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Indoor Environmental Interventions and their Effect on Asthma Outcomes

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Abstract

Purpose of Review The use of environmental interventions to improve outcomes in asthmatics has long been an elusive goal. While numerous interventions have been studied, the results of clinical trials have been mixed. This review aims to identify combinations of interventions that have been proven to be effective and to propose a model for using them in a clinical setting.

Recent Findings An NIH workshop emphasized a need for research to identify effective interventions for reducing indoor exposures and improving asthma outcomes. A number of innovative measures were described, though evidence supporting their use was lacking. A recent systematic review described various interventions for which evidence is available. The greatest challenge for this approach is the same as that for the medical approach to treatment: nonadherence.

Summary Given evidence for effective interventions, control of environmental exposures should lead to improved asthma outcomes. Methods to improve adherence need to be identified.

Keywords Environment · Asthma · Allergens · Remediation

Introduction

The use of environmental assessment and exposure reduction to improve asthma outcomes has long been promoted as a way to reduce asthma morbidity by reducing a patient's exposure to environmental triggers. It has been studied as a means for primary, secondary, and tertiary prevention of asthma. A workshop held by the NIH emphasized the need for further research to better define which interventions are effective for reducing indoor exposures leading to improved asthma outcomes [1••]. In addition, a recent systematic review described various interventions and the evidence behind them [2••].

The idea is straight forward: A patient with asthma is evaluated for sensitivity to environmental triggers. In addition, their environment (home, work, school) is evaluated for the presence of those triggers. Once identified, an intervention is recommended that is targeted to reduce exposure to relevant triggers. When done correctly, this should, in principle, lead to improved asthma outcomes.

While this approach sounds good in theory, in practice, it is not easily achieved. The problem is that patients may be sensitized to multiple environmental triggers many of which have no readily available means for measurement to determine exposure. In addition, feasible interventions frequently are not able to reduce exposure to triggers sufficiently to improve asthma outcomes. Finally, patients in the real world often are not willing to perform the necessary interventions [3].

Asthma symptoms can be triggered both by outdoor and indoor allergens. Americans spend up to 90% of their time indoors. In most homes, this indoor environment is a closed system with poor ventilation in which airborne contaminants can be more concentrated indoors than outdoors and dust allergens can accumulate over time [4]. Therefore, it is reasonable for interventions intended to reduce allergen exposure to be focused on the indoor environment.

This review will describe our current understanding of interventions to reduce indoor exposure to allergens including the evidence for whether they work and, if so, whether they can be used to improve asthma outcomes. While reduced

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exposure to triggers could also be used to prevent sensitization or the development of disease, our focus in this review will be on tertiary prevention that involves use of interventions to treat asthma after it is present.

Environmental Triggers

Environmental substances can trigger asthma by a variety of mechanisms, though the best understood is when they function either as allergens or irritants. A recent systematic review of 69 studies that focused on modifiable indoor exposures found evidence for a causal relationship between asthma morbidity and exposure to indoor dampness and mold, rodents, dust mites, cockroaches, and pet dander as well as with tobacco smoke and other pollutants [5••]. Each of these exposures is present in a large proportion of houses, each has been shown to trigger asthma in susceptible individuals, and each has a method for measurement or at least for estimating exposure. In addition, sensitization to each allergen can be determined either by skin prick test (SPT) or in vitro test for specific IgE. The goal of environmental control is to recommend specific interventions based on the results of allergy testing to reduce an individual patient's allergen exposure.

Allergens are produced by organisms that live indoors at least part of the time. Such organisms require what we have referred to previously as facilitative factors such as water, food, shelter, and warmth to survive in the build environment [6]. Their emanations are excreted and accumulate over time to form a reservoir of allergens that can persist after the organism has been eliminated. Allergens from these reservoirs periodically become airborne permitting transport via pathways to building occupants where they can trigger allergic symptoms. Because of this reservoir, interventions aimed at reducing allergen-producing organisms alone are unlikely to be successful. To be most effective, strategies should involve a combination of interventions that together address facilitative factors, organisms, reservoirs, and pathways to occupants.

