

SHORT REPORT

THE PRESCHOOL ASTHMATIC –

AT AN INTERFACE OF MARCHES – IMPLICATIONS FOR DIAGNOSIS AND TREATMENT

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The concept of the allergic or atopic march is well known to paediatricians and allergists. This phenomenon is one of a progression of allergic or atopic disease expression from food allergy in early infancy, through atopic eczema, then to allergic rhinitis in early childhood and finally to asthma, the final expression (Fig. 1).¹ By age 5 or 6 years most atopic infants will have outgrown eczema but will be on a path to significant airway disease, the final insult born of genetic, epigenetic and environmental interactions in early life. The pathophysiology of this state appears to be driven by TH2 cytokines operating in excess, while TH1 pathways, as well as many innate immune structures, are somehow downregulated.²

While this atopic march progresses relentlessly in some children, two other processes are marching on in parallel with, and continuously abutting on, the atopic paradigm. The first of these is what could be termed a 'wheeze march'. It is well known that roughly half of all infants will develop an acute wheezy lower respiratory tract infection known as bronchiolitis.³ This condition is caused by respiratory syncytial virus (RSV) in the main³ but also human rhinovirus (HRV), parainfluenza virus, influenza virus, human metapneumovirus and boca viruses. Bronchiolitis is more common in certain infants with risk factors (Table I), but is generally a mild disease, requiring no intervention. However, around 45% of bronchiolitics will wheeze on at least one subsequent occasion and many will wheeze frequently thereafter.⁴ Most of these children who wheeze again have a postviral wheeze driven by RSV and the natural history is in the main cessation of wheeze by 3-6 years of age.⁵ Only a few persistent wheezy preschool children have asthma. The development of asthma has been intimately linked to atopy but a number of other risk factors are now being uncovered (Table II). Despite a large number of wheezy preschool phenotypes most children have normal lung function at the outset.⁵ Only 'transient wheezers' have low lung function at birth and this might reflect relatively 'small airways'.⁵

The final march operating in preschool children is a viral one. Children < 2 years old are more susceptible to RSV, while HRV predominates from 2 years old. HRV then becomes increasingly linked to children where the former two marches are setting up a child for asthma.

Asthma occurs where the THREE marches interact (Fig. 2), but unfortunately our understanding of the critical X factor, that turns on asthma, is still missing. This may be the missing genetic link, where all the former envi-

Table I. Risk factors for RSV infection⁶

Environmental risk factors – poverty, passive smoke exposure, pollution, overcrowding, seasonality, day care centre attendance

Host risk factors – prematurity, congenital heart disease (CHD), congenital lung disease (CLD), young age (< 6 months especially those who have older school-attending siblings), family history of atopy, lack of breastfeeding, malnutrition, immunodeficiency

Table II. Possible aetiological factors for asthma⁷

- Atopy
- Bacterial super antigens
- Pollutants (indoor, tobacco smoke, vehicle emissions)
- Dietary factors (allergens, lack of immunomodulatory factors, genetically modified foods, toxins, salt)
- Lack of physical activity
- Obesity
- Drugs (including paracetamol)

ronmental factors function as epigenetic phenomena to switch on the asthma phenotype.

The consequence of this thought process on asthma and asthma causation is important to understanding the limitations of our current paradigm of inflammation causing airway hyper-responsiveness, in turn leading to airway obstruction and finally airway symptoms of asthma (Fig. 3). This logical process is under threat, especially in preschool children with asthma symp-

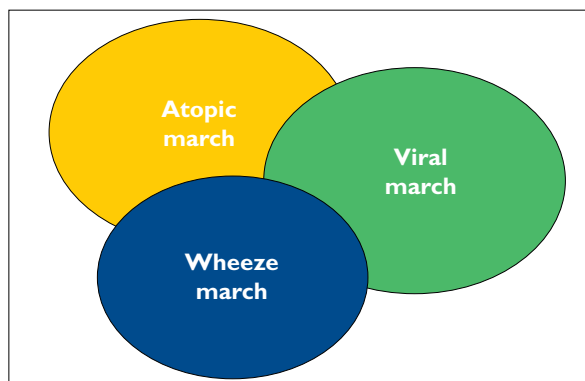


Fig. 2. The various marches operational in setting up asthma.

