

Täiskasvanute astma käsitlemine esmatasandil

Tõendusmaterjali kokkuvõte

Kliiniline küsimus nr 2c

Kas astma kahtlusele tuleks diagnoosimiseks kasutada järgmist meetodit vs meetodi mittekasutamistega:

c. testid võimalike allergeenide selgitamiseks

Kokkuvõte, sh kriitiliste tulemusnäitajate kaupa:

Otseselt selle küsimuse (allergiatestide roll astma diagnostikas) kohta käivaid süstemaatilisi ülevaateid ei leidnud.

On avaldatud mitmeid süstemaatilisi ülevaateid allergeenidest hoidumise kohta astma ravis. Cochrane andmebaasi süstemaatilises ülevaates ei leitud tõendeid, et ükski tolmu-ekspositsiooni vähendamisele suunatud sekkumine aitaks parandada astma tulemusnäitajaid, sh sümptomite esinemine, hooravi vajadus, paranemise osakaal, aga ka PEF hommikused väärtused (Gøtzsche 2008-2011). Seetõttu ei ole mõistlik soovitada tolmu-ekspositsiooni vähendamiseks sekkumist.

Lemmikloomaallergia korral sekkumised allergeeni vähendamiseks on pigem väheefektiivsed (Wood 1989, Wood 1998), tõendusmaterjal selle kohta on puudulik (Cochrane DSR Kilburn 2003, Labre 2012). Kas lemmiklooma-allergeenide testimine mõjutab astma tulemusnäitajaid, selle kohta uurimusi ei leidnud.

Astmahaigete laste haiguslugudel põhinevas uuringus ei leitud kliinilisi tunnuseid, mis aitaks eristada allergilist astmat mitteallergilisest astmast (Sinisgalli 2012), mistõttu selle artikli järelduses soovitatakse kõigile astmaga lastele teste võimalike allergeenide selgitamiseks.

Ravijuhendid

Testid võimalike allergeenide määramise osas - soovitused ravijuhendites on erinevad:

- jah (ISCI-2012, GINA-2012, GEMA-2009, SPLF)
- jah, vähemalt kõigil püsiva astmaga patsientidel (EPR-3 2007, GEMA-2009)
- soovitatav (VA/DoD)
- SIGN-2012 juhendis allergiatestide tegemist juhendis ei käsitleta. Ennetuse peatükis tõdevad, et ei ole häid tõendeid, et sekkumised allergeenide ekspositsiooni vähendamiseks/vältimiseks leevendaks astma kulgu, sh sekkumised tolmu-ekspositsiooni vähendamiseks (Gøtzsche 2008), sekkumised kassiallergeeni eemaldamiseks (Wood 1989, Wood 1998).

Lisaks on Saksamaa erinevate erialaühenduste poolt koostatud allergia ennetamise juhend (Muche-Borowski 2010), mille aluseks on teaduskirjanduse süstemaatiline ülevaade ja tõenduse taseme hindamine. Ka selles juhendis on loobutud tolmu-ekspositsiooni vähendamise soovist.

Süstemaatilised ülevaated

Kokkuvõte	Viide kirjandusallikale
The further increase of allergies in industrialized countries demands evidence-based measures of primary prevention. The recommendations as published in the guideline of 2004 were updated and consented on the basis of a systematic literature search. Evidence from the period February 2003-May 2008 was searched in the electronic databases Cochrane and MEDLINE as well as in reference lists of recent reviews and by contacting experts. The retrieved citations were screened for relevance first by title and abstract and in a second step as full paper. Levels of evidence were assigned to each included study and the methodological quality of	J Dtsch Dermatol Ges. 2010 Sep;8(9):718-24. doi: 10.1111/j.1610-0387.2009.07313.x. Epub 2009 Oct 29. Allergy prevention. [Article in English, German] Muche-Borowski C, Kopp M,

