DOWNLOAD PDF DIAGNOSIS AND MANAGEMENT OF MULTIPLE SCLEROSIS

Chapter 1 : Current Strategies in the Treatment of Multiple Sclerosis

Instead, a diagnosis of multiple sclerosis often relies on ruling out other conditions that might produce similar signs and symptoms, known as a differential diagnosis. Your doctor is likely to start with a thorough medical history and examination.

Medications[edit] In interferon beta-1b was the first drug to ever be approved for MS, being soon followed by interferon beta-1a and glatiramer acetate. It is injected subcutaneously on a daily basis. Dimethyl fumarate is taken twice daily. This led the pharmaceutical to discontinue commercialization and withdraw all marketing applications. Side effects[edit] Injectable medications can produce irritation or bruises at injection site. The bruise depicted was produced by a subcutaneous injection. Irritation zone after injection of glatiramer acetate. Both the interferons and glatiramer acetate are available only in injectable forms, and both can cause skin reactions at the injection site, specially with subcutaneous administration. They are responsible of many of the symptoms of influenza infections, including fever , muscle aches , fatigue , and headaches. Careful adherence to the administration and monitoring guidelines is therefore essential; this includes obtaining an echocardiogram and a complete blood count before treatment to decide whether the therapy is suitable for the patient or the risks are too great. It is recommended that mitoxantrone be discontinued at the first signs of heart damage, infection or liver dysfunction during therapy. After a safety review the drug was returned to the market in as a monotherapy for MS under a special prescription program. Nevertheless, there have been reports of liver failure, and PML. During a CIS, there is a subacute attack suggestive of demyelination but the patient does not fulfill the criteria for diagnosis of multiple sclerosis. A wide range of medications have been used to try to slow the progression of the disease, with results that have been at best fair. Mitoxantrone has shown positive effects in people with a secondary progressive and progressive relapsing courses. It is moderately effective in reducing the progression of the disease and the frequency of relapses in people after two years. It is also not approved in Europe. Natalizumab has shown efficacy and has been approved for secondary progressive MS with relapses. Studies on the use of Interferon-beta-1b in secondary progressive and progressive relapsing MS do not support that it slows progression of the disease, although it is effective in reducing the number of relapses. There have been several trials investigating the efficacy of different drugs for PPMS without positive results. Drugs tested include interferon beta, mitoxantrone, glatiramer acetate or riluzole. As multiple sclerosis progresses, the symptoms tend to increase. The disease is associated with a variety of symptoms and functional deficits that result in a range of progressive impairments and handicap. Management of these deficits is therefore very important. Physical therapy[edit] Symptoms of MS that can be improved include fatigue , spasticity , depression , bladder dysfunction, and neurological symptoms. These symptoms can be improved by physical therapy and medication. Physical therapists can show strengthening exercises and ways to stretch; ultimately making daily tasks easier and reduces fatigue while muscle strength increases as flexibility increases. All symptoms are common amongst MS patients. Both drug therapy and neurorehabilitation have shown to ease the burden of some symptoms, even though neither influence disease progression. For other symptoms the efficacy of treatments is still very limited. Although there are relatively few studies of rehabilitation in MS, [52] [53] its general effectiveness, when conducted by a team of specialists, has been clearly demonstrated in other diseases such as stroke [54] or head trauma. The comprehensive rehabilitation process for patients with multiple sclerosis is generally managed by physiatrists. Allied treatments such as physiotherapy , [57] [58] speech and language therapy [59] or occupational therapy [60] can also help to manage some symptoms and maintain quality of life. Treatment of neuropsychiatric symptoms such as emotional distress and clinical depression should involve mental health professionals such as therapists , psychologists , and psychiatrists , [61] while neuropsychologists can help to evaluate and manage cognitive deficits. More specifically psychological interventions seem useful in the treatment of depression, while evidence on effectiveness for other uses such as the treatment of cognitive impairments or

vocational counseling is less strong. Robotic-assisted body weight-supported treadmill training may be an effective therapeutic option in MS patients with severe walking impairments. Care should be taken not to overheat a person with MS during the course of exercise. There is some evidence that cooling measures are effective in allowing a greater degree of exercise: These strategies are effective when attempting to decrease core temperature post-exercise, and as a method of pre-cooling prior to physical activity or heat exposure. These effects translate to reduced patient safety and performance of ADLs, however there are viable prevention strategies. Behavioral strategies to minimize heat exposure include performing outdoor physical activity when temperatures are cooler, or installing an air conditioner. Medical treatments for symptoms[edit] Further information: Multiple sclerosis signs and symptoms Multiple sclerosis can cause a variety of symptoms including changes in sensation hypoesthesia , muscle weakness, abnormal muscle spasms, impaired movement, difficulties with coordination and balance, problems in speech known as dysarthria or swallowing dysphagia , visual problems nystagmus , optic neuritis , or diplopia , fatigue and acute or chronic pain syndromes, bladder and bowel difficulties, cognitive impairment, or emotional symptoms mainly depression. At the same time for each symptom there are different treatment options. Treatments should therefore be individualized depending both on the patient and the physician. Symptomatology of the urinary tract is common in MS. The former is commonly related to inmobility or secondary effects from drugs used in the treatment of the disease. Cognitive impairment is a frequent complication of MS even after the introduction of disease-modifying treatments in the last 20 years. A speech and language therapist may give advice on specific swallowing techniques, on adapting food consistencies and dietary intake, on techniques to improve and maintain speech production and clarity, and on alternative communication approaches. This second system, although more invasive , has better results in the long term than nasogastric intake. There is some evidence indicating that sildenafil citrate may be a useful treatment. Fatigue is therefore a very difficult symptom to manage for which no drugs are recommended. Treatment will depend on cause. Chronic pain is very common and harder to treat as its most common cause is dysesthesias. Acute pain due to trigeminal neuralgia is usually successfully treated with anticonvulsants such as carbamazepine [] or phenytoin. It has been shown to increase walking speed, although its high cost over dollars a month limits its usage. Multiple sclerosis research Chemical structure of alemtuzumab Research directions on MS treatments include investigations of MS pathogenesis and heterogeneity; research of more effective, convenient, or tolerable new treatments for RRMS; creation of therapies for the progressive subtypes; neuroprotection strategies; and the search for effective symptomatic treatments. These drugs are expected to gain in popularity and frequency of use at the expense of previously existing therapies. Alemtuzumab , daclizumab and CD20 monoclonal antibodies such as rituximab , ocrelizumab and ofatumumab have all shown some benefit and are under study as potential treatments for MS. Nevertheless, there can also appear important drawbacks such as antagonizing mechanisms of action or potentiation of deleterious secondary effects. Many of the newest drugs as well as those under development are probably going to be evaluated as therapies for PPMS or SPMS, and their improved effectiveness when compared with previously existing drugs may eventually lead to a positive result in these groups of patients. The rationale behind the use of Vitamin D supplementation is that studies show an association between vitamin D deficiency and increasing progression of MS, as well as the anti-inflammatory effects of vitamin D.

