บทความพิเศษ

Non - pharmacologic preventions of allergic diseases

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Development of atopic disease seems to depend on both genetic factors and exposure to several environment factors. AT present there is evidence that the mode of infant feeding influences the development of food allergy whereas daily exposure to inhalant allergens and daily exposure to tobacco smoke is found to be associated with an increased risk of recurrent wheezing/asthma and inhalant allergy. In infants with atopic predisposition (first – degree relatives) exclusively breast feeding > of = 6 months is found associated with a significant reduction of the cumulative prevalence of cow's milk allergy (CMA) during the first 1 – 2 years of age. When breastmilk is insufficient or lacking a substitute formula is needed. Several recent prospective studies show a preventative effect of extensively hydrolysed formula (eHF) or partially hydrolysed formula (pHF) in combination with avoidance of cow's milk protein and solid food during > or = 6 months in high – risk infants on the cumulative prevalence of food allergy and atopic dermatitis during the first 2 – 4 years of life, Partially hydrolysed formula (pHF) or extensively hydrolysed formula (eHF) may be effective in allergy prevention. The protective effect on the development to cow's milk allergy is a real prevention and not only a postponement of the onset of symptoms. No studies have demonstrated a prevention effect of dietary measures as regards asthma/inhalent allergy at present until the age of 4 years. As no studies concerning the preventive effect of avoidance of milk and other foods after the age of 4 – 6 months of life have been performed recommendation of preventive elimination diets beyond this age is empirically based. In order to reduce the cost to minimize the risk of stigmatization and the risk of mainutrition it is important to avoid unnecessary restrictive and

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prolonged diets. A diet period of 4 – 6 months seems sufficient in most infants. At present eHF or pHF are recommended for avoidance of cow's milk. Some high – risk infants may benefit from maternal diet during lactation but there is no documented beneficial effect of maternal diet during pregnancy.

Exposure to various environmental factors in predisposed infants causes first sensitization and later leads to symptoms when further exposure occurs. Prevention of atopic symptoms in high – risk individuals may be possible if measures are taken in infancy to avoid exposure to important allergens such as house – dust mites. Food allergens may be specially important in infants, while aeroallergens are important later. Some authors have suggested a combined approach, and initial studies are encouraging.

Tobacco smoke exposure during pregnancy and after birth can be considered an adjuvant factor, which facilitates atopic sensitisation, expecially to food protein, during the first three years of life. The highest risk of atopic sensitisation was observed in families where the mother did not stop smoking until the end of pregnancy. Exclusive human milk feeding during the first six months of life, with delayed introduction of solids, is the recommended feeding for high – risk atopic infant. Human milk reduces the incidence and morbidity related to infection and allergy to cow's milk proteins. Dietary maternal restrictions during late pregnancy or lactation cannot be recommended, but may be advised in special cases. A maternal elimination diet seems more effective if associated with environmental hypoallergenic interventions. Milk form mother consuming cow's milk proteins contains small amounts of beta-lactoglobulin, which appear to introduce in the majority of infant both atopic and non-atopic tolerance rather than sensitisation. However, it is uncertain whether breast feeding also reduces the incidence of later atopic disease, since its etiology is mutifactorial.

