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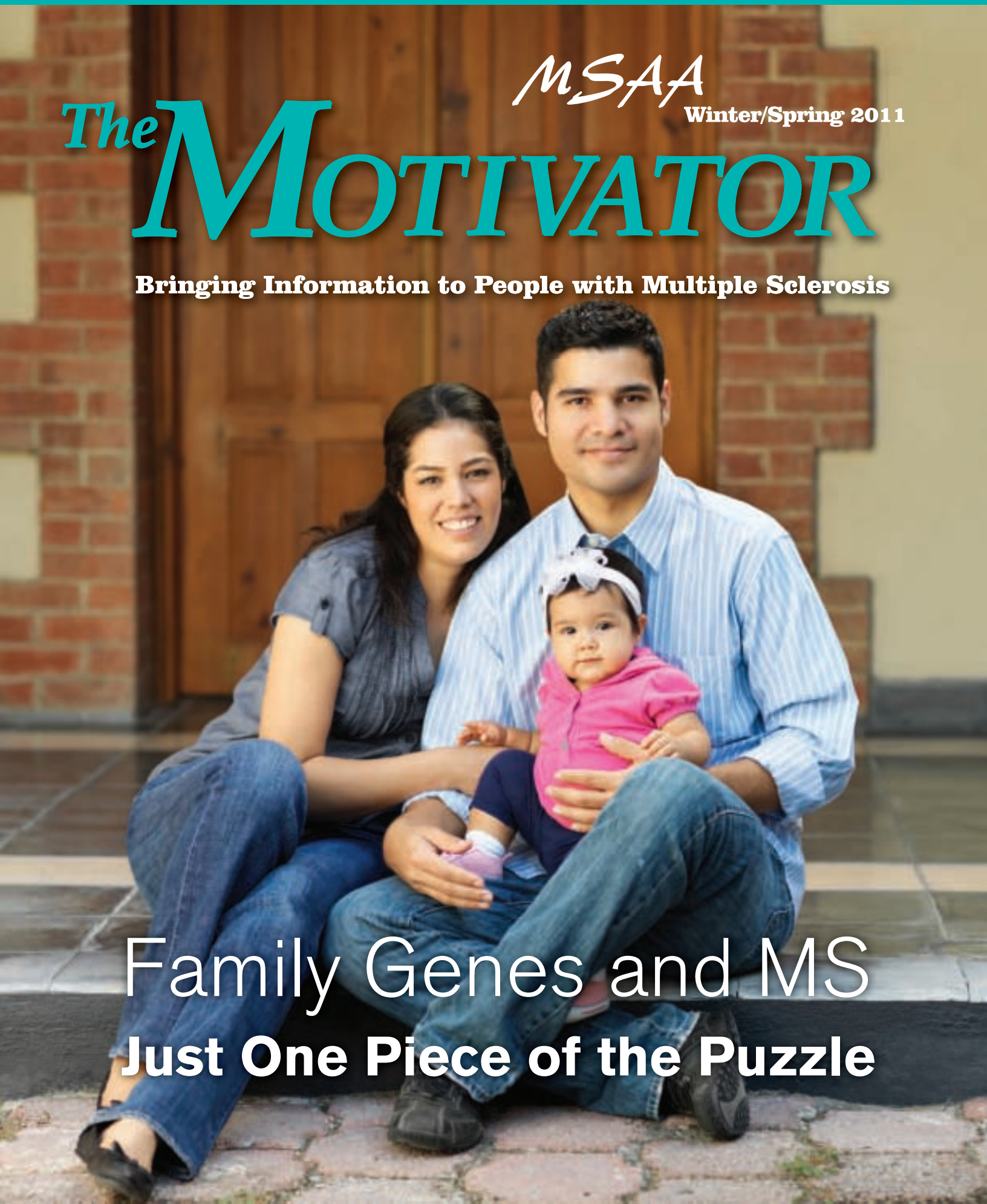

MSAA
Winter/Spring 2011

The Motivator

Bringing Information to People with Multiple Sclerosis

Family Genes and MS

Just One Piece of the Puzzle

The MOTIVATOR

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The Motivator's purpose is to inform and educate those with MS and their families. MSAA does not endorse or recommend any specific products, services, therapies, or activities mentioned in articles or advertisements that appear in *The Motivator.* MSAA, its staff, and those affiliated with the writing of this publication cannot be held responsible for any unintentional errors.

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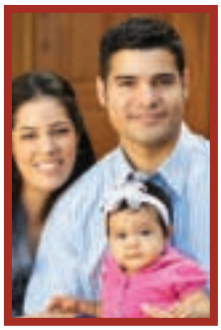

COVER STORY

Family Genes and MS: Just One Piece of the Puzzle

This issue's cover story reveals many important findings about genetics and environmental risk factors associated with MS.

DEPARTMENTS

MSAA™ Multiple Sclerosis Association of America

The Multiple Sclerosis Association of America's mission is to enrich the quality of life for everyone affected by multiple sclerosis.

MSAA strives to provide useful, up-to-date information on matters of concern to MS patients and their families. This material is intended for general informational purposes only, and it does not constitute medical advice. You should not use the information presented as a means of diagnosis or for determining treatment. For diagnosis and treatment options, you are urged to consult your physician.

Up Front

By Douglas G. Franklin
MSAA President and CEO

Douglas G. Franklin

After a particularly harsh winter, we are all looking forward to the promise of spring and warmer weather. Thankfully, regardless of the season or the weather, MSAA's programs and services are always in full swing enriching people's quality of life every day! We are welcoming applications for our MRI programs from individuals in need of advocacy or financial assistance for an MRI to help diagnose or assess MS activity. Our cooling vests and assistive equipment are also in stock and ready to ship! Please contact MSAA's Helpline at **(800) 532-7667** or visit **www.msassociation.org/programs** for more information about these and other MSAA programs.

I am also proud to announce that MSAA's first mobile phone application *My MS Manager* is now available for anyone to download for free to their iPhone, iPad or iPod touch. *My MS Manager* was developed with Ringful Health as a tool to help monitor daily activities related to managing one's MS. Features include tracking MS flare-ups, logging side effects of medications, and journaling other important MS details. This information can then be generated into various reports and shared with your healthcare providers. Please visit **www.msassociation.org/mobile** for details!

Our Swim for MS program is making a big splash this spring season.

Our Swim for MS program is making a big splash this spring season. We've had great events organized across the country, including several group swims, personal challenges and even a teen who dove into action with "Cannonballs for Cash" to honor his aunt with MS. Any pool, any time, Swim for MS is a great way to support MSAA!

In addition, I want to note that all eight member organizations of the MS Coalition met for an annual meeting while attending the National MS Society's Public Policy Conference on March 7th. Having everyone unite to help advocate for critical issues to the welfare of our MS constituency is a priority for all of us and I am proud to lead this effort as the MS Coalition's President. ◆

Doug Franklin joined MSAA as President & CEO in 1999. He has a distinguished career in nonprofit leadership and is a former national trainer in strategic planning for the Peter Drucker Foundation. A published international expert in social marketing and corporate social investment, he is a graduate of four universities. He currently serves on the National Board of the Key Philanthropic Organizations Committee of the American Society of Association Executives; on the Executive Committee of Health First – America's Charities Board in Washington, DC; and as President of the Multiple Sclerosis Coalition.

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FAMILY GENES & MS

JUST ONE PIECE OF THE PUZZLE

Genetics and Environmental Risk Factors Associated with MS

Written by A. Dessa Sadovnick, PhD
Professor, Medical Genetics and Neurology, University of British Columbia
Director, MS Society of Canada endMS Western Pacific Regional Research and Training Centre

Edited by Susan Wells Courtney

Reviewed by Jack Burks, MD

Multiple sclerosis (MS) is the most common cause of neurological disability in young adults, other than trauma. The etiology (cause) of MS remains unknown, but it is increasingly recognized that genes, environment, and interactions thereof are all important. Thus, while it is clear that genes have roles in MS susceptibility and probably disease progression, understanding and dissecting the relative roles of genes and environment remain topics of intensive research.

To assist with our understanding of genetics, we have included brief descriptions of a few basic terms.

DNA is deoxyribonucleic acid, which is a long, spiral-shaped molecule that carries our genetic information. Humans have approximately three billion base pairs of DNA. Just as letters of the alphabet are building blocks for words, DNA is the building block for genes (http://www.genetics.com.au).

Shown is an illustration of the DNA spiral-shaped molecule that carries our genetic information.

Genes are the fundamental units of inheritance (or heredity) and are segments of a DNA molecule, containing all of the information required for the development of a living organism. Humans are estimated to have 30,000 to 40,000 genes.

Chromosomes are strands of DNA that determine the characteristics inherited from one generation to another.

Chromosomes are strands of DNA that contain genes. They determine the characteristics that are inherited from one generation to another. This structure is in the nucleus of each cell and carries all of the genetic information. Humans usually have 23 pairs of (or 46 total) chromosomes, including the XX and the XY pairs that determine a person's gender. Simply put, a chromosome is similar to a book -- a book is a collection of words, and a chromosome is a collection of genes (http://www.genetics.com.au/).

Karyotype is a group of symbols, using numbers, letters, and other images, to represent the chromosomal makeup of an individual.

Locus refers to a specific location on a chromosome. Each gene is located at a specific locus and the 30,000 to 40,000 human genes are carried on different chromosomes.

Genome is an organism's full set of chromosomes, giving the entirety of genetic information.

Alleles are one of two or more alternative forms of a gene. These can occur at a certain locus (location) on a chromosome and can determine alternative, inherited characteristics (such as the color of one's eyes or hair).

Linkage refers to the association of genes being located ("having loci") close to one another on the same chromosome, which has a tendency to be associated with inherited characteristics.

Recombination is the process that creates new combinations of genes by shuffling the linear order of DNA.

Genotype is an individual's genetic makeup.

Phenotype is the observable characteristics of an individual, which are determined by a combination of genotype and environmental factors.

EDITOR'S NOTE: This article contains many references, which are noted within the copy as a number in parentheses. Please refer to pages 30 and 31 for the articles associated with each reference. In addition, a website is sometimes included in parentheses within the copy; this specifies the source of a definition provided.

FAMILY GENES & MS
JUST ONE PIECE OF THE PUZZLE

GENETICS

Each one of us inherits 50 percent of our genetic material (DNA) from our mothers and 50 percent from our fathers. Thus, within biological family members, there is more common DNA sharing than compared to the general, unrelated population. To illustrate, brothers and sisters (siblings) share 50 percent of their DNA, half-siblings (with only one parent in common) share 25 percent of their DNA, and first cousins share one eighth, or 12.5 percent, of their DNA. Sharing DNA increases the chance that family members will have similar genetic risks for disease.

Hermann Eichhorst was a German-Swiss internist and director of the medical clinic in Zurich. In the late 1800's, he was the first to describe MS as "an inherited transmissible disease."[1] By 1950, there were 85 reports of families with two or more members having "disseminated sclerosis"[2] (another name for multiple sclerosis that has not been used for decades). However, it is important to note that this report of 85 families with two or more members with MS was before standardized diagnostic criteria for MS were developed[3, 4] and before scientists had an understanding of the complexity of genes and chromosomes.

An allele is one member of a pair of genes, each inherited from one parent and is an "alternative" gene. An allele is located at a specific position on a specific chromosome (http://biology.about.com/od/geneticsglossary/g/alleles.htm). Until relatively recently, the standard approach for identifying "susceptibility alleles" (those genes which may increase one's risk of disease) has been linkage and association studies.

Genetic linkage assesses the co-transmission of alleles (alternative genes) and disease within families. In the mid-19th century, an Austrian monk named Gregor Mendel was able to categorize patterns of genetic inheritance through gardening and observation of nature. Mendel's laws are still used today to assist with our understanding of alleles, linkage, and the possible relationship between genes and disease.

GENETICS AND MS

In the absence of a solid understanding of the mechanisms that underlie MS, there are no compelling primary candidate genes for MS. Hence, the list of genes which have been investigated for MS susceptibility is long and continually expanding.

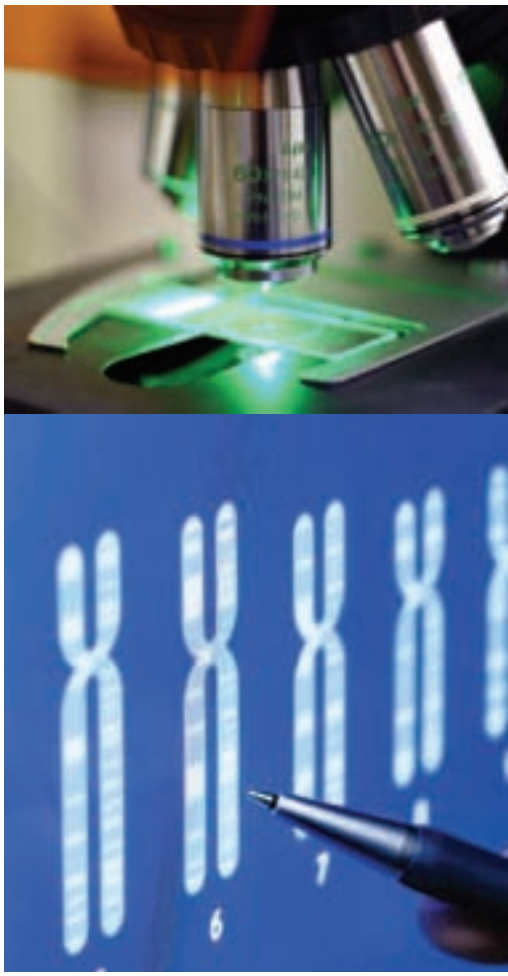
Linkage studies can detect a major susceptibility allele. These studies are less powerful when genetic effects are small, as suggested in MS. MS linkage screens highlight a locus (or location on a chromosome) with the strongest genetic effect in MS. This is the major histocompatibility complex (MHC), which is a cluster of genes on chromosome 6.

