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SUPPORT EDUCATION RESEARCH ADVOCACY

GUILLAIN-BARRÉ SYNDROME

An Overview for the Layperson

SERVING PATIENTS WITH GBS, CIDP AND VARIANTS WITH SUPPORT, EDUCATION, RESEARCH AND ADVOCACY

A PUBLICATION OF THE GBS|CIDP FOUNDATION INTERNATIONAL

11th Edition, 2019

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By
Joel S. Steinberg, M.D., Ph.D.
Vice President, GBS|CIDP Foundation International
and
Carol Lee Koski, M.D.
Medical Director, GBS|CIDP Foundation International

A PUBLICATION OF THE GBS|CIDP FOUNDATION INTERNATIONAL

11th Edition, 2019

IN HONOR OF

ROBERT & ESTELLE BENSON

A publication of the
GBS|CIDP
Foundation International 11th Edition, 2019

GBS|CIDP FOUNDATION INTERNATIONAL

International Office
375 East Elm Street
Suite 101
Conshohocken, PA 19428
866-224-3301
info@gbs-cidp.org
www.gbs-cidp.org

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This pamphlet is provided as a service of the GBS|CIDP Foundation International.

PREFACE TO THE 11TH EDITION

The origin of this overview dates back to 1982 when Estelle Benson, emotionally traumatized by her husband Robert's bout with paralyzing Guillain-Barré Syndrome (GBS), sought a means to help others deal with this disorder. She brought some recovered patients together around her dining room table in suburban Philadelphia to start a support organization. Attending this meeting were Joel Steinberg, a still-recovering physician, as well as experts on GBS, Arthur K. Asbury MD, Professor of Neurology at the local University of Pennsylvania, and two of his trainees, David Cornblath, MD, and Gareth Parry, MD. The group recognized the need of patients and loved ones for emotional support and accurate, understandable information to carry them through the often fearful ordeal of GBS. Out of that meeting the GBS Support Group was born, an organization that now serves patients with this and related disorders worldwide as the GBS|CIDP (chronic inflammatory demyelinating polyneuropathy) Foundation International. The GBS|CIDP Foundation has over 170 local chapters and sister organizations on 5 continents to serve patients and families. You the reader are invited to contact the Foundation to continue this growth. The Foundation's goals are to:

- Expand our network of global support groups and chapters to provide patients and caregivers with support and accurate information
- Provide educational programs to heighten awareness and improve the understanding and treatment of GBS, CIDP and variants
- Expand research support and patient advocacy

Foundation membership is over 28,000 and growing. We are supported by a medical advisory board of internationally recognized experts who have made major contributions to the understanding and treatment of GBS and variants.

As part of the Foundation's educational outreach, Dr. Steinberg wrote an overview in 1982 to provide a comprehensive, detailed source of information for the lay and medical communities. The last decade has seen significant advances in our understanding of GBS and related disorders. Some of these advancements were supported through research grants awarded by the Foundation. Carol Lee Koski, MD, a GBS expert, has played a key role in facilitating much of this research. This current 2010 edition of the overview has the added benefit of her input to explain many of these advances. We are grateful to the many investigators and clinicians who have contributed to the material in this booklet. Finally, we extend thanks to Mary Beth Brooks for professional editing of this publication.

Joel Steinberg, MD, PhD
- Internal and vascular medicine, wound care
- Hospitalist, Aria Health System
- Founding member, GBS|CIDP Foundation International
- Montgomery County, Pennsylvania; 2010

Carol L. Koski, MD
- Professor of Neurology, University of Maryland School of Medicine Baltimore, Maryland (retired)
- Medical Director, GBS|CIDP Foundation International
- Santa Fe, New Mexico; 2010

Overview: Guillan-Barré Syndrome

INTRODUCTION

The disorder called Guillain-Barré (ghee'-yan bah-ray') syndrome, or GBS, is a rare illness causing victims to develop the rapid onset of weakness, often along with and sometimes even preceded by abnormal sensations, such as a "pins and needles" feeling in your skin, tingling or pain. These various abnormal conditions are due to damage to peripheral nerves, that is, nerves located outside the brain and spinal cord. Peripheral nerves, discussed in more detail below, include motor nerves to muscles that allow you to move, sensory nerves from the skin and joints that allow you to feel texture, the position of your arms and legs in space, , and autonomic nerves that automatically control functions such as your heart beat, blood pressure, eye pupil size, and a sense of when your bladder feels full. GBS can occur at any time without warning; you are not born with it, it is acquired some time during life. It affects both genders and all age and ethnic groups. It varies greatly in severity, from mild cases of brief weakness that may not even cause you to seek a doctor's attention, to a devastating, life threatening illness, with complete paralysis, respiratory failure and inability to swallow. Fortunately, GBS is rare. Most people have never heard of it, or if they have, know little about it. The goal of this overview is to acquaint the reader with the clinical features, causes, and treatments of GBS and some of its variants, as well as the effect of these disorders on the life of patients and their families. The sections in brackets are intended for health professionals. References are provided in the back of the booklet.

WHAT IS GBS:
Historical Background and Clinical Features

In 1859, a French neurologist, Jean-Baptiste Landry, described ten patients who, over days to two or so weeks, developed ascending weakness and paralysis of, in sequence, the legs, arms, neck and breathing muscles of the chest (*Landry, 1850*). The weakness was

sometimes preceded by abnormal feelings in the toes and fingers. Deep tendon reflexes, such as the knee jerk found in most people, were absent. Most of the patients recovered spontaneously over time. Some patients had difficulty breathing and an abnormal heart beat. During recovery, the paralysis improved in the reverse order of development, with the upper body improving first, followed eventually by return of leg strength. Landry called the disorder "acute ascending paralysis." Several similar reports followed from other countries. The demonstration by Quinke in 1891 of spinal fluid, removed for testing by passing a needle into the low back, paved the way for three Parisian physicians, Georges Guillain, Jean Alexander Barré and Andre Strohl to report, in 1916, the characteristic abnormal findings of GBS, of increased spinal fluid protein concentration when the cell count in the spinal fluid was normal. Neurologists call this cytoalbuminologic dissociation, meaning simply that the fluid contains a normal number of cells, (indicated by use of the prefix 'cyto,' meaning cells) but elevated amount of protein (or albumin) in the fluid.. Studies have shown that this disorder can affect any of the types of peripheral nerves mentioned above: motor, sensory and autonomic nerves. GBS is usually self-limited; that is, recovery starts spontaneously. Most patients will usually improve and often fully recover so long as, while they are still getting weaker, their vital functions, such as breathing, are supported. GBS is usually monophasic; that is, a patient gets worse only once, then improves, and his symptoms do not worsen again. Additional episodes rarely occur. The underlying problem causing symptoms in most GBS patients is damage to the protective membrane covering the peripheral nerves, the myelin sheath (discussed below).

THE SEVERAL NAMES FOR GBS

GBS has several other names, including "acute inflammatory demyelinating polyneuropathy (AIDP)" (acute, for sudden onset; inflammatory, to indicate inflammation in the nerves; demyelinating, to indicate damage to the outer protective covering of the nerve called myelin sheath; polyneuropathy, a disorder involving many nerves, not just one); "acute inflammatory polyneuropathy;" "acute idiopathic polyneuritis" (inflammation of nerves, hence -"neuritis"; of many nerves; due to "idiopathic," or unknown causes); "acute idiopathic polyradiculoneuritis; Landry's ascending paralysis; "acute dysimmune polyneuropathy (dys- for abnormal, as explained below);" "French polio (reflective of the neurologists who first recognized it);" and "post-infectious neuropathy" (since many cases develop after ['post'], an infection). Currently, however, this syndrome is most commonly referred to as the "Guillain-Barré Syndrome," or GBS.

WHAT'S A SYNDROME?

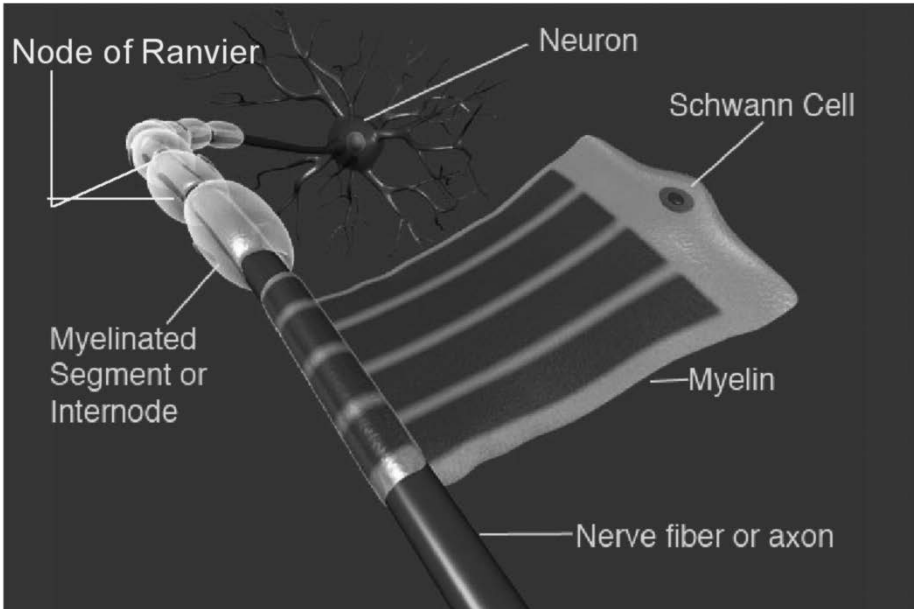
The term "syndrome" instead of "disease" indicates that GBS is diagnosed by identifying or recognizing a specific combination of findings, characteristic of the disorder. In GBS these findings include the symptoms (what the patient feels and describes, such as difficulty walking), signs (what is found on physical examination, for example, lack of knee jerk or other deep tendon reflexes), clinical course (rapidly progressive, ascending weakness), along with confirmatory laboratory tests (for example, slow conduction of nerve signals, and elevated spinal fluid protein).

TYPES OF PERIPHERAL NERVES

An explanation of the function of peripheral nerves helps to understand what happens to the patient in GBS. For a person to perform an activity, such as walking, the brain sends an electric signal down a nerve path to stimulate nerve cells or neurons in the spinal cord. These cells in turn conduct the electric impulse out of the cord and along the nerve's axon, a long narrow branch of the neuron. The axon travels out of the spinal cord along nerve roots, through openings between the backbones or vertebrae, and eventually out to the target muscle, where the impulse stimulates muscle fibers. Nerves that carry signals to muscles are called motor nerves. If enough motor nerves excite enough muscle fibers, the muscle contracts, or shortens, producing limb movement, e.g. walking. Individual axons are too small for the naked eye to see; they are microscopic. Hundreds of nerve axons are bundled together and called a "peripheral nerve." An example is the sciatic nerve, a major nerve to the muscles of the leg. If motor nerve axons are damaged, muscles don't get a sufficiently strong signal to contract when stimulated; the result is that the muscle is "weak," or even paralyzed.

Sensory nerves carry information from various parts of the body, such as from skin and joints, to the spinal cord and then up into the brain, where the signal is recognized as a particular sensation. Examples of these sensations include temperature, pain, hard versus soft textures and joint position, such as whether your elbow is bent or straight.

Autonomic nerves carry signals to and from the internal organs to automatically regulate their activities such as heart rate, blood pressure and the feeling that you have to empty your bladder.



MYELIN AIDS PERIPHERAL NERVE SIGNAL CONDUCTION

Peripheral nerves carry electrical signals from the spinal cord to muscle, and from skin and joints to the spinal cord. (within the spinal cord, part of the central nervous system, fibers take the impulses to the brain.) Most nerves, made up of many axons, are covered by an outer insulating protective sheath called myelin (my'-eh-lin). In GBS, the part of the nerve most commonly initially damaged is the myelin covering. Myelin acts like the insulation on electrical household wires, and assists rapid and accurate conduction of the electrical impulses, preventing the axon signal from short circuiting or slowing down.

Myelin is produced by specialized cells called Schwann cells. Myelin is wrapped around segments of axons and aligned end to end. Small gaps between the segments are called "the nodes of Ranvier." In these gaps, a thin porous surface of the underlying axon, the outer part of the nerve membrane called the "axolemma," is bare and exposed. Chemical ions [eye'-onz], such as potassium and sodium, have an electric charge and can move rapidly through the channels in the axolemma, to create the electric signal of a nerve impulse. The signal jumps from one node of Ranvier to the next, a process called "saltatory conduction." If myelin is damaged or lost, conduction of the nerve impulse is slowed, or even lost altogether, and leads to muscle weakness (or paralysis) in motor nerves, or changes in, or loss of sensations for sensory nerves.

NERVE DAMAGE IN GBS

The main feature in GBS patients occurs at the microscopic tissue level, namely damage to the peripheral nerve myelin. The body's own immune system, which normally fights infection, causes this damage via abnormally programmed, special white blood cells, called "macrophages" (mac'-ro-fages). Indeed, finding cells of the immune system, lymphocytes (limf'-o-sites) and macrophages, at the microscopic sites of myelin damage in GBS patients, gave rise to our current understanding, that GBS is caused by an abnormal reaction of the immune system.

GBS is considered an "autoimmune disorder" since the immune system, normally protective of the patient's own tissues, accidentally ALSO attacks the patient's own tissue, hence use of the prefix, "auto" (against "self"). Just why the immune system acts out of control in some people but not others is not fully understood. Myelin damage, on average, occurs over about 3 weeks, although it can develop as rapidly as hours to days. During this time the patient experiences progressive weakness and sensory loss. If conduction in the nerve is sufficiently slowed or completely blocked, the muscle it innervates becomes paralyzed. This can be life-threatening if the muscle is, for example, the diaphragm, a major muscle needed for breathing. After the peak of damage, the nerves usually undergo a slow healing process during which the myelin is replaced or repaired; during this process, the patient regains strength and sensation. In some cases, however, recovery may be slow or incomplete, resulting in long term weakness, especially if the nerve axon is damaged. Such damage may be primary or secondary, and will be discussed later.

As noted above, sensory nerves allow us to feel temperature, limb position, coarse and smooth fabric surfaces, etc. When the sensory nerves are damaged, the patient may experience decreased or even abnormal sensations, poor balance and even pain. The brain and spinal cord in cases of GBS clinically appear to be spared, although some studies have shown damage of small areas of myelin in the brain and spinal cord as well. Rarely, some patients may develop vision loss, if the myelin around their optic nerves is affected. GBS is not just a disorder of paralysis and abnormal sensations. Damage to myelin and axons of autonomic nerve fibers can cause abnormal heart beat, high or fluctuating blood pressure, impotence, urinary retention (from loss of the sensations of having a full bladder, and needing to empty it) and bowel paralysis.