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Chapter 2 : Multiple sclerosis - Symptoms and causes - Mayo Clinic

A handful of patience is worth more than a bushel of brains â€" Dutch proverb Controversy exists concerning almost every aspect of the diagnosis and management of multiple sclerosis (MS), the most common nontraumatic cause of neurologic disability in young adults.

A Review of Diagnosis and Management â€" Published on: Natalizumab is a humanized monoclonal antibody that antagonizes the alpha-4 integrin of the adhesion molecule very late in the activating antigen VLA -4 on leukocytes. The efficacy of natalizumab in patients with RRMS was established in 2 phase 3 pivotal trials. Serious hypersensitivity reactions have been reported in 1. Other adverse events including mild lymphocytosis and increased liver function have also been reported. Several months after the FDA approval of natalizumab, the product was withdrawn from the market because of 2 cases of PML. The product was later allowed back on the market in the United States, with the requirement that all patients and prescribers register with a mandatory REMS program Table 5. Alemtuzumab, a humanized monoclonal antibody, binds to the cell surface of CD52 on T and B lymphocytes, natural killer cells, monocytes, and macrophages. The efficacy of alemtuzumab was established in 2 phase 3 pivotal trials of alemtuzumab versus interferon beta 1-a, known as CARE-MS. MRI measures also proved superior with alemtuzumab versus interferon beta-1a SQ, as there were significantly fewer Gd-enhancing lesions, fewer new or enlarging T2 lesions, and less brain atrophy. Respiratory tract and urinary tract infections are the most common reported infections. There is also a small but serious risk of developing immune thrombocytopenia. Ocrelizumab is a humanized monoclonal antibody. Ocrelizumab is structurally similar to rituximab, a product commonly used off-label for the treatment of MS. The most common adverse events with ocrelizumab are infusion reactions and upper respiratory tract infections, which are generally mild to moderate in severity. Treatment with ocrelizumab also increases the risk of upper respiratory tract infections, lower respiratory tract infections, skin infections, and herpes-related infections. Because of the increased risk of infection, ocrelizumab is contraindicated in patients who are experiencing active hepatitis B infections and should be avoided in patients with active infections until the infection has resolved. There also appears to be an increased risk of breast cancer with ocrelizumab, based on the phase 3 clinical trials. PML and suicide have been reported in 1 patient each. Daclizumab is a humanized monoclonal antibody that targets CD25, a subunit of the human high-affinity IL-2 receptor. Targeting CD25 causes several immunological effects, including expansion of immunoregulatory CD56bright natural killer cells, inhibition of T-cell activation by dendritic cells, and reduction in lymphoid tissue inducer cells. The approval of daclizumab was supported by data from two phase 3 clinical trials. Among the most common adverse events with daclizumab are nasopharyngitis, upper respiratory tract infections, rash, influenza, dermatitis, oropharyngeal pain, bronchitis, eczema, and elevated liver function. Conclusions Since , the field of multiple sclerosis has been characterized by significant advances. Fourteen branded products, of varying levels of safety and efficacy, have been approved and are now routinely prescribed. Economics and cost-effectiveness of multiple sclerosis therapies in the USA. Doshi A, Chataway J. Multiple sclerosis, a treatable disease. Drugs approved for the treatment of multiple sclerosis: Expert Opin Drug Saf. Treating relapsingâ€"remitting multiple sclerosis: Asian Pac J Trop Biomed. Cleve Clin J Med. Gray matter damage in multiple sclerosis: Loma I, Heyman R. Safety concerns and risk management of multiple sclerosis therapies. Optimizing treatment success in multiple sclerosis. Biogen, Inc; March Mortality in multiple sclerosis: Psychopathology in multiple sclerosis: Ther Adv Neurol Disord. Common clinical and imaging conditions misdiagnosed as multiple sclerosis: Wu GF, Alvarez E. The immunopathophysiology of multiple sclerosis. Advances in imaging multiple sclerosis. Giorgio A, DeStefano N. Effective utilization of MRI in the diagnosis and management of multiple sclerosis. Recommended diagnostic criteria for multiple sclerosis: Diagnostic criteria for multiple sclerosis: Diagnosis of multiple sclerosis: Definition, prevalence and predictive factors of benign multiple sclerosis. Therapeutic strategies for relapsing-remitting multiple sclerosis: Diagnosis and