<p>the studies was assessed as high or low. Finally the revised recommendations were formally consented (nominal group process) by representatives of relevant societies and organizations including a self-help group. Of originally 4556 hits, 217 studies (4 Cochrane Reviews, 14 meta-analyses, 19 randomized controlled trials, 135 cohort and 45 case-control studies) were included and critically appraised. Grossly unchanged remained the recommendations on avoiding environmental tobacco smoke, breast-feeding over 4 months (alternatively hypoallergenic formulas for children at risk), avoiding a mold-promoting indoor climate, vaccination according to current recommendations, and avoidance of furry pets (especially cats) in children at risk. The recommendation on reducing the house dust mite allergen exposure as a measure of primary prevention was omitted and the impact of a delayed introduction of supplementary food was reduced. New recommendations were adopted concerning fish consumption (during pregnancy / breast-feeding and as supplementary food in the first year), avoidance of overweight, and reducing the exposure to indoor and outdoor air pollutants. The revision of this guideline on a profound evidence basis led to (1) a confirmation of existing recommendations, (2) substantial revisions, and (3) new recommendations. Thereby it is possible to give evidence-based and up-to-date recommendations on primary prevention of allergies.</p>	<p>Reese I, Sitter H, Werfel T, Schäfer T; German Society for Allergology and Clinical Immunology (DGAKI); Society of German Allergologists (ADA); German Society for Pediatric and Adolescent Medicine (DGKJ); German Society of Dermatology (DDG); German Society of Pediatric Allergology (GPA).</p> <p>http://www.ncbi.nlm.nih.gov/pubmed/19878402</p>
<p>BACKGROUND: The major allergen in house dust comes from mites. Chemical, physical and combined methods of reducing mite allergen levels are intended to reduce asthma symptoms in people who are sensitive to house dust mites.</p> <p>OBJECTIVES: To assess the effects of reducing exposure to house dust mite antigens in the homes of people with mite-sensitive asthma.</p> <p>SEARCH STRATEGY: last searches Nov 2007, updated July 2011, no change of conclusions</p> <p>SELECTION CRITERIA: Randomised trials of mite control measures vs placebo or no treatment in people with asthma known to be sensitive to house dust mites.</p> <p>MAIN RESULTS: Fifty-four trials (3002 patients) were included. Thirty-six trials assessed physical methods (26 mattress encasings), 10 chemical methods, and 8 a combination of chemical and physical methods. Despite the fact that many trials were of poor quality and would be expected to exaggerate the reported effect, we did not find an effect of the interventions. For the most frequently reported outcome, peak flow in the morning (1565 patients), the standardised mean difference was 0.00 (95% confidence interval (CI) -0.10 to 0.10). There were no statistically significant differences either in number of patients improved (relative risk 1.01, 95% CI 0.80 to 1.27), asthma symptom scores (standardised mean difference -0.04, 95% CI -0.15 to 0.07), or in medication usage (standardised mean difference -0.06, 95% CI -0.18 to 0.07).</p> <p>AUTHORS' CONCLUSIONS: Chemical and physical methods aimed at reducing exposure to house dust mite allergens cannot be recommended. It is doubtful whether further studies, similar to the ones in our review, are worthwhile. If other types of studies are considered, they should be methodologically rigorous and use other methods than those used so far, with careful monitoring of mite exposure and relevant clinical outcomes.</p>	<p>Cochrane Database Syst Rev. 2008 Apr 16;(2):CD001187. Updated July 2011</p> <p>House dust mite control measures for asthma.</p> <p>Gøtzsche PC, Johansen HK.</p> <p>http://www.ncbi.nlm.nih.gov/pubmed/18425868</p>
<p>Asthma is a chronic respiratory disease increasingly prevalent in the</p>	<p>Public health interventions</p>

[Type text]

<p>U.S., particularly among children and certain minority groups. This umbrella review sought to assess and summarize existing systematic reviews of asthma-related interventions that might be carried out or supported by state or community asthma control programs, and to identify gaps in knowledge.</p> <p>EVIDENCE ACQUISITION:</p> <p>Eleven databases were searched through September 2010, using terms related to four concepts: asthma, review, intervention, and NOT medication. Reviews of the effectiveness of medications, medical procedures, complementary and alternative medicine, psychological interventions, family therapy, and nutrients or nutritional supplements were excluded. Two coders screened each record and extracted data from the included reviews.</p> <p>EVIDENCE SYNTHESIS:</p> <p>Data analysis was conducted from May to December 2010. Of 42 included reviews, 19 assessed the effectiveness of education and/or self-management, nine the reduction of indoor triggers, nine interventions to improve the provision of health care, and five examined other interventions. Several reviews found consistent evidence of effectiveness for self-management education, and one review determined that comprehensive home-based interventions including the reduction of multiple indoor asthma triggers are effective for children. Other reviews found limited or insufficient evidence because of study limitations.</p> <p>CONCLUSIONS:</p> <p>State or community asthma control programs should prioritize (1) implementing interventions for which the present review found evidence of effectiveness and (2) evaluating promising interventions that have not yet been adequately assessed.</p>	<p>for asthma: an umbrella review, 1990-2010.</p> <p>Labre MP, Herman EJ, Dumitru GG, Valenzuela KA, Cechman CL.</p> <p>Am J Prev Med. 2012 Apr;42(4):403-10</p> <p>http://www.ncbi.nlm.nih.gov/pubmed/22424254</p>
<p>BACKGROUND:</p> <p>Although pet removal has been recommended in guidelines on the management of allergic asthma, pet ownership remains high in families where one or more members have an allergy to pet dander. Allergen control measures such as air filtration units placed in the homes of pet-allergic asthmatics have been used as a means of reducing allergen exposure.</p> <p>OBJECTIVES:</p> <p>To determine the clinical efficacy of pet allergen control measures in the homes of people with pet-allergic asthma.</p> <p>SEARCH STRATEGY:</p> <p>An electronic search of the Cochrane Controlled Trials Register was carried out. No restriction was placed on language of publication.</p> <p>SELECTION CRITERIA:</p> <p>Randomised controlled trials comparing an active allergen reduction measure with control were considered for analysis. Participants had stable pet-allergic asthma.</p> <p>DATA COLLECTION AND ANALYSIS:</p> <p>34 references were identified by electronic searching, but only three</p>	<p>Kilburn S, Lasserson TJ, McKean M. Pet allergen control measures for allergic asthma in children and adults. Cochrane Database Syst Rev 2003(1):CD002989.</p> <p>http://www.ncbi.nlm.nih.gov/pubmed/12535446</p>