This cluster of genes (MHC) produces human lymphocyte antigens (HLA genes), which enable the immune system to respond appropriately to an antigen (determining if the antigen belongs to one's own body or if it is foreign). Should anything go wrong with the unique order of the HLA alleles (alternate genes), self antigens could be misinterpreted as non-self (or foreign), triggering an inappropriate immune response and potentially leading to an autoimmune disorder.

Additionally, other genes must make considerably weaker contributions to MS disease risk. Learning about these other genes requires genetic association studies which are sensitive to differences in allele frequencies between individuals with MS and the general population.[6] This will also require a large number of genetic markers at different stages, as well as large sample sizes.[7] More recently, genome-wide association studies (GWAS) have become technically feasible. A consortium of more than 50 British groups, known collectively as the Wellcome Trust Case Control Consortium,[8] set the benchmark for genome-wide association studies in terms of sample size, quality control, and statistical analysis.

The first direct evidence for a relationship between genes and MS susceptibility came in 1972 when MS researcher C. Jersild and others[9] reported an association between MS and the major histocompatibility complex (MHC) on chromosome 6. A decade later, MS researcher G. C. Ebers and others provided insight into the familial nature of MS with a report of genotyping (identifying an individual's genetic makeup) sibling pairs affected with MS for human lymphocyte antigens (HLA).[10]

The International Multiple Sclerosis Genetics Consortium published the first genome-wide association studies for MS in 2007.[11] The group screened 931 MS trios (two unaffected parents and one affected offspring). From this report, several genes appear to have a modest effect on suceptibility to MS[11] and these results have also been replicated in other studies. These genes include the interleukin 7 receptor alpha gene (IL7RA); interleukin 2 receptor alpha



Researchers are working to identify genes that may increase one's susceptibility to MS, using a Karyotype (chart) to show the chromosomal makeup of an individual.

(IL2RA); C-type lectin domain family 16, member A (CLEC16A); and the CD58 genes. However, the strongest genetic effect in MS remains within the MHC, although these findings are far from straightforward with complex gene-gene interactions at play.[12, 13]

Despite ongoing research and advanced techniques, genotyping an unaffected individual cannot predict who, in the future, will develop MS. In addition, the complexity of gene-gene interactions, even within the MHC, makes understanding the roles of genes in MS even more complex.

What can be said at present is that genes have some role in susceptibility to MS but exact mechanisms remain unclear. Nevertheless, genetic epidemiological studies in MS have clearly shown that the increased frequency of MS seen within families is a result of relatives sharing DNA and not the common family environment.

FAMILY MEMBERS AND MS

The most widely accepted definition of genetic epidemiology is "a science which deals with the etiology, distribution, and control of disease in groups of relatives and with inherited causes of disease in populations" (http://www.dorak.info/epi/genetepi.html). In the 1980's, it was recognized objectively for the first time that first-degree relatives (parents, children, and siblings) of MS patients had the disease more often than more distant relatives and those who did not have a relative with MS.[14] Nevertheless, "familial aggregation," or the grouping of a specific disease (i.e., MS) within a family, is not necessarily related to genetic sharing. Hence, it is important to test the relative roles of genes and environment (nature versus nurture) within MS families.

A number of strategies has been used to separate the environmental components from the genetic components underlying MS susceptibility. To date, several genetic epidemiological studies have been conducted through the longitudinal, population-based Canadian Collaborative Project on Genetic Susceptibility to MS (CCPGSMS).

Based on earlier work on familial rates,[14] first-degree relatives were shown to have a recurrence risk (RR) for MS of 3 to 5 percent. Recurrence risk in medical genetics is defined as "the chance that a genetic (inherited) disease present in the family will recur in that family and affect another person (or persons)" (http://www.medterms.com/script/main/art.asp?articlekey=5257).

Adoptees and their adoptive relatives were studied with respect to MS risks.[15] The study focused on individuals who were adopted as infants by persons to whom they were not biologically related (e.g., no DNA sharing), and the adoptee subsequently developed MS.

When these non-biological relatives of adoptees with MS were studied, the occurrence of MS reflected the rate for the general population and in no way approached the estimated 3-to-5 percent recurrence risk reported for biological brothers and sisters. Thus, being raised in the same household as someone destined to develop MS does not increase your own risk to develop MS. The risk was no different than that for the general population if you did not share DNA.

Of importance is the fact that these findings were shown again with stepsiblings,[16] half-siblings,[17, 18] and spouses,[19, 20] according to the Canadian Collaborative Project's population. While stepsiblings (as in "The Brady Bunch") can be raised together, they do not share any genetic material. A study of the Canadian Collaborative Project's population looked at 687 stepsiblings of individuals with MS and found that only one stepsibling had MS, which is the same rate as expected for the general population.[16]

Half-siblings[17, 18] share only one parent in common (a mother or a father) and thus only share 25 percent of their genetic material, compared to full siblings (with both parents in common) who share 50 percent of their DNA. Half-siblings share their childhood environment to various degrees if "raised together," or "raised apart" in separate environments, depending on the family situation. Data from the Canadian Collaborative Project clearly show that the risk for half-siblings to develop MS is approximately 2 percent, regardless of whether they were raised apart or together. This reflects 25-percent DNA sharing, regardless of environmental sharing.

Studies of MS in couples[19, 20] have shown that "spouses" (long-term sexual partners) of MS patients develop MS no more often than the general population.

Thus, taken together, adoptee, stepsibling, half-sibling, and couple studies clearly show that it is the sharing of DNA and not the shared family environment that is responsible for the increased occurence of MS within families compared to the general population.

ENVIRONMENT

In very general terms, there are two kinds of "environments" which individuals can share. The first is the "common family environment" as discussed earlier in

this article, and the second is the more wide-spread, population-based environment. While DNA sharing is key in families with more than one member with MS, this does not mean that MS is entirely a genetic disease. In fact, this is confirmed by twin studies[21] among other evidence.

Monozygotic (identical) twins share 100 percent of their genetic material and yet, if one female monozygotic (MZ) twin has MS, the risk for the co-twin is 340 in 1,000, or 34-percent recurrence risk.[21] The fact that only one-third of identical twins will both have MS if one twin has the disease, suggests that environmental factors also play a role. Some environmental risk factors for MS must act at a very early time period, as some factors at the beginning of life (e.g., in utero) are determinants of the future MS risk.

Commonly Asked Questions and Answers

1. Can my family members also "inherit" MS if I have MS?

MS itself cannot be directly inherited as is the case for a single gene disorder (such as cystic fibrosis and Huntington's disease). However, a genetic susceptibility ("risk") to develop MS does exist. This is highlighted by the fact that the increased frequency of MS among family members only holds true for family members who share genetic material (DNA). Family members who grow up together in the same environment but do not share genetic material (e.g., adopted brothers and sisters, as well as stepsiblings) have no increased risk to develop MS compared to the general population.

Conversely, if you do share genetic material, your risk does not change whether you were "raised together" or "raised apart" from the family member who eventually develops MS. The risk of MS among family members can be influenced by several factors including gender, ethnicity, the country/location of where one grows up, age, and biological relationship (percentage of DNA sharing) to other family members with MS, etc.

If you are concerned about your risk to develop MS because you have other family members with MS, or you have MS and are worried about the risk of passing it on, please contact genetic counseling services in your area for more information (http://www.nsgc.org; ccmg-ccgm.org).

2. Can my child catch MS if he or she hugs, kisses or shares a cookie with someone who has MS?

MS is not a transmissible disease and cannot be caught by human contact either during childhood or adulthood. This is clearly shown by a variety of genetic epidemiological studies which have repeatedly shown this finding in separate groups (e.g., adoption studies, couples studies, and others as discussed earlier in this article).

3. If my relative also develops MS, will he or she have the same clinical course of the disease that I do?

The clinical course of MS does not appear to "run true" in families if more than one family member is affected. Thus, if you develop MS, you cannot assume that you will have the same disease course as your mother, sister, or other relative with MS.

4. Can you predict, in advance of any signs or symptoms, who is destined to develop MS in the future?

There are no definitive biomarkers for MS. A bio-

Latitude

Incidence is the number of newly diagnosed cases during a specific time period (http://www.medterms.com/script/main/art.asp?articlekey=11516) and prevalence is the number of cases of a specific disease present in a given population at a certain time (http://medical-dictionary.thefreedictionary.com/prevalence). In general, within regions of a temperate climate, the incidence and prevalence of MS increases with latitude (or distance from the equator).[22] The clearest example of this effect is seen in Australia.[23] The prevalence of MS in Hobart (southern Australia; temperate climate; farther from the equator) is 75.6 per 100,000 compared with a prevalence of 11 per 100,000 in northern Queensland (northern Australia; tropical climate; closer to the equator). Some of the geographical distribution of MS can be explained on the basis of ethnicity (or

marker can be "anatomic, physiologic, biochemical, or molecular parameters associated with the presence and severity of specific disease states" (http://www.biomarkers.org/NewFiles/faqs/definition.html#Anchor-What-35882). This means that if you study two large groups – for example, 1,000 MS patients and 1,000 unaffected controls – you may find "risk factors" occurring more often in the affected group than in the controls, but these risk factors will still exist in both groups. Thus, you cannot test an unaffected person for a specific biomarker (such as HLA genotype or low levels of vitamin D) and then state with any certainty whether a person with or without this factor will end up being affected or unaffected by MS in the future. Hence we use the term "susceptibility" with respect to MS risk rather than "causal."

5. Can MS be prevented?

There is no way to prevent MS. No fault can be assigned if someone develops MS. There are no clear protective preventive measures that can be taken.

6. If I have MS, should I have children?

Much is still to be known about reproduction and MS. If you have MS and are planning to get pregnant or to father a child, you may want to discuss various issues involved in the decision-making process with your healthcare professionals. There is no right or wrong answer. Each couple must make their own informed decision. Topics to consider include the risk of pregnancy on MS, the risk of MS on pregnancy, possible risks of MS therapy at the time of conception and/or gestation, psychosocial issues, and the long-term commitment to raising a child (see references 56 and 57). Please note that while several factors should be considered in advance, many individuals with MS have been able to successfully raise children and enjoy the countless benefits of a loving family. For more information on pregnancy and raising children with MS in the family, individuals may speak with one of MSAA's Helpline consultants at **(800) 532-7667**.

7. If I am from a region where MS is rare (i.e., Shanghai, China) and am Chinese, do I change my risk to develop MS when I move to Canada? Do my genes change?

Although your genes do not change when you move, your environment does. Thus, by moving from Shanghai to Canada, you may have a higher risk to develop MS than if you stayed in Shanghai. This may be due to different environmental exposures as well as genetic and environmental interactions.

race) and genetic factors,[24] but latitude remains the strongest factor for risk after taking race into consideration.[25]

Place of Birth

The effects of migration between low- and high-risk geographic regions for MS (i.e., from Asia or Japan or the Mediterranean, to Canada or the northern United States) have been examined in several populations. These studies consistently show that MS risk is influenced at least to some extent by a person's country of origin.[26] This is highlighted by the observation that first-generation Afro-Caribbean and Asian citizens (individuals living in countries closer to the equator) relocating to Britain[27] and Canada (countries at higher latitudes, farther from the equator), have a much lower incidence of MS than the next generation who are born in the high-risk geographic regions. It is important to point out that immigrants, while changing their geographic place of residence, obviously do not change their genetic makeup.

Gender

An increase in the incidence of MS specifically in women has been documented.[25, 28, 29] A recent Canadian Collaborative Project study was able to show that this increase was real and not merely a reflection of improvements in case identification and diagnosis.[30] Year of birth was shown to be a significant predictor of the female-to-male (F:M) gender ratio of MS over the period of birth years from 1931 to 1980, with the ratio increasing from 1.9 (almost twice as many women as men) to 3.2 (more than three times as many women as men) during this time.[30] There was no evidence to suggest decreasing incidence in males,[30] but rather that the rate of MS in males is more constant over time. This observed increase of women with MS has since been confirmed in a number of other populations (in addition to that of the Canadian Collaborative Project).[31 to 33]

Hygiene Hypothesis

In developed countries, strong evidence of steady rises in the incidence of allergic and some autoimmune diseases parallels a decreasing incidence of childhood infections. Antibiotics, vaccinations, or improved hygiene and better socioeconomic conditions have been credited. The "hygiene hypothesis" proposes that early life infections help to reduce the risk of allergic and autoimmune disorders.[34] Simply put, the earlier in life you are exposed to infections, the sooner your autoimmune system becomes effective. Thus, it is consistent with this hypothesis that, for example, first-born children are less exposed to infection at an

continued on page 27

Expressing emotions shouldn't be left to chance

- People with pseudobulbar affect (PBA) suffer sudden, involuntary outbursts of crying or laughing throughout their day
- PBA can occur in people with an underlying neurologic condition—such as Lou Gehrig's disease (ALS), multiple sclerosis (MS), stroke, or traumatic brain injury
- Though it may sometimes seem like it, a person with PBA is not alone. More than a million Americans suffer from the condition

If you or someone you care for shows signs of having PBA, talk to your doctor or visit PBAinfo.org. You can also share your PBA experiences at facebook.com/PBAinfo

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Program Notes

Much like the design of a GPS navigation system, MS patients and their physicians can employ the S.E.A.R.C.H.℠ model to navigate through this dynamic, ever-changing landscape to reach their desired destination.