Key words : *Prevention, Allergic diseases.*

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โรคภูมิแพ้เกิดได้จากสาเหตุหลายประการ โดยเฉพาะอย่างยิ่งมักจะมีประวัติโรคภูมิแพ้ในครอบครัวซึ่งถ่ายทอดทางพันธุกรรม และการสัมผัสกับสารก่อภูมิแพ้จากอาหารและสิ่งแวดล้อมในบรรยากาศ ในปัจจุบันพบว่าสารอาหารที่ทารกได้รับตั้งแต่แรกเกิดมีอิทธิพลต่อการเกิดโรคแพ้อาหาร ในขณะที่การสัมผัสกับสารก่อภูมิแพ้ในอากาศ รวมทั้งควันบุหรี่เป็นประจำจะทำให้เพิ่มอัตราเสี่ยงต่อการเกิดโรคหอบหืดและโรคภูมิแพ้ที่เกิดจากการสูดหายใจ จากการศึกษาพบว่าในเด็กแรกเกิดที่มีประวัติภูมิแพ้ในบิดาและมารดา ถ้าได้รับประทานนมแม่อย่างเดียวเป็นเวลานานมากกว่า 6 เดือนจะทำให้ลดอัตราการเกิดการแพ้นมวัวในช่วงอายุ 1-2 ปีแรก ในกรณีที่ไม่สามารถรับประทานนมแม่ได้หรือมีปริมาณไม่เพียงพอ ก็จำเป็นต้องหานมอื่นมาทดแทน มีการศึกษาจากหลาย ๆ แห่งพบว่าการใช้นมวัวที่ย่อยพิเศษแบบ extensive หรือ partial hydrolysed formula ร่วมกับการหลีกเลี่ยงการรับประทานนมวัวและอาหารเสริมอื่น ๆ ก่อนอายุ 6 เดือน ในเด็กกลุ่มที่มีอัตราเสี่ยงสูงที่จะเกิดโรคภูมิแพ้ สามารถป้องกันและลดอุบัติการณ์การเกิดโรคแพ้อาหารและ atopic dermatitis ในช่วงอายุ 2 - 4 ปีแรกเกิดได้ ซึ่งการป้องกันการเกิดการแพ้นมวัวถือว่าเป็นการป้องกันอย่างแท้จริงไม่ได้เพียงแต่เป็นการเลื่อนระยะเวลาการเกิดอาการและยังไม่มีการศึกษาวิจัยใด ๆ ที่ให้งดนมวัวหรืออาหารเสริมอื่น ๆ หลังอายุ 6 เดือนไปแล้ว เพราะอาจจะทำให้เกิดสภาวะขาดสารอาหารในเด็กถ้าให้งดอาหารเสริมนานเกินไป ในปัจจุบันมีการแนะนำให้ใช้ extensive หรือ partially hydrolysed formula เป็นนมทดแทนนมวัวสูตรปกติได้ ในเด็กกลุ่มที่เสี่ยงสูงที่จะเกิดโรคภูมิแพ้ ยังมีบางคนเสนอให้งดอาหารบางชนิดเช่นนมวัว ไข่ อาหารทะเลในมารดา ขณะที่ให้นมบุตรด้วย แต่ยังไม่มีรายงานที่สนับสนุนการให้มารดางดอาหารที่จะก่อให้เกิดการแพ้ในขณะตั้งครรภ์ น้ำนมแม่ที่รับประทานนมวัวจะพบปริมาณ β - lactoglobulin ในจำนวนเล็กน้อย ซึ่งพบว่าปริมาณดังกล่าวนี้ จะทำให้เกิดการยอมรับ (tolerance) มากกว่าเป็นการกระตุ้นให้เกิดการแพ้ (sensitization) ทั้งในเด็กปกติ และเด็กที่มีโอกาสเสี่ยงสูงที่จะเกิดโรคภูมิแพ้

การได้รับควันบุหรี่ในขณะตั้งครรภ์และหลังคลอดเป็นองค์ประกอบสำคัญที่ส่งเสริมให้เกิดการกระตุ้นต่อการได้รับสารก่อภูมิแพ้ง่ายขึ้น โดยเฉพาะอย่างยิ่งโปรตีนจากอาหารในช่วง 3 ปีแรกเกิด สำหรับการสัมผัสกับสารก่อภูมิแพ้อื่น ๆ ในบรรยากาศ จะกระตุ้นให้มีการสร้างภูมิต่อต้าน (sensitization) และทำให้เกิดอาการตามมาในภายหลัง ถ้าได้รับสารก่อภูมิแพ้ชนิดนั้นอีกเป็นระยะเวลานาน ๆ ต่อมา ดังนั้นการป้องกันที่ดีที่สุดในเด็กทารกที่มีโอกาสเสี่ยงสูง ก็ควรจะหลีกเลี่ยงการสัมผัสกับสารก่อภูมิแพ้ตั้งแต่แรกเกิด ที่สำคัญ เช่น ฝุ่น ตัวไรในฝุ่น ซากแมลงสาบ วัสดุที่ทำด้วยนุ่น เป็นต้น ในเด็กทารก สารก่อภูมิแพ้ที่มีปัญหาและทำให้เกิดอาการได้ช่วงขวบปีแรก ก็คือ โปรตีนจากอาหาร โดยเฉพาะอย่างยิ่งนมวัว ในขณะที่สารก่อภูมิแพ้ในบรรยากาศจะกระตุ้นและทำให้มีอาการแสดงในระยะต่อมาหลังจากอายุ 2 - 3 ปีไปแล้ว