[Type text]

appeared suitable for potential inclusion in the review. Two met the inclusion criteria for the analysis. Both examined the effectiveness of air filtration units. Two reviewers extracted data independently. A limited amount of data were usable for a meta-analysis.

MAIN RESULTS:

Both trials were small (n=22 and n=35). No significant differences were detected between active intervention and control on the primary and secondary outcome measures reported in the studies. Data on absence from school or work were not reported in either study. No meta-analysis could be performed due to lack of common outcomes.

REVIEWER'S CONCLUSIONS:

The available trials are too small to provide evidence for or against the use of airfiltration units to reduce allergen levels in the management of pet-allergic asthma. Adequately powered trials are needed. There are no trials of other allergen reduction measures, such as pet washing or possibly pet removal.

Otsing 17.08.2013:

Põhiotsing: "Asthma/diagnosis"[Mesh] AND ("Immunoglobulin E/diagnostic use"[Mesh] OR "Skin Tests/methods"[Mesh]) AND (Clinical Trial[ptyp] OR Comparative Study[ptyp] OR Randomized Controlled Trial[ptyp] OR systematic[sb]) n=31

Põhiotsingu raames eraldi süstemaatiliste ülevaadete ja kliiniliste uuringute otsingud:
"Asthma/diagnosis"[Mesh] AND ("Immunoglobulin E/diagnostic use"[Mesh] OR "Skin Tests/methods"[Mesh]) AND systematic[sb], n=2, asjakohaseid ei ole.

"Asthma/diagnosis"[Mesh] AND ("Immunoglobulin E/diagnostic use"[Mesh] OR "Skin Tests/methods"[Mesh]) AND (Clinical Trial[ptyp] OR Comparative Study[ptyp] OR Randomized Controlled Trial[ptyp]) 29 vastet, nendest teemakohane (kuigi mitte käsitusala kohane, sest kästleb lapsi): Sinisgalli 2012 (vt allpool)

"allergic asthma"[All Fields] AND "nonallergic asthma"[All Fields] AND (Clinical Trial[ptyp] OR Comparative Study[ptyp] OR Randomized Controlled Trial[ptyp]) n=14. Asjakohaseid ei ole.
Kui piirangud eemaldada, st lihtotsing "allergic asthma"[All Fields] AND "nonallergic asthma"[All Fields], siis tulemuseks on 46 vastet, millest asjakohane on: Romanet-Manent 2002 (vt allpool) ja mõned enne 1994 avaldatud publikatsioonid.

Kokkuvõte (abstrakt või kokkuvõtlikum info)	Viide kirjandusallikale
<p>OBJECTIVE:</p> <p>Environmental allergens are a major trigger of asthma, but not all asthmatics are allergic. This study was designed to review clinical characteristics in children with allergic and non-allergic asthma, based on responsiveness to allergy skin tests, in order to identify a combination of features that could distinguish allergic from non-allergic asthma in children.</p> <p>METHODS:</p> <p>Medical records of 321 children who had allergy skin testing were reviewed, and demographic and clinical data were compared between allergic and non-allergic patients.</p> <p>RESULTS:</p>	<p>J Asthma. 2012 Feb;49(1):51-6. doi: 10.3109/02770903.2011.631244. Epub 2011 Dec 2.</p> <p>Clinical features cannot distinguish allergic from non-allergic asthma in children.</p> <p>Sinisgalli S, Collins MS, Schramm CM.</p> <p>http://www.ncbi.nlm.nih.gov/pubmed/22136286</p>

