following list of procedures—in alphabetical order—describes some of the other tests used to help diagnose a neurological condition.

Angiography is a test that involves injecting dye into the arteries or veins to detect blockage or narrowing. A cerebral angiogram can show narrowing or obstruction of an artery or blood vessel in the brain, head, or neck. It can determine the location and size of an aneurysm or vascular malformation. Angiograms are used in certain strokes where there is a possibility of unblocking the artery using a clot retriever. Angiograms can also show the blood supply of a tumor prior to surgery or embolectomy (surgical removal of a blood clot or other material that is blocking a blood vessel).

Angiograms are usually performed in a hospital outpatient or inpatient setting and may take up to 3 hours, followed by a 6- to 8-hour resting period. The person, wearing a hospital or imaging gown, lies on a table that is wheeled into the imaging area. A physician anesthetizes a small area of the leg near the groin and then inserts a catheter into a major artery located there. The catheter is threaded through the body and into an artery in the neck. Dye is injected and travels through the bloodstream into the head and neck. A series of x-rays is taken. The person may feel a warm to hot sensation or slight discomfort as the dye is released. In many situations, cerebral angiograms have been replaced by specialized MRI scans, called *MR angiograms* (MRA), or *CT angiograms*. A *spinal angiogram* is used to detect blockage of arteries or blood vessels malformations in the vessels to the spinal cord.

Biopsy involves the removal and examination of a small piece of tissue from the body. Muscle or nerve biopsies are used to diagnose neuromuscular disorders. A small sample of muscle or nerve is removed under local anesthetic (pain-relieving medication) and studied under a microscope. The muscle sample may be removed either surgically, through a slit made in the skin, or by needle biopsy, in which a thin hollow needle is inserted through the skin and into the muscle. A piece of the nerve may be removed through a small surgical incision near the ankle, or occasionally near the wrist. Muscle and nerve biopsies are usually performed in an outpatient testing facility. A skin biopsy can be used to measure small nerve fibers or to test for certain metabolic disorders. A small piece of skin is removed under local anesthesia, usually in an office setting. A brain biopsy, used to determine tumor type or certain infections, requires surgery to remove a small piece of the brain or tumor. A brain biopsy is an invasive procedure that carries its own risks.

Cerebrospinal fluid analysis involves the removal of a small amount of the fluid that surrounds the brain and spinal cord. The procedure is commonly called a *lumbar puncture* or *spinal tap*. The fluid is tested to detect evidence of brain hemorrhage, infection, multiple sclerosis, metabolic diseases, or other neurological conditions Pressure inside the skull can be measured to detect conditions such as a false brain tumor.

The lumbar puncture may be done as an inpatient or as an outpatient procedure. During the lumbar puncture the person will either lie on one side, with knees close to the chest, or lean forward while sitting on a table, bed, or massage chair. The perosn's back will be cleaned and injected with a local anesthetic. The injection may cause a slight stinging sensation. Once the anesthetic has taken effect, a special needle is inserted between the vertebrae into the spinal sac and a small amount of fluid (usually about three teaspoons) is withdrawn for testing. Most people will only feel a sensation of pressure as the needle is inserted. Generally, people are asked to lie flat for an hour or two to reduce the after-effect of headache. There is a small risk of nerve root injury or infection from a lumbar puncture. The procedure takes about 45 minutes.

Electroencephalography, or EEG, monitors the brain's electrical activity through the skull. EEG is used to help diagnose seizure disorders and metabolic, infectious, or inflammatory disorders that affect the brain's activity. EEGs are also used to evaluate sleep disorders, monitor brain activity when a person has been fully anesthetized or loses consciousness, and may be used to confirm brain death. This painless, risk-free test can be performed in a doctor's office or at a hospital or testing facility. A person being tested usually reclines in a chair or on a bed during the test. A series of cup-like electrodes are attached to the scalp with a special conducting paste. The electrodes are attached to wires (also called leads) that carry the electrical signals of the brain to a machine. During an EEG recording session, a variety of external stimuli, including bright or flashing lights, noise or certain drugs may be given. Individuals may be asked to open and close their eyes, or to change their breathing patterns. Changes in brain wave patterns are transmitted to an EEG machine or computer. An EEG test usually takes about an hour. Testing for certain disorders requires performing an EEG during sleep, which takes at least 3 hours.

In people undergoing evaluation for epilepsy surgery, electrodes may be inserted through a surgical opening in the skull to reduce signal interference. This is called an intracranial EEG. People typically remain in a hospital epilepsy monitoring unit while implanted electrodes are in place. During this time, the brain is monitored for seizures in order to determine where the seizures originate. People may also be asked to perform certain types of tasks (e.g., reading, speaking, or certain limited motor activities) so that the EEG can be used to identify brain regions that are important for normal function.