โดยสรุป การป้องกันโรคภูมิแพ้ในทารกที่มีโอกาสเสี่ยงสูง ควรจะรับประทานนมแม่ตั้งแต่แรกเกิดจนถึงอายุ 6 เดือนร่วมกับการเริ่มอาหารเสริมที่อาจจะก่อให้เกิดการแพ้เช่น ไข่ หลังอายุ 6 เดือน เช่นกัน ในกรณีที่ไม่สามารถรับประทานนมแม่ได้นานพอหรือมีปริมาณไม่เพียงพอ การใช้ extensive หรือ partially hydrolysed formulaมาแทนก็สามารถลดอุบัติการณ์การเกิดโรคภูมิแพ้ได้ดีเช่นเดียวกับนมแม่ นอกจากนี้ควรต้องดูแลให้หลีกเลี่ยงสารก่อภูมิแพ้ในอากาศที่สำคัญ เช่น ตัวไร ฝุ่น และสารระคายเคือง โดยเฉพาะอย่างยิ่ง ควันบุหรี่ เพื่อลดการมากระตุ้นให้เกิดอาการของโรคภูมิแพ้ในระบบทางเดินหายใจเมื่อเด็กโตขึ้นด้วย

The occurrence of allergic diseases depends on genetic and environmental factors. Genetic factors determine individual risk and these persons should undergo early, testing. However, the methods currently available (mainly clinical history and IgE in umbilical cord blood) have poor predictive values so their use in the general population is not practical. It is now established that allergen exposure in the first few months of life is important in the development of specific allergic sensitizations. [1,2] Furthermore, the immune response of infants born to families with a strong history of allergic diseases is relatively immature at birth in comparison to infants with no family history of allergies, with reduced production of interferon-gamma (IFN-gamma)[3-5] and lower levels of T cell activation and memory. [6]

Warner JA showed that positive peripheral blood mononuclear cell proliferative responses to specific allergens can be detected from 22 weeks gestation, and that these responses were higher in babies whose mothers were exposed to increased allergen concentrations after 22 weeks of pregnancy. So exposure in the first trimester might have no effect and very low or very high maternal exposure to allergens in the 2nd trimester might have no response or induce tolerance, but moderate maternal exposure in the second trimester caused primary sensitization. Early feeding with foreign proteins is associated with an increased risk for allergic disease, but mostly so in genetically susceptible individuals.[8] The pattern of IgE response to ingested and inhaled allergens differs in at least two significant aspects. [9] Firstly, the latter responses rarely appear until one year of age, i.e. at a higher age than the IgE responses to foods. Secondly, whereas IgE responses against foods do not usually persist beyond early childhood, a much larger proportion of children continue to produce IgE antibodies against one or more inhalant allergens into adulthood. Exposure to high levels of allergens early in life after birth appears to be a risk factor for sensitization and allergic manifestations later in life and this has prompted studies of the possible effects of allergy prevention.

Effect of breast feeding on allergic sensitization and allergic diseases

Human milk is another source of immunological information that may be transferred from the mother to her offspring. Besides numerous components involved in the protection against infection, human milk contains components that enhance the maturation of the immune system of the newborn infant [10] Observations include an early stimulation of IgA antibody synthesis in breast fed infants [11-12] and transfer of cell-mediated immunity [13-14] and cytokines.[15] Thus, human milk would not only provide passive protection against infections, but also actively stimulate infant immunity. There are considerable individual variations in the composition of human milk, however, suggesting that maternal immunity may represent an environmental factor influencing the risk for allergic manifestations in her child, possibly even several years later.

Clinical aspects of allergy prevention

Eseverri JL et al [16] evaluated 200 allergic children ranging in age from 1 month to 15 years; 59.5 % had respiratory allergy, 23 % had food allergy and 27.5 % had medication allergy. Among the risk factors, 69 % had a family history of allergy, and

63.5 % were exposed to smoking. The natural history of allergic disease showed the following sequence: food allergy, respiratory allergy and medication allergy.