GBS AND OTHER INFLAMMATORY NEUROPATHIES

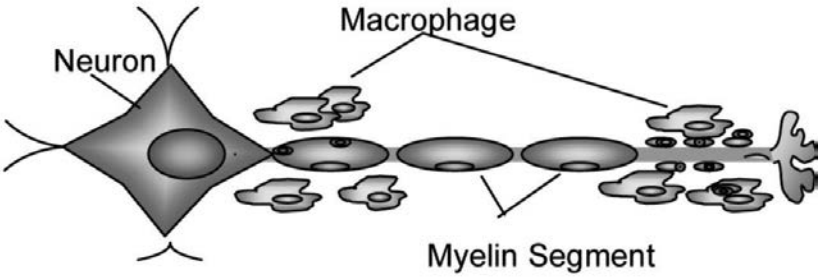
A Family of Disorders

The disorders discussed in this booklet have in common the principal features of GBS: they are all 1) acquired rather than inherited, and 2) likely due to immune-mediated damage to the peripheral nerves. These various disorders differ by their onset, duration, symmetry of clinical findings, and whether the damage is primarily to the myelin, the axon or involves peripheral nerve fibers primarily dedicated to motor, sensory or autonomic function. An accurate diagnosis of these various disorders is important since treatment and outcome among them varies.

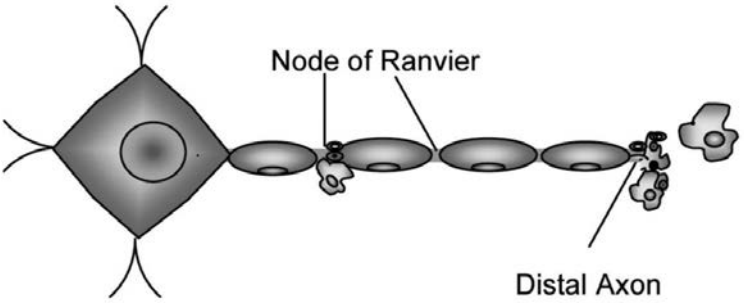
THE RAPID ONSET (ACUTE) DISORDERS

Acute inflammatory demyelinating polyneuropathy (AIDP). This disorder is most commonly called GBS. Its other names were described earlier. The incidence is rare and occurs in 1-2 people per 100,000 population each year. In the Western world, 75% to 80% of cases of acute acquired inflammatory neuropathies fall into this category of AIDP or "classic GBS" with the immune attack directed at myelin.

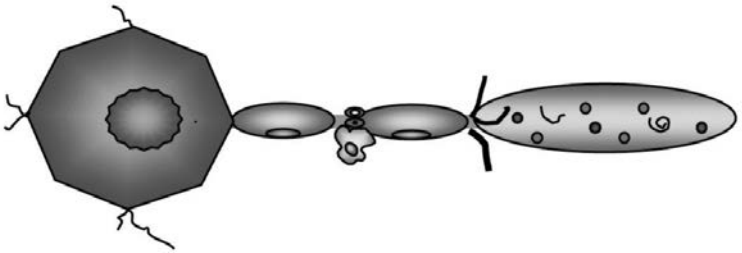
The usual pattern of myelin damage leads to symmetrical weakness and sensory loss or changes (tingling, etc.). Note that in medical terminology, "symmetrical" means equal on both sides of the body. This contrasts with some disorders, such as many strokes, where only one side of the body is affected. Such disorders are thus "asymmetric". Patients with AIDP develop the most, or all, loss of their function over one to four weeks. Ten percent of patients continue to worsen for up to six weeks from onset, but otherwise follow the same course as AIDP; we call their disease "subacute inflammatory demyelinating polyneuropathy."



Acute motor axonal neuropathy (AMAN). This variant was initially recognized upon studying yearly summer epidemics of paralysis in children in rural areas of northern China . It has also been called the "Chinese paralytic syndrome". Clinically it is similar to AIDP, with rapid onset of relatively symmetrical paralysis, but *without any sensory changes*. Outbreaks of AMAN have also occurred in Mexico and South America, and sporadic cases occur throughout the world, including the United States, Europe and Japan; that's why we call it AMAN without regard to the geography. In this variant, nerve damage occurs at areas of the exposed axon, such as myelin gaps at the nodes of Ranvier, and at the end of the axon that is not covered with myelin, just prior to where it has a junction with the muscle fiber.



Acute motor sensory axonal neuropathy (AMSAN). This is a fulminant, severe form of GBS that usually develops rapidly over days, resulting in paralysis and sensory loss due to severe axonal damage. Recovery is poor. Its recognition as a variant dates back to a report by Feasby in 1986. This variant is more prevalent in Asia and South and Central America and is often triggered by a bowel infection with a bacterium called *Campylobacter jejuni*.



Miller Fisher syndrome, or simply Fisher syndrome, is named after Dr. C. Miller Fisher. In its purest form, it is characterized by three features: **1.** double vision from weak eye muscles, **2.** a wobbly or ataxic walk or gait, appearing as loss of balance, and **3.** loss of deep tendon reflexes.

Injury to the myelin of nerves controlling eye muscles causes them to be weak, so the eyes can't move together, creating double vision. Sensory nerves in leg and body muscles detect muscle length and strength and allow us to walk normally, that is, smoothly. Autoimmune

antibodies specific for molecules on their surface damage these sensory nerves, affecting the ability to know where ones limbs are in space, causing an "ataxia" (wobbly or unsteady gait) along with double vision. Blurred vision can also occur and is caused by paralysis of muscles controlling the pupil of the eye. Some patients also develop some weakness in the limbs as well as facial paralysis and difficulty swallowing, thus overlapping with features of GBS. The reverse can also be true, in that patients with GBS can have eye muscle weakness and double vision.

THE SLOW ONSET (CHRONIC) DISORDERS

Chronic inflammatory demyelinating polyneuropathy (CIDP). This neurologic cousin of GBS, described by Austin in 1958, develops slowly, over two months or longer, and is also characterized by symmetrical weakness and sensory changes. Deep tendon reflexes are lost in the involved extremities. It may occur as a single (or monophasic illness) that extends over one to three years with one occurrence and a very slow recovery. Although this variety is self-limiting, if untreated, the nerve damage can be severe and permanent; the nerves may not recover completely. More often CIDP is recurrent, with "relapses" (worsening) and remissions (improvements) occurring several times over the course of years. Occasionally the disorder may run a slowly, progressively deteriorating course over years without improvement. In contrast to GBS, it is often responsive to treatment with corticosteroids and other immunosuppressive agents; both respond to immune globulin (Ig, given intravenously [IgIV]). The incidence of CIDP is rare compared to GBS but because CIDP can persist for years, it is probably the most commonly seen chronic inflammatory neuropathy. Its "prevalence" in the general population, the number of people who have the disorder at any one time, is estimated to be as high as 8 patients per 100,000 population.

Multifocal motor neuropathy (MMN). This rare, asymmetric inflammatory neuropathy affects multiple motor nerves. Major features are the slow or stepwise development of weakness starting with the distal muscles in the upper limb, i.e., the hand, more so than the lower limb. Sensory nerve fibers are not affected. Remember that in GBS, the lower extremity is usually affected before the upper extremity, and there are almost always sensory abnormalities as well. In MMN, the weakness slowly worsens over month to years, much slower than in GBS, and affects primarily the hands. It does not improve by itself over time.

Multifocal acquired demyelinating sensory and motor neuropathy (MADSAM). Also called LewisSumner syndrome after two neurologists who described it, this neuropathy is another rare variant of CIDP. It shares many features with multifocal motor neuropathy, but in addition to asymmetric weakness, the patient experiences sensory changes, i.e., tingling or loss of sensation, in the distribution of the damaged nerves.

Rarer variants of GBS and CIDP are beyond the scope of this overview. Examples include disorders with only autonomic nerve damage, acute autoimmune axonal neuropathies and focal autoimmune disorders, involving weakness of the arm or leg.

CAUSES OF GUILLAIN-BARRÉ SYNDROME

Factors involved in the development of Guillain-Barré Syndrome are not completely understood. Evidence indicates that a variety of events can trigger the disorder in otherwise healthy people. GBS is self-limiting so that most patients eventually recover if they are given any supportive care they might need, like a respirator if their breathing is affected. The recurrence of GBS is rare; fewer than 5% of patients suffer a second episode. In the United States and Europe, 60% to 80% of GBS cases occur within four weeks of a preceding infectious illness. Of these, about three-quarters follow an upper respiratory infection or "cold" and 25 percent seemed to be precipitated by a diarrheal illness. A list of several infectious agents implicated as likely 'triggering' events are listed in Table 1.

The mechanism(s) by which some micro-organisms might lead to GBS are slowly being made clear. Other cases appear to occur during pregnancy or follow seemingly unrelated events such as surgery, insect bites and various injections including spinal anesthesia and vaccinations. Since these events occur commonly in the general population, it is difficult say that an episode of GBS showing up afterwards was caused by them. One of the most striking clusters of GBS cases occurred in the fall of 1976, among people immunized with the swine influenza vaccine used that year. The incidence of GBS is normally 12 new patients per 100,000 population each year. Some estimates suggested the incidence of GBS increased 7-fold in those who received the influenza vaccine that year; however, it is

TABLE 1:
Infectious Agents Associated with GBS

DNA VIRUSES Cytomegalovirus Epstein Barr virus Hepatitis B Herpes Zoster Herpes Simplex Papovavirus	**BACTERIA** Campylobacter jejuni Legionella pneumophilia Salmonella typhi Shigella boydii Yersinia
RNA VIRUSES HIV Echo virus Coxsackie virus Parainfluenza Influenza Polio vaccine	**PARASITES** Malaria **OTHER ORGANISMS** Mycoplasma Jacob Creutzfeldt Psittacosis

hard to know the real incidence of GBS among those people NOT immunized that year. Other outbreaks or clusters of GBS have been reported, including summer epidemics in rural northern Chinese children (see AMAN described above), a outbreak in Jordan in 1978 after exposure to polluted water, and an outbreak in Finland after a nationwide oral poliovirus vaccination campaign, among others. The bacterium, *Campylobacter jejuni*, a very common cause of diarrhea in the world, is implicated as a triggering factor in the Chinese paralytic syndrome (AMAN); in other clusters contamination of drinking water by Shigella or Salmonella have been implicated. On rare occasions, GBS develops in patients with other systemic illnesses, including some cancers, such as Hodgkin's disease, other lymphomas, multiple myeloma, other monoclonal gammopathies, and solitary plasmacytomas, as well as such disorders as systemic lupus erythematosus (an autoimmune disease) and infection with the human immunodeficiency virus (HIV) prior to progression to acquired immune deficiency syndrome (AIDS).

Although GBS often seems to follow a viral or diarrheal illness, there is no evidence that the disorder can be transmitted from one person to another. In fact, often the suspected virus or bacteria is no longer present in the patient when the peripheral nerve damage is developing. It is of interest that literally millions of people are exposed to events such as infections, surgery, and vaccines that have been identified as triggering agents for GBS, yet only a very small number of the people develop GBS. Why only certain people develop GBS is unclear. Might they have some unique genetic predisposition? Since it is rare for more than one member of a family to develop GBS, it does not seem that genetic factors play a significant role. Yet some research indicates that genetic factors can correlate with severity of disease. Indeed, GBS and variants may reflect a unique interaction between certain strains of an infectious agent (*e.g., C. jejuni, Penner strains 0:19 and 0:41*) and the genetically determined immune system composition of the patient . The bottom line is that we do not understand very well what causes someone to develop GBS. Future research will hopefully improve our understanding of how and why GBS occurs.

THE BIOLOGY OF GBS

The different GBS variants likely reflect immune reaction to molecules associated with specific groups of nerves. Unique clinical features distinguish the GBS variants. Examples include ascending paralysis with sensory changes in classic GBS, double vision in Fisher syndrome, and weakness in AMAN and MMN. The unique features of each variant appear to reflect immune system mediated damage to those nerve fibers responsible for a specific function (such as eye muscle movement). Specific nerves appear to be attacked because they have molecules on their surface that are similar to those on the patient's triggering infectious agent. This condition of similar molecules on the microbe and nerve is called "molecular mimicry." It is best demonstrated in AMAN which can be triggered by an

infection with a bacterium, *Campylobacter jejuni, (C. jejuni)* that causes diarrhea. *C. jejuni* is commonly found in chicken droppings and mud where children play in rural villages in China. The bacterium's outer covering contains complex fat (lipid) molecules. Complex lipids on *C. jejuni* contain a group of sugars also present on a sugar-containing lipid, GM1, found on motor nerve axon membranes. Thus, some nerve molecules have pieces on their surface that are chemically similar to, or mimic, those on the surface of the bacterium. When an infection occurs, the immune system mounts a protective response to fight off the bacterium, but the antibodies it produces to do this attack not only the microbe, but also the similar-appearing molecules on the patient's nerve fiber. The patient's nerve becomes the innocent bystander, injured in error by the patient's own immune defense system trying to protect itself.

The immune system, which fights infections, is complex. It has two major parts: a group of special cells, the cellular system, and groups of special molecules within the body's fluids, the humoral system. These two parts work together to help fight infection. Examples of immune system cells are specialized white blood cells, called lymphocytes and macrophages. The humoral system consists of several groups of molecules in solution within the body's liquid compartments (such as plasma). Being dissolved in the liquid parts of the body they are called the 'humoral' system, as historically the ancients suspected that "humors," some unknown material in the body's liquids, was responsible for some body functions and diseases. They were right, even without being able to identify those humors that we now recognize as specific families of molecules. We now know that the humoral system consists of antibodies, chemical signaling agents such as chemokines, and a group of protein molecules that make antibody activity more efficient, called complement. These humors, 'good humors' if you will, work with cells and dissolved proteins to fight infection. Antibodies and complement likely play an role in starting the immune activity, by recognizing an infecting agent as foreign. Their selective, although mis-directed, recognition of and binding to myelin and other nerve parts might likely be a key early event in causing the nerve damage in GBS disorders.

Another factor that likely determines the course of GBS is access of the immune system to nerves. A 'blood-nerve' barrier protects the peripheral nerve. The barrier is composed of "endothelial cells" that line the inside of blood vessels (supplying nutrients to the nerve) and fibrous tissue (connective tissue) that surrounds each individual nerve fiber and nerve fiber bundle. To allow entry into the nerve of immune system components, activated cells such as lymphocytes and macrophages bind to the endothelial cell surface and release signaling chemicals, called "cytokines" and "chemokines," to disrupt this barrier. The disruption exposes the nerve to not only to immune cells but also to proteins, including antibodies, complement and cytokines, parts of the complex immune system. The mechanisms of barrier disruption are being studied as potential places to create treatments for GBS disorders by interfering with the breakdown of the 'blood-nerve' barrier.

The "molecular mimicry" concept outlined above does not explain some cases of GBS and variants, such as those that appear to be triggered by surgery or that occur during pregnancy. Nevertheless, molecular mimicry and the "innocent bystander" theories remain helpful working models to explain most of the GBS family of neuropathies.

EARLY FINDINGS WITH GUILLAIN-BARRÉ SYNDROME

The presenting symptoms of GBS can be quite varied, depending on which particular nerves are involved. Often, initial symptoms may be abnormal sensations, called "paresthesias," which occur in several forms. Examples are numbness, "pins and needles," tingling, an "asleep" feeling, a sense of something crawling under the skin, electricity, or vibrations. They may initially only occur in one limb but quickly become symmetric. They are often experienced at the ends of the limbs, the distal aspects, in the feet and toes or hands and fingers, prior to the onset of weakness in that limb. Weakness can affect any extremity, but initially may be so mild as to be ignored, until it progresses enough to interfere with motor functions that allow us to walk, breathe, talk, etc.; changes in sensation reflect damage to sensory nerves that detect our surroundings (hot, cold, smooth, rough, other textures, limb position, etc.).

