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Multiple Sclerosis: Prevention of Serious Illness — Vision of a Desired Future for Newly Ascertained Patients

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Abstract — The increased prevalence of MS worldwide and the resultant high frequency of serious illness among young adults urges that the developed methods of prophylaxis are fully tested. Reference is made to the hypothesis of a circulating toxin playing a role in disease development. Insights from basic research now in progress may expand or amend the scenario. This discussion pertains to biological reasoning and a prophylactic treatment which is able to postpone or avoid disability in MS.

Introduction

20 years ago Henzi* wondered about the relevance of the similarity of the clinical phases of optic neuritis in multiple sclerosis (MS) and in methanol poisoning and whether this observation might lead to an aetiological explanation and ultimately to a useful therapy. The following statistics and discussions pertain to MS as a biological phenomenon.

100 years ago the affliction we call MS was uncommon and medical professionals in Switzerland considered the condition as a curiosity. This changed in the following 3 decades and by 1921 the result of a countrywide investigation gave a prevalence of 23 MS-patients per 100 000 inhabitants. The investigation was repeated in 1957; by then the prevalence had risen to 50 per 100 000. In the yearly report of the Swiss MS-Society of 1983 the estimate was given, that the prevalence had now risen to between 130 and 170 per 100 000. This is reflected at the Society's meetings where the plight of handicapped MS-patients and wheelchair cases is exposed.

The observation that the more recent investigations show a higher MS prevalence has been reported in various countries (1, 2, 3). MS is the most common and dreaded demyelinating disease of young adults.

The therapy–results of Henzi (1) and others seem to suggest that if prophylaxis against relapses is,

*Hugo Henzi, as a medical doctor and a family man, became involved with MS in the 1940's. In the 1960s he made the observations which led him to believe in a link between MS and a form of methanol poisoning. Attempts to bring the facts together and caring for patients became '*raison d'être*'.

Due to illness he retired from patient care in 1989. He passed away on 10 May 1991.

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from now on, systematically applied — most importantly to all newly ascertained cases of MS — as soon as the first symptoms (e.g. optic neuritis) show, the MS patient in a wheelchair may, by the year 2021, again be a curiosity. How much suffering would be prevented in this manner?

Scientific background

MS research indicates that signs of the MS-process are observable in macroscopically normal white matter surrounding MS-lesions often referred to as plaques of demyelination. The intense demyelination occurring at the contour of an active plaque seems to be a secondary effect in a semi-secluded brainspace which has better diffusion pathways to the bloodstream than to cerebrospinal fluid. Plaque development — as a result of a circulating toxin (4) capable of entering the matrix of membranes and exerting an effect on myelin — has been discussed (5) and the circumstances leading to eye-symptoms have been explored (6). In this plaque-space completely different processes from those in surrounding white matter are under way (7, 8).

These processes are probably associated with some puzzling features which have been observed in MS patients' eyes, e.g. venous sheathing (6, 9) and insidious atrophy of retinal nerve fibres (2 [p.57], 10).

Obviously biological thinking demands that plaques do not evolve by chance but out of necessity under certain circumstances and under the influence of the arrow of time. This scenario was published to promote its investigation; our model has yet to be elucidated in terms of the experience embedded in NMR studies and the complexities of the components of the immune system.

So in spite of advances in understanding the origin and early development of the MS-process, there remains large gaps. Apart from trying to grasp what causes the eye observations (as mentioned), perhaps the biggest challenge in the future will be the search for the antigens of autoimmunity in long-term ill MS-cases and for methods to manipulate the immune response in these patients (11).

For the so-called beginning cases of MS, the position appears to be more hopeful as the Methanol Hypothesis (MeHyp) provides a therapeutic strategy which helps cooperative patients to repress the MS-process. Hence a stage may ultimately be reached in which further increase in disability does not occur any longer (1 [p.81]).

Henzi recognized MS as an allergy, a conclusion supported by various lines of reasoning (1, 2, 12, 13). The process seems to start with transient periods of elevated blood methanol content, which may lead to sensitization. These periods of a mildly toxic condition cannot be felt by the individual and are transient. The process in MS corresponds to other allergies. More than a decade may elapse between sensitization and first signs and symptoms of the clinical disease.

The primary allergen for MS (according to the MeHyp) is protein or glycoprotein in myelin which has been altered by exposure to formaldehyde. The side chains of the amino acids form Schiff-bases. Myelin so changed will not revert to normal myelin. The source of formaldehyde is methanol which has been absorbed ex-pectin in the intestines. It is assumed that the alcohol dehydrogenase — which is required for degradation of formaldehyde — is commandeered (higher affinity) by glycerine aldehyde so that formaldehyde is not promptly degraded and therefore available to react with myelin (1 [p.20]). Glycerine aldehyde is the first metabolite of fructose and thus the level of fructose and of methanol in arterial blood may be critical. In connection with these studies (2, 13), the importance of folic acid was appreciated (adsorption of formaldehyde by tetrahydrofolic acid (2 [p.24])).