Tobacco smoke exposure during pregnancy and after birth can be considered an adjuvant factor which facilitates atopic sensitization, especially to food protein, during the first three year of life. The highest risk of atopic sensitization was observed in families where the mother did not stop smoking until the end of pregnancy.[17]

Food allergy [18] has its specific age-conditioned and geographical features. In childhood, sensitivity to the protein of cow's milk, egg white and also soya or flour pre-dominates. With advancing age, allergies to nuts, fruit, vegetables, spices, cheese, and sea food increase. Host A [19] had reviewed cow's milk protein allergy, and since 1970 widely varying estimates of the incidence from 1.8 % to 7.5 % have been reported. Based on strict diagnostic criteria, the incidence of confirmed CMPA in infancy seems to be about 2-5 % in developed countries. Symptoms suggestive of CMPA may be encountered in about 5 - 15 % of infants emphasizing the importance of controlled elimination / milk challenge. In breast fed infants, reproducible clinical reactions to CMP in human milk have been reported in about 0.5 %. Most infants with CMPA develop symptoms before one month of age, often within one week after introduction of cow's milk base formula. The majority have > or = 2 symptoms and symptoms from > or = 2 organ systems. About 50 % - 70 % have cutaneous symptoms, 50-60% gastrointestinal symptoms, and about 20 – 30 % respiratory symptoms. In exclusively breast fed infants with CMPA, severe atopic eczema is a predominant symptom. The basic treatment is complete avoidance of CMP. The prognosis is good with a remission rate about 45 – 50 % at one year, 60 – 75 % at two years, and 85 – 90 % at three years. Associated adverse reactions to other foods develop in about 50 %, and allergy against inhalants in 50 – 80 % before puberty.

Halken S et al [20] concluded that in high-risk infants fed exclusively with breastmilk and/or eHF combined with avoidance of cow's milk proteins and solid foods during at least the first 4 months of life, a significant reduction of the cumulative incidence of food allergy, especially CMPA, in the first 4 years can be been documented. Also, a reduction in the cumulative incidence of atopic dermatitis during the first 2 - 4 years of life is found . In order to reduce the costs and to minimize the risk of stigmatisation and the risk of malnutrition, it is important to avoid unnecessary restrictive and prolonged diets. A diet period of 4-6 months seems sufficient in most infants. At present, eHF are recommended for avoidance of cow's milk. A few high risk infants may benefit from maternal diet during lactation, but there is no documented beneficial effect of maternal diet during pregnancy.

Substitute Formulas

- Soy formulas

Businco L et al [21] suggested that soy-protein formulas are widely used for feeding babies with cow-milk allergy. When they were first marketed, these formulas were the only available cow-milk substitute and they ensured a normal life for many children who were affected by the large spectrum of clinical manifestations of cow milk allergy. Soy-protein formulas were also given to allergy-prone infants for

the prevention of atopic diseases when breast milk was not available. Several researchers have studied the prevalence of soy sensitization in allergic disease. Few studies used a challenge test for the diagnosis of soy allergy, even those in patients in whom soy allergy was suspected. In most studies the diagnosis of soy allergy was based on anecdotal case histories reported by parents and was not substantiated by scientific diagnostic criteria, no challenge test to soy was made nor were data available on specific immunoglobulin E to soy. They critically reviewed literature on the safety of feeding soy-protein formulas to babies with cow-milk allergy as well as on the prevention of cow-milk allergy.

Some studies show that feeding soy protein formulas for the first six months of life significantly reduces the prevalence of atopic disease in high risk babies. [22] Soy allergy is not common in atopic children.[23] Burks AW et al[24] said that 25 - 40 % of CPMA children may develop clinical hypersensitivity to protein present in soy-based formulas.

- Hypoallergenic Protein hydrolysate formulas

Maldonado J et al[25] had reviewed the special formulas in infant nutrition and concluded that at present, there is no concensus on the appropriateness of soy formulas for the treatment and prevention of nutritional allergies and current opinion seems to favour hydrolyzed protein formulas. High-degree protein hydrolysate formulas are used to treat lactating infants with an allergy to cow milk proteins or with serious nutritional problems. These formulas are not without risk, as they may contain residual epitopes capable of provoking a severe allergic reaction. Before using these formulas, allergenicity tests should be performed, particularly for highly sensitive infants. The unpleasant taste and high cost of these formulas, in addition to possible nutritional problems, limits their use in the prevention of atopic disease, although their efficacy is well established. Partial protein hydrolysate formulas are only used for preventive purposes and are not suitable for lactating infants with a proven allergy to cow milk.