A common scenario in developing GBS is first a sense of paresthesias, such as tingling in the toes and/or fingers. This may be followed shortly, in hours or a day, by slowly worsening weakness, progressing up the body from the feet and legs to the hands and arms, and then to the face. Less often, the weakness could start at the upper parts of the body and work its way downwards. The weakness, initially mild, becomes sufficiently noticeable over days, and drives the patient to seek medical attention. Weakness of thigh and hip muscles causes a problem climbing stairs or getting up from a chair. If the arms or shoulder muscles become weak, the patient may not be able to shave, comb his hair or lift a heavy object. If the fingers or hands become weak or numb, handling common objects, such as a comb, pencil, button etc., may become difficult. Aches or cramps often accompany muscle weakness. Severe muscle cramps, often described as a 'charley horse,' in the back, buttocks, or thighs may cause the physician to suspect a variety of disorders other than GBS, such as a back strain, an arthritic problem, etc. However, the development of widespread and worsening weakness, loss of tendon reflexes, etc., helps to identify the patient's disorder as likely to be GBS. The symmetry of weakness and sensation changes in GBS, and development of symptoms over days, rather than minutes to hours, are important features that differentiate it from a stroke. In the form of GBS affecting only motor nerves, called AMAN, weakness develops without any sensory symptoms. In 70% of GBS patients, the muscles that control breathing can become weak and the patient may feel short of breath. In 40% of patients, the respiratory muscles become so weak that the patient will require temporary placement on a ventilator. If muscles in the throat become too weak, or throat nerves that sense and manage liquids can no longer do that, the patient may experience difficulty talking or swallowing, and may begin choking on their own secretions. Facial muscle weakness, if on one side (that is, unilateral) can cause a lopsided expression or, if affecting both sides (that is, bilateral) will create the inability to smile; or, food may collect in a weak cheek pouch. Rarely, difficulty in urinating or inability to hold one's urine may be a patient's initial problem. As noted earlier, the syndrome may also involve the automatic or autonomic nerves of the

body and alter blood pressure, heart rate, temperature and vision. Even brain and hormonal control of kidney function can be affected and lead to low serum sodium levels.

An occasional patient presents with a picture quite different from the classical ascending paralysis of GBS. Rather, in these patients nerve damage may occur elsewhere from the legs and arms, and the presenting findings in turn reflect that damage. An example would be damage to some cranial nerves resulting in facial weakness, difficulty swallowing and talking, and neck weakness. Very rarely only the phrenic nerves that supply the diaphragm, the major muscle for breathing, may be involved. The Miller Fisher syndrome is another example of atypical or limited nerve involvement, in which the muscles of the eyes are selectively involved; the primary findings then are a triad of double vision, ataxic gait and loss of deep tendon reflexes. Some variants involve only sensory or autonomic fibers. All these various clinical syndromes are diagnosed and treated in the same fashion and with some exceptions all have good outcomes.

DIAGNOSIS

No single test can confirm the diagnosis of GBS. Rather, the disorder is suspected and diagnosed when a patient presents with findings typical of GBS, subacute onset of weakness, first of the legs, then the arms, often with numbness and/or tingling of the affected limbs. The neurological examination showing the loss of deep tendon reflexes (such as at the ankle or knee) supports the diagnostic suspicion of GBS. These findings are often sufficient to admit the patient to a hospital with anassumed diagnosis of GBS, for close observation, in case it progresses. In the hospital a further work-up will usually be undertaken with confirmatory tests. These usually include spinal fluid examination to include protein and cell analysis, and electrophysiological testing of the peripheral nerves. As noted above, the clinical presentation can be varied. But GBS is the most common cause of symmetric weakness developing over days to up to 3 or 4 weeks. Because of the potential for progressive paralysis, failure of breathing and cardiovascular complications, suspected GBS is treated as a medical emergency: even the suspicion of GBS may suffice to warrant hospital admission for observation.

Deep tendon reflexes (DTR) can be elicited in most normal persons. Since peripheral nerves carry the impulse signal required to generate these reflexes, the absence of tendon reflexes suggests peripheral nerve damage. Loss of DTRs occur in weak or paralysed extremities in GBS. (In contrast to the knee jerk that reflects peripheral nerve damage, damage in the central nervous system usually causes brisk or very strong deep tendon reflexes, and abnormal reflexes such as an up-going toe upon stimulation of the sole of the foot, the "Babinski sign.")

Early in the clinical course of GBS, the neurologic exam may also find loss of some skin sensations carried by large myelinated sensory nerves susceptible to demyelination. Thus

position sense, the ability to tell where one's toes or limbs are in space, may be lost, as might be the ability to feel vibrations in the fingers and toes. The patient will likely still sense pain and temperature, as these are felt by nerve impulses that travel in thinly myelinated or unmyelinated nerve fibers and thus usually remain intact early on in GBS. Unmyelinated fibers may become impaired later in the course of GBS, if axonal damage occurs.

Once the history and exam findings direct the physician to a diagnosis of GBS, the disorder can be confirmed by "electrodiagnostic testing" of the nerves, and spinal fluid analysis. Nerve conduction velocity (NCV) studies, measuring the actual speed of stimulated nerve impulses in the nerve, can determine whether nerve damage affects myelin, axons or a mixture of both. The speed with which a peripheral nerve carries an electrical impulse (the conduction velocity of the signal) and stimulates a muscle to contract slows down as myelin is progressively damaged; if damage is severe, impulse conduction in a nerve is blocked altogether. (In contrast to slowing of impulse conduction in GBS and other demyelinating peripheral neuropathies, when the axon is the primary target of damage, electrodiagnostic testing shows reduction in the size of the action potential, the strength of the conducted nerve electrical impulse, while the conduction velocity is largely unchanged. In GBS, the nerve impulse conduction velocities continue to slow over the clinical course, but may not be measurably slowed until 1-4 weeks after onset. Another measure of nerve function is the "distal latency." A nerve exiting the spinal cord conducts an electrical impulse to its end, at the nerve-muscle junction. At the junction, the nerve releases a chemical called acetylcholine (ACH) into a small space between the nerve and muscle. The ACH travels across this space to the muscle, causing it to contract. The time it takes for the electrical nerve impulse at the end of the nerve to stimulate the muscle to contract is called the distal (for end) latency (time). This latency is abnormally long in GBS and the change can be seen within 1-3 days of onset. Therefore, the finding of either slow nerve impulse conduction and/or prolonged distal latency on the study of nerve conduction velocity confirms demyelination of the nerve and thus helps to rule out other causes of peripheral neuropathy. Other causes of peripheral neuropathies, caused by metabolic conditions like diabetes, or various toxins, first cause damage to the axon rather than the myelin.

By the second to fourth week of symptoms, and often within 10 days, fluid bathing the spinal cord usually contains abnormally elevated protein levels, while the white blood cell count in the spinal fluid remains normal. The combination of these findings is supportive of GBS and other inflammatory neuropathies. Therefore, spinal fluid examination provides an important confirmatory test for GBS.

To obtain the spinal fluid, a physician inserts a long thin needle through the skin in the middle of the lower back, between two lumbar vertebrae near the waist. Fluid is obtained from the spinal canal that surrounds and protects the spinal cord and the peripheral nerves branching off it and examined. Protein elevation reflects mostly the accumulation of albumin in the spinal fluid, due to active inflammation of peripheral nerves in the canal. If the white blood cell count is elevated, conditions other than GBS have to be considered, such as infections (such as Lyme disease) or inflammatory disorders of blood vessels. In rare cases, cancer cells may be detected, thus redirecting the physician's diagnostic considerations.

TABLE 2:
Diagnostic Criteria for Guillain-Barré Syndrome

- Rapid onset, over a few days to 1-4 weeks of symmetrical weakness, in the extremities
- Altered sensations, numbness, tingling or pain, in affected limbs
- Elevated spinal fluid protein, usually within 1-4 weeks of symptom onset, with normal cell count
- Nerve conduction velocity-electromyography (NCV-EMG) evidence of nerve conduction slowing or blockage
- Absence of other causes of a peripheral neuropathy, such as:
  1. A history of organic solvent inhalation, lead intake or intake of certain drugs, such as nitrofurantoin or dapsone
  2. evidence of infectious causes of neuropathies, such as Lyme disease, HIV, diphtheria, and, in unvaccinated populations, poliomyelitis
  3. findings of acute intermittent porphyria as evidenced by normal urine studies for porphyrin metabolites (see Appendix)

Findings supportive of the diagnosis of Guillain-Barré Syndrome

- Monophasic course with return of strength starting at about 2 to 8 weeks
- Associated changes in blood pressure such as mild hypertension and rapid heart beat
- A preceding infection, such as an upper respiratory infection, or diarrhea, at 1 to 6 weeks before neurological symptom onset

HOSPITAL CARE

The diagnosis of Guillain-Barré Syndrome is made or suspected most often in a hospital emergency department, when the patient presents for progressive difficulty walking. Sometimes the patient presents to their family doctor with these complaints and is referred to a neurologist for further evaluation, leading to the diagnosis. GBS is usually self-limiting, with the progression of weakness stopping on its own, followed by a slower recovery. That pattern of illness might make a person not familiar with GBS suspect that the patient can be followed without admission to see how they do. This thinking and plan of care is usually not advised. At its onset, the early and subsequent course of this syndrome is not predictable. Progressive weakness with impaired breathing or swallowing can occur over a few hours or up to three to four weeks. The onset of autonomic nerve dysfunction can cause dangerous changes in blood pressure, heart rate, airway clearance and bladder control. Since many of these events can be life threatening, GBS is considered a medical emergency.

Except in very mild cases, careful observation in the hospital is indicated, often in the intensive care or step-down unit, where changes in heart rate, blood pressure and breathing can be monitored. Rapid treatment can then be given if problems arise. One cannot underestimate the importance of supportive nursing care throughout the patient's hospital stay. Much of the nursing care is directed toward preventing the many potential complications of muscle paralysis, including decubitus ulcers or bed sores, pneumonia, contractures of the joints, and thrombosis in the deep veins of the legs. In summary, the newly suspected GBS patient warrants close attention.

The many potential challenges for patient care can be conveniently grouped into **1.** internal organ problems, including breathing management, so called supportive care, **2.** emotional issues, **3.** treatments that modulate or modify the immune system to reverse autoimmune causes of GBS, and **4.** rehabilitation.

INTERNAL ORGAN PROBLEMS

Impaired Breathing. This is a particularly dangerous problem caused by weakness of the diaphragm, the major muscle of respiration, and other muscles used for breathing. Respiratory function can be measured at the bedside every 1-2 hours, by measuring the volume of air in a patient's deep breath with a hand-held monitor or "spirometer." If serial breathing tests and the physical exam indicate sufficient weakness of breathing muscles, mechanical ventilation using a respirator (or "ventilator") may be needed. For example, if an adult patient's "vital capacity," (the volume of air taken in and breathed out with a deep breath) falls below 2 liters or quarts, respiratory failure may be imminent. A further drop of even 500 ml or half a quart may signal a need for intubation, (the insertion of a breathing tube through the nose or mouth into the windpipe or trachea,) to support the patient's breathing with a ventilator. Decreasing levels of oxygen and increasing levels of carbon dioxide in blood are signs of poor breathing and can also be measured to confirm inadequate breathing. For example: a pulse oximeter, a small plastic sensing device gently clipped to the patient's finger or ear lobe, provides an ongoing display of the patient's blood oxygen content and indirectly their breathing ability. Values above 92% oxygen saturation of the blood are normal. Lower values can reflect decreased lung ventilation and suggest an urgent need to place patient on mechanical ventilation. About 40% of GBS patients develop sufficient weakness of breathing muscles to require mechanical ventilation. A professional, one well-trained in intubation, (such as an anesthesiologist,) should intubate the patient. Intubation is best done by such trained personnel, under optimal conditions, such as in an intensive care unit in the hospital. An emergency intubation under less other conditions may be associated with complications and is thus best avoided if possible.

Intubation and mechanical ventilation, although often necessary, are not without risk. Mechanical ventilation does not fully duplicate the natural mechanisms used by healthy people to clear their airway and open the lungs (e.g., cough, sigh, yawn etc.) and makes patients more susceptible to pneumonia. Intubation through the nose limits drainage of the sinuses on the side of the tube placement with the potential to cause sinusitis. Other complications include incomplete expansion of the lungs with collapse of lung segments, called atelectasis, making patients more susceptible to pneumonia; low blood oxygen; and high levels of carbon dioxide in the blood. Measures taken to reduce these complications include frequent suctioning of the airway or trachea, and percussion or "thumping" on the chest wall over the lung bases, to mobilize and loosen accumulated mucous to facilitate its clearing. Percussion is done by positioning the patient on their side and thumping on the upper side of the chest with an open hand or with a machine.

Despite the risks of mechanical ventilation, it can often be life-saving, and it should be used without hesitation if the patient's breathing is failing. Mechanical support of breathing is continued until sufficient respiratory muscle strength returns. This can take days, occasionally weeks, and, rarely, even longer. Various methods are used to determine when strength is adequate to allow unassisted breathing and weaning from a respirator.

Airway Protection. Some patients may require intubation because of inability to swallow. This can lead to aspiration of mouth or stomach contents into the lungs and subsequent pneumonia. Indeed, choking, dribbling or other evidence of poor secretion-handling can signal the need to intubate the patient, to protect their airway from aspiration, even if the patient is able to breathe adequately. (Poor secretion-handling is likely mediated through damage of cranial nerves that control the tongue and palate, which handle the gag and cough reflexes.)

Decubitus Ulcers. The paralyzed patient on long bed rest is prone to breakdown of tissue over boney prominences. The skin breakdown andresulting ulcers are called bed sores or "decubitus ulcers.". Decubitus ulcers can be difficult to heal, so preventing them is important. Common sites of decubitus ulcer formation include the back of the heels, lower back (sacrum) and hips. Several methods are available to help prevent and treat these skin ulcers. These include frequent turning of the patient, every two hours, to reposition the patient off boney prominences; and the use of a foam or gel mattress to spread the patient's weight more evenly. Special beds designed to reduce local pressure, called low-air-loss beds or mattresses, and an air-fluidized bed (e.g., Clinitron®), may be helpful for patient with prolonged paralysis.

