

# Encasement of Bedding Does Not Improve Asthma in Atopic Adult Asthmatics

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## Key Words

House dust mite avoidance · Encasement of bedding · Adult asthma · Atopy

## Abstract

**Aim:** We evaluated the impact of impermeable bed covers on asthma in asthmatics with clinically relevant house dust mite (HDM) sensitization. **Methods:** The study included 32 HDM-sensitized asthmatics in whom HDM allergy was considered as a significant factor in their asthma. They were randomized into either an intervention group whose bedding was encased with impermeable covers, or a control group who received cotton covers. Before and 3 and 6 months after encasement, dust samples were collected from the bedding and assayed for Der p 1. Clinical outcomes included quality of life, lung function, bronchial reactivity to methacholine, symptoms, medications and peak flow rates. **Results:** Baseline Der p 1 levels in both the active and the placebo groups were comparable and high (19.2 vs 18.9 µg/g of dust). There was a significant reduction in Der p 1 levels in the active group after 6 months, but not in the placebo group (7.3 vs 21.9 µg/g of dust). Quality of life improved significantly in both the intervention and control groups, but there was no significant difference in the improve-

ments between the groups. There was no significant change in lung function, symptoms, and requirements for medications. **Conclusions:** Encasement of bedding significantly reduced the Der p 1 levels. However, this was not sufficient to produce worthwhile clinical improvement in those in whom dust mite avoidance might well have been recommended as part of their clinical management.

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## Introduction

House dust mites (HDM) of the family Pyroglyphidae are amongst the most important sources of indoor allergens [1, 2]. HDM allergens are widely distributed in modern homes, especially in bedding [3]. Exposure to HDM allergens is known as a risk factor for exacerbation of symptoms of asthma, especially among sensitized patients [4].

Several methods of HDM control have been investigated in the past, but currently available evidence of chemical and physical approaches does not yet provide a secure basis for advice and policy [5]. Whilst multifactorial mite avoidance measures are recommended in the current clinical guidelines, patients are more likely to

comply with single interventions. The encasement of bedding is a simple single intervention that needs minimal ongoing compliance.

There is some evidence that encasement of bedding reduces HDM allergen levels in bedding [6–9]. However, it has not yet been shown that encasement of bedding is associated with clinical benefits [5]. Clinical benefits of this intervention are likely to be confined to the subgroup of atopic asthmatics whose asthma is precipitated by HDM allergen exposure. Three randomized controlled trials [10–12] that included encasement of bedding investigated patients with mild to moderate asthma and sensitization and showed substantial reductions in Der p 1 levels, but these reductions had no clinical impact.

The current study was conducted to assess the impact of HDM-impermeable covers as a single intervention on different clinical asthma outcomes among adult atopic asthmatics attending specialist clinics, whose HDM allergy played a significant role in their asthma.

## Methods

### *Study Design*

This was a parallel group double blind randomized controlled trial with encasement of bedding utilizing impermeable covers in the intervention group and identical-appearing non-impermeable cotton covers in the control group.

### *Study Population*

The study sample comprised young adults with 'current asthma' (i.e. wheeze and bronchial hyperreactivity), allergy to HDM as determined by skin prick test and referred by specialist clinicians because exposure to dust was a trigger factor for their asthma. These patients were recruited from Asthma and Allergy clinics at the Alfred Hospital and the Respiratory Clinic at the Monash Medical Centre, Melbourne. After initial recruitment, participants' eligibility was confirmed by a questionnaire, skin prick test to HDM and a Methacholine (MCh) Challenge Test. An eligible subject was defined as a patient having all of the following inclusion criteria and none of the exclusion criteria.

**Inclusion criteria:** Patients in whom dust exposure was considered a trigger factor for asthma, who have taken short-acting  $\beta$  agonists during the last 2 weeks, who have a positive MCh challenge test ( $PD_{20}$   $FEV_1 < 2$  mg MCh), a SPT wheal of  $\geq 5$  mm for HDM allergen extract with a positive histamine control and a negative saline control and have perennial asthma.