Furry Animals

According to the American Pet Products Manufacturers Association survey from 2010, there are 93.6 million cat owners and 77.5 million dog owners in the USA [7]. Exposure to furry animals can lead to the development of sIgE resulting in manifestations of asthma and rhinitis if exposure persists [8]. Ongoing exposure to furry animal allergens in a sensitized person is likely to lead to poorer asthma outcomes. The time when the exposure occurs is important since early exposure to pet allergens may have a protective effect in some individuals by preventing sensitization and possibly development of asthma [9, 10•]. Once sensitization and asthma have developed, it becomes necessary to reduce exposure to improve outcomes.

Rodents

Rodent infestation and subsequent allergen exposure can occur in a wide range of environments including homes, schools, hospitals, stores, restaurants, and animal laboratory facilities [11]. Low-income housing in urban areas are more likely to have high levels of rodent allergens and rodent-sensitized occupants than suburban homes. In a study of inner-city homes, all had detectable mouse allergen in settled dust with a median level of 14 mcg/g, while another study reported detectable airborne mouse Mus m 1 in > 80% of bedrooms of children with asthma [12]. In a subset of homes from the National Cooperative Inner-City Asthma Study, 95% of all homes had detectable Mus m 1 in at least one room. Homes with evidence of mice such as droppings or stains had higher levels of mouse allergen than those without such evidence [13]. Thirty-three percent of inner-city homes also had detectable rat allergen Rat n 1 [14].

Mouse and rat allergens are carried on particles ranging from 1 to 20 μm in diameter. Both can remain airborne for 60 min or longer after disturbance of the environment giving them an ability to migrate throughout a building [12]. Exposure to rodent allergen levels above 1.6 mcg/g of dust has been shown to be associated with an increased risk of developing rodent-specific IgE and subsequent morbidity from asthma [15]. A recent study of low-income, minority, mouse-sensitized children found that mouse sensitization was associated with a greater need for asthma medication and with greater asthma severity [16]. A recent practice guideline recommended reducing rodent exposure to improve asthma outcomes [17].

Cockroaches

It is estimated that 30–40% of children with asthma who live in urban centers are sensitized to cockroach with as many as 70–80% sensitized in some inner cities [18]. In contrast, one suburban population had a sensitization rate of only 21%. The multicity NCICAS conducted in the 1990s found that bedroom concentrations of Bla g 1 were directly correlated with cockroach sensitization as determined by skin testing [19].

While exposure to cockroaches is associated with a lower rate of asthma in infants, exposure in older children is associated with higher rates of asthma in inner-city areas both within the USA and in other countries. In one study, cockroaches were found in 77% of apartments and 37% of those had at least one resident with asthma. In addition, apartments with Bla g 2 levels > 8 U/g had 1.7 times greater odds of having a resident with asthma [20]. A recent practice parameter recommended cockroach exposure reduction as component of treatment for asthma in sensitized individuals [21].

Dust Mites

Dust mites are found in locations with climates that have sufficient humidity to elevate moisture inside of buildings. Arid areas and locations with high elevations generally do not support indoor dust mite colonies. It is estimated that 84% of US homes have detectable dust mite allergen with higher concentrations occurring in older homes with lower household income and higher bedroom humidity [22]. Little dust mite allergen can be detected in the air of an undisturbed room; however, up to 30 ng/M^3 can be detected during activities that disturb the dust [23]. This is because dust mite allergens are carried on fecal pellets, each measuring 10 to 24 μm in diameter. Dust mite allergens tend to settle within 15 min due to their size and weight [24].

Early sensitization to dust mite at age 1 or 2 years seems to predict development of asthma [25, 26]. The Institute of Medicine noted that houses with greater than 2 mcg mite allergen/g dust had an increased likelihood of dust mite sensitization in children with asthma [27]. Once an individual is sensitized, a number of studies have demonstrated that exposure reduction can reduce asthma morbidity [28].

Fungi

Indoor fungal growth tends to occur in micro-environments where there are nutrients and moisture sufficient for germination leading to subsequent growth into colonies and eventual generation of spores and hyphae. Approximately 10% of US homes are reported to have water damage from exterior leakage, while 8% have damage from interior leakage [29]. One of the biggest challenges with determining fungal exposure is that there are numerous allergen-producing genera most of which have no readily available assays for measurement. The most common assay using impact samplers to collect fungal spores has never been validated and research that has tried to associate this method with health effects varies greatly [30]. Proxy measurements of fungal content have been proposed including measurements of beta-glucans, ergosterols, and even DNA methods using quantitative PCR [31], though none have gained wide application.