Contractures. GBS patients develop weakness of muscles controlling the ankles and wrists. If weakness is substantial, foot drop and/or wrist drop can develop if the patient is too weak to overcome the effects of gravity, and keep their feet and hands in a natural, upward or flexed position. Over time, the Achilles tendon and calf muscles can become shortened. Fixed shortening of the Achilles tendon interferes with upward movement of the foot and the ability of the patient to stand flat on their feet; instead they stand on their toes, interfering with normal walking and rehabilitation. Similar problems can occur with

the forearm muscles and hand movement, as well as the shoulders. To prevent shortening of tendons and muscles, passive range of motion exercises are given by a physical therapist several times a day. In addition, splints or braces are placed around joints at risk for contractures to maintain the ankle and wrist in more functional or normal positions. A brace is a thin, stiff piece of plastic molded to conform to the shape of the extremity, designed to hold the foot and hand in the desired position. For the foot, the usual preferred position is a 90° or right angle to the leg; for the hand, the usual position is slightly angled upwards, at about 20–30° above the forearm. Prevention of contractures facilitates patient participation in rehabilitation and shortens recovery time.

Deep Vein Thrombosis ('phlebitis'). Muscle paralysis and inactivity increase the risk of blood clot development; an abnormal blood clot is called a "thrombosis." Decreased calf muscle activity from paralysis and bed rest can lead to vein inflammation and formation of blood clots (thrombi) in the deep veins of the legs and pelvis. A bedside clue to formation of blood clots in deep veins, that is, deep venous thrombosis (DVT), is swelling of the leg(s), or "edema." If blood clots break off from leg veins, the moving clot (called an embolus") can travel to the lungs, where they are called "pulmonary emboli." If sufficiently large in size or number, these emboli can interfere with blood flow through the lungs, diminish oxygenation of blood, and can be life-threatening.

Measures used to reduce the development of DVTs include injections of blood thinners (heparin injections); elastic, thigh-length, anti-embolism stockings, (e.g. TED®), and use of an air-filled inflatable bladder wrapped around the calves, that intermittently inflates and deflates (pneumatic limb compression therapy). This helps move blood along in leg veins, reducing the sluggish blood flow of inactivity and the risk of clots.

Autonomic Dysfunction. Damage can occur to any of the many autonomic nerves, both sympathetic and parasympathetic, in the body that serve the heart, blood vessels, bowel etc. Damage to autonomic nerves that regulate internal organ function can make these organs over reactive to medications. This over-reactivity is called "denervation sensitivity." Because of the risk of denervation sensitivity, the smallest effective dose of any drug being newly started should always be used. For example, treatment of elevated blood pressure with midrange dosing could run the risk of over-correcting and result in too low a blood pressure, light-headedness, and even fainting.

Blood Pressure, Heart Rate. Both high and low blood pressure, as well as unusually slow or rapid heart rates, can occur in Guillain-Barré Syndrome. Low blood pressure resulting when the patient is placed in an upright position from lying down (called orthostatic hypotension) may result from expansion or dilation of veins in legs with flaccid muscles. As a result of dilation and muscular inactivity, blood may quickly settle in the dilated veins and not return to the heart as rapidly as usual. Intravenous fluids to increase total blood volume, as well as elastic stockings, mild leg elevation and sometimes medications can be used to correct this condition. Other medications are available to treat low heart rates as well as rapid heart rates (e.g., beta blockers, calcium channel blockers and digoxin), and blood pressure elevation.

Urine retention. Nerve damage to the bladder can reduce the feeling one has of having to empty one's bladder. This contributes to delayed or inadequate emptying of urine. Urine retention may require short-term use of a tube called a Foley catheter, inserted into the bladder to keep it draining until the patient's normal bladder function returns. To keep the catheter in place, a balloon at its inner end, in the bladder, is inflated after it is inserted. If a catheter is used, its loose outer end is usually anchored to the thigh with tape, to avoid pulling on the catheter and the inner balloon end inside the bladder. Such pulling risks moving the inner balloon end downward, where it can traumatize the narrow channel of the natural tube to the outside with its fragile soft tissues, and block urine flow. Urine retention and enlarged bladder can cause a bulge, or fullness, as well as discomfort in the lower abdomen, just above the pubic bone. If pelvic fullness and poor urine flow develop, a first step in evaluation is for the physician either to perform a non-invasive ultrasound study of the bladder or place a catheter and check for urinary retention. If a catheter is already in place, it should be checked for flow..

Constipation. This may result from several factors including bed rest, lack of exercise, interruption of one's daily routine, reduced dietary fiber, decreased gut motility from autonomic nerve damage, the strange hospital environment, and the change in diet. A variety of methods can be used to treat constipation. These include simple measures such as administering prunes, milk of magnesia, bowel softeners such as sodium sulfosuccinate (Colace®), or agents such as psyllium (Metamucil®) and lactulose (Chronulac®). A suggested starting dose of lactulose is 3 tablespoons or 45cc 4 times a day until the patient has a bowel movement, then 1 to 3 tablespoons daily. Bowel stimulants in the short term can be effective for the neurologically compromised patient. Examples include bisacodyl suppositories (Dulcolax®, Corectal®) and senna tablets (Ex-Lax®, Senekot®).

Blood Chemistries. Blood chemistries are usually normal unless the patient has other underlying diseases, with the following exception. In GBS, the blood sodium level may be decreased due to excess secretion of a hormone used to decrease urine output (antidiuretic hormone or ADH). Excessive ADH secretion leads to more retention of water by the kidneys with its recirculation into the body, resulting in increased total body water and fluid volume, diluting the blood sodium level. Treatments for this disorder may include restriction of water intake, and on occasion, intravenous administration of salt or saline solutions, such as normal saline solution.

EMOTIONAL PROBLEMS

During the early stages of the illness, especially for the patient in an intensive care unit, events can be frightening. Most patients with GBS were formerly healthy. Finding themselves suddenly paralyzed, helpless, with intravenous lines, a bladder catheter, and a heart monitor that continuously and monotonously beeps, can be upsetting. If one'sr arms are too weak, even brushing teeth, feeding oneself or scratching an itch becomes impossible. If a ventilator is required for breathing, the inability to talk and communicate leads to a sense of isolation. Helplessness and thoughts of possible death, the threat of permanent disability, dependence, and income loss can be overwhelming. It is helpful for both patient and family to be reminded that most Guillain-Barré patients get better, eventually walk again, and many ultimately resume a normal life, same as they had before GBS. During the hospital course the patient may benefit from the following suggestions for the hospital staff and family as shown in Table 3.

TABLE 3:
Measures Healthcare Providers Can Take to Reduce Anxiety in the Paralyzed Patient

- Express optimism and emphasize to the patient and family the relatively good chance for full recovery
- Provide the paralyzed patient on a respirator with a method for communication to reduce frustration. Communication Cards are available from the GBS Foundation. These list in large print common problems that a patient may develop. A nurse or family member can flip through these cards with the patient, pointing to various items and getting the patient's "yes" or "no" response indicated by a head nod, eye movement to the right or left or eye blink
- Explain all immiinent procedures to the patient to alleviate anxiety
- Identify a key family member to serve as contact with a hospital representative with good rapport (a physician or nurse), to provide accurate information on the patient's status and care plans. Multiple members of the family calling causes confusion and health-care provider fatigue
- Encourage frequent visits by family and friends to provide needed emotional support
- Provide a clock, electric calendar, radio and night light to help the patient keep track of day and night hours, maintain awareness of the outside world and minimize confusion while in the ICU
- Encourage the patient to express emotions (anger, frustration, and fear) and help them deal with these issues
- Encourage family and friends to reduce patient isolation during a prolonged hospital stay by participating in bedside activities (e.g,, grooming, reading get-well cards,...)

SPECIFIC TREATMENT
Immune System Modulating (Modifying) Therapy

Several studies support the effectiveness of aggressive treatment with some therapies that modify the immune system. Two types of therapy that have been shown to shorten the course of GBS are plasma exchange and high dose intravenous immunoglobulin.

PLASMA EXCHANGE (PE)

Introduction. Plasma exchange PE), also called "plasmapheresis,"was the first immune therapy found effective for GBS. "Plasma" means something molded, or without shape, and, as plasma is the liquid part of blood, it does, like all liquids, automatically mold to fit the shape of its container, in this case the blood vessels and body organs. "Plasmapheresis" is a procedure described in more detail below, by which disease-causing substances in a patient's blood can easily be removed. A similar procedure of PE is also used to collect plasma from normal healthy donors, to be further processed into other biological treatments. Indeed, this method is used to produce immune globulin which is used to treat GBS, as described in a later section.

The Procedure. As it applies to GBS, plasmapheresis (or plasma exchange) is used to collect the patient's blood, a little amount at a time, process it and then discard the liquid or plasma portion. The plasma contains antibodies which most evidence suggests are instrumental in targeting nerve fibers for damage. To perform PE, first one or two tubes or catheters are inserted into a large vein in the neck or groin through which blood can be removed. The blood is withdrawn into a machine, where it is spun rapidly (centrifuged) to separate and remove the plasma, and then the red and white blood cells are returned to the body, along with fresh plasma. The procedure is done either on small amounts at a time or by a continuous flow process, and takes 1-3 hours.

Studies performed since the 1980's showed that plasmapheresis significantly shortens a GBS patient's illness. Benefits of PE include shortening of the length of time on a ventilator and time until patients can walk independently. Such benefits from PE support that the humoral immune system, (antibodies), plays an important role in the demyelination process that occurs in GBS. Five studies have evaluated the effects of PE on GBS patients. In a large U.S. multicenter trial, PE, when started within the first two weeks of onset of neurologic symptoms, significantly reduced the number of days a patient had to be on a respirator and improved their six-month outcome. PE resulted in about a 50% improvement in outcome: about 60 percent of PE-treated patients showed measurable improvement within four weeks, compared with about 40 percent in the group given only supportive, or "conventional" care. For older patients, 60 years of age or older, who were respirator-dependent and had rapid onset of paralysis (needing to be on a ventilator within 7 days), PE improved outcome and shortened duration of chronic deficits. Patients treated

with plasma exchange were twice as likely to walk independently at three and six months after onset of GBS than those treated with conventional supportive treatment alone.

PE is usually given in courses of five to 6 treatments over 10 days to 3 weeks. In the North American trial, patients were started on treatment an average of 11 days after developing neurologic symptoms. In each exchange, the plasma equivalent to 55ml (~2 ounces)/Kg (2.2 pounds) body weight was removed and replaced by solution of five percent protein in a salt solution (albumin in physiologic saline). A typical exchange rate is a total of 200-250 ml/kg body weight over 7-14 days. Plasmapheresis removes plasma and thus all molecules within it, including immunoglobulin or antibodies as well as complement proteins, clotting factors, and cytokines, signaling chemicals produced by white blood cells. In theory, if factors that cause demyelination are antibodies and complement, it should be possible to tailor therapy to remove only these agents. However, such procedures are still not commonly available. Furthermore, it is possible that PE is also beneficial because it is also removing cytokines that may be participating in nerve damage and dysfunction. If so, current PE procedures may be actually be optimal treatment to treat GBS.

Plasma exchange is best performed by an experienced medical team to minimize complications. Not every hospital has the professional expertise or equipment to perform PE, and sometimes patients must be transferred to a center where this is available. In experienced hands, risks are uncommon. Side effects and risks include an irregular heart beat from salt imbalance, low serum calcium, infection and blood clots at the site of venous catheter, and allergic reactions that can be severe, with airway obstruction and collapse of circulation (that is, anaphylaxis and activation of coagulation, complement, fibrinolytic cascades, and aggregation of platelets). Patients are given blood thinners during treatments. PE does decrease the number of circulating platelets, used by the body for clotting, and clotting factors are removed, but return to normal within 24 hours, except in the occasional patient with liver disease. Because of upper extremity weakness, it is frequently necessary to use a large bore rigid intravenous catheter to perform the procedures. Attempt at catheter placement in the central (subclavian) vein under the collar bone may cause lung puncture and collapse (pneumothorax) and, rarely, arterial bleeding or an abnormal connection between the artery and vein, an arteriovenous fistulae. In the U.S. multicenter trial, there was no increase in complications between the plasma exchange and conventional therapy groups. Thus, despite potential complications, the actual risks from PE are low.

HIGH DOSE IMMUNOGLOBULIN (IVIG)

Another treatment for GBS is high-dose immunoglobulin, that is, the intravenous administration of high concentrations of normal antibodies purified from the plasma of normal, healthy donors. This treatment is abbreviated IgIV.

Two large trials of almost 600 patients compared PE with IgIV in GBS patients. In the Dutch trial, IgIV was given at a dose of 0.4 grams of immunoglobulin/Kg body weight daily for 5 days in newly diagnosed GBS patients. After four weeks, 54 percent of patients

treated with IgIV had improved at least one grade of function (e.g., walking ability) compared with 33 percent of patients treated by plasma exchange. A second multicenter, 383-patient trial organized in the UK was designed to compare the efficacy of IgIV versus plasma exchange (*Plasma Exchange/Sando. GBS Study Group, 1997*). Patients were treated either with plasma exchange (200-250 ml/kg body weight over 5 treatments) or IgIV (at a dose of 0.4g immunoglobin/Kg body weight for 5 days). Both studies, although they found the treatments were equally effective, concluded that IgIV was the preferred therapy, since immune globulin infusion were usually well tolerated and could be readily given through a small, safe peripheral intravenous line. The second trial also looked at a combination of IgIV followed by PE. Patient outcomes suggested that this combined regimen might be somewhat more effective than IgIV alone (improvement at four weeks was 1.1 grade of function and 0.8 grade of function respectively), but the difference was not statistically significant.

Complications and side effects from IgIV are usually mild. Temporary headache, chills, muscle aches and nausea are common and can be managed with non-steroidal anti-inflammatory medication (e.g., ibuprofen [Motrin®], etc.) and/or slowing the infusion rate (*Koski, 2005*). Other potential side effects include fever, hypertension, lightheadedness and flushing. Severe headaches and other intolerable side effects may be prevented, or their intensity reduced by the administration, of steroids (e.g., methylprednisolone [60-100 mg IV] and diphenhydramine [Benadryl® 25-50 mg IV] 30 minutes prior to IgIV treatment. Immunoglobulin administration can occasionally lead to "aseptic meningitis" characterized by severe headache, stiff neck, vomiting, fever and increased white cells in the spinal fluid. Contraindications to receiving immunoglobulin are uncommon but include complete deficiency of immune globulin A (IgA), a prior history of systemic hypersensitivity reactions to immune globulin infusion, and poor kidney function. In older patients with accompanying atherosclerotic cardiovascular disease, IgIV use can potentially contribute to excessive thickening (hyperviscosity) of the blood with, in turn, slower blood flow or sludging of the blood in vessels. Slow blood flow can potentially place the patient at greater risk for a heart attack (acute myocardial infarction), chest pain due to inadequate blood flow to the heart (angina) and stroke.

The mechanism of action of IgIV is less clear than that for plasmapheresis. Several mechanisms have been proposed, such as suppression of harmful white blood cells, supplying a large pool of naturally occurring and safe antibodies to neutralize harmful auto-antibodies ("anti-idiotypic antibodies"), blocking production of harmful auto-antibodies, interference with the immune system's complement protein cascade (that in GBS may cause nerve damage) and inhibition of cytokines that attract myelin-damaging macrophages. Alternatively, IGIV may work by inhibiting macrophage function via upregulation of the Fc IIb receptors, by containing pools of naturally occurring anti-idiotypic antibodies, by blocking antibody generation through both B and T cell mechanisms or limiting production of certain cytokines. It may also work by inhibiting natural killer cell activity or by modulating activation of neurological symptoms of the complement cascade preventing formation of C5b-9.