Fructose is not utilizable as such by most cells of the body and is normally converted by the liver. Individuals consuming 40 g or (as often the case) 100 g or more of sugar within an hour (at a meal or in between meals in tea, coffee, cold drinks, ice cream, sweets, compote, cake etc), may, depending on their enzymes, cause a temporary liver overload. Metabolic complexities which have unfavourable side effects ensue (2 [p. 22]). The one of importance in this discussion is a temporarily elevated methanol and fructose level in arterial blood entering the brain. Depending on genetic endowment and other factors this type of eating habit may lead to sensitization for the allergy MS.

Explanations of pregnancy related immune suppressive substances, which influence the course of an allergic affliction, were originally given by Beer & Billingham (14). Korn-Lubetzki et al. (15) and Poser & Poser (16) contributed observations of MS patients during pregnancy and post-partum. Their results are invaluable and statistically significant as they had large numbers of pregnant MS patients under their care. Henzi mentions (13) 2 cases — MS patients diagnosed as definite MS cases by neurologists — who followed the MeHyp dietary regimen and further recommendations. In

view of the increased demand for folic acid during pregnancy, the folacin status of these patients was carefully monitored and adequate supplements were given. These 2 patients remained free of relapse prior and during pregnancy as well as during the observed period of 6 months post-partum.

The allergy can be grouped as per Coomb & Gell as type II cytotoxic which for MS would be called 'myelinotoxic' (2 [pp.10, 11, 34]).

The 2 cases mentioned above — MS patients which were guided through pregnancy and the post-partum period without relapses — contrast favourably with the case histories recorded in the large series. Cohorts of several hundred patients (15, 16) were observed which led the authors to conclude: in MS there is a reduced rate of relapses during pregnancy (as compared to the relapse frequency of a matched group of non-pregnant female MS patients) and an abnormally high rate (statistically significant) in the first 6 months of the post-partum period.

In recent years important work has come to the fore (17–20) which opens up scientific inquiries around fructose, methanol, myelin and health – *see* (20) re formaldehyde derivatives, and (19) re molecular mechanisms, myelin/opioid peptides. It certainly marshals new evidence and may confirm the MeHyp-scenario or offer an alternative perspective for the early evolution of plaques.

The therapy which has been found useful for prevention of disability

MS is known only since 1823, at a time when agricultural and technical advance had lowered the price of sugar and food habits started to change. Saccharose (releasing glucose and fructose in equal amounts), began to cover an appreciable percentage of daily energy requirements. MS prevalence has increased in line with this trend.

Henzi's therapeutic approach (applied since the early 1970s) which includes a diet low in fructose and methanologenic pectin, has had encouraging results (1). In 1985 testing of the folacin status of the MS patients was introduced. The frequently observed deficit had to be corrected by green vegetables in the diet and vitamin supplements.

With this regimen the formation of further formaldehyde-altered myelin (the presumed primary allergen) is slowed down. However, the difficulty exists that the patient does not feel an immediate benefit. The reason being is that the patient's brain still contains various active plaques in which the processes leading to future relapses are under way. For the ultimate benefit long-term adherence to the diet and other recommendations of the MeHyp regimen is essential.

According to the model discussed (5, 6, 12) relapses are events which occur after a lengthy complex prehistory (*see* 6, Fig. 6) and are due to myelinolysis (2nd step of demyelination). Such active plaques in which the disease process maintains itself — macrophages digesting myelin-debris rest in perivascular space of brain capillaries for long periods (21) — may precipitate relapses long after the start of the therapeutic regimen.

In this phase good communication between the doctor and the patient and the patient's family is very important. Relapses must be curtailed timeously and patients must receive sound advice and moral support, as they have to cope with exacerbations and relapses occurring in spite of adherence to a strict curative regimen.

Those who are able to persist gradually start to feel better. Within 9–12 months the chronic fatigue disappears and the patient is on the way to become a benign case of MS in permanent remission.

It is to be understood that the allergy remains lifelong, but the process can be kept under control by maintaining the recommended routine for prophylaxis against relapses.

MS appears to be analogous to diabetes mellitus in that adherence to a strict dietary regimen is beneficial. This returns the patient to metabolic balance and is thus able to ameliorate the condition. Education regarding diet and self-discipline should be an essential part of the treatment.

It is an understandable development that MS societies and neurological research have been mainly involved with assistance to very ill patients in need of care. The well supervised long-term studies tend to consist exclusively of cohorts of such patients. Present insights in biology and preventive medicine make it necessary to carefully monitor freshly ascertained cases and to check regularly re impending disease activity. Cohorts of MS patients during gestation and post-partum are presumably a good opportunity to study effectiveness of the treatment. Such investigations would supply decision makers with the tools to address this health-care problem of the economically active population.

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