In a systematic review by Quansah, a relationship was found between exposure to dampness and fungi early in life and the risk of subsequently developing asthma [32]. In particular, dampness (defined as sufficient moisture to permit growth of microorganisms), and visible mold and moldy odors each were associated with this increased risk. A quantitative meta-analyses of 33 studies that were reviewed by the IOM [33] found a statistically significant association between the presence of fungal growth and dampness and the development of cough, wheeze, current asthma, and ever-diagnosed asthma [34].

Interventions Used to Reduce Exposure

Environmental control involves a variety of interventions designed to reduce exposure to allergens. Some act on facilitative factors while others focus on the organisms that create allergens and yet others act on reservoirs of allergens. In theory, it is necessary to act on all three of these factors in addition to blocking pathways to occupants for allergen exposure to be reduced sufficiently to be clinically useful. A recent systematic review identified 33 randomized controlled trials of interventions that individually or in combination were evaluated for allergen reduction as a means of improving asthma outcomes. Table 1 shows the most commonly used interventions and the allergens they are intended to act on.

Facilitative Factors

Facilitative factors are conditions that are necessary for the growth of allergen-producing organisms. The most important factors are a source of water, food, shelter, and a means of ingress into the building. Microorganisms such as fungi can also use condensation on cold surfaces as a water source while dust mites can absorb humidity directly from the air. Though we intentionally provide pets with food and water, cockroaches and rodents often gain access to those same sources. Elimination or at least control of facilitative factors makes it difficult for unwanted organisms to survive in a given building which makes their removal a useful intervention.

Integrated Pest Management

Integrated pest management (IPM) has been shown to be effective for reducing exposure to rodents and cockroaches. It involves removing facilitative factors including food, water, and shelter leading to a reduced environmental carrying capacity for these unwanted pests. In addition to removing these factors, IPM also involves blocking means of ingress and, when necessary, killing or trapping them using either chemical or mechanical methods. Once the pests are removed, professional cleaning is necessary to reduce residual allergens that have accumulated in reservoirs. For IPM to be effective, residents need to be taught how to monitor their home for a recurrence of the infestation and to continue the intervention until pests are completely eliminated. They may also need to be taught better home cleaning and food management strategies to reduce the potential for food and water to become available to pests.

Several randomized, controlled studies have demonstrated the effectiveness of IPM in reducing cockroach exposure

Table 1 Interventions with at least some evidence that they can reduce allergen exposure when used correctly, mechanisms of action and allergens that are removed

Intervention	Mechanism of action	Allergen(s) removed
Facilitative factors (mitigation)		
Integrated pest management (IPM)	Remove food, water, shelter, means of ingress	Cockroach, rodent
Fix leaks, intrusion, remove moldy materials	Remove moisture	Fungi
Ventilation, dehumidification, insulation	Prevent condensation	Fungi, dust mites
Source control		
Chemical (acaricides/insecticides/rodenticides/fungicides)	Chemical—kills target organism	Dust mite, rodents, cockroaches, fungi
Mechanical (traps, gel baits)	Mechanical—traps target organism	Rodents, cockroaches
Pet avoidance/regular washing	prevents allergen release into reservoirs	Dogs and cats
Reservoir (abatement)		
Repeated carpet cleaning and vacuuming	Removes accumulated allergens	Dust mite, fungi, pets
Remove carpet/furniture	Prevents accumulation of allergens	Dust mite, fungi, pets
Washing of bedding	Removes accumulated allergens	Dust mite, pets
Change mattress	Removes accumulated allergens	Dust mite, pets, fungi
Pathway to occupants		
HEPA air filtration (central and portable units)	Removes airborne particles	Fungi, pets, rodents
Mattress/pillow encasements	Block allergen transport to patient	Dust mites, pets

[35–37]; however, only one included patient outcomes. Since multiple interventions were used in that study, it was not possible to determine the role of IPM alone in improving the outcomes [38]. IPM was used to control mice in one study; however, even with a significant reduction in mouse allergen levels, no significant improvement in asthma symptoms or forced expiratory volume (FEV_1) was demonstrated [39]. Recently, the aggressive use of insecticidal bait alone to reduce cockroach exposure in the home of children with asthma was shown to reduce asthma symptoms and unscheduled healthcare utilization [40•]. The success of this intervention over previous attempts was attributed to measures that ensured that it was performed persistently and correctly.