How to S.E.A.R.C.H.℠ for the Right MS Therapy

The Changing Landscape

The first treatment for relapsing-remitting multiple sclerosis (RRMS) was approved by the United States Food and Drug Administration (FDA) in 1993. This forever changed the landscape of how MS could be managed. The approval of Betaseron® (interferon beta-1b) for RRMS ushered in a remarkable surge of MS treatments designed to reduce the number and severity of exacerbations and help lessen disease progression. Throughout the 1990s and into the 2000s, several effective medications for MS have become available, giving neurologists and patients a variety of treatment options for slowing disease activity.

Along with these treatments, known as disease-modifying therapies (DMTs), came the expanded use and improved technology of magnetic resonance imaging (MRI). Through diagnostic and follow-up MRI scans of the brain and spinal cord, physicians could now better diagnose, treat, track and manage the ever-changing course of MS in a more definitive and proactive manner.

As the recommendation and usage of MRIs grew, MSAA recognized the need to assist MS patients who required these valuable tests but lacked insurance coverage or the financial means to pay for the exams. As a result, MSAA developed and implemented the MRI Diagnostic Fund and MRI Institute programs. To date, these two programs have combined to serve nearly 5,000 MS clients who have benefited from an initial or follow-up MRI exam. For more details on these two programs, please visit MSAA's website, **www.msassociation.org**, or call **(800) 532-7667, extension 120**.

Advances in MRI techniques, along with years of consistent research data, have demonstrated that most patients who begin and maintain a DMT will experience fewer active lesions on the brain and spinal cord, fewer and less severe exacerbations, a reduction in symptoms, and a delay in disease progression and disability. In addition, more recent clinical trials have found that many of these DMTs also delay time to a second MS-like event, in cases of clinically isolated syndrome (CIS). CIS refers to the first presenting symptom of MS, prior to a confirmed diagnosis.

These impressive results led the MS medical community to universally adopt and support the position of treating MS with approved DMTs as early as possible and for patients to maintain adherence. Since the mid-2000s, the issue of treatment adherence has been aggressively advocated by leaders in the MS medical and healthcare communities, including MSAA.

Framing the Discussion

To support the critically important message for patients to begin and stay on an MS therapy, MSAA launched a national public awareness campaign in 2007 titled "*These Treatments Work, Let Them Work for You*." This campaign featured brochures, articles and other print materials distributed to MS patients and MS centers across the country. It also included a series of radio and television public service announcements and airport dioramas. Over the last few years, this national initiative has been widely successful, generating nearly 70,000 broadcasts and $6 million of free radio and television airtime to support the message of treatment adherence.

While the issue of treatment adherence continues to gain awareness and momentum, MSAA also recognizes the complexity of the situation. Healthcare providers continue to encourage their patients to become more health literate and to take an active, decision-making role in selecting a treatment. In doing so, an extraordinary number of factors need to be considered when choosing an appropriate MS therapy or switching from one DMT to another. Among the numerous questions to consider include: What are the therapies? Am I a candidate? What should I know about each one? How will my body react to taking one of these medications? How are the different medications administered? What about the costs or insurance? Once I have begun taking a DMT, how do I know if the one I am prescribed is working?

These and other important considerations require ongoing conversations with your doctor and other healthcare professionals. The treatment decision for each patient is unique and must be addressed individually between the person and his or her healthcare team. Additionally, patients must recognize the need to prioritize their issues, questions, and concerns in order to maximize the time with their doctor and healthcare team. With so much information to remember, organize, and prioritize, MSAA recognized the need to help frame these important discussions and

has implemented a new program titled, "S.E.A.R.C.H." Through this program, MSAA is able to support patients and their physicians in their S.E.A.R.C.H. for the most appropriate therapy for each individual.

What is S.E.A.R.C.H.?

Designed as a memory aid, the S.E.A.R.C.H. acronym represents the key areas that should be considered when "searching" for the most appropriate MS treatment. Each letter represents an important topic to be addressed by patients, physicians, and other healthcare and social service professionals. S.E.A.R.C.H. stands for:

Safety
Effectiveness
Affordability
Risks
Convenience
Health outcomes
(overall wellness and quality of life)

"The S.E.A.R.C.H. acronym is not only a useful tool to help frame and remember these important issues, but gives patients a way to start the conversation with their healthcare team," explains MSAA President and CEO Doug Franklin. "Our goal is to foster a positive doctor-patient relationship and allow the dialog to take its own course. MSAA recognizes that MS is a uniquely individual disease that affects each person differently. We are not advocating any one treatment or approach, but rather looking to help guide the conversation between patients and their medical team toward issues that matter most."

To assist with this conversation, MSAA has prepared a sampling of key questions within each aspect of S.E.A.R.C.H. These questions represent a broad overview of many different factors to consider and investigate. They also allow the flexibility for patients to adapt their specific medical history, current disease state, experiences and other physical, emotional, and financial aspects into the decision-making process.

The S.E.A.R.C.H. Questions

MSAA has developed the following S.E.A.R.C.H. questions to serve as a sample, or guide, for you to consider when evaluating your own healthcare needs. These S.E.A.R.C.H. questions merely reflect a starting point to help you think about your own medical situation, issues to prioritize, and ways to develop questions which address your specific healthcare needs.

When using the S.E.A.R.C.H. model, it is also important to recognize that reviewing key topics and questions will likely require more than one office visit with members of your healthcare team. The S.E.A.R.C.H. framework can also be helpful when conducting your own research before or after visiting your healthcare provider. Please see a comprehensive resource guide at the end of this article.

Maximizing S.E.A.R.C.H.

As mentioned in the beginning of this article, the MS landscape has dramatically changed over the past two decades. With the recent introduction of an oral medication, and with new investigational drugs nearing completion of their trials, changes in this landscape continue to evolve at a rapid pace.

Much like the design of a Global Positioning System (GPS), MS patients and their physicians can employ the S.E.A.R.C.H. model to navigate through this dynamic, ever-changing landscape to reach their desired destination. Also, similar to a GPS's feature to recalculate direction, patients can continue to utilize the S.E.A.R.C.H. tool to "recalculate" their decisions and adjust treatments if necessary in order to optimize health outcomes.

Another way to derive maximum benefit from S.E.A.R.C.H. is to use it as a time saver. Unfortunately, doctors today face an increasing workload of patients, restrictive managed-care regulations, and other factors that prevent many physicians from spending as much time with their patients as they were able to do in the past. The reality of these brief and often rushed doctor visits can leave both the patient and physician feeling dissatisfied with the outcome and "searching" for a better way to manage their time.

"As a neurologist, I find tremendous value in the S.E.A.R.C.H. model because

SAFETY

- What are the long-term safety profiles of these FDA-approved MS disease-modifying therapies (DMTs)?
- What tests are required prior to taking DMTs? What tests are required while receiving DMTs?
- How will DMTs interact with my current medical treatments, other medical conditions, and any complementary and alternative medicines?

EFFECTIVENESS

- How effective are these DMTs in reducing MS relapses, disability, and MRI activity?
- What are my realistic expectations regarding the effectiveness of these DMTs?
- How can I tell if my DMT is working?

AFFORDABILITY

(These questions could be directed to other healthcare team members including your social worker, insurance representative, MS organization, etc.)

- What are the costs and insurance coverage for these DMTs?
- Does the insurance coverage have caps, gaps, or limitations?
- Are there assistance programs through the pharmaceutical companies, government, or charities?

RISKS

- What are the risks of side effects associated with these DMTs?
- How frequent and severe are the side effects? How soon do they subside?
- Can these side effects be managed, and if so, how?

CONVENIENCE

- How are the DMTs administered?
- How often do I take these DMTs?
- Must I have regular tests or visits to other healthcare providers to monitor the effects of my treatment?

HEALTH OUTCOMES

- How will my general health and quality of life be affected by these DMTs?
- Will taking a DMT lower my immune system and cause other problems?
- Can these DMTs assist with my mobility, cognition, and other health factors?

it brings to light the key issues involved in treating MS in a way that focuses the conversation," explains MSAA Chief Medical Officer Dr. Jack Burks. "Patients can present their questions and concerns in a clear cut, easy, and efficient way. I see S.E.A.R.C.H. as a template from which patients can choose the issues most important to them."

"Patients sometimes call or revisit me after an appointment with additional questions that they forgot to ask. S.E.A.R.C.H. will effectively reduce the time needed to cover the important topics. This will give patients more confidence in their medical decisions."

The S.E.A.R.C.H. Toolkit

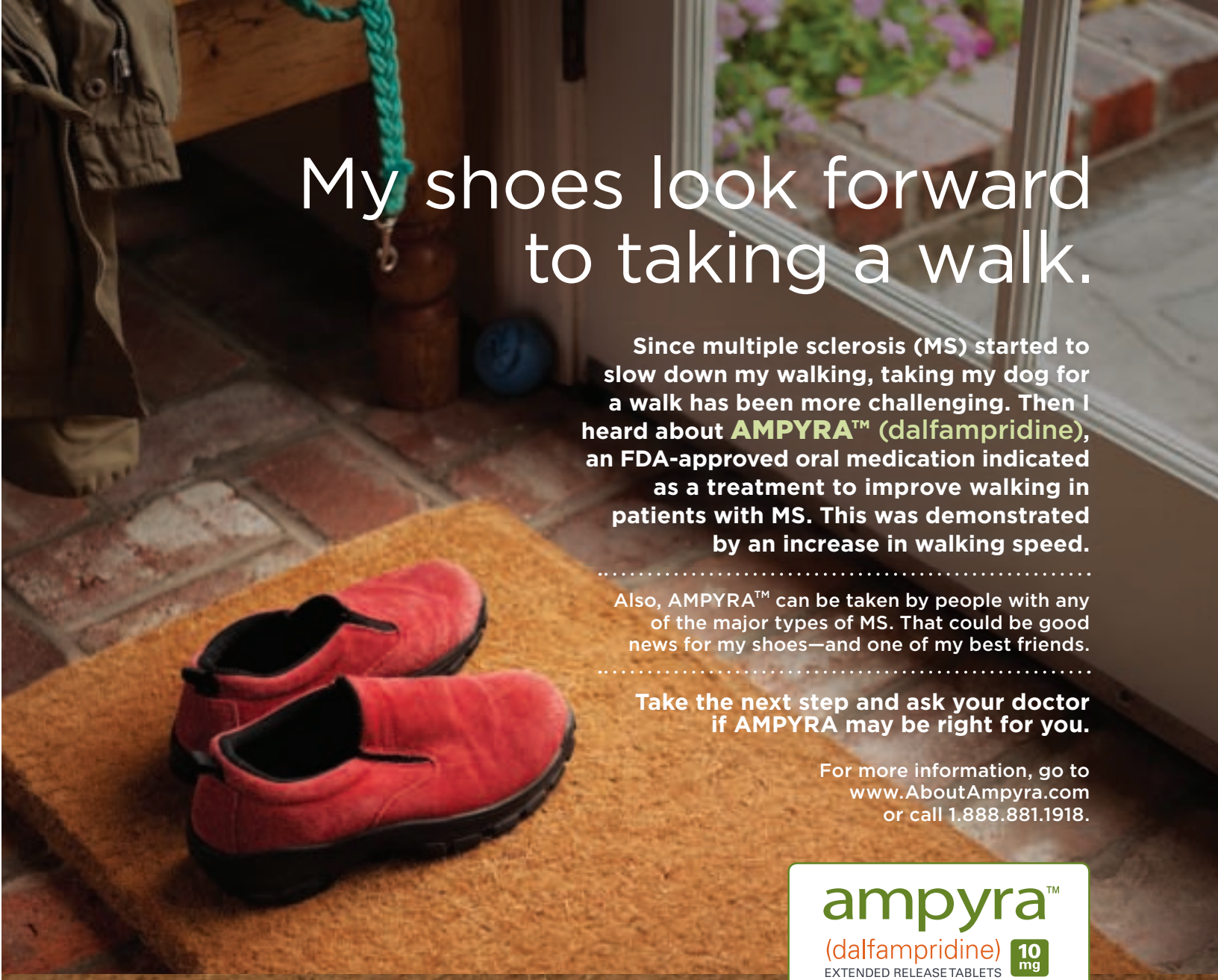
In addition to this article, MSAA has produced a variety of informational tools to help people maximize their success with S.E.A.R.C.H. The first tool is a wallet-size reference card which includes the six key elements of S.E.A.R.C.H. (see insert in this issue of *The Motivator*). Designed as a simple guide that is convenient to carry and readily available, this four-sided card provides a basic explanation of S.E.A.R.C.H. and offers suggested questions to begin the conversation with your healthcare team.

As a secondary and more comprehensive tool to help organize and manage the many aspects of S.E.A.R.C.H., MSAA has created a very useful patient workbook. The S.E.A.R.C.H. Patient Workbook includes an easy-to-follow chart which organizes and provides current MS treatment options; a comprehensive listing of suggested questions within each aspect of S.E.A.R.C.H.; ample writing space to develop questions and take comprehensive notes; an extensive resource guide; and an office-visit questionnaire to help prioritize questions for the doctor. You can download your free copy of the MSAA S.E.A.R.C.H. Patient Workbook online at **www.msassociation.org/search** or you can request a copy be mailed to you by calling **(800) 532-7667**.