<p>Approximately two-thirds of the asthmatic children had at least one positive skin test. These allergic patients were more likely to have a history of eczema or Medicaid insurance, but these findings had poor predictive value. There was no difference between allergic patients and non-allergic patients in terms of family history of atopy or asthma, home tobacco smoke exposure, age of onset of asthma, gender, rate of obesity, or asthma severity. Among the allergic asthma patients, neither the number of positive skin tests nor specific individual allergic sensitivities correlated with age of onset of asthma or asthma severity.</p> <p>CONCLUSIONS:</p> <p>This study failed to identify any combination of features that could reliably distinguish allergic from non-allergic asthma in children. Thus, all children with asthma should undergo allergy testing in order to identify potential allergic triggers in allergic patients and to avoid the institution of unnecessary environmental control measures in non-allergic patients.</p>	
<p>BACKGROUND:</p> <p>The aim of this work was to describe clinical similarities and differences between allergic and nonallergic asthmatics, notably concerning the nasosinusal involvement.</p> <p>METHODS:</p> <p>A total of 165 asthmatics (122 allergics and 43 nonallergics) and 193 controls (40 allergics and 153 nonallergics), recruited in the frame of EGEA study (Epidemiological study on the Genetics and Environment of Asthma, bronchial hyperresponsiveness and atopy), were included. Asthmatics were included on the basis of positive answer to four standardized items. To establish differences and similarities between allergic and nonallergic asthmatics, general characteristics (age, sex, smoking habits, history of hay fever and allergic dermatitis), history of asthma, severity and nasosinusal involvement were examined. Clinical assessment was based on the answers to a detailed questionnaire, and spirometry.</p> <p>RESULTS:</p> <p>Greater age, female sex, sinusal polyposis, and FEV1 below 80% of the predicted value increased the risk of displaying a nonallergic type of asthma, whereas history of hay fever, seasonal exacerbation of asthma, and asthma duration lowered this risk. Unexpectedly, we found no difference in terms of rhinitic symptoms between both groups, probably resulting from distinct causes.</p> <p>CONCLUSION:</p> <p>These results give new insights into the contrasts between clinical features of allergic and nonallergic asthma. The terminology of extrinsic asthma was first introduced by Rackeman in 1947 (1) and referred to the triggering role of allergens in asthma. By symmetry, he described intrinsic asthma as a disease characterized by later onset in life, female predominance, higher degree of severity, and more frequent association to nasosinusal polyposis. As these asthmatics were not improved by conventional treatment, this author considered their disease as caused by a nonallergic, unknown phenomenon. It is now widely admitted that nonallergic asthma can be objectively distinguished from allergic asthma based on negative skin tests to usual aeroallergens. On the other hand, positive skin test shows a tendency to produce IgE antibodies in response to low doses</p>	<p>Allergy. 2002 Jul;57(7):607-13.</p> <p>Allergic vs nonallergic asthma: what makes the difference?</p> <p>Romanet-Manent S, Charpin D, Magnan A, Lanteaume A, Vervloet D; EGEA Cooperative Group.</p> <p>http://www.ncbi.nlm.nih.gov/pubmed/12100301</p>

[Type text]

of allergens. "Atopy" and "atopic" are the terms used to describe this clinical trait and predisposition (2). Allergic clinical manifestations of atopy are of various types, for example rhinitis and asthma. Nowadays the terminology of "extrinsic" and "intrinsic" asthma should no longer be used, and should be replaced by the terminology of "allergic" or "nonallergic" asthma (2).	