Relapses of GBS can occur after the use of either IGIV or PE in about 5% to 10% of patients. Patients who relapse usually improve with another course of treatment. Thus, close monitoring of the patient's breathing, strength and overall clinical condition is still warranted after they receive IgIV or PE, to watch for deterioration. General weakness, difficulty breathing, softer voice, poor secretion or mucous handling, and drop in blood oxygenation via pulse oximetry readings are some markers to prompt careful re-evaluation of the patient for relapse and possible need for retreatment in an acute care setting. Close monitoring of the patient is important during the weeks after IgIV or PE to watch for evidence of relapse following initial improvement, particularly if they are promptly transferred to a rehabilitation or other facility.

Corticosteroids. Corticosteroids ("steroids") are anti-inflammatory medications that were used in the past to treat GBS patients. This class of drugs consists of medicines such as cortisol, prednisone, prednisolone and methyl-prednisolone. Since GBS is understood to be caused by autoantibodies, , it might seem reasonable to expect that steroids could be a helpful treatment. To address this possibility, more than six randomized controlled trials were performed and the findings were summarized in a review article, that found that steroids are not helpful to speed recovery, and in fact at least one study suggested that steroids actually may delay improvement). Accordingly, corticosteroids are not usually recommended for the treatment of GBS.

RECOMMENDED IMMUNE THERAPIES FOR NEW GBS PATIENTS

Recommendations by the American Academy of Neurology based on a comprehensive medical literature review concluded that IgIV and PE are equally effective treatments for GBS. Either should be started within 4 and preferably within 2 weeks of the onset of symptoms. Either can be considered for use in children. Using both treatments, PE then IGIV, does not provide any greater benefit than using either alone. Corticosteroids are not recommended.

INVESTIGATIONAL TREATMENTS

Both PE and IgIV are, to some extent, non-specific methods of treatment. They are designed to block ongoing nerve damage, such as antibody-mediated nerve demyelination by inhibiting the immune system. Not all patients respond to these treatments. Drugs focused on blocking specific steps in immune system activity might facilitate improvement in more patients. Such potential therapies are in the investigational stage. One currently being considered for human studies is eculizumab (marketed as Soliris®). It is a unique antibody that blocks parts of the complement system, the series of protein molecules that help antibodies damage nerves. In laboratory mouse models, eculizumab blocks nerve damage by complement (*Halstead et al, 2008*). Eculizumab has already been shown to effectively treat another rare autoimmune, but non-neurological disorder, paroxysmal nocturnal hemoglobinuria (PNH). In this disorder, complement damages red blood cells, leading to nighttime episodes of bloody urine and reduced numbers of circulating

red blood cells. Studies are planned to determine if eculizumab will limit ongoing nerve damage in GBS and hasten recovery, by blocking antibody-mediated complement activation.

PAIN AND OTHER ABNORMAL SENSATIONS

During the earliest stages of GBS, as well as throughout its entire course, the patient may experience significant pain. The pain can be severe, difficult to control and under-appreciated by hospital personnel. The GBS patient also experience other unique sensations, such as having a sense of vibration in the limbs while lying perfectly still in bed.

Pain in GBS occurs in over half of newly diagnosed patients. Several mechanisms are implicated to explain the pain, including inflammation and swelling within the nerve, mechanical contact of enlarged nerves by boney ridges, and damage to the nerve's conducting core, the axon. Pain, by definition, is a noxious or unpleasant sensation. It can be a challenging problem in GBS for several reasons. These include lack of physician awareness that pain can occur in GBS, inability of the patient to communicate their pain if they have been intubated for respiratory support, , and a lack of response of the pain to standard therapies. Pain in GBS may develop early in the illness, even before the diagnosis is made, as well as during both disease progression and recovery.

Pain during the onset of GBS is often felt in the lower back, buttocks, and/or thighs and sometimes between the shoulders and the arms. It may be achy, crampy or stab-like, or sometimes described as feeling like a Charlie horse, with a deep muscular pain quality. It may be mild to severe in degree, and last for several weeks. Interestingly, the very first symptom in GBS may occasionally be low back pain that radiates into the buttocks and/or thighs, thus mimicking a sciatica type condition usually caused by pinched nerves in the back; or referred pain from a kidney stone. Such a scenario may lead the physician to think of these or other disorders rather than GBS, and delay the correct diagnosis until those other findings more typical of GBS develop, such as weakness and loss of reflexes.

Several options can be used to treat pain in the early or acute phase of GBS. It may simply improve with the standard treatments of PE or IgIV. Turning, positioning and having someone move the legs and arms passively may be helpful to relieve back and shoulder pain. Severe pain can contribute to increasing (or even decreasing) blood pressure and an increased or rapid heartbeat. In such situations, aggressive use of ipain medications, even narcotics, may help relieve vital sign instability [. Pain may improve with administration of medications commonly used to treat neuropathic pain such as gabapentin, carbamazapine and amitriptyline (see below for more information). Rarely, a patient may develop a sciatica syndrome, with low back and/or thigh pain, and may benefit from local injections of

narcotics or anesthetics at the site of pain or around the outer covering of the spinal cord (epidural injections) to provide relief. An experienced anesthesiologist would usually insert a needle into the low back to deliver the medicine. This method avoids the side effects from narcotic medicines given orally, intramuscularly (IM), or intravenously (IV) (such as constipation, grogginess, decreased breathing and altered blood pressure). Non-steroidal anti-inflammatory drugs, also called NSAID's (pronounced en'-seds), such as ibuprofen (marketed as Motrin® and Advil®,) are very popular to treat arthritic, muscle and other types of pain. Although sometimes beneficial, published experience with this drug class for the pain of GBS is limited. Clinical judgment may help guide its use.

Pain during recovery from GBS may change in character from that during the acute phase, since it reflects axonal damage from the acute inflammatory process. It is often a burning pain but can have a stabbing quality or may be felt as increased sensitivity, with even the touch of bed sheets causing pain. This type of pain may persist for weeks or occasionally years. As damaged sensory nerves undergo healing, the sensitive regenerating tip of the nerve generates abnormal signals with minimal stimulation, that can be exacerbated by exercise and weight bearing, and thus can interfere with rehabilitation. This type of pain typically occurs distally, in the feet and sometimes hands. Interestingly, some sensations may be rather subtle and difficult for the patient to describe. Some patients might, for example cough, choke and aspirate ice cold water but could easily tolerate room temperature water. Such seemingly trivial problems can lead to aspiration and pneumonia. Changing from ice water to room temperature water can be a simple but important intervention.

Most sensation problems resolve with time. Persistent pain, if sufficiently bothersome, may respond to various treatment modalities. Over-the-counter enteric-coated aspirin, acetaminophen (Tylenol®) or ibuprofen, local heat application (especially moist heat), cold or creams such as capsaicin may be helpful. Capsaicin is a cream made from the ingredient in cayenne peppers and marketed as Zostrix® as well as other product names (Capzasin-P). Application of capsaicin cream to painful areas of skin can reduce local pain in arthritis and painful neuropathies. It comes in various strengths. Local pain can sometimes be relieved by a transcutaneous electrical nerve stimulator (TENS). TENS is a portable battery-powered device that supplies electric current to the skin and underlying nerves. Immersion in a therapeutic pool and exercise may also relieve pain. Should these relatively safe initial measures prove inadequate, alternative approaches, such as prescription medications, are used.

Prescription strength arthritis medications, the non-steroidal antiinflammatory drugs, have not been widely used to treat neuropathic pain and may only be of modest benefit. Side effects, such as internal bleeding, heart and kidney damage, can limit their safe use. Prescription medications in common use for neuropathic pain include antiepileptic, antidepressant and narcotic drugs. Antiepileptic drugs act to stabilize nerve membranes and are often helpful to relieve pain. These include two rather old drugs, phenytoin (Dilantin®) and carbamazepine (Tegretol®). Gabapentin, more recently developed to treat epilepsy, is safer and thus more commonly used to treat neuropathic pain. Its side effects

can include dizziness, a cloudy mind, lower extremity edema and weight gain. A starting dose is 100–300 mg, taken at bedtime. The dose may be increased in a few days to twice a day, and thereafter increased to 3 to 4 doses a day, or the twice a day dose doubled every 3–5 days, until the patient's symptoms are relieved or side effects interfere with further dose increases. A slower increase in dose may reduce side effects and allow tolerance of a higher dose. Doses as high as 2,700 to 3,600 mg a day have been tolerated and effective. The more recently introduced prebagalin (Lyrica®) is part of the same family of drugs but requires lower doses twice a day. Other products such as levetiracetam (Keppra®) and lacosamide (Vimpat®) can be of benefit to treat neuropathic pain.

Other effective drugs for management of pain are antidepressants. Examples are the tricyclics such as nortriptyline (Pamelor®) and amitriptyline (Elavil®) at bedtime. Another class are the serotonin and norepinephrine reuptake inhibitors (SSRIs and SNRIs). The main drug in this group is duloxetinem (Cymbalta®). Its potential side effects include nausea, sweating, insomnia and sedation. Not infrequently, a combination of drugs such as a tricyclic plus an anti-seizure drug such as gabapentin, may more effectively control pain at a lower dose than either drug used alone. If narcotics are used, long acting products are often safer, such as a slow release fentanyl patch (Duragesic Patch®), slow release morphine (MS Contin®), etc. It is however important to remember that side effects such as confusion and constipation are common as well as a need to gradually increase the amount of drug to maintain the same benefit.

When treating complications of GBS, it is important to realize that the effects of therapeutic interventions may not be predictable. Therapies should be tailored to each individual patient and monitored carefully.

INTERMEDIATE COURSE AND REHABILITATION

The progression of disability during the acute phase of Guillain-Barré Syndrome can vary from a few days to four weeks, and, infrequently, six weeks. Then a low stable level of impairment (paralysis, weakness, etc.) continues for a variable length of time, days to weeks, and, less often, months or longer.

When the patient has recovered from acute life-threatening complications such as breathing difficulty and infections, and muscle strength has stabilized and perhaps even begun to return, treatment in an acute care hospital is usually no longer required. However, many patients will still require rehabilitative care including intensive physical and occupational therapy. Where this care is provided will depend in part on several factors. Choices available for further rehabilitation include:

1. In-patient care in a rehabilitation hospital. A common requirement to justify this intensive rehabilitation is the patient's ability to participate in at least 3 hours of therapy a day.
2. Sub-acute rehabilitation, in a nursing/rehab facility.
3. (So-called) Day hospital care. The patient sleeps at home, and is transported, by a wheelchair-accommodating van, to the rehabilitation hospital or center regularly (daily) for daytime therapy.
4. Out-patient rehabilitation.
5. Home-based therapy, via visiting therapists or by following instructions set up by a therapist for a home therapy program.

The decision as to the type and location for rehabilitation should be individualized to each patient's particular needs, taking into consideration such factors as overall physical condition, strength, endurance, amount of return of use of arms and legs, and insurance. For example, patients with mild impairment, who can walk with assistance of a quad (four-footed) or straight cane may not need an in-patient rehabilitation facility, and may obtain sufficient care in an out-patient setting. In contrast, patients who can't walk, or require substantial assistance to do so, but are showing some improvement, may be transferred to an in-patient rehabilitation hospital setting for optimal care.

Physicians may occasionally be reluctant to place Guillain-Barré Syndrome patients in rehabilitation hospitals because of concern about depression or relapse of symptoms that could require readmission to an acute care facility for further treatment. Regardless, transfer of a patient to a rehabilitation center should be considered as a positive next step in the patient's recovery.

The rehabilitation process itself does not improve nerve regeneration. Rather, the major goal of rehabilitation is to assist the patient in optimal use of muscles as their nerve supply returns, and to adapt to a lifestyle within their functional limitations. In addition to helping the patient regain use of muscles, the rehabilitation center treats any remaining medical complications. These can include control of high blood pressure, antibiotics for infections, treatment or prevention of blood clots, etc.

Strength usually returns in a descending pattern, so that arm and hand strength usually returns towards normal before leg strength. Often, right-handed persons note more rapid return of strength to the left side and vice versa. As arm strength returns, the patient is again able to perform some restricted things that used to be taken for granted, such as brushing their teeth, feeding, grooming and dressing themselves, cutting meat and so forth. As ability to perform activities of daily living improves, the success can be emotionally gratifying.

Rehabilitation in many centers is accomplished by the coordinated efforts of several groups of professionals in a team approach. The team members may include, depending upon the particular patient's needs, a physiatrist (rehabilitation doctor), physical therapist, occupational therapist, registered nurse, neurologist, internist, psychologist, social worker,

etc. Each team member contributes their specific expertise and experience to the patient's care. Team conferences may be held at intervals, for example, weekly, to assess the patient's status, determine progress and plan further care. The team's overall goal is to assist the patient to maximize use of returned function and ultimately return to normal activity. Most patients will eventually lead a normal or near normal life. For those patients with incomplete recovery, the goal is to adapt their lifestyle to their persisting functional limitations.

The physiatrist (pronounced: fiz-eye'-a-trist) (not to be confused with a psychiatrist) is a physician who specializes in physical medicine and rehabilitation. A physiatrist usually coordinates and oversees the total rehabilitation program.

Principles of Rehabilitation for the GBS Patient. During the rehabilitation process, certain issues are unique to GBS patients. Most rehabilitation patients are exercised to maximum ability, to fatigue. This should be avoided in GBS patients as exhaustion requires some time to resolve and will delay the rehabilitation process without benefitting the patient. Substitution of stronger muscles for weaker ones will delay uniform return of strength and optimal function. The physical therapist should be cognizant of the potential for substitution and customize exercises to strengthen weak muscles. Neuropathic pain can limit the patient's ability to undergo rehabilitation and should be recognized and adequately treated.

Occupational Therapy: An occupational therapist instructs the patient in exercises to strengthen the upper limbs (shoulders, arms, hands and fingers) and help prepare them for return to their occupation. Usually arm strength and use returns before hand and finger dexterity. Help is given to re-learn activities previously taken for granted such as holding a pencil, using an eating utensil, etc. Muscle testing may be performed, and exercises designed to strengthen the weaker muscles. Repetitive squeezing of a rubber ball or putty can strengthen the hand grip while spreading two fingers apart against a rubber band placed across the fingers can be used to increase finger strength.

Tests may be utilized to determine the status of hand sensation. For example, the patient may be instructed to look away or close their eyes while articles of varied consistency and shape are placed into their hand are placed into their hand, such as a marble, key, eraser, pen, closed safety pin, and the like. The ability of the patient, without looking, to discern the presence of these objects and identify what they are indicates that their sensory nerves can perform fine touch discrimination. In another test, the patient inserts their hand, with eyes closed, into a bowl of sand or rice containing such items as chalk, keys, eraser, etc. The ability of the patient to locate these, and, upon removing them, identify their particular shape and consistency provides an index of return of finger sensation. Some patients may experience persistent difficulties in using their hands and fingers to perform such activities as using a zipper, buttoning a shirt, writing, using utensils and handling coins. Methods are available to compensate for these problems. For example, to circumvent difficulty in buttoning clothes, a button-hook device may be utilized. Velcro® straps or zippers with large pull handles may sometimes be practical alternatives to buttons. Because of the potential for fatigue, severely affected patients are taught energy conservation techniques that include using shortcuts to maximize hand and arm use. Splints may be used to position

the wrist in a slightly bent position, and to support the thumb, to optimize hand use.

