ASTHMA IN TRANSITION: FROM CHILDHOOD THROUGH ADOLESCENCE TO ADULTHOOD

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THE PROBLEM

Childhood asthma and wheezing illness has become a major health concern, with a significant rise in wheezing illness over the past 30 years.[1-3] Despite the high prevalence childhood asthma has not been clearly defined,[4] although it is well established that childhood wheezing, particularly in infancy and early childhood, represents a heterogeneous group of syndromes.[5,6] Wheezing in infancy is common and affects up to 40% of all pre-school age children, with up to 60-70% remission in mid-late childhood.[7-9] A significant number of these early symptomatic individuals have a subtle but definite reduction in airway function which may have either a genetic origin or intrauterine environmental cause.[10] Maternal smoking during pregnancy is the most clearly defined risk factor.[11] By mid-childhood (8-14 years) most symptomatic patients are assumed by doctors to have classic atopic asthma as a family history of atopy is often associated, and most of the affected children are atopic themselves as defined by positivity in skin prick tests to common inhaled allergens and/or specific IgE sensitisation.[12-15] The presence of atopy has been shown to be associated with persistence of symptoms into adult life,[15-17] and atopy appears to be associated with an increased rate of decline in pulmonary function in mid-late adult life.[18]

The long-term significance of other childhood lower respiratory symptoms such as cough is less clear cut. Cough without wheeze is common in childhood and its incidence appears to decrease with age,[19] and there is growing evidence that this symptom, when present in isolation, does not form part of the 'asthma' spectrum.[20-22] Indeed, there is a lack of association between cough, atopy and airway hyper-responsiveness when wheeze is taken into consideration, and this therefore questions the relevance of cough as a useful identifier of asthma in childhood.[19] Although asthma and wheezing illness in childhood does remit in the transition to adult life,[23] significantly increased risk of the symptoms continuing exists in the presence of atopic disease. The long-term consequences of childhood atopic asthma in studies of such population cohorts demonstrate that the majority of such individuals (60-70%) are likely to continue with symptoms into adult life.[24,25]

For other less clearly defined recurrent symptoms, such as cough and wheezing only in the presence of viral infection (previously labelled as bronchitis or wheezy bronchitis), the long-term consequences are becoming clearer[24] despite the fact that distinctions previously made between asthma and wheezy bronchitis fell out of favour in the 1970s and 80s as they were shown to be associated with a tendency to underdiagnose and undertreat childhood asthma.[26,27] The concern about what has been termed the 'asthma generation' must be that the increase in symptomatic children appears to have been in the group labelled as atopic[6,28,29] and in whom the long-term prognosis into adult life is unfavourable.[24,25]

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ADOLESCENCE: A TIME OF TRANSITION

As a consequence of this increased recruitment of patients to atopic asthma, an ever-increasing number of young people are having to make the journey from childhood to adulthood with an additional challenge and burden. How is this period of life from childhood to adult life (adolescence) defined? In North America a separate medical specialty has developed within an age-band spanning 15-25 years of age. It encompasses a period of life when physical, psychological and sociological maturity and independence are intermingled.[30] Physical maturation becomes established in girls at about the age of 12, with the onset of menarche occurring at approximately 13 years, although a wide variation from 9-18 years is recorded. No such clear-cut identifier is found in boys but peak height velocity, which is associated with sexual maturation, occurs at around the age of 12 in girls and approximately two years later in boys.[31] This gender difference has important implications as girls not only mature physically in advance of boys but they also tend to achieve other adult attributes ahead of boys; this is reflected in the fact that the young women leave the family home and establish their independence several years ahead of their male counterparts.[32]

LEGAL ASPECTS

Ratification of the UN Convention on the Rights of the Child by the Government of Great Britain and Northern Ireland in 1991 has been reflected in legislation and has significant consequences for parents, young people and their carers. The Children Act (England and Wales: 1989, Scotland: 1995) enshrines some of the rights of young people and the responsibilities of their carers. These acts support previous legislation on the age of majority and although 18 years (16 years in Scotland) is commonly regarded as the age of achieving full adult rights and responsibilities, children of any age able to understand what is being proposed for them, whether it be medical or surgical treatment, or custody arrangements, must now be involved directly in the decision-making process if the attending physician believes that they have the appropriate mental capabilities to so do. The age at which a child must be included in these important decisions does not have a lower age limit, but certainly by the age of 12 years, children and young people should be involved in consent for any medical interventions proposed for them.[33] Strict confidentiality

must also be maintained unless there are overriding reasons why this should not be so. Young people have the right to have personal information withheld from their parents/guardians if they so desire. This has been tested in the English courts (the Gillick case) for contraceptive advice in young people under 16 years of age.