management of multiple sclerosis. Symptomatic therapy in multiple sclerosis: EMD Serono; November Biogen, Inc; July Teva Neuroscience, Inc; August Sandoz, Inc; April East Hanover, NJ; December Biogen, Inc; December Genzyme Corporation; November Biogen, Inc; August Genzyme Corporation; December South San Francisco, CA: Genentech, Inc; March Hospira, Inc; April Interferon beta-1b is effective in relapsing-remitting multiple sclerosis. MRI analysis results of a multicenter, randomized, double-blind, placebo-controlled trial. Intramuscular interferon beta-1a for disease progression in relapsing multiple sclerosis. Mechanism of action of glatiramer acetate in treatment of multiple sclerosis. Optimizing the initial choice and timing of therapy in relapsing-remitting multiple sclerosis. Rottlaender A, Kuerten S. Int J Mol Sci. Oral fingolimod or intramuscular interferon for relapsing multiple sclerosis. N Eng J Med. A placebo-controlled trial of oral fingolimod in relapsing multiple sclerosis. Progressive multifocal leukoencephalopathy information page. National Institutes of Health Website. Accessed February 6, Placebo-controlled phase 3 study of oral BG for relapsing multiple sclerosis [published correction appears in N Eng J Med. Placebo-controlled phase 3 study of oral BG or glatiramer acetate in multiple sclerosis. Randomized trial of oral teriflunomide for relapsing multiple sclerosis. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. Alemtuzumab verus interferon beta-1a as first-line treatment for patients with relapsing-remitting multiple sclerosis: Alemtuzumab for patients with relapsing multiple sclerosis after disease modifying therapy: Ocrelizumab versus interferon beta-1a in relapsing multiple sclerosis. Ocrelizumab versus placebo in primary progressive multiple sclerosis. Daclizumab HYP versus interferon beta-1a in relapsing multiple sclerosis.

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Chapter 3 : Multiple sclerosis - Diagnosis and treatment - Mayo Clinic

Diagnosis and Management of Multiple Sclerosis Out of Print--Limited Availability. Clinically focused text discusses diagnosis, timing of treatment initiation, and treatment regimen options.

October 1, Diagnostic Evaluation Establishing a definitive diagnosis is often difficult, with much uncertainty concerning prognosis once the diagnosis is made. Multiple sclerosis can be difficult to diagnose since its signs and symptoms may be similar to other medical problems. Medical organizations have created diagnostic criteria to ease and standardize the diagnostic process especially in the first stages of the disease. Historically, the Schumacher and Poser criteria were both popular. Currently, the Mc Donald criteria focus on a demonstration with clinical, laboratory and radiologic data of the dissemination of MS lesions in time and space for non-invasive MS diagnosis, though some have stated that the only proved diagnosis of MS is autopsy, or occasionally biopsy, where lesions typical of MS can be detected through histopathological techniques. Clinical data alone may be sufficient for a diagnosis of MS if an individual has suffered separate episodes of neurologic symptoms characteristic of MS. Since some people seek medical attention after only one attack, other testing may hasten and ease the diagnosis. The most commonly used diagnostic tools are neuroimaging, analysis of CSF and evoked potentials. MRI of the brain and spine shows areas of demyelination lesions or plaques. Contrast can be administered to highlight active plaques and, by elimination, demonstrate the existence of historical lesions not associated with symptoms at the moment of the evaluation. The nervous system of a person with MS responds less actively to stimulation of the optic nerve and sensory nerves due to demyelination of such pathways. These brain responses can be examined using visual and sensory evoked potentials. MRI scan of the spine are important to help diagnose and follow MS. Management MS treatment is dynamic and rapidly evolving, covering two main areas: Treatment is aimed at relieving symptoms and helping the patient function. However, a therapeutic relationship between the patient and nurse creates a critical and strong bond that is essential across the long trajectory of the illness. Although there is no known cure for multiple sclerosis, several therapies have proven helpful. As with any medical treatment, medications used in the management of MS have several adverse effects. Alternative treatments are pursued by some patients, despite the shortage of supporting, comparable, replicated scientific study. The treatment most commonly used to control exacerbations is I. Solu-Medrol ethylprednisolone is one of the most commonly used corticosteroids in MS. Disease-modifying treatments Disease-modifying treatments are expensive and most of these require frequent up-to-daily injections. Others require IV infusions at 1â€”3 month intervals. Current Disease-Modifying Drugs Corticosteroids or adrenocorticotropic hormone are used to decrease inflammation, shorten duration of relapse or exacerbation. Immunosuppressive agents may stabilize the course. Interferon beta-1a and interferon beta-1b are being used for treatment of rapidly progressing symptoms in some patients. Copolymer-1, a mixture of synthetic polypeptides composed of four amino acids, has been effective in reducing relapse rates and disability in patients with relapsing-remitting MS. Immunomodulator are used in relapsing-remitting disease. Mitoxantrone Novantrone , a chemotherapeutic agent used for the treatment of secondary chronic progressive, progressive relapsing, or worsening relapsing-remitting Multiple sclerosis to reduce neurologic disability and frequency of clinical relapses. After this approval, there are six disease-modifying treatments for MS approved by regulatory agencies of various countries, being the other five: A third medication is glatiramer acetate, a non-interferon, non-steroidal immunomodulator. The fourth medication, mitoxantrone, is an immunosuppressant also used in cancer chemotherapy. The fifth is a humanized monoclonal antibody immunomodulator, natalizumab. The interferons and glatiramer acetate are delivered by frequent injections, varying from once-per-day for glatiramer acetate to once-per-week but intra-muscular for Avonex, Natalizumab and mitoxantrone are given by IV infusion at monthly intervals. All six kinds of medications are modestly effective at decreasing the number of attacks in relapsing-remitting MS RRMS while the capacity of interferons and glatiramer acetate is more controversial.