Viited SIGN-2012 juhendist

Kokkuvõte (abstrakt või kokkuvõtlikum info)	Viide kirjandusallikale
<p>To evaluate the effect of cat removal on cat-allergen content in the home, serial house dust samples were collected from 15 homes during a 9- to 43-week period after cat removal. Samples were obtained with a hand-held vacuum cleaner, and allergen content was quantitated by a radioimmunoassay specific for the major cat allergen, Fe1 d I. Baseline Fe1 d I content ranged from 7.8 FDA units per gram of dust to 436.7 U/gm (median 61.2 U/gm), consistent with levels found in homes with a pet cat. Fe1 d I levels declined gradually in most homes, and by 20 to 24 weeks after cat removal, eight of 15 reached levels consistent with levels found in control homes without cats. In two of those homes, allergen levels fell much more rapidly after aggressive environmental control measures were undertaken. In the other seven homes, however, the decline occurred at a much slower rate, with three homes demonstrating persistent elevations in Fe1 d I content for 20 or more weeks. These data demonstrate that the task of allergen elimination from an indoor environment is extremely difficult, even when the source of a specific allergen can be identified and removed.</p>	<p>Wood RA, Chapman MD, Adkinson NF Jr, Eggleston PA. The effect of cat removal on allergen content in household-dust samples. J Allergy Clin Immunol 1989;83(4):730-</p>
<p>To evaluate the effect of a room high-efficiency particulate air (HEPA) cleaner on cat-induced asthma and rhinitis, 35 cat-allergic subjects who were living with one or more cats were studied in a double-blind, placebo controlled trial. After a 1 mo baseline period, subjects' bedrooms were equipped with an active or placebo air cleaner for the following 3 mo. Evaluations included monthly measurement of cat-allergen levels, daily morning, afternoon, and nighttime nasal- and chest-symptom scores, twice-daily measurement of peak-flow rates, daily medication scores, monthly spirometry, and methacholine (MCh) challenge testing before and after the study.</p> <p>Airborne allergen levels were reduced in the active-filter group as compared with the placebo group ($p = 0.045$). However, no differences were detected in settled-dust allergen levels ($p = 0.485$), morning, afternoon, or nighttime nasal-symptom scores ($p = 0.769$, 0.534, and 0.138), chest-symptom scores ($p = 0.388$, 0.179, and 0.215), sleep disturbance ($p = 0.101$), morning or afternoon peak-flow rates ($p = 0.424$ and 0.679), or rescue medication use (nasal, $p = 0.164$, chest, $p = 0.650$), respectively. Although the combination of a HEPA room air cleaner, mattress and pillow covers, and cat exclusion from the bedroom did reduce airborne cat-allergen levels, no effect on disease activity was detected for any parameter studied.</p>	<p>Wood RA, Johnson EF, Van Natta ML, Chen PH, Eggleston PA. A placebo-controlled trial of a HEPA air cleaner in the treatment of cat allergy. Am J Respir Crit Care Med 1998;158(1):115-20.</p>
<p>Võimalik, et püsiv kõrge ekspositsioon allergeenile aitab kaasa tolerantsi tekkele.</p> <p>BACKGROUND:</p> <p>Although asthma is strongly associated with immediate</p>	<p>Platts-Mills T, Vaughan J, Squillace S, Woodfolk J, Sporik R. Sensitisation, asthma, and a modified Th2 response in children exposed to cat allergen:</p>

[Type text]

<p>hypersensitivity to indoor allergens, several studies have suggested that a cat in the house can decrease the risk of asthma. We investigated the immune response to cat and mite allergens, and asthma among children with a wide range of allergen exposure.</p> <p>METHODS:</p> <p>We did a population-based cross-sectional study of children (aged 12-14 years), some of whom had symptoms of asthma and bronchial hyper-reactivity. Antibodies to mite (Der f 1) and cat (Fel d 1) allergens measured by isotype (IgG and IgG4) specific radioimmunoprecipitation assays were compared with sensitisation and allergen concentrations in house dust.</p> <p>FINDINGS:</p> <p>226 children were recruited, 47 of whom had symptoms of asthma and bronchial hyper-reactivity. Increasing exposure to mite was associated with increased prevalence of sensitisation and IgG antibody to Der f 1. By contrast, the highest exposure to cat was associated with decreased sensitisation, but a higher prevalence of IgG antibody to Fel d 1. Thus, among children with high exposure, the odds of sensitisation to mite rather than cat was 4.0 (99% CI 1.49-10.00). Furthermore, 31 of 76 children with 23 microg Fel d 1 at home, who were not sensitised to cat allergen had >125 units of IgG antibody to Fel d 1. Antibodies to Fel d 1 of the IgG4 isotype were strongly correlated with IgG antibody in both allergic and non-allergic children ($r=0.84$ and $r=0.66$, respectively). Sensitisation to mite or cat allergens was the strongest independent risk factor for asthma ($p<0.001$).</p> <p>INTERPRETATION:</p> <p>Exposure to cat allergen can produce an IgG and IgG4 antibody response without sensitisation or risk of asthma. This modified T-helper-2 cell response should be regarded as a form of tolerance and may be the correct objective of immunotherapy. The results may also explain the observation that animals in the house can decrease the risk of asthma.</p>	<p>a population-based cross-sectional study. Lancet 2001;357(9258):752-</p>