COMMON THEMES

Growing up involves the adolescent in a variety of learning experiences and experimentation in 'testing the boundaries' of rules and accepted social practices. A desire to take part in 'risk-taking' is normal in the transition to adulthood.[32]

The development of various lifestyles can have important implications for emerging adult patterns of health behaviour across the life-span as evidenced by smoking, drinking, diet and physical activity. Young people with a chronic health problem such as asthma may be particularly 'at risk' in adolescence by acquiring certain habits which in the long term affect lifestyle such as smoking, in order to remain accepted within their peer group, to imitate an admired adult role model, or to protest against parental values. Attempting to prevent the development of unhealthy lifestyles in adolescence may be the best way of reducing a number of health risks in adult life, particularly for those with an established chronic illness.

A number of models of adolescent behaviour have been proposed including the 'focal' theory of Coleman (Figure 1) which suggests that concern about gender role peaks around the age of 13 years, concerns about acceptance or rejection by peers become more important at around 15 years, and issues regarding the gaining of independence from parents climbs steadily to peak beyond 16 years and then tail off towards the early to mid-20s.[32] The fact that adolescents do not usually cope with these challenges at the same time, but meet them sequentially, may provide some resolution of the paradoxes of the huge amount of disruption and crisis implicit in adolescence, and yet the relatively successful adaptation to adulthood and maturity in the majority.

In young people with the additional burden of chronic illness, attention needs to be given to their own and their parents'/guardians' coping skills. A recurrent theme is the need to establish independence while helping parents come to terms with 'the loss' of their dependent sick child for whom they have hitherto taken full responsibility. Compliance (or concordance) with treatment is also a major concern as failure to maintain a regular therapy can have serious immediate and long-term consequences for the health of the affected individual.

All responsible parents invest huge amounts of time and emotional energy into child rearing but these efforts are often redoubled by the presence of chronic disease and illness. Most parents experience feelings of loss at the passing of childhood and the changes in their children as they make the transition to adult life. A common challenge is to achieve a balance between acceptance of the illness by the child and their parents and at the other extreme the denial of the severity of the disease and resultant harm by failing to comply with best possible medical treatments.

ISSUES FOR THE HEALTH CARE PROFESSIONAL

A pattern of transitional care is commonly adopted for children in their early teens as a first step towards full independence and regular follow-up in an adult-oriented service with full transfer somewhere between 16 and 18 years of age. Parents often find it difficult to separate from their children, particularly when they have hitherto been largely responsible for their medical management. Unless responsibility for day-to-day management is transferred to young people, there is a danger that the medical management itself may become part of the natural testing of boundaries and the need to establish independence.

In a potentially life-threatening illness such as asthma, compliance with therapy can become a source of conflict. Parents are aware of the potential dangers of poor compliance and risk-taking such as smoking but, as with many young people, present behaviour is not often linked to long-term consequences and the young person himself

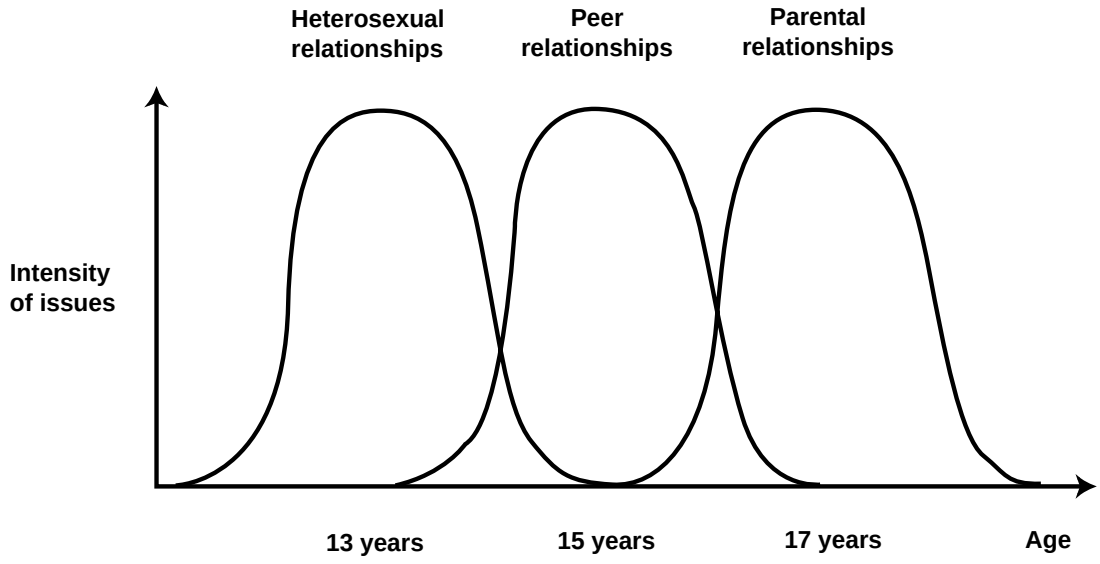

FIGURE 1
Coleman's focal theory conceptualises the issues facing young people in the transition from childhood to adult life.[32]