Studies of their long-term effects are still lacking. Comparisons between immunomodulators all but mitoxantrone show that the most effective is natalizumab, both in terms of relapse rate reduction and halting disability progression. Mitoxantrone may be the most effective of them all; however, it is generally not considered as a long-term therapy, as its use is limited by severe secondary effects. Treatment with interferons during an initial attack can decrease the chance that a patient will develop clinical MS. Treatment of progressive MS is more difficult than relapsing-remitting MS. Mitoxantrone has shown positive effects in patients with secondary progressive and progressive relapsing courses. It is moderately effective in reducing the progression of the disease and the frequency of relapses in patients in short-term follow-up. No treatment has been proven to modify the course of primary progressive MS. As with many medical treatments, these treatments have several adverse effects. One of the most common is irritation at the injection site for glatiramer acetate and the interferon treatments. Over time, a visible dent at the injection site, due to the local destruction of fat tissue, known as lipoatrophy, may develop. Interferons produce symptoms similar to influenza; some patients taking glatiramer experience a post-injection reaction manifested by flushing, chest tightness, heart palpitations, breathlessness, and anxiety, which usually lasts less than thirty minutes. Under the direction of a physiotherapist, participation in physical activity can be safe and has been proven beneficial for patients with MS. Research has supported the rehabilitative role of physical activity in improving muscle power, mobility, mood, bowel health, general conditioning and quality of life. However, it is important to be cautious about not overworking or overheating the patient during the course of exercise. Physiotherapists have the expertise needed to adequately prescribe exercise programs that are suitable for the individual. Determining an appropriate and safe exercise program is challenging and must be carefully individualized to each patient being sure to account for all contraindications and precautions. Medicines to reduce muscle spasms such as Lioresal Baclofen , tizanidine Zanaflex , or a benzodiazepine Cholinergic medications to reduce urinary problems Antidepressants for mood or behavior symptoms Amantadine for fatigue The following may also be helpful for people with MS Physical therapy, speech therapy, occupational therapy, and support groups Assistive devices, such as wheelchairs, bed lifts, shower chairs, walkers, and wall bars A planned exercise program early in the course of the disorder A healthy lifestyle, with good nutrition and enough rest and relaxation Avoiding fatigue, stress, temperature extremes, and illness Changes in what patient eat or drink if there are swallowing problems Making changes around the home to prevent falls and ease in moving around Social workers or other counseling services to help you cope with the disorder and get assistance such as Meals-on-Wheels Part1 Part2 Part3 Part4 Part5 Amanda Johnson Dr. Amanda Johnson is a senior nursing professional in a tertiary level health care institute.

Chapter 4 : Multiple Sclerosis

Introduction. Multiple sclerosis (MS) is the immune-mediated demyelinated disease of the human-beings that mostly entangle young adults. Nevertheless, children MS estimated to be 10% of all cases.

Headache, influenza, diarrhea, back pain, liver transaminase elevations, and cough 1. Targets the sphingosinephosphate receptor that is necessary for lymphocyte egress from lymph nodes 2. Interferon beta lNFB Previous studies suggested that INFB is able to effect on MS through inhibition of proinflammatory cytokines, induction of anti-inflammatory mediators, reduction of cellular migration and inhibition of autoreactive T cells Side effects of INFB have been reported as: Liver function tests LFTs in younger children taking interferon obviously showed abnormality Glatiramer acetate GA Glatiramer acetate is a heterogenous mixture ofsynthetic polypeptides consisting of four amino acids L-alanine, L-glutamic acid, L-lysine, L-tyrosine found in myelin basic protein. Role of GA is to act as human myelin basic protein, activate myelin specific response of suppressor T lymphocytes and inhibit specific T lymphocytes. The safety and well toleration of drug in pediatric MS patients is reported 14 , Three retrospective studies have been published assessing the efficacy of GA in pediatrics 16 , 24 , 25 Table 2. Headache, transient elevation of the liver enzymes, leucopenia, anemia, thrombocytopenia, and thyroid dysfunction require monitoring during the process of treatment with IFN. These side effects are diminished usually by reduction of drug dosage. Exacerbation of depression symptoms by IFN should be mentioned in depressed patients and thus it is better to avoid IFN usage in these patients. GA Most common side effects is pain and indurations at the site of injection and transient systemic reactions Transient skin retraction at the injection site as well as chest pain and flushing are complications happening immediately after the injection 21 , 24 Table 2. Treatment in condition of exacerbation Methyl Prednisolone pulse Methyl prednisolon is an important drug in treatment of MS, especially in the acute phase of relapse. Decreasing the inflammatory process done through different pathways: Exacerbations in children have not been carried out yet, as far as we know. Thus, treatment for acute MS in the pediatric is extremely based on adult treatment. Notably, not all children who experience acute, receive treatment. Supportive care may be recommended by some physicians if clinical manifestations are mild and do not lead to disability 28 Table 2. Plasmapheresie Plasma exchange PE is an efficient therapy for severe relapses of acute inflammatory CNS demyelinating diseases in adults. Therapeutic plasma exchange TPE has been useful in the treatment of several pediatric diseases. However, the safety and efficacy of this management in pediatric patients need to be more developed 31 Table 2. Therapy evaluation The patients follow up should be done within 1, 3 and 6 month after therapy and then every 6 month. Efficacy of treatment was evaluated by following the patients in mentioned time and performing the neurological examination. MRI scan should be repeated yearly in patients with stable condition If serious side effects are appearing or when side effects are not tolerated by patients and leading to reduced compliance, alteration in treatment is necessary. Furthermore, when the therapy is not as effective as expectation, drug choice should be changed. Yet, nostudies or suggestion for pediatric MS are available to guide the decision if therapy should be changed or not 6. No overlap or time delay between discontinuing the first drug and initiation of second one is acceptable. Dosage of INFB should be gradually increased as it introduced first as described above. Supporting the suboptimal response to DMT is based on the above mentioned suggestion and needs at least 6 month time after the starting the treatment. However, individual decision for each patients must be taken as there is not follow a strict algorithm Second-line therapies Therapy failure is a concern in the pediatric MS individuals. Failure in treatment is defined differently with a high controversy among physicians treating adult-onset MS. Noncompliance and intolerable side effects were observed in a notable percentage of these patients. Yet, there is not any approved algorithm for the treatment of partial responsiveness, natalizamab, cyclophosphamide, mitoxantrone, and rituximab are the immunomodulatory and cytotoxic agents reported in pediatric MS patients resistant to therapy Escalation therapy Cyclophosphamide, mycophenolatemofetil,