Protein nutrition based exclusively on a partially hydrolysed formula does not impair the response to immunization in both preterm and term infants.[26]

Vandenplas Y had studied the effect of partially hydrolysed formula for a programme preventing atopic disease in high risk infants during the first 6 months of life. The incidence of atopic disease was decreased up to the age of 12 months[27] and 5 years[28] It is also unclear if a high - degree hydrolysate would result in a more efficient prevention than a partial-degree hydrolysate, or that a partial degree hydrolysate would result in a better development of tolerance than a high degree hydrolysate. [29] Milk from mothers consuming cow's milk proteins contains small amounts of beta - lactoglobulin, which appears to introduce in the majority of infants both atopic and non-atopic tolerance rather than sensitization.[30] Both extensively and partially hydrolysed protein hydrolysate compared with cow milk formula or soy formula have been reported to reduce atopic dermatitis, cow milk allergy and even asthma. Outcomes appear similar to exclusive breast feeding. [31-33] Fukushima Y [34] et al suggested that consumption of hypoallergenic formula for pregnant and lactating women and for infants could be helpful in preventing allergy development in infants.

Alllergic sensitization : food vs aeroallergen

The natural history of atopic sensitization as well as development of atopic disease is currently being investigated in a prospective birth cohort study in Germany (Multicenter Atopic Study, MAS). [17,35] In a cohort of 1,340 children who were carefully followed from birth, It was demonstrated that the first manifestation of atopy in most cases is atopic dermatitis, which has its highest incidence during the first three months of life. The risk of atopic dermatitis manifestation during infancy is strongly related to family history, particularly the parental phenotype of atopic dermatitis, suggesting that there are phenotype-specific genes involved in the development of atopy in general. Atopic dermatitis must be considered as a strong risk factor for subsequent development of allergic airway disease. Together with a particularly maternal (rather than a paternal) history of asthma, it increases the risk of subsequent asthmatic symptoms during childhood.

Recurrent episodes of wheezing in many children are observed during infancy, however, these early symptoms do not seem to be related to an atopic susceptibility in the family and are not associated with atopic sensitization to either indoor or outdoor allergens during the first two years of life. The first specific IgE responses during infancy are usually induced by food proteins, especially by allergens from cow milk and egg, which are strong risk factors for subsequent sensitization to indoor or outdoor allergens two years later. From the third year on, however, the presence of specific IgE antibodies to indoor or outdoor allergens , a family history of asthma, or elevated total serum IgE are strong risk factors for wheezing, which in many cases may persist into adolescence or adulthood. By contrast, early wheezers without indicators for atopy tend to have a good long-term prognosis. The role of indoor allergen exposure in the MAS study, domestic allergen exposure, was assured from birth onwards by determining the amount of major allergens from dust mites (Der p 1, Der f 1) and cat (Fel d 1) in carpet dust. There was a dose – response relationship between domestic allergen exposure and risk for sensitization during the first three years of life. Tobacco smoke exposure during pregnancy and after birth can be considered an adjuvant factor which facilitates atopic sensitization, especially to food protein. There is now convincing evidence that daily exposure to tabacco smoke results in an increased risk of developing wheezy bronchitis, asthma and bronchial hypereactivity in children.[36] Early introduction of pets into households of children at risk of atopy must be considered a risk factor for later development of allergic airway disease.

Ngamphaiboon J [37] et al had studied the common aeroallergens in allergic Thai children by intradermal skin testings, and the most common indoor aeroallergens were house dust mites, house dust, cockroaches and kapok.

Environmental controls include air - conditioning systems which both reduce humidity and filter large fungal spores, and lowers the molds, mites and yeast counts indoors.[38,39] Air cleaners (high efficiency particulate air, HEPA filters) remove particles 0.5 mm in diameter and larger with an efficiency of approximately 85 %.[40] Carpeting and bedding made from kapok should not be allowed. No pets and cockroach controls are recommended. Respiratory irritants such as cigarette smoke, and cleaning, cooking and cosmetic fumes should be eliminated

from the home environment or confined to well - ventilated areas.

Conclusions

Exclusive human milk feeding during the first 6 months of life with delay introduction of solids food is the recommonded feeding for infants to reduce the risk of atopic disease. Maternal dietary restrictions during pregnancy or lactation cannot be recommended, but may be advised in special cases. They might be more effective if associated with environmental hypoallergenic interventions such as mites, cock-roaches, house dust, kapok and tobacco smoking. Hypoallergenic formula is recommended if breastmilk is insufficient or lacking, especially in atopic prone babies. The protective effect on the development of cow's milk allergy is a real prevention and not only a postponement of the onset of symptoms.

Exposure to various environmental factors in predisposed infants causes first sensitization and later leads to symptoms when further exposures occurs. Food allergens may be specially important in infants, while aeroallergens are important later. Thus a combined approach is suggested.

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