Physical Therapy: The physical therapist emphasizes strength and function of the lower limbs, and ultimately teaches the patient to walk as independently as possible. A variety of methods are used to accomplish these goals. Initially, the patient, fitted with a life jacket (personal flotation device), may be lowered into a pool, and assisted into a suitable depth of water so they can walk on the bottom of the pool with partial weight bearing, the life jacket and water providing buoyancy to enable this. Immersion in a therapeutic pool may also relieve muscle pain. As strength returns, exercises are performed on mats to help strengthen various muscle groups against gravity and resistance. For example, the patient may be placed on a mat on his back, with the knees raised on a triangular foam support; progressively increasing weights are placed on the ankle and the patient is directed to slowly and repeatedly straighten and lower the leg. This exercise can help the patient increase thigh muscle endurance. Slowly raising and slowly lowering the leg affords greater use of muscles and facilitates better development of thigh muscle strength, rather than allowing the lower leg to fall with gravity. Other exercises are used to strengthen the hip musculature, such as lifting the upper leg with the patient on their side and maintaining it in an upward position against gravity. As nerve innervation returns, other exercises can be used to maintain muscle strength. A stationary rehabilitation exercise bicycle may be used to apply an adjustable force to the leg as it pedals the bike, thus providing progressive resistive exercise to improve strength and endurance.

As leg strength improves sufficiently for the patient to bear weight and begin walking, assistive devices provide added support and balance. The patient may be placed between two railings, called parallel bars, positioned at about waist level. These provide the patient with maximal support while walking, by their holding the bars with both hands. Their upper body can support some of their weight, that their legs no longer have to support. As balance improves, a wheeled walker may be used. The patient rolls or slides the walker forward to provide support as they walk. As balance improves further a standard, non-wheeled walker can be used with the patient lifting the walker forward and placing it down ahead repeatedly as they walk. The next progression may then be to the use of forearm crutches or directly to the use of underarm crutches and then canes. A quad cane, with four small feet close together, provides a fair amount of stability. If the patient has enough balance and strength, a straight cane may be sufficient. Eventually, if possible, independent walking without an assistive device is accomplished. During the rehabilitation process emphasis is placed on proper body mechanics, avoidance of substitution of stronger muscles for weaker ones, prevention of muscle strain and fatigue, and safety.

For patients with persisting muscle group weakness, various methods (orthotic devices) can be used to increase function and independence. For example, a "foot drop" can be treated with a molded ankle foot orthosis (MAFO), a thin lightweight plastic device that fits behind the lower leg and under the foot. For the patient with a weak grip, utensil handles can be wrapped with a thick cylinder of foam rubber to enable better gripping of the utensil; the edge of a plate can be fitted with a metal wall so the patient can push food against it with a fork or spoon to help get the food onto the utensil. A Velcro® strap around

a cane handle can hold the hand of a patient with a poor grip onto the handle and enable him to use the cane. Progressive resistive exercises may be designed to strengthen specific muscle groups and functions.

In addition to occupational and physical therapists, other persons may participate in rehabilitation, including speech therapists, nurses, social workers, and psychologists. The latter can play an important role in assisting the patient and family in dealing with the new and sometimes overwhelming problems of paralysis, dependency, lost income, and a multitude of associated emotional problems including frustration, depression, self-pity, denial, and anger. Since the prognosis for the Guillain-Barré patient is optimistic, in spite of the potential gravity of the illness, a practical approach is to take one day at a time. Recovery, although greatest during the first year, can continue over two to five or more years. Participation in active physical therapy can be a positive factor in a patient's recovery both mentally and physically.

Speech Therapy: Speech is impaired in about 40% of GBS patients. Patients on a respirator will be unable to speak because the tube placed into the airway does not allow the vocal cord movement required to produce speech. These patients can usually communicate via Communication Cards. Typically, after an endotracheal tube is removed, the patient's speech returns within a few days. Even off a respirator, a patient may still have difficulty talking if the muscles used for speech are weak. These muscles control the vocal cords, tongue, lips, and mouth. Slurred speech or difficulty swallowing may occur. A speech therapist can help the patient learn exercises for the affected muscles, to improve speech patterns and clarity of voice, as well as recommend dietary changes to facilitate safe swallowing with adequate nutrition.

LONG-RANGE PLANS

As the patient progresses through the rehabilitation program, it may be appropriate to plan for multiple long-range problems. These problems include learning to drive and using convenient parking, re-employment, learning to pace activities, sexual activity, limitations of the wheelchair-bound patient and so forth. A social worker may assist in handling many of these problems. The majority of patients who were in a rehabilitation center may be placed on an out-patient therapy program when sufficient strength has returned. At home, living on a floor that has a bathroom and bed may be temporarily helpful until the patient is able to climb stairs. As sufficient strength returns, driver retraining may be appropriate, especially if the patient had been hospitalized and not driving for a long time. Driver retraining, and adaptation of an automobile for hand controls, is available through some rehabilitation and hospital centers.

The frustration of physical exhaustion, or shortness of breath associated with prolonged walking, may be reduced in the recovering patient by parking near a building entrance in a handicapped parking space. A special parking placard or license plate is available in some states.

As the patient approaches the end of in-hospital rehabilitation, it is usually appropriate to plan for return to their employment or reemployment. This is hopefully a cooperative effort between patient, social worker, current employer and, if available, a state bureau of vocational rehabilitation. A potential barrier to returning to work, as well as resumption of a normal overall lifestyle, is the onset, following a certain amount of activity, of muscle aches, physical exhaustion, and abnormal sensations, such as tingling and pain. These problems may be circumvented by returning to work part-time initially, and if possible, timing activity with intermittent periods of rest. Many patients learn by trial and error how much activity they can tolerate.

After discharge from a formal hospital-based in or out-patient rehabilitation program, there is often a role for continued exercise. Usually, some of the physical and occupational therapy exercises done as an inpatient can be performed at home. Also, activities of daily living, such as bathing, dressing, walking, and stair climbing may suffice as a practical outpatient exercise program. Should muscle or joint cramps or aches develop with activity, over-the-counter mild pain medications such as aspirin or acetaminophen (Tylenol®) may provide relief. Since pain relief does not relieve the muscle, tendon, or joint strains, rest periods or a temporary reduction of activity may be helpful.

Some caution is warranted with respect to the gradual institution of non–hospital-based exercise programs, jogging, and sports. Each recovering patient should be evaluated for their individual needs. Care should be taken to gradually expand activities to avoid tendon, joint, and muscle injury. Upon discharge, the patient can usually resume sexual activity. Positions that minimize muscle exertion, such as lying on the back, may prevent exhaustion until pelvic and other muscle strength has improved. A male patient that experiences erectile dysfunction not present prior to GBS should have his physician review his medications to screen for those that might inhibit normal erections or see a urologist experienced in these problems. In some cases medications for erectile dysfunction, such as sildenafil (Viagra®), may be helpful.

For the wheelchair-bound patient, architectural barriers (e.g., stairs) may be overcome by ramps to enter the home and other buildings. One-floor living, a stair lift, or an elevator may be required. A visiting nurse and physical therapist can treat the patient at home. Significantly handicapped patients are referred to their local rehabilitation center or other resources.

FATIGUE

Fatigue is a common problem during the early part of recovery and can even persist in some patients who appear to have recovered. Such patients may have normal strength with standard testing of muscle function, and can perform normal activities, such as walking. Yet, with sustained activity, they may develop weakness or fatigue, and even frank exhaustion and collapse. Fatigue may be preceded or accompanied by flare-ups of muscle pain, or abnormal sensations such as tingling. This problem of persisting poor endurance and fatigability in people with prior GBS was documented in a study of members of the United States Army who had apparently recovered . Despite some people having been able to return to their usual activities, formal physical fitness testing (a 2-mile run, sit-ups and push-ups) showed that some "recovered" patients still had decreased endurance compared to their abilities pre-GBS. Two of the studied patients had normal electrodiagnostic tests (nerve conduction velocity-electromyography), despite having diminished endurance capacity. In summary, both patient and physician should realize that limited endurance is a valid, persisting problem in recovered GBS patients that is difficult to measure objectively with standardized office tests of muscle strength. At least one study suggests that formal endurance exercise training may help improve a patient's work capacity. Another study showed that three, 20 minute aerobic courses of exercise per day also improved the symptoms of fatigue.

As noted in the "Long-Range Plans" section, if a GBS patient senses impending weakness or, by experience, learns to recognize a flare-up of abnormal sensations that signal impending fatigue, the practical treatment is for them to learn how to pace their activities by resting as needed, to avoid exhaustion. Decreased endurance may necessitate a shortened workday or, alternatively, a less physically-demanding job.

NATURAL HISTORY AND PROGNOSIS

The overall outlook for most GBS patients is good, but the course of the illness can be quite variable. An occasional patient may experience a mild illness, with a brief period, days or weeks, of a waddling or duck-like gait, and perhaps some tingling and upper limb weakness. At the other extreme, more often in the elderly, the patient may rapidly develop almost total paralysis, respirator dependency, and life-threatening complications, such as abnormal heart beat and blood pressure, lung congestion, and infections. Rarely, paralysis may be so complete that the patient may not even be able to shrug a shoulder or blink an eye to communicate. The patient is said to be 'locked in.' Fortunately, hearing is usually preserved, enabling the patient to hear and fully understand those around them, despite

not being able to respond at all. Thus, as always, conversations about problems may best be spoken away from the patient.

Estimates of outcomes are based on several studies. Up to 80 percent of patients will be able to walk without aid at three months after onset of their symptoms, and by the end of a year will experience only minor residual symptoms, such as numbness of the bottom or ball of the foot. A full recovery can be expected, eventually. A patient may experience persisting, but mild, abnormalities that will not interfere with long-term function. Examples include abnormal sensations such as tingling, achy muscles, or weakness of some muscles that make walking or other activities awkward or difficult.

At least 20% of patients have significant residual symptoms and these patients benefit the most from treatment intervention to modify the immune system. Perhaps 5 to 15 percent of GBS patients will have severe, long-term persisting disability that will prevent complete return to their prior lifestyle or occupation. Factors that often predict greater severity of the disorder, with a longer course and incomplete recovery, include older age, more rapid onset of symptoms, becoming respirator dependent within 7 days and preceding diarrhea. Such patients are more likely to have a prolonged hospital course followed by rehabilitation for 3 to 12 months and may never be able fully to walk independently.

Strength returns at various rates. Some generalizations about speed of recovery can be made based upon the data published in 1988 by the Hopkins-based GBS Study Group and by the 2007 Erasmus University study in the Netherlands. In the latter study patients, were scored based upon their age, preceding diarrhea, and degree of weakness. The patients who could readily walk without assistance were assigned a disability score of 1. Non-walking patients were given a score of 5. The total score can range from the least impaired, 1, to the most impaired, 7. Patients with a low score of 1-3 have an excellent (95%) chance of recovery, being able to walk unassisted within 3 months from onset of their illness. Those with a score of 7 are less likely to have a good recovery . The scoring system they used is summarized in Table 4:

Children with GBS seem to fare at least as well as do young adults, and some studies suggest that pediatric patients actually recover faster and more completely than young adults, who, in turn, appear to recover faster than older patients.

Since GBS rarely strikes twice, if, after recovery, a patient again develops abnormal sensations, it is usually appropriate to look for causes other than Guillain-Barré Syndrome. Evaluation by a neurologist would be warranted. Sometimes, for example, there may be a need for a repeat nerve conduction velocity test, a glucose tolerance test, and other studies to confirm the presence of nerve damage and then to look for its cause. Recurrence or persistence of abnormal sensations or weakness may also conceivably signal the development of chronic idiopathic relapsing or progressive polyneuritis. These disorders are rare and the persistence or redevelopment of abnormal sensations should not be taken as an indicator of the presence of this disorder unless a neurologist experienced with chronic relapsing polyneuritis confirms the diagnosis. This disorder is described later in the section on CIDP.

TABLE 4:
Erasmus Prognostic Score

PROGNOSTIC FACTORS	CATEGORY	SCORE
Patient Age (year)	≤ 40	0
	> 40	1
Diarrhea (within 4 wks. before GBS symptoms)	absent	0
	present	1
GBS disability score	0-1	1
	2	2
	3	3
	4	4
	5	5
EGOS Erasmus GBS Outcome Score		1-7

IMMUNIZATION SAFETY

Foreign Travel

Since the illnesses prevented by immunizations often lead to substantial medical complications, the benefits of most immunizations outweigh their risks, even for someone with a history of GBS. Most immunizations and medications used for foreign travel (outside the USA) are safe and mentioned at the end of this section.

Influenza vaccine. The influenza vaccine developed in 1976 for a swine- influenza-derived virus (swine flu) immunization program was implicated as the trigger of many GBS cases. Some studies reported a sevenfold increase in the number of GBS cases following immunization. Because of the large number of GBS cases the program was halted. Another study reported a smaller increase in GBS cases (about 1 extra person per 1,000,000 persons vaccinated each year) following administration of influenza vaccine for more common human strains of influenza during the 1992-93 and 1993-94 seasons.

The greater-than-expected number of GBS cases associated with the 1976 swine flu vaccine led to a concern by some patients that influenza immunization shots or even other

vaccines might trigger a recurrence of their illness. Compared to the risk of developing significant complications from the flu, the risk of new onset or recurrent episodes of GBS resulting from the flu vaccine is very low. In patients 65 and over, the typical higher-risk candidates for a flu shot, 1,000 people per 100,000 population will require hospitalization if they get the flu, with a death rate as high as 1,500 per million. In contrast, the average number of GBS cases is only 0.5-2 per 100,000 people each year (a very small percent of which is related to influenza vaccine), with a mortality rate of only 3% to 5% in that group. This translates to 1,000 people getting very sick from the flu if not given a flu shot, compared to one or fewer people in the general population given a flu shot actually developing GBS. Accordingly, the risk of developing a significant complication from getting the flu is much greater than the risk of developing GBS. For these reasons, most experts recommend that even former GBS patients, who fulfill standard criteria to receive the flu shot, should receive it. The Centers for Disease Control today recommends virtually everyone over six months old receive the influenza vaccine, unless they have a bona fide medical contraindication (severe allergic reaction [such as anaphylaxis] to prior influenza immunization; have had acute GBS in the past 6 weeks; or currently have an acute illness or fever.)

There is an exception to this guideline. If a patient developed GBS within 6 weeks of receiving a flu shot or other vaccine, such a time relationship increases the possibility that the injection might have triggered the original episode of GBS and thus may, if repeated, cause a recurrence. In such situations, the vaccine should likely be avoided indefinitely and if exposed to the virus, the patient should be preemptively treated with an anti-influenza agent such as Tamiflu®.