daclizumab, mitoxantrone, rituximab and natalizumab have been used in pediatric MS patients 35 - However, their prescription in children has not been suggested yet. Natalizumab Natalizumab is a humanized monoclonal antibody that targets the a4 subunit of a4b1 and 4b7 integrins, molecules involved in the transmigration of immunecells into the CNS In only one pediatric study performed in Italy, natalizumab mg, every 28 days was used in 19 children with severe active MS. After month follow up relapses and MRI lesions suppressed in all patients and no serious side effects were reported In Portugal, cases were enrolled in natalizumab therapy and treatment with natalizumab was more effective in patients with less disability and without prior disease modifying therapy However, natalizumab is not approved for patients less than 18 yr old and in some cases leads to progressive multifocal leukoencephalopathy PML. Thus, natalizumab therapy must be restricted to specialized centers 6 , 35 , 37 , 40 , 42 Table 2. Cyclophosphamide Cyclophophamide has not been approved for the treatment of MS. But, prescription of pulse cyclophosphamide decrease disease activity in adult MS patients 43 , In a retrospective study, 17 children aged 9 to 18 yr were treated with cyclophosphamide at either pulse or induction therapy most of the cases indicated improvement of relapse frequency and EDSS 1 yr after the initiation of cyclophosphamide therapy 37 Table 2. Rituximab Rituximab is not accepted for the treatment of MS, but positive effects has been indicated in adult RRMS that showed noticeable decrease of brain lesions and clinical relapses. A recent study assesses 8 pediatric neuromyelitisoptica and 3 MS patients and reported that the use of rituximab in our pediatric neuromyelitisoptica and multiple sclerosis cohort was overall safe and effective 45 - 48 Table 2. Daclizumab Intravenous daclizumab, has been used off-label in adult MS patients 49 - 52 and another subcutaneous form is being tested in clinical trials in adult MS. Recently, a study assessed the efficacy intravenousdaclizumab in 7 pediatric MS patients treated largely in combination with beta interferons. This study indicated that treatment with daclizumab was in association with reductions in ARR, number of contrast enhancing lesions, and reduction or stabilization of EDSS in each patient. However, 4 patients had relapses and new contrast enhancing lesions during daclizumab treatment 53 Table 2. Hypersensitivity reactions and development of antibody to the drug. The most important side effect is a 1: Side effects of cyclophosphamide include vomiting, transient alopecia, osteoporosis, and amenorrhea. Development of bladder carcinoma has been seen in one patients that was successfully treated 57 , Probable side effect of rituximab is development of PML and other severe infection 50 - 52 Daclizumab: Elevated liver function tests, infections, psoriasis and oral ulcers are adverse effects related to intravenous daclizumab treatment 50 - 53 , 59 , 60 Table 2. Oral agents Fingolimod, and cladribine for adult MS patients, influence the lymphocytes by various mechanisms. Yet, no study about usage of these two oral agents in pediatric MS patients has been published. However, negative effects founded in association with these agents in adult MS patients, consisting of cancer and lethal herpetic infections. Thus, adopting these therapies in pediatric population requires serious attention 61 - Fingolimod Fingolimod is an orally administered small molecule that targets the sphingosinephosphate receptor that is necessary for lymphocyte egress from lymph nodes. Fingolimod was approved for adult patients with MS. No information currently exists about fingolimod with regard to safety, tolerability and dosage in children 62 , 64 - 66 Table 2. In conclusion, Children appear to accrue locomotor disability more slowly, but they can have significant cognitive deficits, even early on in the course of the disease. There have been no randomized-controlled studies of disease-modifying therapies. However, firstline therapies, beta interferon, and glatiramer acetate are extensively used off-label. Therapies in pediatric MS are being developed and may be implemented in the next few years. Acknowledgements We wish to thank Dr, FarzanehNajafi, for her valuable assistances. Author Contribution Mohammad Amin Najafi: Study concept and design, Development of original idea, writing the manuscript, collecting data and Statistical analysis, Final approval of the version Dr. Study concept, Development of original idea, edition of manuscript, Final approval of the version Zahra Nasr: Conflict of Interest None declared References 1. Inaloo S, Haghbin S. Multiple sclerosis in children. Iran J Child Neurol. CD24 gene allele variation is not associated with oligoclonalIgG bands and IgG index of multiple sclerosis patients. Multiple Sclerosis in Children. MS disease-modifying therapies in children.

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Natalizumab therapy for highly active pediatric multiple sclerosis. Magnetic resonance imaging characteristics of children and adults with paediatric-onset multiple sclerosis. Recommended diagnostic criteria for multiple sclerosis: Diagnostic criteria for multiple sclerosis: International Pediatric Multiple Sclerosis Study Group criteria for pediatric multiple sclerosis and immune-mediated central nervous system demyelinating disorders: Consensus definitions proposed for pediatric multiple sclerosis and related disorders. Cognitive and psychosocial features of childhood and juvenile MS. Disease-modifying drugs in childhood-juvenile multiple sclerosis: Effectiveness of early beta interferon on the first attack after confirmed multiple sclerosis: MRI in the diagnosis of pediatric multiple sclerosis. Intramuscular interferon beta-1a for disease progression in relapsing multiple sclerosis. Treatment of early onset multiple sclerosis with subcutaneous interferon beta-1a. Safety and tolerability of interferon beta-1b in pediatric multiple sclerosis. Interferon beta-1a treatment in childhood and juvenile-onset multiple sclerosis. Treatment of pediatric multiple sclerosis and variants. Glatiramer acetate treatment in patients with childhood and juvenile onset multiple sclerosis. Immunomodulatory treatment of early onset multiple sclerosis:

Chapter 5 : Diagnosis of multiple sclerosis - Wikipedia

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Problems with bowel and bladder function When to see a doctor See a doctor if you experience any of the above symptoms for unknown reasons. Disease course Most people with MS have a relapsing-remitting disease course. They experience periods of new symptoms or relapses that develop over days or weeks and usually improve partially or completely. These relapses are followed by quiet periods of disease remission that can last months or even years. About 60 to 70 percent of people with relapsing-remitting MS eventually develop a steady progression of symptoms, with or without periods of remission, known as secondary-progressive MS. The worsening of symptoms usually includes problems with mobility and gait. The rate of disease progression varies greatly among people with secondary-progressive MS. Some people with MS experience a gradual onset and steady progression of signs and symptoms without any relapses. This is known as primary-progressive MS. In the case of MS, this immune system malfunction destroys myelin the fatty substance that coats and protects nerve fibers in the brain and spinal cord. Myelin can be compared to the insulation coating on electrical wires. When the protective myelin is damaged and nerve fiber is exposed, the messages that travel along that nerve may be slowed or blocked. The nerve may also become damaged itself. A combination of genetics and environmental factors appears to be responsible. Risk factors These factors may increase your risk of developing multiple sclerosis: MS can occur at any age, but most commonly affects people between the ages of 15 and Women are about twice as likely as men are to develop MS. If one of your parents or siblings has had MS, you are at higher risk of developing the disease. A variety of viruses have been linked to MS, including Epstein-Barr, the virus that causes infectious mononucleosis. White people, particularly those of Northern European descent, are at highest risk of developing MS. People of Asian, African or Native American descent have the lowest risk. MS is far more common in countries with temperate climates, including Canada, the northern United States, New Zealand, southeastern Australia and Europe. You have a slightly higher risk of developing MS if you have thyroid disease, type 1 diabetes or inflammatory bowel disease. Smokers who experience an initial event of symptoms that may signal MS are more likely than nonsmokers to develop a second event that confirms relapsing-remitting MS. Complications People with multiple sclerosis also may develop: Muscle stiffness or spasms Paralysis, typically in the legs Problems with bladder, bowel or sexual function Mental changes, such as forgetfulness or mood swings Depression.

Chapter 6 : Management of multiple sclerosis - Wikipedia

In the above transmission electron micrograph, a myelin sheath surrounds a neuronal axon. Multiple sclerosis (MS) is a chronic, immune-mediated disease of the central nervous system (CNS) that is characterized pathologically by inflammation, demyelination, and, ultimately, axonal loss.

Identify and address contributing MS symptoms i. Healthy Lifestyle and Wellness In addition to conventional pharmacologic therapy, there is growing interest in the use of lifestyle strategies to support wellness and mitigate disease-related outcomes in MS. This interest is based on a growing appreciation of the role of certain comorbidities and lifestyle factors on disease activity, disability, mortality, and overall quality of life. For example, key observational studies suggest an association between vascular comorbidities eg, hypertension, hyperlipidemia, and type 2 diabetes and an increased risk of disability and mortality. Outcomes MS is a heterogeneous disease with a variable clinical course. Patients can progress rapidly over several years to significant disability or may have a few relapses and then remain clinically stable for many decades. The accumulation of disability in MS is slower than previously thought and varies widely between individuals. Early studies reported a relatively quick progression from disease onset to walking with a cane, with a median time of about 15 years. Likewise, in PPMS, early studies reported short median time from disease onset to cane of less than 10 years, whereas more current studies showed that median time is closer to 15 years. It is difficult to predict which patients will progress and which patients will remain relatively stable over time. Although there are clearly patients in whom the disease remains relatively mild, it is very difficult to predict which patients will eventually follow this course. There are several prognostic factors for unfavorable clinical outcomes. Older age at onset, Black race, Hispanic ethnicity, and initial symptoms involving cerebellar, spinal cord or pyramidal systems, and higher initial clinical activity eg, high attack frequency and increased disability progression in the first 5 years are all unfavorable prognostic factors. Prognostic radiologic measures include brain and spinal cord atrophy and number of GdE lesions. In general, DMTs are not recommended during pregnancy, so efficient family planning with the help of the obstetrician can help minimize the amount of time the patient is off DMT. Pregnancy during MS is associated with a decreased incidence of relapses, but there is a rebound in relapse frequency in the postpartum period. A mid-pregnancy visit with the treating neurologist is recommended for postpartum planning. It is also generally recommended that patients who were previously treated with DMT prior to pregnancy resume treatment immediately postpartum unless they plan to breastfeed. If breastfeeding is pursued, cranial MRI 2 months after delivery for disease surveillance is appropriate. If there is evidence of active disease, the benefits of breastfeeding should be balanced with the need to resume DMT. Unfortunately, no DMT is proven to be safe during pregnancy or while breastfeeding, and so they are generally not recommended. The potential impact of brief exposures to DMTs ie, during the first few weeks of pregnancy, before pregnancy is recognized is relatively unknown, but appears to be minimal. Accordingly, although women who become pregnant while taking DMTs are generally recommended to discontinue DMTs, they can be reassured that the potential impact on their pregnancy is very low. As stated above, teriflunomide is pregnancy category X and should not be used in women of childbearing potential without effective contraception and counseling. Vaccines and MS The effect of vaccines on MS has been studied very carefully and there appears to be no adverse effect of vaccines on the course of disease. Inactivated vaccines are generally preferred, including in patients taking DMTs. Live attenuated vaccines are generally not recommended for a person with MS because of their theoretical ability to stimulate MS inflammation, although there is no compelling evidence showing an increased risk in the MS population of live attenuated vaccines at this time. Back to Top Summary Multiple sclerosis MS is a chronic inflammatory, demyelinating, and neurodegenerative disorder affecting the brain, optic nerve, and spinal cord. Symptoms of MS can involve almost any neurologic function; therefore, accurate diagnosis relies on a combination of clinical history, neurological examination, and paraclinical testing such as magnetic resonance imaging MRI