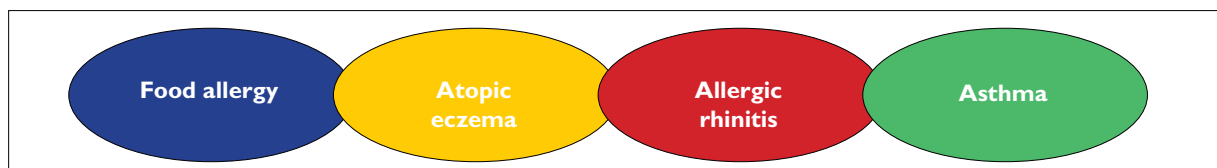


Fig. 1. The atopic march.

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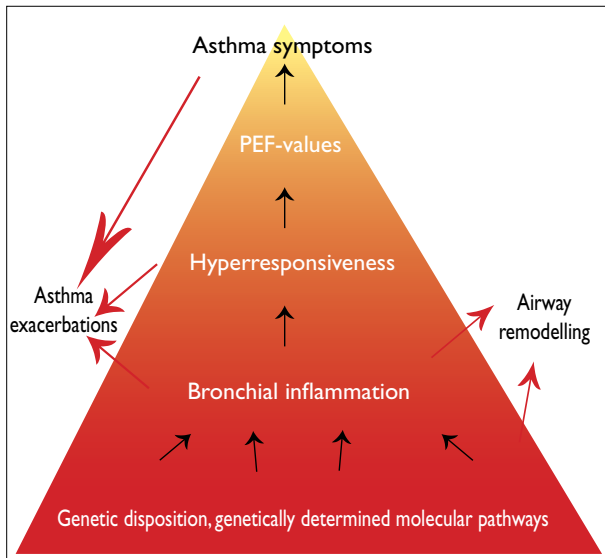


Fig. 3. The relationship between asthma pathophysiology (PEF – peak expiratory flow).

toms. Different factors are probably responsible for symptoms, natural history, control and exacerbations of asthma, especially in the preschool child. A logical flow of events in asthma, and especially preschool asthma, seems unlikely and we may need to think of this condition, at least pathophysiologically, as a multiple phenotypic state (Fig. 4).

The final implication of a new thinking paradigm relates to therapy of this condition. Obviously placing treatment on an overlay of this disease is not simple and this most probably explains why no one drug will fit all eventualities or treat all children. Selecting therapy for these children, then, just as diagnosing asthma in the preschool child, is an art that needs careful consideration. This is the art we need to teach our colleagues.

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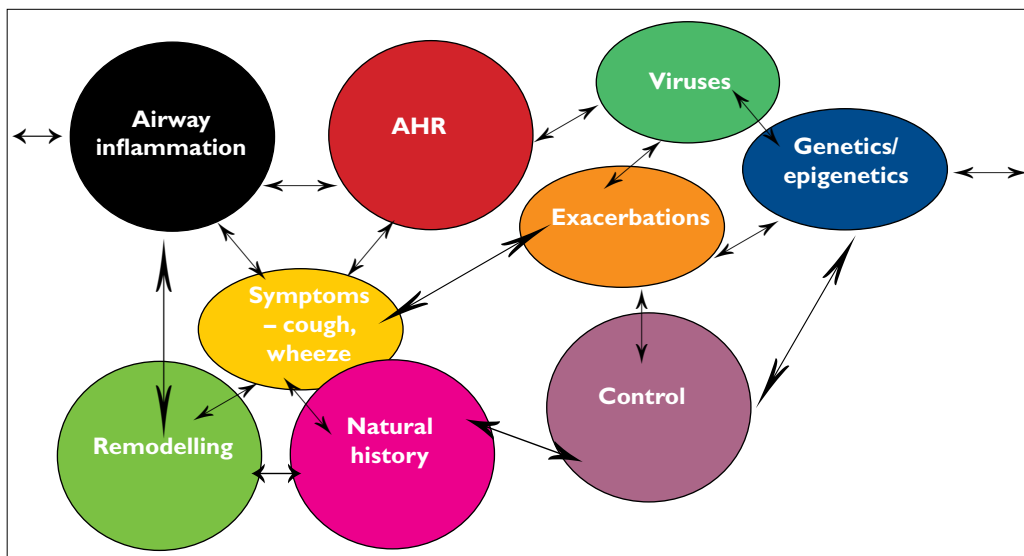


Fig. 4. The chaotic map of asthma-associated phenomena (AHR – airway hyperresponsiveness).