The GBS patient who is still recovering presents a different situation from recovered patients. During recovery, the immune system may be more vulnerable to exposure to foreign proteins. Immunization in these patients is likely best deferred until they are stable, at least six months out from onset of their illness.

Sanofi-Pasteur received FDA approval to market a H1N1 swine flu vaccine. The product's literature does not include an absolute contraindication for former GBS patients to receive it and in the subsequent vaccination campaign, this virus strain was not associated with any unusual increase in GBS cases. It is recommended to discuss its use with a patient's treating physician.

Other vaccines. The following list of vaccines are likely safe for recovered GBS patient, especially if they have underlying chronic illness (diabetes, heart failure, chronic lung disease, etc.) that make them more susceptible to infections in general, or if the person plans travels to any area where the disease is common.

- Vaccines for cervical cancer/human papillomavirus vaccine (Gardasil®)
- Pneumococcal vaccine for pneumococcal pneumonia (Pneumovax®23; Prevnar®13))
- Zoster vaccine (Zostavax®) to reduce the risk of developing shingles (herpes zoster)
- Hepatitis A and B vaccines
- Yellow fever vaccine (YF-Vax® by Sanofi-Pasteur)

Sporadic cases of GBS are reported following administration of these vaccines. The pros and cons of using these is usually best discussed with the patient's physician who can take the entire medical history into consideration.

Meningitis vaccine (Menactra®). Bacterial meningitis is a rare but potentially fatal infection, affecting primarily children and young adults. It can be caused by some strains of *Neisseria meningitidis*. The vaccine, meningococcal polysaccharide diphtheria toxoid conjugate vaccine (marketed by Sanofi-Pasteur as Menactra®) reduces the risk of developing meningitis. However, because of reports of cases of GBS following its use, a prior history of GBS is a contraindication to using Menactra®.

Guidelines for immunizations for foreign travel. Travel to some parts of the globe, such as much of Asia and Africa, carries risk of contracting infectious and other disorders. That risk often warrants the use of immunizations and/or medication. Most of these treatments are safe for most former GBS patients. Travelers can obtain recommendations for medical care and health precautions from the web site of the Centers for Disease Control, at http://wwwn.cdc.gov/travel. Recommendations are provided for immunizations as well as medications and health precautions during the trip ('Staying Healthy during Your Trip'). Plan in advance so immunizations have sufficient time to become effective. If more than one vaccine is recommended, for example, for hepatitis B and yellow fever, it is best to receive each one at a separate visit, spacing them apart by at least several days to identify which was the trigger if a reaction occurs. Even if they are administered on the same day, multiple vaccines will each still be effective at providing immunity.

Sources of medication and immunization for foreign travel. Family doctors do not usually stock travel medications and may not be aware of recommended regimens. As an alternative, the CDC, local yellow pages, and other resources can direct the traveler to medical centers/doctors who specialize in travel medicine, and who have ready access to vaccines to provide these special immunizations.

SUMMARY

Guillain-Barré Syndrome, also called acute inflammatory demyelinating polyneuropathy (AIDP), is characterized by the rapid onset of weakness and even paralysis of the legs, arms, and other parts of the body, as well as abnormal sensations. Within four weeks in 90% of patients the disease plateaus and recovery proceeds over several weeks to months. About eighty percent of patients will have a complete or near-complete recovery. Long-term severe disability is uncommon. GBS frequently follows a viral or bacterial infection. The illness can present in several ways, at times making the diagnosis difficult to establish in its early stages. Early care is often given in an intensive care unit, as the disease is evolving, so potential complications can be recognized and treated quickly.

Treatments to limit the progression of disease and speed recovery include plasma exchange (plasmapheresis) and high-dose intravenous immune globulins. The administration of immunoglobulin is easier, making this an attractive option over plasma exchange. In the early stages of the illness, treatments are also directed at preventing complications of paralysis. If breathing muscles become too weak, a ventilator is used to support respirations. After acute hospital care is completed, and the patient is recovering but still has significant weakness, a comprehensive rehabilitation program in an appropriate recovery center is often utilized. As muscle strength returns, efforts are directed towards returning the patient to as close to their former lifestyle as possible. Patient care may involve the coordinated efforts of a neurologist, physiatrist (rehabilitation physician), internist, family physician, physical therapist, occupational therapist, social worker, nurse, and psychologist or psychiatrist. Emotional support from family and friends, and information about this rare disorder from the GBS-CIDP Foundation International, may help the patient learn to deal with this frustrating, disabling, and potentially catastrophic illness.

Particularly frustrating consequences of this disorder are long-term recurrences of fatigue and/or exhaustion, as well as abnormal sensations, including pain and muscle aches. These problems can be aggravated by normal activities such as walking or working, and can be alleviated or prevented by pacing activity and rest.

PERTINENT FACTS ABOUT GUILLAIN-BARRÉ SYNDROME INCLUDE THE FOLLOWING:

- Incidence: 1 to 2 cases in 100,000 population each year (0.001-0.002%).
- Greater than 50% of cases follow a viral or bacterial illness.
- Diagnosis can be difficult in the early stages of the syndrome.
- The disorder is not contagious.
- About 50% of patients initially develop abnormal sensations; 25% present initially with muscle weakness (often difficulty walking); 25% present initially with both, abnormal sensations and weakness.
- High-dose immunoglobulin infusion or plasma exchange may hasten recovery. Rehabilitation helps during the recovery phase. Corticosteroids are not helpful.
- Recovery may occur over 6 months to 2 years or longer.
- From 10% to 20% of patients have long-lasting disability.
- Death rate is low (3%), particularly in centers experienced with GBS management.

Appendix

DISORDERS POTENTIALLY SIMILAR TO GUILLAIN-BARRÉ SYNDROME

This section may be of interest only to patients in whom a diagnosis of Guillain-Barré Syndrome has been raised but other disorders are still being considered. Several disorders can affect the nervous system or muscles and cause symptoms similarto Guillain-Barré Syndrome. Some of these disorders are even more rare than Guillain-Barré Syndrome, so their existence need not be of concern to most patients ("It is only rare until you have it!). However, if a patient's findings raise concern about them, your physician may wish to do studies to exclude their presence. In many of these disorders some findings that are typical of Guillain-Barré Syndrome are not found. These include spinal fluid protein elevation, weakness of breathing, facial and eye muscles, and loss of deep tendon reflexes. The presence of such abnormalities is supportive of a diagnosis of Guillain-Barré Syndrome. The absence of these findings, however, helps tell Guillain-Barré Syndrome apart from other possible disorders. The following paragraphs supply brief descriptions of some disorders with clinical presentations similar to GBS.

Lyme disease is more prevalent in some parts of the United States. It is caused by the tick-borne (spirochete) bacterium *Borrelia burgdorferi* and was named after the Connecticut town (Lyme) where early cases were identified. Manifestations of this disease can include a GBS-like picture of acute peripheral neuropathy with pain. Appropriate blood tests and spinal fluid examination can establish the diagnosis so that proper antibiotic therapy can be instituted.

Poisoning with **heavy metals** such as arsenic (found in some insecticides), lead, and mercury can cause abnormal sensations and/or weakness. These symptoms can also be caused by other **industrial and environmental substances** including thallium, present in some pesticides, and rodent poisons; organic solvents including n-hexane, inhaled with glue sniffing; methyl n-butylketone, a solvent for some glues; acrylamide; and organophosphorous compounds. An appropriate history and urine and/or blood tests can help identify these substances as the source of the symptoms.

Attacks of acute intermittent **porphyria**, a genetic metabolic disorder, sometimes include muscle weakness and loss of sensations and tendon reflexes. Thus, attacks of porphyria can produce symptoms similar to those seen in Guillain-Barré Syndrome. However, with porphyria, abdominal pain, rapid heat beat, seizures, and behavior changes are common. Appropriate screening blood and/or urine studies can help determine the presence of this rare disorder.

Post-Polio Syndrome is the term used to describe a recurrence of weakness in some patients who had previously developed paralytic poliomyelitis in the 1940s and 1950s. The syndrome is thought to represent a delayed death of spinal cord motor neurons previously injured during the acute polio infection. Thus, these patients' history of prior polio years before helps to distinguish the cause of their weakness from Guillain-Barré Syndrome. Also, with polio, as well as Post-Polio Syndrome, the weakness may affect the legs or arms unequally, there are few if any sensory problems, and the spinal fluid protein is not elevated.

A disorder similar or identical to Guillain-Barré Syndrome in symptomology, with both the features of abnormal sensations and weakness, can occur with some **malignancies**. These malignancies include those of lymph glands (including Hodgkin's disease and lymphoma) and of certain white blood cells (including chronic lymphocytic leukemia). Other malignancies in which similar neurological changes can occur include those of the lung, stomach, and special white blood cells (plasma cells) which make abnormal protein substances (multiple myeloma).

As with Guillain-Barré Syndrome, the disorder **transverse myelitis**, an inflammatory condition of the spinal cord, may occur after a viral illness and immunizations. It is characterized by the development, over hours to several days, of weakness and abnormal sensations of the legs. Other common findings may include difficulty in controlling urination, as well as bowel disorders, and back pain. Typically, there is a lack of sensation below a certain level of the body indicating disease in the spinal cord. In contrast to Guillain-Barré Syndrome, transverse myelitis does not affect the upper limbs or face. Also, unlike Guillain-Barré Syndrome, in which loss of deep tendon reflexes is common, in transverse myelitis, the knee and ankle reflexes are brisk or exaggerated, indicating an *upper* motor neuron lesion (as opposed to *lower* motor neuron lesions in GBS). Spinal fluid protein can be elevated in transverse myelitis.

People with **Diabetes mellitus** can develop abnormal sensations of the feet, and also the fingers. They can also develop muscle weakness (diabetic amyotrophy), but often the weakness is asymmetric, affecting one lower limb more than the other, and does not involve the breathing muscles, as may occur in Guillain-Barré Syndrome.

Some drugs can cause nerve damage as side effects. For example, nitrofurantoin (Macrodantin®), used for urinary tract infections, has been associated with severe and even irreversible peripheral nerve damage. Dapsone, used to treat leprosy and some skin disorders, has been associated with muscle weakness related to nerve damage. Muscle strength usually returns if the medication is stopped.

Some abnormal **blood chemistries** can cause weakness. An example is **low serum potassium**, caused by several diuretics ("water pills") and occasionally by a genetic disorder, hypokalemic periodic paralysis. A simple history and blood test for electrolytes can make the diagnosis. Supplemental potassium medication or adjustment of diuretic medication can usually correct the low serum potassium level and resulting weakness.

Some autoimmune **connective tissue or collagen vascular disorders**, including polyarteritis nodosa, systemic lupus erythematosis, Sjogren's syndrome, and progressive systemic sclerosis (scleroderma) may be complicated by abnormal sensations related to nerve changes.

Acute polymyositis and **dermatomyositis** are inflammatory conditions of muscle, causing muscle weakness and pain. However, nerve conduction is not affected, reflexes are preserved, and spinal fluid protein is not elevated. Abnormal blood studies (elevated CPK-MM fraction and aldolase) support the diagnosis of muscle "necrosis" (death of the muscle cells) which can be confirmed by a muscle biopsy. Other conditions that lead to muscle necrosis and weakness include acute thyrotoxicosis (overproduction of thyroid hormone), and malignant hyperthermia from sensitivity to certain anesthetics.

In **tick paralysis**, weakness of the legs is followed, usually within a few days, by paralysis of the rest of the body, including muscles for breathing and swallowing. Deep tendon reflexes are decreased, as with Guillain-Barré Syndrome, but spinal fluid protein does not rise and nerve conduction velocity (NCV) tests show disease of the nerve muscle junction. Several kinds of ticks, including female wood ticks, the Rocky Mountain wood tick of western North America, the common dog tick of eastern North America and the Australian tick, have been associated with reversible muscle paralysis. If the patient recovers promptly following removal of a tick, they probably didn't have Guillain-Barré Syndrome.

Botulism can resemble a *descending* form of Guillain-Barré Syndrome. It is a paralyzing disorder caused by food poisoning with the bacterium Clostridium botulinum, which is rarely found in improperly prepared canned foods and meats. Typically, within a half to one-and-a-half days of eating the contaminated food, patients develop weakness of the eye muscles, with double vision, and difficulty swallowing, as well as gastro-intestinal upset. The weakness pattern then descends and can involve breathing muscles. It can quickly become potentially fatal.

Polio, a disease caused by the poliomyelitis viruses, is virtually eradicated in the USA by the successful vaccine program. The occasional unvaccinated patient may experience weakness which, in this disorder, predominates over sensation abnormalities. The weakness may affect one side of the body more than the other and the breathing muscles may also become weak enough to require ventilator support. Fortunately, as is the case with diphtheria (*see below*), in countries with widespread immunization programs, polio is a very rare disorder.

West Nile virus can also cause severe and sometimes irreversible damage to neurons in the spinal cord, leading to rapid onset of asymmetrical paralysis.

A few weeks after the onset of **diphtheria**, a descending pattern of muscle weakness may

develop and first affect the throat and eyes (with blurring of vision) and then other muscles of the face. Thus, it eventually produces a *descending* Guillain-Barré Syndrome-like phenomenon. Fortunately, this disease is quite rare in the United States and other countries with widespread immunization programs.

There are many non-nerve-causes of weakness, including anemia; low blood potassium levels (hypokalemia) caused by some water pills or diuretics (e.g., hydrochlorothiazide [*HCTZ*], used to treat high blood pressure [*hypertension*], or furosemide [*Lasix®*], used to treat a weak heart [*congestive heart failure*]); and underactive thyroid gland hormone production (hypothroidism). Presence of the latter disorder can be confirmed by finding an elevated thyroid stimulating hormone (TSH) level and a low normal or decreased thyroid hormone (T4) level in the blood. Diagnoses of the enumerable causes of weakness can usually be accomplished via an appropriate history, physical examination, and laboratory studies.

REFERENCES

GBS

1. Asbury AK, Arnason BG, Adams RD. The inflammatory lesion in idiopathic polyneuritis. Its role in pathogenesis. Medicine (Baltimore) 1969; 48: 173-215.

2. Austin JH. Recurrent polyneuropathies and their corticosteroid treatment; with five-year observations of a placebo-controlled case treated with corticotrophin, cortisone, and prednisone. Brain 1958; 81: 157-92.

3. Blumenthal D, Prais D, Bron-Harlev E, Amir J. Possible association of Guillain-Barre syndrome and hepatitis A vaccination. Pediatr Infect Dis J 2004; 23: 586-8.

4. Burrows DS, Cuetter AC. Residual subclinical impairment in patients who totally recovered from Guillain-Barre syndrome: impact on military performance. Mil Med 1990; 155: 438-40.

5. Dyck PJ, O'Brien PC, Oviatt KF, Dinapoli RP, Daube JR, Bartleson JD, et al,.Prednisone improves chronic inflammatory demyelinating polyradiculoneuropathy more than no treatment. Ann Neurol 1982; 11: 136-41.