As the S.E.A.R.C.H. campaign gains awareness and momentum, MSAA plans to roll out additional activities and tools including an on-demand educational video, live webcasts, a series of in-person public education programs, a smartphone application, the development of support materials for healthcare professionals, and many other tools to help patients and their doctors work together and make informed decisions.

Treatment Chart

Please see the easy-to-follow reference chart on page 21 titled "Current Approved MS Disease-Modifying Therapies" that shows the currently approved and available MS disease-modifying therapies. This chart does not address the issues of efficacy, safety, and risk. All of the disease-modifying therapies for MS have different benefits and risks. The effectiveness and side effects of each drug may vary from one patient to another. Additionally, patients who do not respond well to one DMT may benefit by switching to a different treatment. Individuals need to consult with their healthcare team to determine which treatment might be the best option for them. ◆



My shoes look forward to taking a walk.

Since multiple sclerosis (MS) started to slow down my walking, taking my dog for a walk has been more challenging. Then I heard about AMPYRA™ (dalfampridine), an FDA-approved oral medication indicated as a treatment to improve walking in patients with MS. This was demonstrated by an increase in walking speed.

Also, AMPYRA™ can be taken by people with any of the major types of MS. That could be good news for my shoes—and one of my best friends.

Take the next step and ask your doctor if AMPYRA may be right for you.

For more information, go to www.AboutAmpyra.com or call 1.888.881.1918.

ampyra™
(dalfampridine) 10 mg
EXTENDED RELEASE TABLETS

IMPORTANT SAFETY INFORMATION:

Talk to your doctor about AMPYRA to learn if it is safe for you. Do not take it if you've ever had a seizure or if you have certain types of kidney problems as this may increase your risk of seizure. Tell your doctor if you have kidney problems.

Never take more than one tablet of AMPYRA twice a day (about 12 hours apart). Don't take more than 2 tablets in a 24-hour period because it may increase the risk of seizures. If you miss a dose of AMPYRA don't make up the missed dose.

Do not take AMPYRA together with other aminopyridine medications, including compounded 4-aminopyridine (sometimes called 4-AP, fampridine).

AMPYRA may cause serious side effects, including kidney or bladder infections. The most common side effects are urinary tract infection, trouble sleeping (insomnia), dizziness, headache, nausea, weakness, back pain, and problems with balance. Tell your doctor if you have any of these side effects that bother you or do not go away.

For more information, please refer to the Medication Guide. This important safety information is not meant to replace discussions with your doctor. For more information call toll-free 1-888-881-1918.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

AMP166

ACORDA® THERAPEUTICS

MEDICATION GUIDE FOR AMPYRA™ (am-PEER-ah) (dalfampridine) Extended Release Tablets

Read this Medication Guide before you start taking AMPYRA.

Read this Medication Guide before you start taking AMPYRA and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or your treatment.

What is the most important information I should know about AMPYRA?

AMPYRA can cause seizures.

- Your chance of having a seizure is higher if you take too much AMPYRA or if you have kidney problems.
- Do not take AMPYRA if you have ever had a seizure.
- Before taking AMPYRA tell your doctor if you have kidney problems.
- Take AMPYRA exactly as prescribed by your doctor. See "How do I take AMPYRA?"

Stop taking AMPYRA and call your doctor right away if you have a seizure while taking AMPYRA.

What is AMPYRA?

AMPYRA is a prescription medicine used to help improve walking in people with multiple sclerosis (MS). This was shown by an increase in walking speed.

It is not known if AMPYRA is safe or effective in children less than 18 years of age.

Who should not take AMPYRA?

Do not take AMPYRA if you:

- have ever had a seizure
- have certain types of kidney problems

What should I tell my doctor before taking AMPYRA?

Before you take AMPYRA, tell your doctor if you:

- have any other medical conditions
- are taking compounded 4-aminopyridine (fampridine, 4-AP)
- are pregnant or plan to become pregnant. It is not known if AMPYRA will harm your unborn baby. You and your doctor will decide if you should take AMPYRA while you are pregnant
- are breast-feeding or plan to breast-feed. It is not known if AMPYRA passes into your breast milk. You and your doctor should decide if you will take AMPYRA or breast-feed. You should not do both.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins and herbal supplements. Know the medicines you take.

Keep a list of them and show it to your doctor and pharmacist when you get a new medicine.

How should I take AMPYRA?

- Take AMPYRA exactly as your doctor tells you to take it. Do not change your dose of AMPYRA.
- Take one tablet of AMPYRA 2 times each day about 12 hours apart. Do not take more than 2 tablets of AMPYRA in a 24-hour period.
- Take AMPYRA tablets whole. Do not break, crush, chew or dissolve AMPYRA tablets before swallowing. If you cannot swallow AMPYRA tablets whole, tell your doctor.
- AMPYRA is released slowly over time. If the tablet is broken, the medicine may be released too fast. This can raise your chance of having a seizure.
- AMPYRA can be taken with or without food.
- If you miss a dose of AMPYRA, do not make up the missed dose. Do not take 2 doses at the same time. Take your next dose at your regular scheduled time.
- If you take too much AMPYRA, call your doctor or go to the nearest hospital emergency room right away.
- Do not take AMPYRA together with other aminopyridine medications, including compounded 4-AP (sometimes called 4-aminopyridine, fampridine)

What are the possible side effects of AMPYRA?

AMPYRA may cause serious side effects, including:

- Kidney or bladder infections

See "What is the most important information I should know about AMPYRA?"

The most common side effects of AMPYRA include:

- urinary tract infection
- trouble sleeping (insomnia)
- dizziness
- headache
- nausea
- weakness
- back pain
- problems with balance
- multiple sclerosis relapse
- burning, tingling or itching of your skin
- irritation in your nose and throat
- constipation
- indigestion
- pain in your throat

Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of AMPYRA. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

How should I store AMPYRA?

- Store AMPYRA at 59°F to 86°F (15°C to 30°C).
- Safely throw away AMPYRA that is out of date or no longer needed.

Keep AMPYRA and all medicines out of the reach of children.

General Information about the safe and effective use of AMPYRA

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use AMPYRA for a condition for which it was not prescribed. Do not give AMPYRA to other people, even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about AMPYRA. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about AMPYRA that is written for health professionals.

For more information, go to www.AMPYRA.com or call 1-800-367-5109.

What are the ingredients in AMPYRA?

Active ingredient: dalfampridine (previously called fampridine)
Inactive ingredients: colloidal silicon dioxide, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, and titanium dioxide.

Distributed by: Acorda Therapeutics, Inc.
Hawthorne, NY 10532

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ACØRDA®
THERAPEUTICS

Current Approved MS Disease-Modifying Therapies *(listed alphabetically)*

DRUG	FDA APPROVAL	MECHANISM OF ACTION	ADMINISTERED
Avonex (interferon beta-1a) Parent company: *Biogen Idec*	Approved for relapsing forms of MS in 1996 and for individuals with clinically isolated syndrome (CIS).	Avonex is an interferon. Interferons appear to reduce inflammation by modulating a favorable balance between cells that increase inflammation and cells that decrease it.	30 micrograms taken via weekly intermuscular injections
Betaseron (interferon beta-1b) Parent company: *Bayer Healthcare Pharmaceuticals*	Approved for relapsing forms of MS in 1993 and for individuals with clinically isolated syndrome (CIS).	Betaseron is an interferon. Interferons appear to reduce inflammation by modulating a favorable balance between cells that increase inflammation and cells that decrease it.	250 micrograms taken via subcutaneous injections every other day
Copaxone (glatiramer acetate) Parent company: *Teva Neuroscience*	Approved for relapsing forms of MS in 1996 and for individuals with clinically isolated syndrome (CIS).	Copaxone is a synthetic polypeptide that mimics myelin basic protein, a key component of the myelin sheath that is damaged in MS. By a different mechanism of action than the interferons, Copaxone also appears to reduce inflammation by modulating a favorable balance between cells that increase inflammation and cells that decrease it.	20 milligrams taken via daily subcutaneous injections
Extavia (interferon beta-1b) Parent company: *Novartis Pharmaceuticals Corporation*	Approved for relapsing forms of MS in 2010 and for individuals with clinically isolated syndrome (CIS).	Extavia is an interferon beta-1b that is biologically identical to Betaseron and made in an identical process, but marketed by a different company.	250 micrograms taken via subcutaneous injections every other day
Gilenya (fingolimod, FTY720) Parent company: *Novartis Pharmaceuticals Corporation*	Approved for relapsing forms of MS in 2010.	Gilenya blocks potentially damaging T cells from leaving lymph nodes, thereby lowering their number in the blood, central nervous system and tissues.	Oral DMT for MS; 0.5 mg capsule taken orally once per day
Novantrone (mitoxantrone) Parent company: *EMD Serono, Inc.*	Approved for use in secondary-progressive MS (SPMS), progressive-relapsing MS (PRMS) and worsening RRMS in 2000.	Novantrone is an immunosuppressant that has been used for years to treat cancer. It targets rapidly dividing cells, including those believed to be involved in MS.	IV infusion once every 3 months (for 2 to 3 years maximum). 12 mg/m^2 approximately 5 to 15 minutes
Rebif (interferon beta-1a) Parent companies: *EMD Serono, Inc. and Pfizer Inc*	Approved for relapsing forms of MS in 2002.	Rebif is an interferon. Interferons appear to reduce inflammation by modulating a favorable balance between cells that increase inflammation and cells that decrease it.	44 micrograms taken via subcutaneous injections three times weekly
Tysabri (natalizumab) Parent companies: *Biogen Idec and Elan Pharmaceuticals*	Approved for relapsing forms of MS in 2006.	This laboratory-produced monoclonal antibody acts against a molecule involved in the activation and function of lymphocytes and their migration into the central nervous system (CNS). It is thought to prevent damaging immune cells from crossing the blood-brain barrier.	IV infusion every 4 weeks; 300 milligrams (mg) over 1 hour

S.E.A.R.C.H.SM RESOURCES

MSAA: For more information on FDA-approved therapies, symptom management treatments, and MSAA programs and services, please visit MSAA's website at **www.msassociation.org** or contact MSAA at (800) 532-7667. Inquiries may also be emailed to **MSquestions@msassociation.org**.

MS Coalition: The MS Coalition is a collaborative network of independent MS organizations. The MS Coalition's mission is to increase opportunities for cooperation and provide greater opportunity to leverage the effective use of resources for the benefit of the MS community. Please visit **www.ms-coalition.org**.

In addition to MSAA, the MS Coalition members include (listed alphabetically):

Accelerated Cure Project for Multiple Sclerosis
(781) 487-0008; www.acceleratedcure.org

Consortium of Multiple Sclerosis Centers (CMSC)
www.mscare.org or www.narcoms.org

Can Do Multiple Sclerosis
(800) 367-3101; www.mscando.org

International Organization of Multiple Sclerosis Nurses
(201) 487-1050; www.iomsn.org

Multiple Sclerosis Foundation
(800) 225-6495; www.msfocus.org

National Multiple Sclerosis Society
(800) 344-4867; www.nationalMSsociety.org

United Spinal Association
(718) 803-3782; www.unitedspinal.org

S.E.A.R.C.H.SM ASSISTANCE PROGRAMS

The following pharmaceutical companies offer patient programs to provide information, instruction, and resources for advocacy and financial assistance (listed alphabetically).

Avonex - MS ActiveSource
(800) 456-2255; www.avonex.com

Betaseron - Betaplus MS Support
(800) 788-1467; www.betaseron.com

Copaxone - Shared Solutions
(800) 887-8100; www.sharedsolutions.com

Extavia Patient Support Program
(866) 925-2333; www.extavia.com

Gilenya Patient Support Program
(877) 408-4974; www.gilenya.com

Rebif - MS LifeLines
(877) 447-3243; www.MSLifeLines.com

Novantrone - MS LifeLines
(877) 447-3243; www.novantrone.com

Tysabri
(800) 456-2255; www.tysabri.com

The MSAA S.E.A.R.C.H. initiative is made possible through unrestricted educational grants from Bayer HealthCare Pharmaceuticals, Biogen Idec, and Teva Neuroscience. MSAA is solely responsible for the development of S.E.A.R.C.H. and its content.

Equipment Distribution Program Makes A Difference

"I would like to personally thank all involved for the wonderful gift of equipment that I received. I cannot express the difference it has made in my life already. Thank you so much for your care and concern."

– R.B. of Virginia

This very touching and greatly appreciated letter of thanks came to MSAA from one of our clients just before the holidays. We wanted to share this with our readers and remind you that the **MSAA Equipment Distribution Program** offers a wide range of safety products, daily living aids, and mobility items to client members. Equipment ranging from grab bars to wheelchairs are available free of charge to those who qualify for the program. Please let us improve your quality of life…today!

To download an application, please visit **www.msassociation.org/programs**. If you have any questions or want to request an application by mail, please call MSAA at (800) 532-7667.