Electromyography, or EMG, is used to diagnose nerve and muscle disorders, spinal nerve root compression, and motor neuron disorders such as amyotrophic lateral sclerosis. EMG records the electrical activity in the muscles. Muscles develop abnormal electrical signals when there is nerve or muscle damage. During an EMG, very fine needles or wires are inserted into a muscle to assess changes in electrical signals at rest and during movement. The needles are attached through wires to an EMG machine. Testing may take place in a doctor's office or clinic and lasts an hour or longer, depending on the number of muscles and nerves to be tested. Because of a slight risk of bruising or bleeding, people will be asked if they are on aspirin or blood thinners. Most people find this test to be somewhat uncomfortable.

An EMG is usually done in conjunction with a *nerve conduction study* (NCS). An NCS measures the nerve's ability to send a signal, as well as the speed (nerve conduction velocity) and size of the nerve signal. A set of recording electrodes is taped to the skin over the muscles or skin. Wires connect the electrodes to an EMG machine. A small electrical pulse (similar to the sensation of static electricity) is given on the skin a short distance away to stimulate the nerve to the muscle or skin. The electrical signal is viewed on the EMG machine. The physician then reviews the response to verify any nerve damage or muscle disease. There is minimal discomfort and no risk associated with this test.

Electronystagmography (ENG) describes a group of tests used to diagnose involuntary eye movement, dizziness, and balance disorders. The test is performed at a clinic or imaging center. Small electrodes are taped on the skin around the eyes to record eye movements. If infrared photography is used in place of electrodes, the person being tested wears special goggles that help record the information. Both versions of the test are painless and risk-free.

Evoked potentials, also called evoked response, measure the electrical signals to the brain generated by hearing, touch, or sight. Evoked potentials are used to test sight and hearing (especially in infants and young children) and can help diagnose such neurological conditions as multiple sclerosis, spinal cord injury, and acoustic neuroma (small tumors of the acoustic nerve). Evoked potentials are also used to monitor brain activity among coma patients, and confirm brain death.

Testing may take place in a doctor's office or hospital setting. One set of electrodes is attached to the person's scalp with conducting paste. The electrodes measure the brain's electrical response to stimuli. A machine records the amount of time it takes for impulses generated by stimuli to reach the brain.

- Auditory evoked potentials (also called brain stem auditory evoked response) can assess hearing loss and damage to the acoustic nerve and auditory pathways in the brain stem, and detect acoustic neuromas. The person being tested sits in a soundproof room and wears headphones. Clicking sounds are delivered one at a time to one ear while a masking sound is sent to the other ear. Each ear is usually tested twice, and the entire procedure takes about 45 minutes.
- *Visual evoked potentials* detect loss of vision from optic nerve damage (for example from multiple sclerosis). The person sits close to a screen and is asked to focus on the center of a shifting checkerboard pattern. One eye is tested at a time. Each eye is usually tested twice. Testing takes 30-45 minutes.

• Somatosensory evoked potentials (SSEPs) measure responses from electrical stimuli to the nerves. In addition to electrodes on the scalp, electrodes are pasted to the arms, leg, and back to measure the signal as it travels from the peripheral nerves to the brain. Tiny electrical shocks are delivered by electrodes pasted to the skin over a nerve in an arm or leg. SSEPs may be used to help diagnose multiple sclerosis, spinal cord compression or injury, and certain metabolic or degenerative diseases. SSEP tests usually take longer than an hour.

Myelography involves the injection of contrast dye into the spinal canal to enhance imaging of the spine, by CT or by X-ray. Myelograms have mostly been replaced by MRI, but may be used in special situations. For example, myelograms may be used to diagnose tumors of the spine or spinal cord or spinal cord compression from herniated discs or fractures. The procedure takes about 60 minutes and can be performed as an outpatient procedure. Following an injection of anesthesia to a site between two vertebrae in the lower back, a small amount of the cerebrospinal fluid is removed by spinal tap (see cerebrospinal fluid analysis, above). Contrast dye is injected into the spinal canal and a CT scan or a series of x-rays is taken. People may experience some pain during the spinal tap as well as headache following the spinal tap. There is a slight risk of fluid leakage or allergic reaction to the dye.