and sometimes cerebrospinal fluid analysis. The McDonald Criteria simplify the diagnostic process, while preserving high sensitivity and specificity, and allowing early diagnosis of MS and prompt treatment. They decrease the clinical episodes of inflammation, new MRI lesions, and slow the progression of disability. However, the benefit of ocrelizumab on the underlying progressive aspects of PPMS appears to be limited. Despite emerging neurotherapeutics for progressive MS, early diagnosis and treatment are still key in preventing central nervous system inflammation and forestalling progressive disability related to neurodegeneration. Symptom management and healthy lifestyle strategies are important complementary approaches for better outcomes and quality of life for patients with MS. The burden of neurological disease in the United States: A summary report and call to action. Ann Neurol ; Natural history of multiple sclerosis. Ann Neurol ; 36 Suppl: The natural history of primary progressive multiple sclerosis. The natural history of multiple sclerosis: The clinical features and natural history of primary progressive multiple sclerosis. Multiple sclerosis prevalence in the United States commercially insured population. MS International Federation website. Updated March 14 Accessed April 2, Semin Neurol ; Pathological mechanisms in progressive multiple sclerosis. Lancet Neurol ; Iron and neurodegeneration in the multiple sclerosis brain. Inflammatory cortical demyelination in early multiple sclerosis. N Eng J Med ; Axonal transection in the lesions of multiple sclerosis. N Engl J Med ; Premyelinating oligodendrocytes in chronic lesions of multiple sclerosis. Cleve Clin J of Med, ; Problems of experimental trials of therapy in multiple sclerosis: Ann N Y Acad Sci ; Recommended diagnostic criteria for multiple sclerosis: Diagnosis of multiple sclerosis: MRI criteria for the diagnosis of multiple sclerosis: Defining the clinical course of multiple sclerosis: A double-blind controlled trial of high dose methylprednisolone in patients with multiple sclerosis: J Neurol Neurosurg Psychiatry ; Double-blind, randomized, placebo-controlled study of oral, high-dose methylprednisolone in attacks of MS. Oh J, Calabresi PA. Disease-modifying therapies in relapsing multiple sclerosis. Multiple Sclerosis and Related Disorders: Intramuscular interferon beta-1a for disease progression in relapsing multiple sclerosis. Copolymer 1 reduces relapse rate and improves disability in relapsing-remitting multiple sclerosis: Interferon beta-1b in the treatment of multiple sclerosis: Daclizumab HYP versus interferon beta-1a in relapsing multiple sclerosis. Restrictions of use of Zinbryta daclizumab in view of fatal fulminant liver failure. Biogen Health Products Regulatory Authority website. Published July 11, Accessed March 9, A placebo-controlled trial of oral fingolimod in relapsing multiple sclerosis. Oral fingolimod or intramuscular interferon for relapsing multiple sclerosis. Classifying PML risk with disease modifying therpaties. Mult Scler Relat Disord ; Inhibition of dihydroorotate dehydrogenase by the immunosuppressive agent leflunomide. Biochem Pharmacol ; J Immunol ; Randomized trial of oral teriflunomide for relapsing multiple sclerosis. Teriflunomide versus subcutaneous interferon beta-1a in patients with relapsing multiple sclerosis: Mult Scler ; Fumaric acid esters exert neuroprotective effects in neuroinflammation via activation of the Nrf2 antioxidant pathway. J Dtsch Dermatol Ges ; 7: Placebo-controlled phase 3 study of oral BG for relapsing multiple sclerosis. Placebo-controlled phase 3 study of oral BG or glatiramer in multiple sclerosis. Ontaneda D, Fox RJ. Emerging therapies for relapsing multiple sclerosis. Natalizumab plus interferon beta-1a for relapsing multiple sclerosis. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. Risk stratification for progressive multifocal leukoencephalopathy in patients treated with natalizumab. Risk of natalizumab-associated progressive multifocal leukoencephalopathy. Evaluation of patients treated with natalizumab for progressive multifocal leukoencephalopathy. Reassessing the risk of natalizumab-associated PML. J Neurovirol ;

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Chapter 7 : Multiple Sclerosis | Mercy Health

Diagnosis. Since the early s the Poser criteria was used to classify multiple sclerosis. This relied on evidence of at least two relapses typical of multiple sclerosis and evidence of involvement of white matter in more than one site in the central nervous system, the concept of "lesions scattered in time and space.".

Diagnosis A complete neurological exam and medical history are needed to diagnose MS. There are no specific tests for MS. Instead, a diagnosis of multiple sclerosis often relies on ruling out other conditions that might produce similar signs and symptoms, known as a differential diagnosis. Your doctor is likely to start with a thorough medical history and examination. Your doctor may then recommend: Lumbar puncture spinal tap Lumbar puncture spinal tap During a lumbar puncture spinal tap procedure, you typically lie on your side with your knees drawn up to your chest. Then a needle is inserted into your spinal canal â€" in your lower back â€" to collect cerebrospinal fluid for testing. Blood tests, to help rule out other diseases with symptoms similar to MS. Tests to check for specific biomarkers associated with MS are currently under development and may also aid in diagnosing the disease. Lumbar puncture spinal tap , in which a small sample of fluid is removed from your spinal canal for laboratory analysis. This sample can show abnormalities in antibodies that are associated with MS. Spinal tap can also help rule out infections and other conditions with symptoms similar to MS. MRI, which can reveal areas of MS lesions on your brain and spinal cord. You may receive an intravenous injection of a contrast material to highlight lesions that indicate your disease is in an active phase. Evoked potential tests, which record the electrical signals produced by your nervous system in response to stimuli. An evoked potential test may use visual stimuli or electrical stimuli, in which you watch a moving visual pattern, or short electrical impulses are applied to nerves in your legs or arms. Electrodes measure how quickly the information travels down your nerve pathways. In most people with relapsing-remitting MS, the diagnosis is fairly straightforward and based on a pattern of symptoms consistent with the disease and confirmed by brain imaging scans, such as MRI. Diagnosing MS can be more difficult in persons with unusual symptoms or progressive disease. In these cases, further testing with spinal fluid analysis, evoked potentials and additional imaging may be needed. Brain MRI is often used to help diagnose multiple sclerosis Dr. Mark Keegan explains the diagnosis and treatment of multiple sclerosis Treatment There is no cure for multiple sclerosis. Treatment typically focuses on speeding recovery from attacks, slowing the progression of the disease and managing MS symptoms. Some people have such mild symptoms that no treatment is necessary. Multiple sclerosis research laboratory Treatments for MS attacks Corticosteroids, such as oral prednisone and intravenous methylprednisolone, are prescribed to reduce nerve inflammation. Side effects may include insomnia, increased blood pressure, mood swings and fluid retention. The liquid portion of part of your blood plasma is removed and separated from your blood cells. The blood cells are then mixed with a protein solution albumin and put back into your body. It slows worsening of disability in people with this type of MS. For relapsing-remitting MS, several disease-modifying therapies are available. Much of the immune response associated with MS occurs in the early stages of the disease. Aggressive treatment with these medications as early as possible can lower the relapse rate and slow the formation of new lesions. Many of the disease-modifying therapies used to treat MS carry significant health risks. Selecting the right therapy for you will depend on careful consideration of many factors, including duration and severity of disease, effectiveness of previous MS treatments, other health issues, cost, and child-bearing status. Treatment options for relapsing-remitting MS include: These medications are among the most commonly prescribed medications to treat MS. They are injected under the skin or into muscle and can reduce the frequency and severity of relapses. Side effects of beta interferons may include flu-like symptoms and injection-site reactions. People taking interferons may develop neutralizing antibodies that can reduce drug effectiveness. This humanized immunoglobulin antibody medication is the only DMT approved by the FDA to treat both the relapse-remitting and primary progressive forms of MS. Clinical trials showed it reduced relapse rate in

