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MULTIPLE SCLEROSIS: ENVIRONMENTAL RISK FACTORS

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A b s t r a c t. Multiple sclerosis is a disease of unknown etiology characterized by inflammory demyelination of the brain and spinal cord. Epidemiological investigations play important role in study of multiple sclerosis. Geographical distribution of the disease has been described in terms of prevalence and incidence. The possible role of environmental factors as a cause of multiple sclerosis had been hypothesized with observation of unequal geographic distribution of the disease. More interesting, in terms of their biological significance, are attempts to identify associations between multiple sclerosis and situations or events wich could cause blood-brain barrier damages, such as trauma or toxic exposures.

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РАССЕЯННЫЙ СКЛЕРОЗ: ФАКТОРЫ ОКРУЖАЮЩЕЙ СРЕДЫ

Рассеянный склероз является заболеванием неизвестной этиологии с характерной воспалительной димиелинизацией головного и спинного мозга. Важную роль в изучении этиологии рассеянного склероза играют эпидемиологические исследования. Описано географическое распространение заболевания и обсуждена возможная роль факторов окружающей среды как причин его развития. Приведены данные о роли таких биологических факторов, как травма и токсические воздействия, в этиологии заболевания.

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ТАРКАУ ХЭТЕР: ЭЙЛӘНӘ-ТИРӘ ФАКТОРЫ

Баш һәм арка мие ялкынсынулы димиелинизация белән характерланучы, килеп чыгышы билгесез чир. Эпидемиологик тикшеренүләр чәчелгән склерозны өйрәнүдә мөһим роль уйныйлар. Авыруның географик таралышы сурәтләнгән. Әйләнә-тирә мохиткә бәйле факторларның роле РС үсешенең сәбәбе буларак карала. Чирләрнең килеп чыгышында бер рәт биологик факторларның роле турындагы мәгълуматлар китерелә.

Multiple Sclerosis (MS) is a disease of unknown etiology characterized by multiple inflammatory demyelination of the brain and spinal cord. The clinical diagnosis is made by demonstrating symptoms and signs of multiple separate white matter lesions, which are disseminated in time and space. MS features present either as acute attacks or as a progressive neurological involvement. Clinical variants may include benign forms with few attacks and mild disability over time.

MS is difficult to study by epidemiological methods, since it shows unfavourable characteristics for this approach. Low frequency, long latency and long duration pose methodological limits to the epidemiological study [1, 2]. In spite of all these limits, however, epidemiological investigations have undoubtely played a role in the study of MS: it is from them that much of the present view has emerged of MS as a disease caused by multiple factors which appear to act in specific temporal sequence at an age before puberty in genetically predisposed subjects [3]. This unifying hypothesis emphasized on the one hand a possible etiological heterogeneity and lack of specificity, and on the other, the role of a genetic-racial susceptibility in a complex interplay in which the relative contribution of environmental and genetic factors remains a controversial issue [4]. Since mortality data are not adequate to provide an accurate picture of MS, the geographical distribution of the disease has been described in terms of prevalence and incidence. Well conducted descriptive studies have shown that MS has a uneven spatial distribution and a changing incidence over time, at least in several regions. The frequency of MS varies considerably in different parts of the world, but also within the same countries. The geographical pattern described by Kurtzke [5, 6] had identified areas of low, medium or high risk of MS: however, it must be accepted with some cautions because it was based on the comparison of prevalence rates reported from different areas, at different time, and by using different study methods. Moreover, particularly questionable is the assumption that prevalence is a reliable gauge of frequency. Furthermore, the belief that MS frequency is directly related to latitude has been refused by many prevalence studies carried out in Southem Europe since 1980 [1, 7, 8]. Also the comparison of MS incidence rates indicated that the distribution of MS depends on more than just a frequency-latitude relationship. Certainly, MS is more frequent among Caucasians than in other ethnic groups, even if they live in the same geographic areas [6, 9]. The varying susceptibility of MS according to race seems to emphasize the role of genetic factors, which has been confirmed by the increased risk of MS in close blood relatives and above all monozygotic twins of patients [10]. The pattern of recurrence risks in relatives of MS patients is consistent with a model involving more than one susceptibility gene. At present, we are confident that the common Caucasian MHC class II HLA-DR2 plays a role in most populations [11]. The

biological significance of other candidate genes in MS susceptibility remains unclear. The possible role of environmental factors as a cause of MS had been hypothesized at the beginning of the century with the observation of the unequal geographgic distribution of the disease. The postulated higher frequency of MS in northern areas of Europe and America might also be due to latitude-associated variables, and not only ethnic factors. This hypothesis gained greater support from investigations carried out on migrant populations. Prevalence studies carried out on groups of Northern Europeans and North-Americans who left their birthplaces (at high risk) to go to low risk areas revealed that immigrants tended to retain the level of risk of their original countries, but this rule was valid only for those who emigrated after the age of 15 years, whereas those under the age of puberty acquired the risk of the adoptive countries [12, 13]. Other observations have been recorded regarding individuals who moved from low to high risk areas revealing less convincing results. Although these findings have been criticized because of the small sample size of the denominators and the selection bias intrinsic to migrant studies, they represent one of the strongest arguments in favor of the exogenous hypothesis. The difference in risk in relation to age at migration suggests the existence of a critical age of exposure to putative factors, at some time before puberty: they also indicate the existence of a long latency between acquisition and clinical disease onset. Another important aspect suggested by descriptive studies on MS incidence is the temporal pattern of the disease which varies in different geographical areas. Along with areas in which MS frequency was found to be essentially stable [14], there are many region in which the disease risk has changed overtime. Investigations Gamed out in some Canadian provinces, in Northern Europe, North America, and in various communities of Sardinia [15], have reported an increase in frequency of MS which does not appear to be merely related to improved diagnostic tecniques. On the other hand, in some areas the incidence pattern has changed toward lower frequencies. This temporal heterogeneity emphasized the possible influence of exogenous factors. This suggestion is in agreement with reports of a sudden increase in MS incidence in some communities living in North European islands and in Sardinia, indicating the effect of a change in environment during or after the World War Second caused by the end of the cultural and ethnic isolation of native populations [16, 17, 18].