A *polysomnogram* measures brain and body activity during sleep. It is performed over one or more nights at a sleep center. Electrodes are pasted or taped to the person's scalp, eyelids, and/or chin. Throughout the night and during the various wake/sleep cycles, the electrodes record brain waves, eye movement, breathing, leg and skeletal muscle activity, blood pressure, and heart rate. The person may be videotaped to note any movement during sleep. Results are then used to identify any characteristic patterns of sleep disorders, including restless legs syndrome, periodic limb movement disorder, insomnia, and breathing disorders such as sleep apnea. Polysomnograms are noninvasive, painless, and risk-free.

Thermography (also known as digital infrared thermal imaging) uses infrared sensing devices to measure small temperature changes and thermal abnormalities between the two sides of the body or within a specific organ. Some scientists question its use in diagnosing neurological disorders. It may be used to evaluate complex regional pain syndromes and certain peripheral nerve disorders, and nerve root compression. It is performed at a specialized imaging center, using infrared light recorders to take pictures of the body. The information is converted into a computergenerated two-dimensional picture of abnormally cold or hot areas indicated by color or shades of black and white. Thermography does not use radiation and is safe, risk-free, and noninvasive.

Ultrasound imaging, also called ultrasonography, uses high-frequency sound waves to obtain images inside the body. During an ultrasound examination, the person lies on a table or reclines in an examination chair. A jelly-like lubricant is applied to the bare skin and a transducer, which both sends and receives high-frequency sound waves, is passed over the body. The sound wave echoes are recorded and displayed as a computer-generated real-time visual image of the structure

or tissue being examined. Ultrasound is painless, noninvasive, and risk-free. The test is performed on an outpatient basis and takes between 15 and 30 minutes to complete.

Ultrasound can be used to assess changes in the anatomy of soft tissues, including muscle and nerve. It is more effective than an x-ray in displaying soft tissue changes, such as tears in ligaments or soft tissue masses. In pregnant women, ultrasound can suggest the diagnosis of conditions such as chromosomal disorders in the fetus. The ultrasound creates a picture of the fetus and the placenta. Ultrasound also may be used in newborns to diagnose hydrocephalus (build-up of cerebrospinal fluid in the brain) or hemorrhage.

- *Carotid doppler ultrasound* is used to measure flow in arteries and blood vessels in the neck.
- *Transcranial Doppler ultrasound* is used to view blood flow in certain arteries and blood vessels inside the skull. Carotid dopplers and transcranial dopplers are used to assess the risk of stroke.
- *Duplex ultrasound* refers to ultrasound studies that are combined with anatomical ultrasound.

X-rays of a person's chest and skull may be taken as part of a neurological work-up. X-rays can be used to view any part of the body, such as a joint or major organ system. In a conventional x-ray, a concentrated burst of low-dose ionized radiation passes through the body and onto a photographic plate. Since calcium in bones absorbs x-rays more easily than soft tissue or muscle, the bony structure appears white on the film. Any vertebral misalignment or fractures can be seen within minutes. Tissue masses such as injured ligaments or a bulging disc are not visible on conventional x-rays. This fast, noninvasive, painless procedure is usually performed in a doctor's office or at a clinic.

Fluoroscopy is a type of x-ray that uses a continuous or pulsed beam of low-dose radiation to produce continuous images of a body part in motion. The fluoroscope (x-ray tube) is focused on the area of interest and pictures are either videotaped or sent to a monitor for viewing. Fluoroscopy is used to evaluate swallowing and can be used for other procedures, such as a lumbar puncture, angiogram for clot removal, or myelogram.

What lies ahead?

S cientists funded by the National Institute of Neurological Disorders and Stroke seek to develop additional and improved screening methods to more accurately and quickly confirm a specific diagnosis and investigate other factors that might contribute to disease. Technological advances in imaging will allow researchers to better see inside the body, at less risk to the person. These diagnostics and procedures will continue to be important clinical research tools for confirming a neurological disorder, charting disease progression, and monitoring therapeutic effect.

More information about neurological diagnostics is available from the following organizations:

American Association of Neurological Surgeons 5550 Meadowbrook Drive

Rolling Meadows, IL 60008 847-378-0500 888-566-2267 www.aans.org

American College of Radiology

1891 Preston White Drive Reston, VA 20191-4397 703-648-8900 www.acr.org

Radiological Society of North America

820 Jorie Boulevard, Suite 200Oak Brook, IL 60523-2251630-571-2670Patient information: www.radiologyinfo.orgwww.rsna.org

National Library of Medicine

National Institutes of Health 8600 Rockville Pike Bethesda, MD 20894 301-496-6308 www.nlm.nih.gov

For information on specific neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute's Brain Resources and Information Network (BRAIN) at:

BRAIN

P.O. Box 5801 Bethesda, Maryland 20824 301-496-5751 800-352-9424 www.ninds.nih.gov



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