Moisture Control

Elimination of moisture sources including intrusion, leaks, and condensation due to poor insulation can inhibit growth of fungi and other microorganisms that require dampness. Based on intervention studies available at the time, a WHO report concluded that remediation of dampness can improve health outcomes [41]. Interpretation of these results is difficult because each study included multiple interventions of which moisture control was the only one component. A Cochrane systematic review of moisture control by Sauni [42••] that included 12 studies with 8028 total participants found moderate to very low-quality evidence that repairs that included moisture control of fungus-contaminated houses and offices reduced asthma-related symptoms and respiratory infections in adults. A study by Kercsmar [43] demonstrated reduced asthma symptom days and a lower rate of exacerbations following extensive environmental remediation that included moisture reduction. A controlled trial of improved home insulation also showed decreased moisture and mold exposure and improved health outcomes [44].

Dehumidification

Dehumidification operates on the principle that when air is exposed to a surface that is below its dew point, water from the air condenses on the surface and is removed. Since microorganisms such as fungi and dust mites require moisture to survive. Preventing condensation by reducing humidity removes this source of water. Since dust mites also are capable of absorbing moisture directly from the air, dehumidification makes it more difficult for them to grow.

A dehumidifier can operate either centrally within an air handling system, or it can operate as a stand-alone unit. An air conditioning unit intrinsically serves as a dehumidifier since moisture in the air that travels over the cooling coils condenses on the coils leading to its removal. Stand-alone dehumidifiers operate on the same principle and can be placed in damp locations such as a basement. They need to be emptied regularly or they can be set to empty continuously if a drain is available.

Dehumidification alone can lead to reduced exposure to dust mites [45] and to fungi [46]. It is unclear whether this also leads to improved asthma outcomes because most studies include multiple interventions in their protocol. Studies of dehumidification alone have failed to demonstrate improved clinical benefit. For that reason, this intervention should be used as part of a multifaceted approach to reduce mite and mold exposure [47].

Allergen-Producing Organisms

Pet Removal/Hypoallergenic Pets

Removal of pets from the home or at least keeping them from the bedroom where the person with asthma sleeps and breeding of hypoallergenic dogs and cats are strategies that have been proposed for reducing pet allergen exposure. Pet removal can reduce allergens in the home, though it may take up to 6 months for reservoirs to diminish. In a prospective study of patients with asthma who were sensitized to furry animals, some elected to find their pet a new home and others chose to keep it. After 1 year, there was a significant improvement in airway hyperresponsiveness and reduction in ICS use in the pet removal group compared to the pet keeping group [48]. Compliance with this approach is a challenge, however, since most families are unwilling to remove a family pet [49]. Keeping a pet from the bedroom may lead to reduced allergen exposure; however, in homes with central heating and cooling systems, airborne pet allergens can circulate to the isolated room diminishing the effectiveness of that intervention.

Breeding of hypoallergenic pets has become a popular fad. The problem with this approach is that allergens such as albumin and immunoglobulins are necessary for pet survival. For that reason, there is no such thing as a completely nonallergenic pet. While it is in principle possible to breed a Fel d 1-deficient cat or Can f 1-deficient dog, that would help only if those are the only pet allergens triggering a person's asthma.

Pet Washing

Regular washing of pets to remove allergens before they spread into the environment also has been studied. Since pets produce allergens continuously, washing needs to be performed regularly to be effective. Washing can lead to reduced airborne Can f 1 in a home for up to 3 days suggesting a need to wash a dog at least twice a week for the intervention to be effective [50]. An indoor cat should be washed more frequently to reduce airborne Fel d 1 [51]. Even with reduced airborne exposure, studies have not consistently demonstrated reduced asthma symptoms in response to pet washing.