6. Farcas P, Avnun L, Frisher S, Herishanu YO, Wirguin I. Efficacy of repeated intravenous immunoglobulin in severe unresponsive Guillain-Barre syndrome. Lancet 1997; 350: 1747.

7. Feasby TE, Brown WF. Conduction block in early Guillain-Barre syndrome. Lancet 1986; 1: 332.

8. Garssen MP, Bussmann JB, Schmitz PI, Zandbergen A, Welter TG, Merkies IS, et al. Physical training and fatigue, fitness, and quality of life in Guillain-Barre syndrome and CIDP. Neurology 2004; 63: 2393-5.

9. Geleijns K, Laman JD, van Rijs W, Tio-Gillen AP, Hintzen RQ, van Doorn PA, et al. Fas polymorphisms are associated with the presence of antiganglioside antibodies in Guillain-Barre syndrome. J Neuroimmunol 2005; 161: 183-9.

10. Geleijns K, Roos A, Houwing-Duistermaat JJ, van Rijs W, Tio-Gillen AP, Laman JD, et al. Mannose-binding lectin contributes to the severity of Guillain-Barre syndrome. J Immunol 2006; 177: 4211-7.

11. Gorson KC, Ropper AH, Weinberg DH. Upper limb predominant, multifocal chronic inflammatory demyelinating polyneuropathy. Muscle Nerve 1999; 22: 758-65.

12. Guillain G, Barré, J.A., Strohl, A. Sur un Syndrome de radiculonévrite avec hyperalbuinose du liquide céphalo-rachidien sans réaction cellulaire.

13. Bull. Soc. Med. Hop. 1916; 40: 1462.

14. Halstead SK, Zitman FM, Humphreys PD, Greenshields K, Verschuuren JJ, Jacobs BC, et al. Eculizumab prevents anti-ganglioside antibodymediated neuropathy in a murine model. Brain 2008; 131: 1197-208.

15. Hughes R, Bensa S, Willison H, Van den Bergh P, Comi G, Illa I, et al. Randomized controlled trial of intravenous immunoglobulin versus oral prednisolone in chronic inflammatory demyelinating polyradiculoneuropathy. Ann Neurol 2001; 50: 195-201.

16. Hughes RA, Hadden RD, Gregson NA, Smith KJ. Pathogenesis of GuillainBarre syndrome. J Neuroimmunol 1999; 100: 74-97.

17. Hughes RA, Swan AV, van Koningsveld R, van Doorn PA. Corticosteroids for Guillain-Barre syndrome. Cochrane Database Syst Rev 2006: CD001446.

18. Khamaisi M, Shoenfeld Y, Orbach H. Guillain-Barre syndrome following hepatitis B vaccination. Clin Exp Rheumatol 2004; 22: 767-70.

19. Koski CL. Therapy of CIDP and related immune-mediated neuropathies. Neurology 2002; 59: S22-7.

20. Koski CL. Initial and long-term management of autoimmune neuropathies. CNS Drugs 2005; 19: 1033-48.

21. Koski CL, Baumgarten M, Magder LS, Barohn RJ, Goldstein J, Graves M, et al. Derivation and validation of diagnostic criteria for chronic inflammatory demyelinating polyneuropathy. J Neurol Sci 2009; 277: 1-8.

22. Kuwabara S. Guillain-Barre syndrome: epidemiology, pathophysiology and management. Drugs 2004; 64: 597-610.

23. Landry J-B, Gaz, O. Note sur la paralysie ascedante aigue. Hebdom du Med, et de Chir. 1850; 6: 472-4.

24. Lasky T, Terracciano GJ, Magder L, Koski CL, Ballesteros M, Nash D, et al. The Guillain-Barre syndrome and the 1992-1993 and 1993-1994 influenza vaccines. N Engl J Med 1998; 339: 1797-802.

25. Lolekha P, Phanthumchinda K. Optic neuritis in a patient with Miller-Fisher syndrome. J Med Assoc Thai 2008; 91: 1909-13.

26. McKhann GM, Cornblath DR, Griffin JW, Ho TW, Li CY, Jiang Z, et al. Acute motor axonal neuropathy: a frequent cause of acute flaccid paralysis in China. Ann Neurol 1993; 33: 333-42.

27. McKhann GM, Griffin JW. Plasmapheresis and the Guillain-Barre syndrome. Ann Neurol 1987; 22: 762-3.

28. McMahon BJ, Helminiak C, Wainwright RB, Bulkow L, Trimble BA, Wainwright K. Frequency of adverse reactions to hepatitis B vaccine in 43,618 persons. Am J Med 1992; 92: 254-6.

29. Merkies IS, Schmitz PI, Samijn JP, van der Meche FG, van Doorn PA. Fatigue in immune-mediated polyneuropathies. European Inflammatory Neuropathy Cause and Treatment (INCAT) Group. Neurology 1999; 53: 1648-54.

30. Moulin DE, Hagen N, Feasby TE, Amireh R, Hahn A. Pain in Guillain-Barre syndrome. Neurology 1997; 48: 328-31.

31. Nadkarni N, Lisak RP. Guillain-Barre syndrome (GBS) with bilateral optic neuritis and central white matter disease. Neurology 1993; 43: 842-3.

32. Pandey CK, Raza M, Tripathi M, Navkar DV, Kumar A, Singh UK. The comparative evaluation of gabapentin and carbamazepine for pain management in Guillain-Barre syndrome patients in the intensive care unit. Anesth Analg 2005; 101: 220-5, table of contents.

33. Pitetti KH, Barrett PJ, Abbas D. Endurance exercise training in Guillain-Barre syndrome. Arch Phys Med Rehabil 1993; 74: 761-5.

34. Plasma Exchange (PE)/Sandoglobulin GBS Trial Group. Randomised trial of PE, intraven. immunoglob., and combined treatments in Guillain-Barré Syndrome. Lancet 1997; 349: 225-30.

35. Prineas JW. Pathology of the Guillain-Barre syndrome. Ann Neurol 1981; 9 Suppl: 6-19.

36. Ropper AH, Shahani BT. Pain in Guillain-Barre syndrome. Arch Neurol 1984; 41: 511-4.

37. Rudnicki S, Vriesendorp F, Koski CL, Mayer RF. Electrophysiologic studies in the Guillain-Barre syndrome: effects of plasma exchange and antibody rebound. Muscle Nerve 1992; 15: 57-62.

38. Simmons Z, Wald JJ, Albers JW. Chronic inflammatory demyelinating polyradiculoneuropathy in children: I. Presentation, electrodiagnostic studies, and initial clinical course, with comparison to adults. Muscle Nerve 1997; 20: 1008-15.

39. Sindern E, Schroder JM, Krismann M, Malin JP. Inflammatory polyradiculoneuropathy with spinal cord involvement and lethal [correction of letal] outcome after hepatitis B vaccination. J Neurol Sci 2001; 186: 81-5.

40. Van den Berg-Vos RM, Van den Berg LH, Franssen H, Vermeulen M, Witkamp TD, Jansen GH, et al. Multifocal inflammatory demyelinating neuropathy: a distinct clinical entity? Neurology 2000; 54: 26-32.

41. van der Meche FG, Schmitz PI. A randomized trial comparing intravenous immune globulin and plasma exchange in Guillain-Barre syndrome. Dutch Guillain-Barre Study Group. N Engl J Med 1992; 326: 1123-9. van Koningsveld R, Steyerberg, E.W., Hughes, R.A.C., Swan, A.V. van Doorn, P.A., Jacobs, B.C. A clinical prognostic scoring system for GBS. ILancet Neurol 2007; 6: 589-94.

42. van Schaik IN. What's new in chronic inflammatory demyelinating polyradiculoneuropathy in 2007-2008? J Peripher Nerv Syst 2008; 13: 258-60.

43. van Sorge NM, van der Pol WL, Jansen MD, Geleijns KP, Kalmijn S, Hughes RA, et al. Severity of Guillain-Barre syndrome is associated with Fc gamma Receptor III polymorphisms. J Neuroimmunol 2005; 162: 157-64.

44. Vucic S, Kiernan MC, Cornblath DR. Guillain-Barre syndrome: an update. J Clin Neurosci 2009; 16: 733-41.

REFERENCES

For more information, please contact:

GBS|CIDP FOUNDATION INTERNATIONAL

International Office
375 East Elm Street, Suite 101
Conshohocken, PA 19428
866-224-3301
info@gbs-cidp.org
www.gbs-cidp.org

A BRIEF DESCRIPTION OF THE FOUNDATION

The GBS|CIDP Foundation International was founded in 1980 by Robert and Estelle Benson to assist victims of this rare, paralyzing, potentially catastrophic disease of the peripheral nerves. The Foundation:

- Provides emotional support to patients and their loved ones
- Provides, when possible, personal visits by former patients to those currently in hospitals and rehabilitation centers
- Develops worldwide support groups
- Supplies literature about the GBS and CIDP syndromes, a comprehensive Overview for the Layperson, so patients and their families can learn what to expect during these illnesses
- Educates the public and medical community about the Foundation and maintains their awareness of the disorder
- Supports and fosters research into the cause, treatment and other aspects of inflammatory/immune mediated peripheral neuropathies
- Directs patients with long-term disability to resources for vocational and other assistance
- Holds International Symposia
- Encourages financial support for the Foundation's activities
- Advocates for early diagnosis, effective and affordable treatment for patients

The Foundation's Medical Advisory Board includes neurologists active in GBS and CIDP research, leading physicians in rehabilitation medicine and physicians who, themselves, have had the syndrome. Meetings are held by the Foundation's support group chapters to introduce new patients and present speakers who are knowledgeable about the disorder. All contributions to help us help others are appreciated. The GBS|CIDP Foundation International is a nonprofit 501(c)(3) volunteer organization, incorporated in the Commonwealth of Pennsylvania.

ACKNOWLEDGEMENTS, COPYRIGHT, ETC.

Joel Steinberg, M.D., Ph.D. (physiology and biophysics), a specialist in peripheral vascular disease (circulation disorders) and internal medicine, joined the GBS-CIDP Foundation International after developing GuillainBarré Syndrome. His neurologist suggested that he write about his experiences. Further impetus to write this Overview came from the Foundation's founders, Robert and Estelle Benson, who appreciated a need to supply patients with information.

Carol Lee Koski, M.D. is a member of the Medical Advisory Board for the Guillain-Barré Syndrome/Chronic Inflammatory Demyelinating Polyneuropathy Foundation International (GBS|CIDP Foundation International).

She retired from the University of Maryland School of Medicine in Baltimore in April 2006, where she served as professor of neurology and director of the Neuromuscular Division and the Physicians Infusion Clinic in the Department of Neurology.

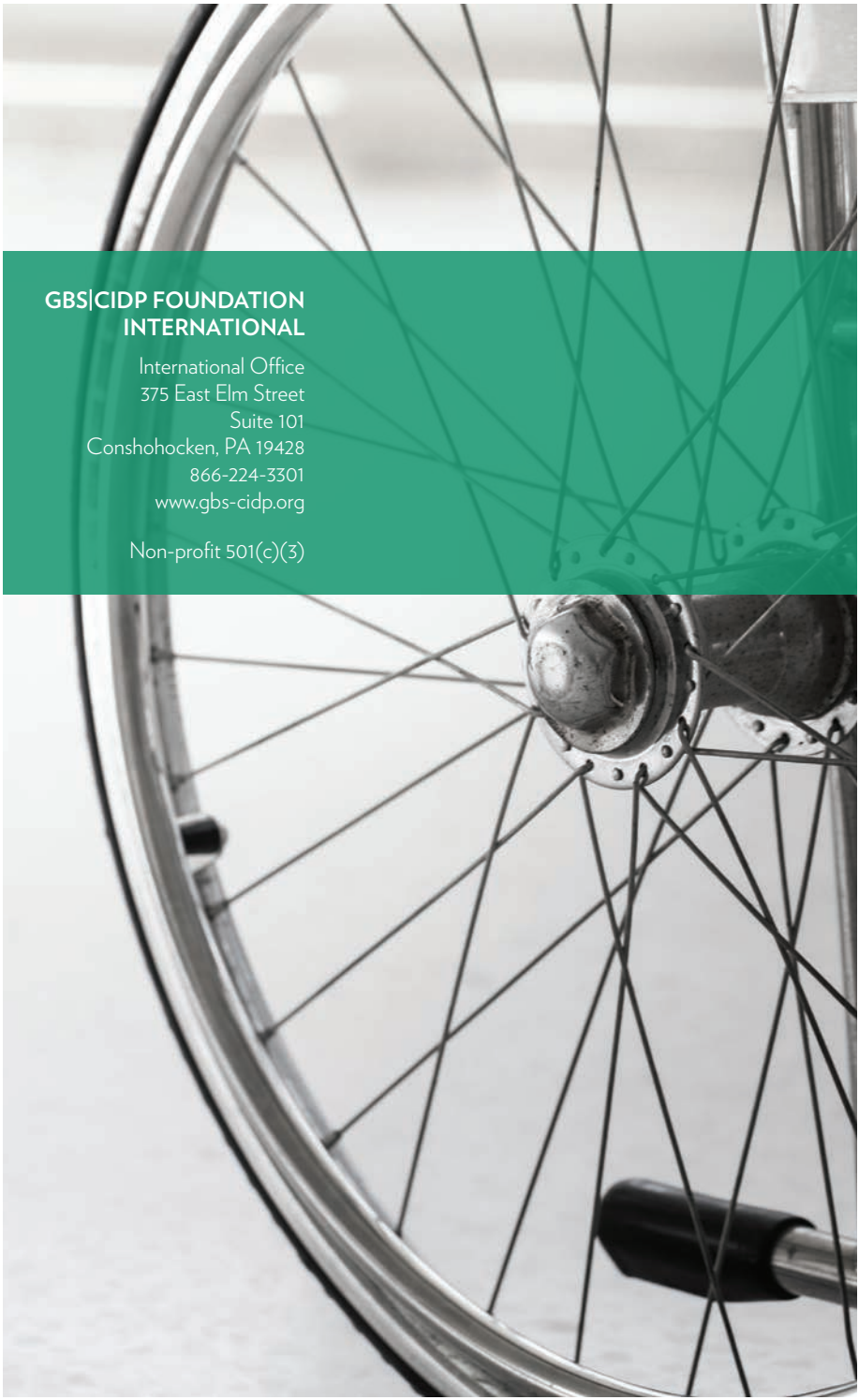
Dr. Koski received her medical degree from the University of Maryland School of Medicine. She completed residencies at the University of Maryland Medical System and Jackson Memorial Hospital in Miami, Florida, and fellowships in neuromuscular disease, neurochemistry, and neuroimmunology at University Hospital in Baltimore; the Eunice Kennedy Shriver Center in Waltham, Massachusetts; and the Neuroimmunology Branch of the National Institutes of Health in Bethesda, Maryland, respectively.

Copies of the Overview, Communication Cards and other literature are available through the:

GBS|CIDP FOUNDATION INTERNATIONAL

International Office
375 East Elm Street, Suite 101
Conshohocken, PA 19428
866-224-3301
info@gbs-cidp.org
www.gbs-cidp.org

Supported by an educational grant from CSL Behring



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