relapsing disease and slowed worsening of disability in both forms of the disease. Ocrevus is given via an intravenous infusion by a medical professional. Side effects may infusion-related reactions including irritation at the injection site, low blood pressure, fever, and nausea among others. Ocrevus may also increase the risk of some types of cancer, particularly breast cancer. Side effects may include skin irritation at the injection site. This twice-daily oral medication can reduce relapses. Side effects may include flushing, diarrhea, nausea and lowered white blood cell count. This once-daily oral medication reduces relapse rate. Other side effects include headache, high blood pressure and blurred vision. This once-daily medication can reduce relapse rate. Teriflunomide can cause liver damage, hair loss and other side effects. It is harmful to a developing fetus and should not be used by women who may become pregnant and are not using appropriate contraception, or their male partner. This medication is designed to block the movement of potentially damaging immune cells from your bloodstream to your brain and spinal cord. It may be considered a first line treatment for some people with severe MS or as a second line treatment in others. This medication increases the risk of a viral infection of the brain called progressive multifocal leukoencephalopathy in some people. This drug helps reduce relapses of MS by targeting a protein on the surface of immune cells and depleting white blood cells. This effect can limit potential nerve damage caused by the white blood cells, but it also increases the risk of infections and autoimmune disorders. Treatment with alemtuzumab involves five consecutive days of drug infusions followed by another three days of infusions a year later. Infusion reactions are common with alemtuzumab. The drug is only available from registered providers, and people treated with the drug must be registered in a special drug safety monitoring program. This immunosuppressant drug can be harmful to the heart and is associated with development of blood cancers. As a result, its use in treating MS is extremely limited. Mitoxantrone is usually used only to treat severe, advanced MS. Treatments for MS signs and symptoms Physical therapy session Physical therapy session Physical therapy can build muscle strength and ease some of the symptoms of MS. A physical or occupational therapist can teach you stretching and strengthening exercises and show you how to use devices to make it easier to perform daily tasks. Physical therapy along with the use of a mobility aid when necessary can also help manage leg weakness and other gait problems often associated with MS. You may experience painful or uncontrollable muscle stiffness or spasms, particularly in your legs. Muscle relaxants such as baclofen Lioresal and tizanidine Zanaflex may help. Medications to reduce fatigue. Medications also may be prescribed for depression, pain, sexual dysfunction, and bladder or bowel control problems that are associated with MS. Request an Appointment at Mayo Clinic Clinical trials Explore Mayo Clinic studies testing new treatments, interventions and tests as a means to prevent, detect, treat or manage this disease. Lifestyle and home remedies To help relieve the signs and symptoms of MS, try to: Get plenty of rest. If you have mild to moderate MS, regular exercise can help improve your strength, muscle tone, balance and coordination. Other types of mild to moderate exercise recommended for people with MS include walking, stretching, low-impact aerobics, stationary bicycling, yoga and tai chi. MS symptoms often worsen when your body temperature rises. Avoiding exposure to heat and using devices such as cooling scarves or vests can be helpful. Eat a balanced diet. Results of small studies suggest that a diet low in saturated fat but high in omega-3 fatty acids, such as those found in olive and fish oils, may be beneficial. But further research is needed. Studies also suggest that vitamin D may have potential benefit for people with MS. Stress may trigger or worsen your signs and symptoms. Yoga, tai chi, massage, meditation or deep breathing may help. Alternative medicine Many people with MS use a variety of alternative or complementary treatments or both to help manage their symptoms, such as fatigue and muscle pain. Activities such as exercise, meditation, yoga, massage, eating a healthier diet, acupuncture and relaxation techniques may help boost overall mental and physical well-being, but there are few studies to back up their use in managing symptoms of MS. Guidelines from the American Academy of Neurology recommend the use of oral cannabis extract for muscle spasticity and pain, but do not recommend cannabis in any other form for other MS symptoms due to a lack of evidence. The guidelines also do not recommend the use of herbal supplements such as Ginkgo biloba and bee venom or magnetic therapy for MS symptoms. Coping and

support Living with any chronic illness can be difficult. To manage the stress of living with MS, consider these suggestions: Maintain normal daily activities as best you can. Stay connected to friends and family. Continue to pursue hobbies that you enjoy and are able to do. Contact a support group, for yourself or for family members. Discuss your feelings and concerns about living with MS with your doctor or a counselor. Preparing for your appointment You may be referred to a doctor who specializes in disorders of the brain and nervous system neurologist. What you can do Write down your symptoms, including any that may seem unrelated to the reason why you scheduled the appointment. Make a list of all your medications, vitamins and supplements. Bring any clinical notes, scans, laboratory test results or other information from your primary care provider to your neurologist. Write down your key medical information, including other conditions.

Chapter 8 : Multiple Sclerosis â€“ Diagnosis, Management | Nursing Journals

Diagnosis and Management of Multiple Sclerosis: Case Studies Douglas A. Woo, MD, Michael J. Olek, DO, Elliot M. Frohman, MD, PhD Multiple Sclerosis Program.*

Chapter 9 : Diagnosis and Management of Multiple Sclerosis in Children

It can be a challenge for doctors to diagnose multiple sclerosis (MS). There's no single test that can prove you have it. And many conditions have symptoms that seem like MS.