therefore has a rather different view. Peer pressure and the need to be accepted as 'one of the crowd' are other influences which are particularly strong in girls and young women.[32] Establishing trust between health care professionals and young people, and transferring responsibility for disease management and a healthy lifestyle to young people themselves are prerequisites for long-term future health, not only in the presence of chronic illness but also in those without health problems. Asthma may be underdiagnosed in teenagers and young people because of communication problems with medical and health care professionals.[34] This is also likely to be compounded by the unease that many practitioners experience in dealing with young people.[35-37] Young people themselves may also be confused about the appropriate route to gain access to health care.[38]

PROGNOSIS

Against this background, which needs to be considered in any young person requiring continuing medical support, a frequently asked question is 'what is likely to happen to my symptoms in the future?' In the early 1960s, Orie proposed that asthma and non-specific lung disease (NSLD), including chronic bronchitis and emphysema, were merely extremes of the same syndrome.[39] This became known as the 'Dutch Hypothesis' which postulated that the expression of asthma or NSLD depended in part on the age of exposure to the adverse environmental factor or factors. It is clear from recent identification of genetic markers and candidate genes associated with asthma and wheezing illness that this unitary hypothesis needs modification as the heterogeneity of these respiratory conditions becomes apparent.[6] It is likely that there are a number of overlapping conditions in the polygenetic and environmentally-influenced disorder that is termed asthma, some of which may also contribute to chronic obstructive pulmonary disease.

Most repeat surveys, and indeed longitudinal studies, have not chosen to separate different wheezing syndromes in childhood but have rather lumped together what used to be called 'wheezy bronchitis' with doctor-diagnosed asthma. Serial cross-sectional surveys in Aberdeen schoolchildren have suggested that the prevalence of this particular syndrome (wheezing only precipitated by intercurrent upper respiratory tract infections) has not changed over a 30-year period.[29] Evidence is emerging for different pathogenetic origins of these two conditions. Stevenson *et al*. have reported different varieties and concentrations of inflammatory cells derived from children undergoing bronchial alveolar lavage (BAL) who have been categorised as asthmatics or as wheezy bronchitics.[40] Indeed this latter group shows features which are more in keeping with similar data in stable adult chronic bronchitics. Different outcomes were shown in the transition from childhood to adult life for these two clinically diagnosed syndromes.[23] As reported in the influential 1969 Melbourne study, it was clear that wheezy bronchitis was used as a separate diagnostic label.[41] At baseline, these children aged 7-9 years appeared to have a gradation in specific sensitisation in terms of skin prick test positivity whether they were labelled as asthmatic, moderate to severe wheezy bronchitics, mild wheezy bronchitics or asymptomatic. The proportion of subjects whose symptoms resolved in adult life were more likely to have been diagnosed as wheezy bronchitics. When these children were followed up 25 years later, it was also noted that non-specific bronchial hyper-reactivity was highest in the atopic asthmatic group, lowest in the controls and intermediate in the wheezy bronchitis population,[42] again suggesting different mechanisms.

If the individual with episodes only precipitated by viral infections has a good prognosis, what are the features that predict early adult onset disease? For doctor-diagnosed asthma, a strong predictor appears to be associated atopy.[43] For young adults with a history of cough and sputum production more suggestive of NSLD, the strongest predictor appears to be active smoking with a significant but smaller contribution from atopy.[43] This would support the Orie hypothesis[39] that there is indeed some overlap between predisposition to classic atopic asthma and COPD in adult life. One of the difficulties in establishing the prognosis for asthma is the relative paucity of prospective studies and the poor retrospective recall of symptoms.