Although the interpretation of these observations is still in dispute, they seem to support the hypothesis of an exogenous origin of the disease.

Analytical studies have attempted to examine the association with some biologically plausible environmental variables. In this respect, in view of the descriptive evidence suggestive of an infectious etiology, various studies aimed at verifying this hypothesis with microbiological, molecular or sere-epidemiological approaches, have yielded unconclusive results. Agents responsible for common childhood diseases and other viruses or retrovirusers have been investigated as possible causative agents. The results of studies with an epidemiological retrospective approach have provided contradictory data in demonstrating associations either with some childhood diseases contacted at a preschool age, or later in childhood, or any other parameters which may indirectly bring about greater likelihood of contact with hypothetical agents such as frequent moves, public jobs, contacts with animals, etc. [19]. There still remains the hypothesis that the disease may be caused or triggered by common, and not necessarily specific agents, as an abnormal immune response in susceptible individuals. The analytical method has also been used to investigate geoclimatic variables whose biological plausibility had been suggested by the spatial distribution of MS, without convincing results.

More interesting, in terms of their biological significance, are the attempts to identify associations between MS and situations or events which could cause blood-brain barrier damages, such as trauma or toxic exposures (for example organic solvents), providing results which, although far from be conclusive, could incourage further investigations. Finally, some studies on dietary habits have indicated that a low intake of polyunsatured fatty acids could predispose to the disease, perhaps by making the product of myelinosynthesis more vulnerable to various types of attack. Other hypotheses on dietary factors have been also investigated [20]. The bulk of scientific data which has emerged from several thousand studies do not lead to any definitive etiological attribution. However, the interpretations from both promoters of the genetic doctrine and proponents of an environmental cause of MS are not necessarily in conflict and a unifying hypothetical model can be proposed. Since genetic susceptibility by itself is not sufficient to cause MS, and since descriptive and analytical studies as well as clinical and laboratory evidence lead to the conclusion that MS etiology cannot be explained by any known environmental factors in isolation, the body of information currently available is concordant that MS is caused by several factors. MS predisposition is probably induced by polygenes, when the environment is conducive. In the same way, considering the presumed long latency, several environmental factors may be involved in the

etiopathogenesis of MS in susceptible individuals. In this context, situations or events, such as childhood or adolescent infectious diseases, hypersensitivity, nutritional habits, exposure to toxicants, significant head or spinal trauma, and other factors may contribute at different times to the acquisition of demyelinating disease, trigger its onset or modify its course [21].

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РАСПРОСТРАНЕННОСТЬ ПРОГРЕССИРУЮЩИХ МЫШЕЧНЫХ ДИСТРОФИЙ В ТВЕРСКОЙ ОБЛАСТИ

Тверская государственная медицинская академия

Р е ф е р а т. Показана частота прогрессирующих мышечных дистрофий в Тверской области. Обследованы 166 больных с различными формами заболевания. Наиболее часто обнаруживалась форма Эрба–Рота (у 60%). Формы Дюшена и Ландузи–Дежерина встречались с одинаковой частотой (по 20%). Выявлено значительное преобладание этой патологии в Тверской области по сравнению с другими регионами России.

Н.А. Дудкина

ТВЕРЬ ӨЛКӘСЕНДӘ КӨЧӘЯ БАРУЧЫ МУСКУЛ ЗӘГЫЙФЬЛЕГЕ (ДИСТРОФИЯСЕ) ТАРАЛУЫ

Автор Тверь өлкәсендә көчәя баручы мускул зәгыйфлеге ешлыгы буенча материаллар китерә. Төрлечә авыручы 166 авыру тикшерелә. Аеруча Эрба-Рота (60% ында), Дюшен формасы һәм Ландузи - Дежерина (бер үк ешлык белән 20%) формалары еш булуы ачыклана. Бу патологиянең Тверь өлкәсендә Россия буенча очрау ешлыгына караганда югарырак булуы ачыклана.

N.A. Dudkina

INCIDENCE OF PROGRESSIVE MUSCULAR DYSTROPHY IN REGION OF TVER

The author represented materials on incidence of progressive muscular distrophy in the region of Tver. 168 patients were investigated with different forms of disease. The most frequent form of disease was Erb's athophy (in 60%); incidence of Duchenne's and Landuzy's forms was the same (in 20%). Compared with the Russia's indices of incidence, significant prevailing of this pathology in the region of Tver was revealed.

Прогрессирующие мышечные дистрофии (ПМД) – группа наиболее распространенных наследственных нервно-мышечных заболеваний. Первичные и вторичные формы ПМД в структуре наследственных заболеваний нервной системы составляют 0,6–0,7 %. Термин "мышечная