For years, Bayer® has been helping people with relapsing forms of multiple sclerosis (MS) understand their treatment options and manage their treatment. Here are some things you should know about BETASERON (interferon beta-1b) and the BETAPLUS® Patient Support Program:

- Early treatment with BETASERON may help delay disease progression[1]
- With 20 years of clinical experience, BETASERON is the longest-studied MS therapy
- BETASERON offers every-other-day dosing with the thinnest needle available in MS therapy[2]
- Only BETASERON comes with BETAPLUS—a FREE support program including 24/7/365 access to an MS-trained BETA Nurse
- Only BETASERON offers $0 monthly copays* to help make treatment affordable

INDICATIONS AND USAGE

BETASERON® (interferon beta-1b) is indicated for the treatment of relapsing forms of multiple sclerosis to reduce the frequency of clinical exacerbations.

Patients with multiple sclerosis in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with multiple sclerosis.

IMPORTANT SAFETY INFORMATION

- **BETASERON** should be used with caution in patients with depression.
- Injection-site necrosis has been reported in 4% of patients in controlled trials. Patients should be advised of the importance of rotating injection sites.
- Severe hepatic injury, including cases of hepatic failure, has been reported. Patients should be monitored for liver enzyme elevations while taking **BETASERON**.
- **BETASERON** should be used with caution in patients with seizure disorders or cardiac disease.
- Female patients should be warned about the potential risk to pregnancy.

* Some restrictions apply. Copay assistance is limited to $9500 per patient per calendar year. Patients who are enrolled in any type of government insurance or reimbursement programs are not eligible. As a condition precedent of the copayment support provided under this program, eg, copay refunds, participating patients and pharmacies are obligated to inform insurance companies and third-party payors of any benefits they receive and the value of this program, as required by contract or otherwise. Void where prohibited by law, taxed or restricted. Patients enrolled in Bayer's Patient Assistance Program are not eligible.

References: 1. Kappos L, Polman CH, Freedman MS, et al. Treatment with interferon beta-1b delays conversion to clinically definite and McDonald MS in patients with clinically isolated syndromes. *Neurology.* 2006;67:1242-1249. **2.** BETASERON (prescribing information). Montville, NJ: Bayer HealthCare Pharmaceuticals Inc; 2010.

BETASERON®
(INTERFERON BETA-1b) FOR SC INJECTION

MEDICATION + SUPPORT™

for the road ahead.

Call 1-800-788-1467 any time or visit us online at BETASERON.com

- Cases of anaphylaxis have been reported rarely.
- The most commonly reported adverse reactions are lymphopenia (low numbers of a certain kind of white blood cell), injection-site reaction, asthenia (general weakness), flu-like symptom complex (flu syndrome and/or a combination of at least two Adverse Events from fever, chills, muscle aches, tiredness and sweating), headache and pain. Gradual dose titration and use of analgesics during treatment initiation may help reduce flu-like symptoms.

See "Warnings," "Precautions," and "Adverse Reactions" sections of full Prescribing Information. More information, including the full Prescribing Information, is available at **www.BETASERON.com**.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see brief summary of Medication Guide on the following page.

Bayer HealthCare
Pharmaceuticals

Model used for illustrative purposes only.

 521-10-0007-10 Printed in USA. December 2010

BETASERON®
(INTERFERON BETA-1b) FOR SC INJECTION
6800503BS

Brief Summary of Medication Guide

Betaseron® (bay-ta-seer-on)

Interferon beta-1b

(in-ter-feer-on beta-one-be)

Please read this leaflet carefully before you start to use Betaseron® and each time your prescription is refilled since there may be new information. The information in this medication guide does not take the place of talking with your doctor or healthcare professional.

What is the most important information I should know about Betaseron?

Betaseron will not cure multiple sclerosis (MS) but it has been shown to decrease the number of flare-ups of the disease. Betaseron can cause serious side effects, so before you start taking Betaseron, you should talk to your doctor about the possible benefits of Betaseron and its possible side effects to decide if Betaseron is right for you. Potential serious side effects include:

- **Depression.** Some patients treated with interferons, including Betaseron, have become seriously depressed (feeling sad). Some patients have thought about or have attempted to kill themselves. Depression (a sinking of spirits or sadness) is not uncommon in people with multiple sclerosis. However, if you are feeling noticeably sadder or helpless, or feel like hurting yourself or others, you should tell a family member or friend right away and call your doctor or health care provider as soon as possible. Your doctor may ask that you stop using Betaseron. Before starting Betaseron, you should also tell your doctor if you have ever had any mental illness, including depression, and if you take any medications for depression.
- **Liver problems.** Your liver may be affected by taking Betaseron and a few patients have developed severe liver injury. Your healthcare provider may ask you to have regular blood tests to make sure that your liver is working properly. If your skin or the whites of your eyes become yellow or if you are bruising easily, you should call your doctor immediately.
- **Risk to pregnancy.** If you become pregnant while taking Betaseron you should stop using Betaseron immediately and call your doctor. Betaseron may cause you to lose your baby (miscarry) or may cause harm to your unborn child. You and your doctor will need to decide whether the potential benefit of taking Betaseron is greater than the potential risks to your unborn child.

  A pregnancy registry has been established to monitor pregnancy outcomes of women exposed to Betaseron while pregnant. Providers are encouraged to obtain information on line at www.BetaseronPregnancyRegistry.com and register patients by calling 1-800-478-7049.
- **Allergic reactions.** Some patients taking Betaseron have had severe allergic reactions leading to difficulty breathing and swallowing; these reactions can happen quickly. Allergic reactions can happen after your first dose or may not happen until after you have taken Betaseron many times. Less severe allergic reactions such as rash, itching, skin bumps or swelling of the mouth and tongue can also happen. If you think you are having an allergic reaction, stop using Betaseron immediately and call your doctor.
- **Injection site problems.** Betaseron may cause redness, pain or swelling at the place where an injection was given. A few patients have developed skin infections or areas of severe skin damage (necrosis). If one of your injection sites becomes swollen and painful or the area looks infected and it doesn't heal within a few days, you should call your doctor.
- **Seizures -** Some patients have had seizures while taking Betaseron, including some patients who have never had seizures before. It is not known whether the seizures were related to the effects of their MS, to Betaseron, or to a combination of both. If you have a seizure while taking Betaseron, you should stop taking Betaseron and call your doctor right away.
- **Heart problems -** While Betaseron is not known to have direct effects on the heart, a few patients who did not have a history of heart problems developed heart muscle problems or congestive heart failure after taking Betaseron. Some of the symptoms of heart problems are swollen ankles, shortness of breath, decreased ability to exercise, fast heartbeat, tightness in chest, increased need to urinate at night, and not being able to lay flat in bed. If you develop these symptoms or any heart problems while taking Betaseron, you should call your doctor right away.

For more information on possible side effects with Betaseron, please read the section on **"What are the possible side effects of Betaseron?"** in this Medication Guide.

What is Betaseron?

Betaseron is a type of protein called beta interferon that occurs naturally in the body. It is used to treat relapsing forms of multiple sclerosis. It will not cure your MS but may decrease the number of flare-ups of the disease. MS is a lifelong disease that affects your nervous system by destroying the protective covering (myelin) that surrounds your nerve fibers. The way Betaseron works in MS is not known.

Who should not take Betaseron?

Do not take Betaseron if you:

- Have had allergic reactions such as difficulty breathing, flushing or hives to another interferon beta or to human albumin.

If you have any of the following conditions or serious medical problems, you should tell your doctor *before* taking Betaseron:

- Depression (a sinking feeling or sadness), anxiety (feeling uneasy, nervous, or fearful for no reason), or trouble sleeping
- Liver diseases
- Problems with your thyroid gland
- Blood problems such as bleeding or bruising easily and anemia (low red blood cells) or low white blood cells
- Epilepsy
- Heart problems
- Are pregnant, breast feeding, or planning to become pregnant

You should tell your doctor if you are taking any other prescription or nonprescription medicines. This includes any vitamin or mineral supplements, or herbal products.

How should I take Betaseron?

Betaseron is given by injection under the skin (subcutaneous injection) every other day. Your injections should be approximately 48 hours (two days) apart, so it is best to take them at the same time each day, preferably in the evening just before bedtime.

You may be started on a lower dose when you first start taking Betaseron. Your doctor will tell you what dose of Betaseron to use, and that dose may change based on how your body responds. You should not change your dose without talking with your doctor.

If you miss a dose, you should take your next dose as soon as you remember or are able to take it. Your next injection should be taken about 48 hours (two days) after that dose. **Do not take Betaseron on two consecutive days.** If you accidentally take more than your prescribed dose, or take it on two consecutive days, call your doctor right away.

You should always follow your doctor's instructions and advice about how to take this medication. If your doctor feels that you, or a family member or friend may give you the injections, then you and/or the other person should be trained by your doctor or healthcare provider in how to give an injection. Do not try to give yourself (or have another person give you) injections at home until you (or both of you) understand and are comfortable with how to prepare your dose and give the injection.

Always use a new, unopened, vial of Betaseron and syringe for each injection. Never reuse vials or syringes.

It is important that you change your injection site each time Betaseron is injected. This will lessen the chance of your having a serious skin reaction at the spot where you inject Betaseron. You should always avoid injecting Betaseron into an area of skin that is sore, reddened, infected or otherwise damaged.

At the end of this leaflet there are detailed instructions on how to prepare and give an injection of Betaseron. You should become familiar with these instructions and follow your doctor's orders before injecting Betaseron.

What should I avoid while taking Betaseron?

- **Pregnancy.** You should avoid becoming pregnant while taking Betaseron until you have talked with your doctor. Betaseron can cause you to lose your baby (miscarry).
- **Breast feeding.** You should talk to your doctor if you are breast feeding an infant. It is not known if the interferon in Betaseron can be passed to an infant in mother's milk, and it is not known whether the drug could harm the infant if it is passed to an infant.

What are the possible side effects of Betaseron?

- **Flu-like symptoms.** Most patients have flu-like symptoms (fever, chills, sweating, muscle aches and tiredness). For many patients, these symptoms will lessen or go away over time. You should talk to your doctor about whether you should take an over the counter medication for pain or fever reduction before or after taking your dose of Betaseron.
- Skin reactions. Soreness, redness, pain, bruising or swelling may occur at the place of injection **(see "What is the most important information I should know about Betaseron?").**
- **Depression and anxiety.** Some patients taking interferons have become very depressed and/or anxious. There have been patients taking interferons who have had thoughts about killing themselves. If you feel sad or hopeless you should tell a friend or family member right away and call your doctor immediately. **(see "*What is the most important information I should know about Betaseron*?").**
- **Liver problems.** Your liver function may be affected. If you develop symptoms of changes in your liver, including yellowing of the skin and whites of the eyes and easy bruising, call your doctor immediately. **(see "What is the most important information I should know about Betaseron?")**
- **Blood problems.** You may have a drop in the levels of infection-fighting white blood cells, red blood cells, or cells that help you form blood clots. If drops in levels are severe, they can lessen your ability to fight infections, make you feel tired or sluggish or cause you to bruise or bleed easily.
- **Thyroid problems.** Your thyroid function may change. Symptoms of changes in the function of your thyroid include feeling cold or hot much of the time or change in your weight (gain or loss) without a change in your diet or amount of exercise you are getting.
- **Allergic reaction.** Some patients have had hives, rash, skin bumps or itching while they were taking Betaseron. There is also a rare possibility that you can have a life-threatening allergic reaction. **(see "*What is the most important information I should know about Betaseron*?").**
- **Seizures -** Some patients have had seizures while taking Betaseron, including patients who have never had seizures before. It is not known whether the seizures were related to the effects of their MS, to Betaseron, or to a combination of both. If you have a seizure while taking Betaseron, you should call your doctor right away. **(See "What is the most important information I should know about Betaseron?")**
- **Heart problems -** While Betaseron is not known to have any direct effects on the heart, a few patients who did not have a history of heart problems developed heart muscle problems or congestive heart failure after taking Betaseron. Some of the symptoms of heart problems are swollen ankles, shortness of breath, decreased ability to exercise, fast heartbeat, tightness in chest, increased need to urinate at night, and not being able to lay flat in bed. If you develop these symptoms or any heart problems while taking Betaseron, you should call your doctor right away. **(See "What is the most important information I should know about Betaseron?")**

Whether you experience any of these side effects or not, you and your doctor should periodically talk about your general health. Your doctor may want to monitor you more closely and ask you to have blood tests done more frequently.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General Information About Prescription Medicines

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. This medication has been prescribed for your particular medical condition. Do not use it for another condition or give this drug to anyone else. If you have any questions you should speak with your doctor or health care professional. You may also ask your doctor or pharmacist for a copy of the information provided to them with the product. Keep this and all drugs out of the reach of children.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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early age than later-born children, who are exposed through their older brothers and sisters. However, using data from the Canadian Collaborative Project, it was found that one's position in birth order does not impact the risk to develop MS.[35]

Later-Acting Environmental Factors

Because the average age of onset of MS is approximately 30 years, there is a long time period from birth to MS diagnosis for the environment to influence one's risk of MS. Migration data highlights adolescence as being important, further illustrated by additional associations, such as the age of menarche (beginning menstruation) and adolescent obesity with the onset of MS.[36, 37] Other epidemiological studies (e.g., occupational data) suggest influences of the environment extending into adult life.[38] The risk of developing MS is age-related and drops off dramatically after the age of 50,[39] so whatever risk factors that do play a role must be unable to stimulate the development of MS after a certain point of time.

