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Asthma and Wheezy Bronchitis in Childhood

Attacks of wheezing are among the commonest illnesses of childhood that general practitioners are called upon to treat. Two studies carried out in general practice showed that at least 20% of children had had one or more attacks during their first ten years of life.[1 2] Some authors consider that the term asthma should be applied to any child who is subject to wheeze. Others[1-3] reserve the term for those children whose wheezing is provoked by such stimuli as exercise, allergens, and emotional disturbance, and exclude children in whom recurrent attacks of wheezing occur only in association with respiratory infection. The terms "wheezy bronchitis" and "pseudo-asthma"[3] are often used to describe the disease in this group of children.

The relationship between asthma and wheezy bronchitis continues to be a matter for controversy, and this is partly a problem of semantics. H. E. Williams and K. N. McNicol[4] carried out a large survey of children in Melbourne and found that groups of children with asthma and wheezy bronchitis showed similar differences from a control group in such characteristics as the liability to recurrent bronchitis, a history of wheezing in siblings, and the capacity of the serum to bind histamine. These and other findings led them to conclude that children with asthma and wheezy bronchitis belong to a single population with a common underlying defect. This view receives support from the finding that children with a previous history of wheezy bronchitis have greater exercise-induced lability of the bronchi than control children, though it is not as great as that found in most children with overt asthma.[5]

While it seems probable that children with recurrent wheezy bronchitis and children with asthma both have the same fundamental abnormality of bronchial hyperreactivity, nevertheless there are evident differences between the two groups. For instance, the Melbourne workers found a much lower incidence of hay fever, eosinophilia in nasal secretions, and positive reactions to skin tests in children with recurrent wheezy bronchitis than in children with asthma, which suggests that in the former allergy is less important as a direct cause of wheezing. Furthermore, in a recently reported study[6] carried out in a London general practice M. E. C. Horn and I. Gregg found that infection by respiratory viruses—particularly rhinoviruses—was frequently associated with episodes of wheezing in children who were known to be predisposed to wheeze, but many of these children had never been observed to wheeze under any other circumstances.

Much of the confusion which surrounds the whole subject of asthma in childhood has arisen as a result of generalizations having been made about a condition which in any case may not be a homogeneous entity and which certainly varies widely in its course and severity. K. N. McNichol and H. E. Williams[7] have now reported their findings of a seven-year follow-up study of 315 children with asthma and 82 control children. In accordance with the conclusions of their previous study[4] the authors have applied the term asthma to any child who had been or was still subject to wheezing. They distinguished four grades of severity in a spectrum ranging from occasional episodes of mild wheezing to severe unremitting asthma which persists into adolescence. An important aspect of their study concerns the number of children who do not "grow out" of asthma. Their findings suggest that about a quarter of all children with asthma continue to wheeze after the age of 13 years, and in a small proportion of these (between 1 and 2% of all asthmatic children) they found radiological evidence of hyperinflation and impairment of ventilatory function when these children were examined at the age of 14. Another and more disquieting finding in this group of severely affected children was deformity of the chest, suggesting that they had irreversible lung damage. McNicol and Williams make the comment that the treatment of some of these children had been inadequate, probably because they were often quiet and inactive and had persistent asthma rather than acute attacks, so that neither their parents nor their doctors had appreciated the seriousness of the situation.

Clearly it is all-important to identify children with severe asthma at as young an age as possible. With the improved methods of treatment which have become available over the last few years (particularly disodium cromoglycate and beclomethasone dipropionate aerosol) it may prove possible to prevent further deterioration and permanent lung damage in these children. The task of identifying them will fall mainly on general practitioners. From the findings of McNicol and Williams it would appear that the most important criteria are the development of even mild deformity of the chest and the presence of auscultatory signs of airways obstruction during periods of apparent remission. Simple tests of ventilatory function, such as peak expiratory flow, which provide reliable

evidence of persistent airways obstruction,[8] should now be regarded as an essential part of the assessment of children with asthma by general practitioners.

An association between allergy and childhood asthma has long been recognized, but, as McNicol and Williams point out in the second of their papers,[9] many features of asthma cannot be explained on the basis of type I (immediate) hypersensitivity. Though they found a higher incidence of hay fever, eczema, and positive reactions to skin tests in the children with asthma, no one feature unequivocally distinguished them from control children. For instance, 15% of control children gave positive reactions to skin tests, and it is probable that a still higher percentage would have done so if McNicol and Williams had included an extract of house-dust mite in the range of skin tests which they performed.[6] Similarly, they found it impossible to define a discriminatory value of serum IgE which was present in most asthmatic children and only rarely present in the controls. While their findings have not thrown any new light on the part which allergy plays in the pathogenesis of asthma, they suggest that bronchial hyperreactivity and allergy are independent factors. This would explain their observation that in some children there was no relationship between the clinical course of asthma and either the first appearance of or subsequent variation in some of their allergic manifestations.