Acaricides

An acaricide is a chemical such as benzyl benzoate that can kill dust mites when applied to carpeting and upholstered furniture. When used as an intervention along with vacuuming to remove the reservoir, use of acaricides can provide a temporary reduction in dust mite exposure. In general, acaricides do not completely eliminate dust mite populations primarily because they are unable to penetrate through the entire depth of carpet or throughout upholstered furniture. Consequently, colonies of mites survive application and regrow over time. A meta-analysis of 23 studies of dust mite control including use of acaricides found no beneficial effect on asthma symptoms or on the development of sensitization [52].

Reservoirs

Vacuuming

Regular use of a high-efficiency vacuum cleaner can remove allergen-associated particles that have settled into carpeting and upholstered furniture. The removal rate needs to be greater than the rate of production for this approach to be successful. Ideally, reservoirs such as carpeting and upholstered furniture should be removed from the environment; however, most homeowners are unwilling to do that. The challenge with vacuuming is that it needs to be done regularly to work. In addition, the vacuum needs to have a high-efficiency bag or filter on it to prevent redistribution of collected particles. Cyclonic vacuum cleaners have an advantage in that they are able to capture particles without the need for filtration. Vacuuming can remove dust mite particles, but if the mites are still present, mite allergens tend to re-accumulate unless the intervention is performed repeatedly and frequently. Regular vacuuming can lead to sustained reductions in exposure to dust mite allergen [53], though these results are not consistent among the numerous studies that evaluated it.

Hot water extraction (known as steam cleaning) could, in principle, provide additional removal of dust mite allergens over vacuuming with the added advantage of scalding and therefore killing the mites. A limitation of this approach is that dust mites move away from heat, so the hot water tends to drive them to the bottom of the carpet pile where they are unaffected by the heat [54]. In addition, the moisture associated with water can be a stimulus for mite proliferation.

Chemical Methods

Sodium hypochlorite bleach (0.05% solution) is capable of denaturing cat and dog allergens [55]. Tannic acid solution also can denature cat allergen in vitro [56], though there are concerns that its presence may interfere with assays for Fel d1 making this reduction activity an artifact. There is no evidence that use of chemical methods alone improves outcomes for pet-allergic patients with asthma.

Pathways

Air Filtration

Air filtration is used to remove allergen-associated particles from the air. A recent Rostrum on air filters and air cleaners described how they work and the evidence for their effectiveness [57]. The efficiency of an air filter is usually described in terms of its minimum efficiency reporting value or MERV rating, which is assigned to filters based on the ASHRAE standard testing method [58]. Ratings range from MERV1 to MERV12, with higher ratings indicating better efficiency. Filters with a MERV12 rating are at least 80% efficient at removing particles in the 1 to 3 μm range and at least 90% in the 3 to 10 μm range. Filtration strategies include whole house filters installed on the central heating and air conditioning system and free-standing portable room air purifiers. Central filters range from inexpensive fiberglass that provides minimal particle removal to pleated polymer filters with a large surface area that can reach a rating as high as MERV11 or MERV12. Stand-alone air purifiers generally contain HEPA (high-efficiency particulate air) filtration; however, they have a limited ability to filter large volumes of air and therefore should only be used in rooms that meet their recommended capacity.

Air filtration is effective only if the allergens of concern are associated with airborne particles that are consistently available for removal. This includes cat, dog, and rodent allergens Dust mite allergens are associated with particles that tend to settle when not disturbed so they are not amenable to air filtration most of the time. It is not clear whether fungal allergens can be removed by air filtration. A review by Wood [59] concluded that HEPA filters are not effective for reducing exposure to mites and mold but that they may be effective for removing pet allergens. Air filters were able to reduce PM 2.5 and black carbon particles in a school setting [60].

Evidence for clinical improvement with air filtration has been difficult to demonstrate primarily because of differences in the results of studies. One controlled trial that evaluated the combined use of HEPA air filtration, mattress encasements, and cat removal showed reduced exposure to allergen but failed to show a significant clinical benefit [61]. Another study found that HEPA filters did improve airways hyperresponsiveness but not symptoms among cat- or dog-allergic children [62]. And yet another study showed clinical benefit even though there was no demonstrated reduction in pet allergens [63]. A Cochrane review found insufficient evidence for clinical improvement with air filters among people with pet allergies and exposure [64]. Studies that have shown decreases in exposure and improved asthma outcomes generally use air filtration as one component in a multicomponent intervention strategy [57].