Suspected Environmental Risk Factors in MS

Although the above data point to the time when environmental factors are likely to increase the risk of MS, we still do not have absolute evidence for the identity of environmental factors involved. To follow is a summary of the factors with the strongest evidence for involvement in MS etiology, namely Epstein-Barr virus (EBV), vitamin D, and smoking.

Epstein-Barr Virus (EBV): There have been many reports suggesting an association between one or more infectious diseases and MS.[40, 41] However, the epidemiological data associating EBV infection with MS has been supported through numerous studies.

Virtually all subjects with MS (more than 99 percent) are infected with EBV compared to approximately 94 percent of age-matched control subjects (individuals without MS).[42] The corollary to this is that MS is very rare in adult subjects who are not infected with EBV; the relative risk of getting MS if you are EBV negative is very low.[42, 43] Further supporting a role for EBV in MS is the finding that individuals with a history of infectious mononucleosis (IM) have an increased risk of developing MS. Infectious mononucleosis is an illness that is caused by EBV. A systematic review and meta-analysis of 14 case-control and

cohort studies (those which observe a group of people over time) reported a relative risk of MS after infectious mononucleosis of 2.3,[44] which is more than twice the risk of MS in the general population.

Vitamin D: Sunlight exposure and associated vitamin D status are potential explanations for the link between geography (in terms of latitude) and the incidence of MS.[45] Levels of past sun exposure during childhood and adolescence are inversely related to MS susceptibility.[46] This means that as one's level of sun exposure during childhood and adolescence increases, the risk of MS susceptibility decreases. Questionnaire-based studies are prone to bias or inaccuracies as individuals answer questions according to their own perceptions and what they are able to recall from the past. Nonetheless, an effect of sun exposure on MS could be confirmed when using the objective measure of long-term skin damage from the sun.

Experimental and epidemiological data suggest that vitamin D is the connection to the sunlight effect. It was noted many years ago that the consumption of fatty seafood and cod liver oil in Norway – both rich sources of vitamin D – provided protection against the risk of MS,[47] although this outcome may also arise from the biological effects of omega-3 fatty acids. A prospective cohort study (observing groups of people over time) found that taking vitamin supplementation which included vitamin D was associated with an approximate 40-percent reduction in the risk of developing MS.[48] However, the amounts of vitamin D taken via vitamin supplementation in this study are thought to be insufficient to make much change in circulating vitamin D levels,[49] and effects of multivitamin intake may be misinterpreted as other factors could contribute to the observed reduction of MS risk.

The strongest evidence of a role for vitamin D comes from a prospective, case-control study in military personnel in the United States who had blood-serum samples systematically stored. This study showed that a lower risk of MS was associated with high serum vitamin D levels (specifically, 25-hydroxyvitamin D).[50] In Caucasians, the risk of developing MS decreased significantly with increasing vitamin D levels in the blood.[50]

Smoking: A recent meta-analysis of several completed studies gave a combined risk estimate for developing MS of 1.51 for "ever smoking" versus "never smoking,"[51] which means that smoking may increase one's risk of MS by 50 percent. Earlier studies showed a dose-dependent (i.e., number of cigarettes smoked) relationship to MS risk.[52] A Swedish study showed that the use of

snuff (a form of tobacco that is inhaled through the nose) does not increase the risk of MS. This suggests that factors present in smoked tobacco, rather than just the route of administration, is important.[53]

CONCLUSIONS

In summary, the etiology of MS is still unclear, but it is now recognized that the degree of complexity is beyond what was previously believed – even as recently as 10 to 15 years ago. The complexity comes from the realization that one cannot predict a person's risk of developing MS just by considering the individual effects of single factors alone. Genes, environment, post-genomic modifications, and chance all appear to be involved and to interact with one another.

The associated risk factors for MS appear to come together to form a "causal cascade," where several things need to occur before developing MS. Factors largely defined from birth (i.e., gender, HLA status, place of birth) appear to need certain environmental factors (vitamin D deficiency, late EBV exposure) to provoke the development of the abnormalities required that subsequently can lead to MS. The effect of where someone lives in early life (in relation to the equator and latitude) and associations with infectious mononucleosis in adolescence would support the notion that vitamin D deficiency precedes EBV infection.[54] However, the Australian migration data and the evidence for vitamin-D related influences on risk during adult life (e.g., outdoor occupations decrease MS risk)[55] suggest that vitamin D has the potential to play a role over a wider time period.

It is not yet clear whether MS susceptibility is a result of a chain of adverse factors that need to occur in a specific order and are dependent on one another (e.g., a domino effect), or whether risk factors are independent of each other but each adds to the collection and strength of factors that push an individual closer to the threshold of developing MS. Since a single cause for the development of MS has not been found in all MS patients, this suggests that "causal pathways" (the events leading to MS) will likely differ in individuals. Should this be the case, this could support the hypothesis where independent risk factors add up, pushing someone closer to developing MS or the hypothesis that the interaction of risk factors is critical.

Although some progress has been made, our understanding of the stages involved in the development of MS is still limited. Further study is vital to identifying and understanding the causes of MS. Once we have these answers, we can work to prevent its occurrence, create more effective treatments, and hopefully one day cure this challenging disease. ◆

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Ask the Doctor

By Dr. Jack Burks
Chief Medical Officer for MSAA

Can Lesions Disappear?

Dr. Jack Burks

Q: I was diagnosed with RRMS in 2009. After trying one MS therapy, I switched to Tysabri, and have steadily improved in function. When I was diagnosed, I only had a couple of lesions on my MRI, but my lumbar puncture was positive for bands and I've had many MS symptoms. My last MRI showed no lesions.

I have just moved and was referred to a new neurologist. Due to this MRI, this neurologist has told me that I "can't possibly have MS," and has stopped all treatment. (I am a veteran and this has been through the VA.) He tells me that lesions never go away, and that he suspects errors in my history. Could he be correct? Can lesions disappear?

A: You are in a difficult situation. I would gather your previous records, including MRIs, lumbar puncture results, and medical evaluations that showed MS and ask your neurologist to review your records. If there is still a conflict, I would get another opinion from a VA doctor with MS center expertise, or a non-VA neurologist if you have the resources. MS lesions can fluctuate, but reverting to a completely normal MRI provides cause for your neurologist to be concerned.

After he reviews your complete records, he will be in a better position to judge. He may want to see the actual abnormal MRIs in the past and not just read the reports. Also, he may want to talk with your previous neurologist to get a better understanding of your MS prior to starting Tysabri.

Q: I was diagnosed with MS in 2004. I've been on a few different injectable drugs and have had bad experiences with them. As an option, I would like to try LDN (low-dose naltrexone).

Which brings me here to ask, why is it so hard to get someone to help me with this? I know it's not specifically approved for MS, but it's been helping people. Is it wrong of me to want to try this?

A: I am sorry that you have had problems with the approved MS therapies. They help most people with MS. LDN is not FDA-approved, so many neurologists are not enthusiastic about prescribing this drug. It appears relatively safe and some people feel better when taking it. However, it is not a substitute for FDA-approved disease-modifying therapies.

Nonetheless, you can probably find a neurologist or general practitioner who is willing to prescribe LDN. To learn about studies of LDN and MS, and to ask for the name of a nearby doctor, you can visit the LDN website (at **www.lowdosenaltrexone.org**).

You might consider revisiting an MS-injectable drug option with an MS expert. Although this has not been helpful in the past, you may still be able to benefit from one of the currently available therapies. If not, another alternative is to ask your neurologist about the new FDA-approved drug called Gilenya. It is the first oral medicine approved for the long-term treatment of MS. Your neurologist can explain the benefits and risks of this new drug, and since it is different from the other medications you have tried, it may be helpful to you. Tysabri is another option that you may want to discuss with your doctor. It also has a different mechanism of action and is given via IV infusion once monthly.

(This question comes from a nurse.)

Q: With new drugs coming on the market that suppress the immune system, combined with the fact that individuals may produce certain white blood cells to fight infection, I am surprised that I do not see any recommendations in the study literature on a "washout" period for other medications that one may currently be on prior to starting these medications once they are approved.

For example, if someone is on high-dose steroids, Tysabri, or cyclophosphamide,* would it be reasonable to have a period of a month or more between the last dose of a current medication and the first dose of new medication? And if so, how would you deal with a relapse during that time?

**Cyclophosphamide (Cytoxan) is a drug not specifically approved for MS but is sometimes prescribed for certain individuals.*

A: Great question! Unfortunately, the treatment trials do not usually address the question of "washout." Without data, it is hard to make any recommendations. Opinions vary when data are lacking.

My opinion (not based on data) is that a washout period for some drugs seems reasonable. The ABCER drugs (Avonex, Betaseron, Copaxone, Extavia, and Rebif) as well as steroids are not likely to need more than a week or two washout. Tysabri washout-period opinions vary from one to six months. I favor a two-to-three month washout with Tysabri before starting Gilenya. Similarly, Gilenya may require a two-to-three month washout before switching to another MS therapy.

If one has an exacerbation during the washout period, I would give this patient a short course of steroids, which has a short "half life" (or duration in the body). Novantrone and Cytoxan are long-acting drugs and I would give a three-to-six month washout period for these drugs.

Remember, these suggested washout periods are based on my opinion and not based on scientific data. These washout periods are subject to individual interpretation and other MS experts may recommend different lengths of time to wait between switching from one MS treatment to another. ◆

To submit questions, please send them to: MSAA, Questions for Ask the Doctor, c/o Dr. Jack Burks, 706 Haddonfield Road, Cherry Hill, NJ 08002; or you may email them to agriese@msassociation.org (please write "Ask the Doctor" in the subject line).

Research News

by Susan Wells Courtney
Reviewed by Jack Burks, MD

Research News presents highlights from some of the recent news items of importance to the MS community. To access the full articles on these and other topics, please visit ***www.msassociation.org****, or call MSAA's Helpline at* ***(800) 532-7667*** *to request a printed copy.*

More Data Needed for Oral Cladribine

On March 2, 2011, EMD Serono, Inc., makers of Cladribine Tablets (an oral formulation of cladribine for the treatment of MS), announced that the United States Food and Drug Administration (FDA) was not able to approve the application for Cladribine Tablets without additional information. According to EMD Serono, the FDA found substantial evidence of Cladribine Tablets' effectiveness as indicated by the CLARITY study (CLAdRIbine Tablets treating MS orallY). While the effectiveness was not in question, the FDA is looking for an improved understanding of safety risks and the overall benefit-risk profile of Cladribine.

EMD Serono notes that they remain committed to completing their ongoing studies with Cladribine Tablets and to continue to seek FDA approval of their drug. Three ongoing studies are nearing completion, and top-line results (the initial, primary outcomes of a study) are expected by the end of 2011 and in the first half of 2012. The safety data from these studies should provide valuable, additional safety data for the FDA to consider. ◆

FDA Approves Nuedexta to treat Pseudobulbar Affect (PBA)

On October 29, 2010, Avanir Pharmaceuticals, Inc. announced the approval of Nuedexta™ by the Food and Drug Administration (FDA) for the treatment of pseudobulbar affect (PBA) associated with certain neurological conditions, including MS. PBA is characterized by uncontrolled, inappropriate, and/or exaggerated episodes of crying, laughing, or other emotional display. PBA occurs involuntarily with little or no stimulation to invoke such a response. It can greatly impact social situations and overall quality of life, both for the patient and his or her family.

Nuedexta is an oral drug in capsule form. Initially, a patient is given one capsule daily for the first seven days. Beginning on the eighth day, the medication is increased to the full dose of two capsules daily (one capsule every 12 hours). No one should take more than two capsules within a 24-hour period, and if a dose is missed, it will need to be skipped, as two doses should never be taken at the same time.

In studies with Nuedexta, episodes of excessive crying and laughing were significantly reduced in the treated group as compared to placebo, both in terms of frequency and severity. According to Avanir, the response to this drug is readily observable within a short time – often within the first week. In the most recent clinical trial (the STAR trial), about half of the patients with PBA

experienced a complete remission of this symptom by the end of the study while taking Nuedexta. Scores on a scale measuring emotional lability (the Center for Neurologic Study-Lability Scale [CNS-LS]) significantly decreased. The approval of Nuedexta comes after 10 years of research and development. ◆

MSAA Survey Reveals Surprising Results *(published online March 1, 2011)*

The Multiple Sclerosis Association of America (MSAA) conducted an independent, online survey of almost 20,000 of its members in the fall of 2010. The purpose of this survey was to better understand the extent and impact of pseudobulbar affect (PBA) among people living with MS. The results were surprising in both areas.

A total of 5,229 people completed the online survey. Of these respondents, 2,504 or 48 percent reported experiencing symptoms of PBA based on their answers to a scientifically developed measurement scale (the CNS-LS). This percentage is higher than the estimated 10 to 15 percent of the MS population that has been cited as potentially being affected by PBA. Of the 2,504 who reported behaviors (experiences) associated with PBA, 2,389 identified themselves as having MS and an additional 115 care partners or family members completed the survey on behalf of a person with MS.

Our results suggest that PBA might be more widespread in the MS population than was previously thought. Additionally, the frequency of these episodes and their impact on daily life were also considerable. ◆

Getting to Know Each Other

Ideally, MSAA would like to be on speaking terms with every donor who, by making a gift, has demonstrated an interest in our mission to help people with MS.