The British birth cohort followed up from 1958 has demonstrated the poor reliability of recall of previous symptoms when this information is requested throughout an individual's life history rather than gathered prospectively.[23] At subsequent follow-up at age 11, 16, 21 and 33 years, a significant number of persons from the original symptomatic group at age seven years had lost their symptoms and others had regained symptoms at different time-points through this period. Prospective studies such as this demonstrate the unreliability of identifying 'asthma' at any single time-point as apparently asymptomatic individuals may have had a prior history which may or may not recur in the future. Indeed only 2% of individuals in the 1958 cohort had symptoms at four of the five follow-up occasions. In common with the Melbourne[42] and Aberdeen cohorts,[24] approximately 35% of individuals presenting before the age of seven expressed a resolution of their symptoms by the age of 33. Bringing these data from early childhood together with subsequent adult-onset disease, it is clear that a number of different wheezing syndromes occur across a lifespan, which contribute to the total symptomatic population at any single age. In population studies in pre-school children, transient viral wheezers who will subsequently resolve through childhood and into early adult life will be over-represented. From school age through to young adulthood, atopic-related wheezing predominates and from mid-adult life onwards, atopy is gradually overtaken by exposure to cigarette smoke and other harmful environmental exposures. In mid-childhood (8-12 years) there is a significant contribution from children who wheeze only in association with viral infections, previously labelled wheezy bronchitis, and which has a good prognosis at least into early middle age. However, it is possible that infant viral wheezers and mid-childhood viral 'wheezers' may present again in late adult life with chronic obstructive pulmonary disease although there are no longitudinal studies or linked family studies to confirm this possible association.[44,45]

GROWTH

Linear growth is a concern to young people and their parents and can become a major concern in adolescence. The growth spurt, or more correctly peak height velocity, is achieved at approximately 12 years in girls and 14 years in boys, and is closely associated with sexual maturation.

Delayed puberty will therefore postpone the growth spurt but have no effect on the final achieved adult height.[31] Chronic illnesses, such as asthma, delay the onset of puberty and thereby slow the pace of linear growth. A slow pace of growth during adolescence has its greatest impact in boys who may require considerable counselling and support if so affected. Whereas it is an advantage for boys to mature early and a disadvantage to mature late this is less of an issue in girls. A basic knowledge of normal patterns of linear growth, and how to identify constitutional short stature and delayed onset of puberty, is an essential skill for all health care professionals dealing with adolescents. This must include an ability to estimate mid-parental height, interpret bone age and work with growth charts.[46] Properly calibrated wall-mounted stadiometers and staff trained in accurate measurement of stature are essential. With increasing concerns about long-term use of inhaled steroids and their possible systemic effects, it is not surprising that there is considerable confusion amongst clinicians, carers, parents and young people which may contribute to undertreatment and/or poor compliance. Despite these concerns modest doses of 400 μg/day or less of beclomethasone diproprionate or equivalent do not have any effect on achieved adult height. It is likely that the observed effects on height, in the short to medium term, may have been at least in part due to the impact of the illness itself on delaying the onset of puberty rather than on a direct systemic effect of the medication.[47]

GENDER DIFFERENCES

An interesting, and as yet unexplained, phenomenon during the transition from childhood to adulthood is the reversal of prevalence between the sexes with boys more likely to lose their symptoms and girls more likely to persist with symptoms or to re-acquire them.[43] This, together with the erroneous view of some health care professionals that asthma is more common in adolescent boys, can lead to under-recognition, poor treatment and compliance in girls.[48]

CURRENT TRENDS AND RISK FACTORS

Evidence is emerging that the recent increase in asthma has been associated with further atopic recruitment within the population with increased sensitisation to common inhaled allergens.[49-51] It has been fashionable and conceptually useful to identify high-risk and low-risk children as those whose parents clearly have atopic disease and those who have none. However, this distinction has recently been questioned, as in two-generation families, clear aggregation of atopy is only apparent in adults but with very little difference in terms of skin test positivity and RAST tests in the younger childhood population regardless of their parentage.[28] This suggests a recent and very significant pressure towards allergen sensitisation in the younger generation born to what has been termed the 'asthma generation'. This complicates extrapolation to the present day of the lessons drawn from historical cohorts. One needs to know what the long-term outcome in later adult life is in those children who present with virus-associated wheeze or 'wheezy bronchitis'. Is there a link between this syndrome and late-onset non-specific lung disease in adult life, and is this risk increased significantly by active smoking and/or exposure to environmental tobacco smoke? Are the different wheezing conditions distinct or do they have overlapping genetic contributions? With recent and future developments in identification of genes contributing to asthma and wheezing illness these questions may well be answered within the coming years. The questions surrounding asthma in the transition from childhood to adulthood are fascinating and require answers. However, in all the current and future research into the different conditions that contribute to what clinicians term asthma, the needs of young people who are travelling through a challenging, and often turbulent, period in their lives should not be forgotten. Knowledge of these challenges and concerns together with a real interest in young people are prerequisites to the practice of good medicine in this setting.

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