Bedding Encasements and Washing

Mattress and pillow encasements are used to prevent movement of dust mites and allergen-containing particles from mattresses or pillows to individuals who sleep on them. Encasements have been shown to be effective for decreasing exposure to dust mites and furry animal allergens; however, when used as an isolated intervention, they have not been found to improve asthma outcomes [65]. Another study that looked at the effect of mattress and pillow encasements along with regular washing of bedding also was not able to demonstrate reduced asthma symptoms [66]. A study that used multiple interventions for mites including tannic acid, encasements, and washing of bedding did show a reduction in mite exposure and improved hyperresponsiveness but did not show an improvement of FeV_1 or asthma-specific quality of life [67].

Multifaceted Interventions

Building occupants are exposed to allergens because of a variety of factors. Strategies that affect multiple factors tend to be the most successful at reducing allergen exposure and improving asthma outcomes [68]. In addition, since most strategies have an effect on multiple allergens, it makes little sense to study an intervention with the goal of reducing a single one. The systematic review by Le Cann [2] illustrated this by pointing out that most controlled studies showing benefit used multiple intervention strategies. The real question is whether it is possible to identify which interventions to use in a given environment if the sensitization status of its occupants is known and its allergen content has been measured. When used this way, individually tailored environmental control practices, if implemented properly, could reduce asthma symptoms and exacerbations as effectively and at similar cost as use of inhaled controller medications [69••]. If both interventions (environmental intervention and pharmacotherapy) are used to their greatest effect, it is possible that asthma morbidity could be further reduced. Since most studies of interventions use a standard strategy regardless of the exposure or sensitization of building occupants, this question cannot currently be answered. Clearly, further research is needed to define these variables.

So Does It Work?

Control of disease by manipulating environmental factors has long been a goal. While a number of interventions have been shown to reduce exposure to target allergens leading to improved asthma outcomes, real-world allergen reduction is difficult to achieve. The most likely reason for reduced environmental control of asthma appears to be interventional noncompliance in much the same way that pharmacologic noncompliance reduces medical control of asthma [2].

Interventions with the best adherence tend to be those with relatively low cost or that would have been done anyway as part of routine cleaning (e.g., mattress encasements, washing bedding, vacuuming) while those with the least adherence either are expensive or interventions that families are unwilling to do (e.g., changing mattresses, removing carpets and furniture, pet removal). In addition, passive interventions that require little patient input are likely to have better compliance than those requiring repeated action. Table 2 shows the estimated adherence for various interventions from two different studies [2, 3].

It is likely that noncompliance can be approached in much the same manner as medication noncompliance. This includes repeated education and use of interventions that families are willing to do and that are feasible given their living and financial situation. In addition, a recent study demonstrated that providing patients with feedback in the form of repeated measurements of dust mite exposure lead to significantly reduced allergen levels than the same interventions without feedback [70••]. Adherence also can be improved if there are regular visits by a community health worker [71]. If asthma education is provided in addition to help with environmental interventions, this combination is likely to be the most effective way to improve asthma outcomes and reduce costs [72].

Table 2 Likelihood that patients will perform various interventions. (low compliance < 33%, medium compliance 34–66%, high compliance > 66%)

	Likely adherence (Schatz)	Likely adherence (Le Cann)
Facilitative factors		
IPM	Medium	Medium
Fix leaks, intrusion, moldy materials	Medium	Low
Ventilation, dehumidification, insulation	High	High
Source control		
Chemical	Low	
Mechanical	Low	
Pet avoidance/washing	Low	Medium
Reservoir		
Vacuuming	Medium	High
Wash bedding	High	High
Remove carpet/furniture	Low	Medium
Change mattress	Medium	
Pathways		
HEPA air filtration	Low	Medium
Encasements	High	High

Conclusions

The use of environmental interventions targeted at exposures to which a patient is sensitized and exposed opens up an exciting new possibility for asthma management. As a strategy to accompany pharmacologic treatment, environmental intervention has the potential to improve asthma outcomes when drugs and allergen immunotherapy alone have been insufficient. The precise combination of interventions to use in specified situation remains to be determined.

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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