The reality is more fortunate than ideal. Each year tens of thousands of donors send voluntary gifts that support MSAA's programs and services. We need and value that support to ensure our mission is fulfilled without interruption or restriction. The volume is especially important because MSAA was built on – and thrives on – many gifts from many donors rather than sustaining grants or whopping gifts from a few. (Although luckily, we receive some larger gifts as well.) The result of so many smaller gifts is a collective mass of donors. Welcome as it is, this prevents us from getting to know individual donors as personally as we'd like.

So we remain curious about what attracts a donor to MSAA. If we could talk to every donor, we could learn whether a family member or a friend faces the challenges of this unpredictable disease. We could find out whether awareness of MS's devastating potential triggers compassion and motivates people to do their part in enriching the quality of life for others. We could also benefit from a dialogue with people whose lives may have been touched directly by MSAA and who contribute because they know about our services firsthand.

There's so much to know and limited time in a day to learn it. But we're trying!

Like the teacher in "The King and I," MSAA works harder and harder towards "getting to know you."

Each day, calls expressing gratitude go out to people whose continuing generosity has attracted our attention. We hope these calls will reveal some of the information described earlier. We also hope that these conversations will take us further towards building a genuine relationship with donors so we not only know why people make gifts, but also know the outcome they expect from their support. We hope that through such conversations, we can learn how we can meaningfully keep donors informed about the life-changing impact of all that MSAA does.

Relationships are what MSAA strives to have. Our name says we are an "Association," and we want donors to feel a part of the MSAA family, to be an active participant in a dialogue that can only make MSAA stronger and make us better stewards of a donor's gifts.

"Getting to know you" means using the telephone and sending personally written cards to say "thanks." So please don't be wary if someone calls and begins the conversation by saying, "I'm from MSAA." We are calling because we are proud and grateful to have you on our team. We hope you are also proud about your role in enriching the quality of life for individuals

The Need for Cooling Equipment

As spring approaches, the demand for MSAA's cooling equipment increases... markedly.

Cooling relieves heat-related fatigue that often prevents individuals with MS from participating in outdoor activities in warm weather. Its benefits go further than helping alleviate fatigue and other symptoms of overheating. Cooling also enriches family life by allowing someone affected by heat to attend picnics, sporting events, concerts, weddings, and other occasions that take place outdoors, warding off isolation that comes from "just not being able to go." Individuals benefit from being able to take walks or garden or just relax in the sunshine without having to worry about wilting in the heat.

Increased demand means increased inventory. The cooling vests and ice packs that do so much good cost MSAA about $126 per set. It would be great if interested donors pitched in to make sure supplies are plentiful. A gift of $126, or any contribution towards the cooling inventory would be greatly welcome, especially during this time of year.

Donors can send their tax-deductible gifts to **MSAA Cooling, 706 Haddonfield Road, Cherry Hill, NJ 08002** and make checks payable to "MSAA." These gifts will help make cooling a breeze.

affected by a chronic disease.

Hearing from donors on a regular basis would lead to the ideal we want to establish. Call me at **(800) 532-7667, extension 128**, or email me at **nzoren@msassociation.org** and tell me about your interest in MS and MSAA. Ask questions. We have answers, and we have so much to learn from each other.

Let's associate. Let's get to know each other better. The result will be a greater affinity with an organization you support and a better understanding about how MSAA uses your gifts to support a mission that directly benefited tens of thousands of people last year.

The true ideal is to tailor a program that lets each donor decide when and how to be asked for support. The resulting relationships would ensure that MSAA could be there as long as it's needed to enrich the safety, mobility, comfort, convenience, security, and dignity of everyone affected by MS.

Maybe if we start talking or writing to each other, the ideal could become a reality. I look forward to those calls and emails.

MSAA's $100,000 Online Challenge to Help Individuals with MS

So an idea is broached at a meeting, and everyone is intrigued.

The idea is to help MSAA expand its work by having a $100,000 online challenge on our website at **www.msassociation.org**, between now and June 30 when our 2011 fiscal year ends. While intriguing, we all wondered, could we reach a goal of $100,000 in time?

I believe that testing the waters is preferable to saying "no" to oneself. So, I'd like to propose the challenge to the readers of this column. More than 12,000 donors

receive our magazine, *The Motivator*. If each donor who receives this magazine went online and made a gift of $8.50, the $100,000 would be reached. Given that not everyone might venture online and perhaps some may miss this part of the article, gifts of two, three, or more times the amount ($17, $25.50, $34, etc.) will help take up the slack. And nothing stops our other readers from joining in!

What do you say? Shall we give it a go?

Please help me to get the ball rolling by going to **support.msassociation.org/nzf** and making a gift of $8.50 or more. If you are able, a gift of $85, which is ten times the initial amount, would really help us to reach our goal! I will get things started by making my own personal donation of $85. But please know that whatever amount you can give – whether large or small – will be of great help to support our urgent mission to enrich the quality of life for everyone affected by MS.

For anyone who prefers not to contribute online, payments may also be mailed to MSAA at 706 Haddonfield Road, Cherry Hill, NJ 08002. Gifts are also gratefully accepted over the phone at **(800) 532-7667, extension 128**.

Thank you so much! Your compassion and generosity are enormously appreciated by MSAA and members of the MS community. ◆

– Neal Zoren
MSAA Director of Development

THE PHILANTHROPY CIRCLE

The following thoughtful corporations and foundations have contributed generously to MSAA to help enrich the quality of life for everyone affected by multiple sclerosis. Organizations providing gifts of $10,000 or more are shown in this listing.

GUARANTORS *($500,000 and up)*
EMD Serono, Inc. and Pfizer Inc
Teva Neuroscience

CHAMPIONS *($100,000 to 499,999)*
Acorda Therapeutics
Bayer HealthCare Pharmaceuticals
Bayer USA Foundation
Biogen Idec
Genentech Foundation
Novartis Pharmaceuticals Corporation

VISIONARIES *($50,000 to $99,999)*
Genentech, Inc.

INNOVATORS *($25,000 to $49,999)*
Medtronic Foundation

ADVOCATES *($10,000 to $24,999)*
Avanir Pharmaceuticals
Catholic Human Services Foundation
The Chatlos Foundation
Grand Lodge Daughters of Scotia
The Ronda Gruber Foundation
The Virginia Dashiell Foundation

CRAFTS for Fun & Function

Written by Maryann B. Hunsberger

Spring is in the air! Without the threat of snow and ice, many people who might otherwise stay in the safety and comfort of their home may venture out for plenty of spring and summer events. These might include bridal showers and weddings, birthday and anniversary parties, spring and summer holidays, and any special occasion throughout the year.

With such events comes the need for gift-giving, which isn't so easy when counting pennies. A great solution is to create your own decorative packaging and gifts. This doesn't just save money, but also provides a fun activity for families and friends to do together. Husbands and wives, parents and children, or just a few good friends, can get together, socialize, and create a personalized work of art.

Gift Packaging

Karen Fennimore, a craft designer from Runnemede, New Jersey, suggested several craft projects that people with MS can do together with family and friends. One is decorating paper takeout boxes to use as small gift boxes. "These are sold in craft stores. Add stickers or sticky-backed rhinestones. Use markers to draw designs, or use stamps with stamp pads to create images. Ribbons can be tied on and curled with a dull knife or children's safety scissors. Make designs with glitter glue pens or sprinkle glitter over designs made from clear-drying white glue (note: tacky glue, which can be found in craft shops, and Elmer's glue, are both clear-drying white glues).

To add a gift tag, cut a small piece of cardstock paper with decorative scissors. These scissors have edges that cut paper into a range of designs. Punch a hole in the piece of cardstock, weave a ribbon through it, attach it to the box handle – and it's a gift tag."

People can also decorate plain gift bags or even brown paper bags. A fun way to enhance paper bags is to dip a slightly moistened sea sponge into washable paint and then lightly dab the paint onto the bag with the sponge to create a pattern. Allow to

dry and add sticky letters to spell the recipient's name. Various colors of tissue paper can be placed around the gift, with the top of the tissue papers peeking out from the opening of the bag. "There's no right or wrong way to stuff the tissue paper. Just do whatever you like," notes Fennimore.

A nice thing about creating gift bags – or any crafts mentioned in this article – is that they don't need to be perfect. People with fine-motor problems can create a design using puffy foam stickers, dimensional stickers, self-sticking letters or rubber stamps. Family members with steady hands can add to designs by filling in rubber-stamped images with markers. Projects needn't be expensive, as products can be found not only in craft shops, but also in dollar stores and discount chain stores.

Bookmarks, Greeting Cards, Scrapbooks, and More

As for gifts to slip into those bags, creating bookmarks is a great way to make a present. Craft these using the same supplies used to adorn the bag. Cut a sheet of cardstock paper into the shape and size of a bookmark with decorative or plain scissors. Add a sponge-painted design, stickers, rub-ons or self-sticking letters to personalize the bookmark.

Let's not forget the card! Begin with a folded piece of cardstock paper. Vellum paper (translucent paper that often has sayings on it) can be attached to the front with vellum tape (thin double-sided tape that is sticky on both sides). Some people like to attach pictures to the front of a card with paper fasteners (also called brads). "Brads come in all shapes and sizes, even holiday shapes. The brad shows through the corners of the pictures. This gives it a look like upholstery nails in a couch."

Those with fine-motor difficulties can decorate the card with the same tissue paper that fills the gift bag. Rip two or three sheets of different colored tissue paper into strips (neatness isn't important). Dip a paintbrush into glue water (three-quarters cup white glue to one-quarter cup water mixed together). Apply the glue water widely to one side of the tissue paper and stick it onto the

Fennimore decorated a plain green gift bag by adding self-sticking shapes, ribbon, cardstock paper and rub-ons. "Rub-ons are pages with various words, characters, flowers and shapes. You cut the shape from the piece of paper, rub it onto a piece of cardstock using a Popsicle® stick, and the design shows on the paper." Fennimore cut cardstock paper with decorative scissors and glued it to the bag. She finished the project by slipping tissue paper into the bag.

card front in any design. Let dry. The finished product will look crinkly.

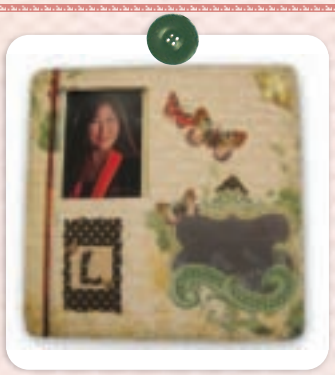
Bookmarks aren't the only presents that can be tucked into a gift bag. Friends and family can also create scrapbooks together and place them into an adorned brown grocery bag. Scrapbook kits – with decorative papers, letters and words – are available in craft shops and some discount chain stores. For a more personal touch, many options are available.

"Scrapbooking isn't just about pictures," says Fennimore. "It's about all the things you put around the picture to embellish it that relate to the picture. Start with a piece of colored cardstock paper. Attach your photo and then add any embellishments. Be sure to insert the decorated cardstock into a protective plastic page. The scrapbook will be thick, but most are. Use scrapbooks with adjustable hinges, as these can be made larger."

Some embellishments Fennimore suggests are as follows:

- **Attach dimensional paper flowers** with white glue.
- **Glue buttons with white glue**. "These can be found in the home or bought at the store. The coolest buttons are available in all sorts of shapes, patterns and colors that don't even look like buttons. With a silk or paper flower, you can glue a button on the middle to make a center."
- **Layer different colors of paper flowers** and attach it at the center with a brad.
- **Cut printed words** from magazines and affix with white glue.

The card Fennimore made was crafted from lavender cardstock paper. After folding it in half, she glued a smaller piece of pink cardstock paper across the middle with red cardstock below it. Above and below the pink cardstock, she glued ribbon. She applied six stickers and wrote with a marker. Inside, she used more cardstock paper and a marker. Stickers with preprinted words could be used in place of writing with a marker.



For this scrapbook page, Fennimore cut a rectangle in a sheet of decorative cardstock paper. Using white glue, she fastened a picture onto a piece of ivory linen paper and glued it to the back of the cardstock. She cut a piece of a different cardstock paper with decorative scissors and glued a precut decorative letter to it. She fastened the letter to the cardstock with metal brads, added a metal charm and a metal page corner with a low-temperature hot-glue gun, and glued on thin ribbon fibers.

- **Square alphabet beads** used to make children's name bracelets can be used to spell out words. On a baby page, spell out the baby's name with these beads and attach with white glue.
- **Silk leaves in seasonal colors** can be glued onto a page to create a seasonal theme.
- **Premade gift tags** with sayings on them such as "Our Wedding" can be added.
- **Carefully glue old, inexpensive charms** from bracelets to the pages or cover of a scrapbook using a low-temperature hot glue gun. "We call these 'found objects' because people can often find them in their homes."
- **Use a hole-punch and weave a ribbon** through cardstock to use as a backing on a scrapbook page or on the cover.

Covers may be the most important aspect of a scrapbook. Some scrapbooks come with an opening on the cover that cardstock and pictures can be slipped into. "Use colored cardstock as a background, then place a cut

The Benefits of Occupational Therapy and Craft Making

Besides creating a lovely gift, making crafts with a group of friends helps people to develop friendships with a purpose. Kathy Zackowski, PhD, OTR, Assistant Professor at the Department of Physical Medicine and Rehabilitation, Kennedy Krieger Institute and Johns Hopkins School of Medicine, spoke with *The Motivator* about this. Zackowski, an occupational therapist (OT) who works solely with people who have MS, says making crafts gives people something in common to share. "This is more binding than casual friendships because you work toward the same goal. People can do this with many mediums, such as sewing, exercise, a book club or other activities. The social interaction is so important. Much evidence says this can help with healing in different ways."