The role of psychological factors in asthma is another aspect of the disease which has caused controversy. Some workers believe that a child's personality and his reactions to emotional stress are primary aetiological factors. Others consider that asthmatic children have a higher incidence of neurotic traits than normal children but are undecided whether these are the consequence or cause of asthma. As the Melbourne workers emphasize in their third paper,[10] one reason for these varying opinions is that often they have been based on studies of highly selected groups of asthmatic children whose clinical and physiological status was not properly defined. In this context the importance of classifying asthmatic children according to the grade of severity is clear from the Melbourne study. Its most important finding was that behavioural disturbances were uncommon in asthmatic children, and only in the group of the most severely affected children was their incidence significantly higher than in the controls. While these findings do not exclude the possibility that severe asthma is especially likely to occur in children of a specific personality type, a more reasonable interpretation might be that severe asthma itself is a potent cause of emotional disturbance in the child and in his family.

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Clues to Multiple Sclerosis

The search for clues to the aetiology of multiple sclerosis has already inspired many hypotheses. Among them is the possibility that heredity may play a part. Recently J. H. McIntyre, of Christchurch, New Zealand, has considered this question in a brief report.[1]

In the space of one year he himself has encountered four cases of multiple sclerosis (he prefers the older word "disseminated") in each of which he noted a well-established familial history. He rightly says that this may be a coincidence but poses the question whether this finding is suggestive of a familial tendency of a "sensitivity to some virus, possibly measles." On this problem at present speculation outweighs fact, but what is worth noting is that the risk of having the disease for a first-degree relative of a patient with multiple sclerosis is at least 15 times that for a member of the general population.[2]

But this increased incidence is not necessarily due simply to an inborn familial tendency to the disease any more than it is, say, in the case of leprosy. Certain other observed facts are worth considering. Firstly, the prevalence of multiple sclerosis is clearly related to latitude, being virtually zero in tropical areas, though there are certainly anomalies in the Japanese distribution. Secondly, there appears to be an interval of perhaps 10 to 15 years between a supposed exposure to infection and the appearance of neurological symptoms. Thirdly, as M. Haire and colleagues[3] have now shown, there seems to be a significant increase in the immunoglobulin G specific for measles (and to a lesser degree herpes simplex) in the cerebrospinal fluid of patients with multiple sclerosis. It is therefore tempting to use this combination of familial frequency, latitudinal prevalence, latent period, and measles immunoglobulin studies to support the hypothesis that in early life close-knit groups are subjected to environmental factors (including exposure to measles), and that they are subsequently influenced by other, as yet unknown, factors to develop clinical multiple sclerosis, which most authorities, including C. E. Lumsden,[4] consider can best be explained in terms of an antigen-antibody reaction.

It is now worth considering some new work which has come from the Medical Research Council's demyelinating disease unit in Newcastle-upon-Tyne. The sequence of events in the evolution of this work is worth summarizing here. R. L. Swank[5 6] has long urged the view that multiple sclerosis is related to the consumption of fats deficient in the unsaturated fatty acids. R. W. R. Baker and colleagues[7] showed that lecithin from the cerebral white matter of patients with multiple sclerosis contained more saturated fatty acids than did the white matter of control patients, and R. H. S. Thompson[8] noted changes in the serum lipid content of patients with multiple sclerosis. Following up these observations, J. H. D. Millar and colleagues[9] in a double blind trial reported a slight advantage to patients treated with linoleic acid, and from this J. Mertin and colleagues[10] put forward the view that supplements of linoleic acid might have an immunosuppressive effect on the development of multiple sclerosis. They report that both linoleic and arachidonic acid inhibited the macrophage electrophoretic mobility and that this inhibition was much higher for patients with multiple sclerosis than for controls. Their initial intention was to try to find laboratory support for the clinical observations of Millar and colleagues, but they then realized that they might use this inhibitory effect as a diagnostic test for the disease.[11] Their next step was to investigate the sera of families of patients with multiple sclerosis,[12] and in so doing they found that 41% of the relatives had the same macrophage anomaly, "though to a lesser degree." Other interesting findings are that sisters of the propositus more frequently gave anomalous results to this test than brothers and that in the group of patients they studied no patient was