Zackowski notes that making crafts can provide some similar benefits to those gained in occupational therapy (OT). "People can gain skills making crafts. It forces people to use their hands in detailed ways, which can help improve motor control. It is huge in helping with eye-hand coordination, since our vision is critical in assuring that we don't hurt ourselves when we use our hands. It gives motivation to complete a task, which is a big deal. We need to be motivated to get out of bed sometimes, so completing tasks is important. Making crafts forces coordination between both hands. Creating crafts helps both gross- and fine-motor skills. For instance, using one's arms to hammer a nail into a board strengthens gross-motor skills, while weaving or drawing strengthens fine-motor skills. Cognitive skills are strengthened when figuring out how to create the craft."

Zackowski says she finds crafts useful for her own patients. "I can assign someone to make a craft at home to improve their motor skills. I am not aiming to teach anyone to be a professional craft person, but instead to help improve their eye-hand coordination. These

piece of themed cardstock at the bottom (such as one with a flowery design), and use other cardstock as frames around pictures. Use sticky shapes on corners of pictures as embellishments," says Fennimore.

For an especially finished look, Fennimore recommends the following: "Buy an inexpensive frame, discard the glass, take off the back of the frame and glue decorative cardstock in its place. Put a picture in the center and embellish with buttons, stickers, glitter glue and ribbons. Before putting the picture in the mat, put sticky dots under the picture to add dimension (small one-quarter inch-thick foam discs). Glue the frame onto the cover with white glue. It gives a shadowbox effect and makes a great gift for grandparents."

Mosaics are another fun craft to create. A mosaic starts with a piece of wood. Craft shops sell unfinished wooden plaques, mirrors, frames and jewelry boxes, as well as

kinds of skills help people do things they need to do in life, such as dressing or driving a car."

Occupational therapy can help many patients with MS to accomplish more. "Many tasks can become difficult for people with MS. An OT is trained to take a task and break it into smaller parts so people can adapt it. For example, if you are on one of the injectable disease-modifying therapies, it may be hard to give yourself an injection, so an OT can help design a method to make the process easier. An OT can also help you devise a strategy for taking your medicines at the right time. An OT can teach you ways to get exercise from working in the kitchen or around your home. Sometimes you need someone to look at the task and figure out how to make it work. The OT can teach you ways to address all of these issues in a practical way."

Zackowski says accommodations can help people with MS to create crafts. "You might have to modify instructions and learn to work within limitations. We all need to do this, even if our limitation is that we're not great at making crafts. Be sure to take advantage of technology to help with limitations. Use a pretty computer font to print words instead of writing words with a pen. Use software and a mouse to draw in place of drawing with a pencil if holding a pencil is difficult. Software is available to read directions out loud, and to increase font size to make reading instructions easier. Don't shy away from using technology to help you reach your goals.

"Neither physical nor cognitive limitations should stop you from enjoying fun activities. Making crafts can be a powerful, inexpensive way to give gifts or decorate your home in bad economic times. The pure enjoyment of doing something you like can't be understated. It makes us happy, and that's important to our quality of life."

tile pieces to apply to the wood. Fennimore uses tacky glue or ceramic glue to fasten the tile pieces to the wood. Using thick tacky glue mixed with sand as grout, she applies the grout with a Popsicle® stick, paintbrush or cake decorator. While still wet, she wipes excess grout with a damp cloth. "You don't need to be precise. Just get as much as possible into the space."

Note: Some Nicole Craft Products™ were used to make the crafts in the photos in this article. All products shown in the photos can be purchased at local craft stores. ◆

George Kaizar, founder of the Kaizar School of Art in Sewell, New Jersey, taught the author's daughter to make this mosaic. "You can be as abstract as you want, so it doesn't matter if someone can't be precise with their hands," says Kaizar. He says that even a piece of plywood can be the base and stones or shells work well in place of ceramic pieces. He affixes the objects onto the wood with epoxy glue, and then applies tile grout (the type that is premixed with sand) between the objects with a putty knife or cake decorator. "You can go over the pieces with a putty knife and then scrape off the excess."

PUSHING THROUGH

How I became inspired to work out at my own personal best – and discovering that my body strengthened with time

By Kristen Mishler

Over the past couple of years, I've become increasingly interested in physical fitness and health issues related to longevity. Last fall, while looking through some books online, I saw Jillian Michaels on the cover of her diet and fitness book, *Making the Cut*. Jillian is one of the trainers on the TV show, *The Biggest Loser*. The book's cover has Jillian posing in a tiny sports top and low-cut sweatpants, showing off her well-toned arms and stomach muscles. I said, "I want to look like that!" My son, who was looking on nearby said, "Gross!" …but I wasn't deterred.

I am not athletic at all, but I had been exercising regularly for about a year and a half prior to starting Jillian's fitness program. I started *Making the Cut* seven months ago – just a few weeks after finishing my first weight-training program. I work out at home and especially during my first time going through it, I really felt like being at home gave me an advantage. I know I didn't do a lot of the exercises with the "proper" form, but I did them the best I could.

I probably looked pretty silly doing just about every exercise, and that's why being alone helped me: there wasn't anyone to laugh at me or tell me I was doing it wrong. I didn't feel inadequate next to anyone else; I just did the best I could. Of course, for safety, you should always exercise with the approval of your doctor and have someone at home should you need assistance. But not having other, more able-bodied people exercising alongside allowed me to focus on my own way of getting into shape.

For instance, if I couldn't do a particular move, I modified it. I still use my bench press bar as a support when I have to do jumps or knee kicks. When a move requires me to jump from one spot to another, I often end up taking two or three (or four) small steps to reach the goal. If my legs won't move, they won't move. All I can do is push them.

My family thought my MS was in a full relapse for at least the first two weeks that I devoted to my newest workout routine. For several days I could hardly move and I was having obvious difficulty walking every day. But I wasn't incredibly sore. The reason for this, I believe, is that a few years ago I had an exacerbation in which I lost feeling in my legs. When the exacerbation ended and feeling returned (mostly), I could do absolutely anything with my legs and not be sore.

Nowadays, I normally do get sore if I push myself, but my lack of soreness harkened me back to that earlier time and made me think that, maybe, the difficulty walking and getting around wasn't an exacerbation; maybe it was how my body coped with physical stress rather than the normal way of getting sore. And this really made sense, considering that I walked much better on rest days than on exercise days. I convinced my family that it was just muscle fatigue that was causing my difficulty; and they trusted me.

By the fourth week of the program, you wouldn't even have known I was working out. I had no symptoms of muscle fatigue or stress. Even though the workouts were getting more and more difficult, I had built up enough resistance and tolerance to the physical stress that I no longer had MS-looking symptoms. I say "MS-looking" because I don't think my symptoms were actually *caused* by MS but, rather, because I *have* MS, my muscle fatigue showed up in forms that *looked* identical to an exacerbation of the disease. In addition, any side effects that I had previously experienced from my medication were gone! No headaches! No sweaty, sleepless nights! I felt incredible.

The before-and-after figures that I received from a local trainer revealed a drop in weight from 155 pounds to 148 pounds, and a drop in body fat from 26 percent to 22 percent. All that in just 30 days! I was very impressed. I don't look like Jillian Michaels, but I'm satisfied!

At one point during this exercise program, I talked to my doctor about my trouble getting around and the program itself, just to make sure I wasn't making things worse for myself. Her response seemed very caring, cautious, and typical: "You don't have to stop taking the stairs; just maybe, instead of walking the whole flight, do half of them and then take the elevator." In other words, "Don't stress yourself so much that you have to deal with MS-like symptoms."

But what I have found is different; this program has shown me that if I stress my body this time, the next time it is stronger and more capable of standing up against

stressors. If I'm completely exhausted after 20 minutes on the elliptical, that's okay. Either I keep doing 20 minutes every day, expecting to be exhausted every time and knowing that three weeks down the road, it will be easier; or, I knock it down to 10 or 15 minutes, bumping it back up to 20 in three weeks when I'm more capable. It's easy for me to say, "I can't do it." But that doesn't help me live a normal life with multiple sclerosis. In my own personal experience, I find that when I push myself physically, I get stronger and more capable; and that helps me live a better life.

At the beginning of most exercise programs, there's some sort of fitness test or assessment to make sure you're not overexerting yourself and that you have the correct level of workouts. Jillian Michaels' *Making the Cut* is a pretty intense workout and I wouldn't recommend it for everyone. I chose to do it for the challenge and because it was so exciting to realize that clumsy ol' me could be fit enough to do a workout as difficult as this one.

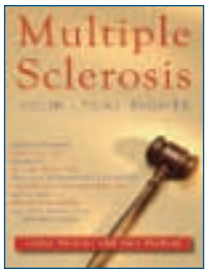
What I do recommend to everyone is to make a commitment to fitness, at whatever level is appropriate for you, to improve overall health. This might mean three minutes every morning and evening on the motor-driven exercise bike for a month, if that level is appropriate. By following a plan consistently, I predict that you will see improvement.

As you master each level of activity, you may be able to challenge yourself more and develop, or recover, even more strength and stamina. Whatever fitness level you're at, when you can consistently challenge yourself over a period of time, if you are like me, you will see improvement. This could be in coordination, in balance, or maybe in some other area. It has been revolutionary for me and I encourage you – under your doctor's supervision – to search out and find, through your personal experience, that you too are capable of pushing through! ◆

Editor's note: Our "Stories to Inspire" column showcases articles written by our readers, all of which have some type of inspiring message. While certain diet and exercise regimens are appropriate for some individuals, they may not be appropriate for others. Please consult a medical professional before making any changes to your diet, activity level, medications, or any other part of your normal routine.

Spread the Word

Multiple Sclerosis: Your Legal Rights



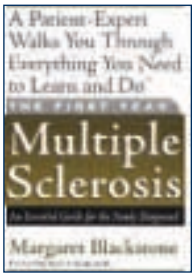
Written by Lanny E. Perkins, Esq. and Sara D. Perkins, Esq.
Published by Demos Health
MSAA Book #8

This legal reference explains many of the legislative changes which may be vital to individuals with MS. Among others, topics include: working with doctors and lawyers; employment, income, and taxes; disability benefits; insurance issues; travel and homeland security; family law; and choices with property and powers. Author Lanny Perkins is an attorney who has worked with many clients with MS, and co-author Sara Perkins is a retired attorney who has MS and continues as an active volunteer advising on legal issues and MS.

MSAA DVD Selections

For individuals without internet access, or for those who prefer to watch a video on DVD versus on a computer, several videos from MSAA's MSi DVD collection are available for loan through our Lending Library program. These videos take "a closer look at MS" and address such topics as: clinically isolated syndrome; employment; managing stress; complementary and alternative therapies; MS symptoms (including MS fatigue); the emotional impact of MS; the value of MRIs; disability benefits; home safety and accessibility; research; and treatment adherence. A full listing of videos (and books) available may be viewed online at **http://www.msassociation.org/Lending**

The First Year: Multiple Sclerosis: An Essential Guide for the Newly Diagnosed



Written by Margaret Blackstone
Foreword by Saud A. Sadiq, MD
Published by Marlowe & Company
MSAA Book # 243

Author Margaret Blackstone has written several books on a variety of medical topics. Diagnosed with MS in 2000, Blackstone has educated herself on virtually every aspect of her condition. In her book on the first year with MS, she provides a step-by-step guide for individuals who are newly diagnosed. Medical research, treatment options, alternative therapies, stress management and exercise, talking with others, and selecting the right medical team, are among the many subjects discussed in this important resource.

MSAA Lending Library

To borrow books featured in this column or any other book in MSAA's Lending Library, please send us your name and address. We will send you an application and a list of books for the Lending Library. MSAA and its clients greatly appreciate any donations made to help build the Lending Library. If you would like to donate a book to the Lending Library you need only send it to us at the address below. Please address all correspondence to:

MSAA Lending Library
706 Haddonfield Road
Cherry Hill, NJ 08002

(Please reference book number)

2011 MSAA *Art Showcase*

Jeanie Spradlin,
The Beautiful Red Cardinal

*MSAA is proud to present our **2011 Art Showcase** for and created by People Living with Multiple Sclerosis. The theme this year is **Inspiration – a reflection on what has been a positive inspiration in your life and experiences**.*

We received 70 works of art submitted by 29 artists living with MS throughout the country. We are delighted to be able to present to you this artwork and we hope that you too are inspired by this wonderful collection.

Each month we will highlight one artist and his or her work, so please be sure to visit often.

*Please go to **support.msassociation.org/artshowcase2011** to view this inspirational showcase. Enjoy!*

Get ready to create your best work for the 2012 Art Showcase! *Details for submitting artwork will be available this summer. Please watch for more information on our website at **www.msassociation.org**, or check your next issue of The Motivator.*

Multiple Sclerosis Association of America
706 Haddonfield Road
Cherry Hill, NJ 08002 USA

CHANGE SERVICE REQUESTED

Looking for a fun activity to plan with your kids this summer?

Make a *splash* with Swim for MS!

Swim for MS provides a unique volunteer fundraising opportunity that can turn a day at the pool into a meaningful way to help the MS community.

To learn more about this program and to see what other swimmers are planning, please visit **msassociation.org/swimforms** or call **(800) 532-7667, ext. 157**

SWIM FOR MS
ANY POOL, ANY TIME
MULTIPLE SCLEROSIS ASSOCIATION OF AMERICA