**Exclusion criteria** were: patients on oral steroids, on inhaled steroids  $>2,400$   $\mu$ g per day, current smokers, ex smokers  $>10$  pack-years and  $FEV_1 < 1.0$  litre.

### *Intervention*

The participants were stratified by the floor coverings in their homes in permuted blocks of size two and randomized into either the intervention group or the placebo group by the toss of a coin. Encasement of the bedding either with impermeable covers (inter-

vention) or with cotton covers (control) was carried out for pillows, mattresses and doonas. The covers were fitted by a research nurse and left for 6 months. Participants were instructed to place conventionally washed bed linen on the bed outside of the encasement of bedding. Both groups were requested to follow their routine cleaning and washing procedures. No specific washing instructions or any other information on avoidance of mites was given to patients in either group.

### *Data Collection Protocol*

A questionnaire was used to gather information on demographic variables at baseline. Before the encasement and again 3 months and 6 months afterwards, home visits were made to collect dust samples. The clinical status of participants was followed longitudinally with lung function tests, a quality of life questionnaire and diary cards. Lung function and quality of life were assessed prior to and 6 months after the intervention. Information on asthma was collected with diary cards prior to, 3 months and 6 months after the intervention.

### *Assessment of Allergen Levels*

At each visit, dust samples were collected from the mattress and the rest of the bedding using a modified Makita 4071D handy-vac (7.2-volt-battery-operated) with a 25- $\mu$ m Nylon filter. Dust was collected from a 2-m<sup>2</sup> area of the mattress over 2 min and from the remaining bedding components over 2 min [3]. Dust samples were sieved (0.3 mm mesh) and Der p 1 levels in the fine dust were measured by a standard immunoassay [13].

### *Assessment of Asthma and Allergy*

#### *Skin Prick Test*

Skin prick testing was carried out using lancets and allergen extracts (Bayer, USA). The allergen extracts used were of *D. pteronyssinus* (Bayer, Sydney), cat dander and rye grass pollen. A positive SPT was defined as a wheal diameter of 3 mm or more to an allergen with a positive reaction to histamine (i.e. 3 mm or more) and a negative reaction to saline.

#### *Lung Function Tests*

Lung function was measured using a rolling seal spirometer (Sensor-Medics, Yorba Linda, Calif., USA). Forced expiratory volume ( $FEV_1$ ) was recorded from the best of five blows, which met the American Thoracic Society criteria. MCh (Methacholine Chloride, USP Methapharm Inc, Brantford, Ontario, Canada) was delivered by a Mefar 3B dosimeter (Mefar srl, Bovezzi, Italy) until  $FEV_1$  fell by 20% from the initial value or up to a cumulative dose of 2 mg. The full protocol has been described elsewhere [14].  $PD_{20}$  was defined as the provocative dose of MCh required to produce a 20% fall in  $FEV_1$  from the initial value. Bronchial hyperreactivity (BHR) was defined as a  $PD_{20}$   $FEV_1 \leq 2$  mg MCh. Bronchial reactivity was also expressed as the dose response slope (DRS) = (% change in  $FEV_1 + 3.5$ )/MCh dose.

#### *Quality of Life*

A validated quality of life questionnaire related to asthma [15] was used to measure the impact of asthma on quality of life. This was a self-administered questionnaire with 20 statements describing situations how asthma or its treatment affected some people. The responses were given on a 5-point Likert scale ranging from very severely to not at all. These items collected information on

four subscales of quality of life, i.e. breathlessness, mood disturbance, social disruption and concern for health. Responses were scored from 0 to 4 and composite scores were calculated for each domain as well as for the total quality of life, (TQL) [15]. TQL ranged from a minimum score of 0 to a maximum score of 10 with higher scores indicating a worse quality of life.

#### Diary Cards

These were self-administered forms where participants recorded peak expiratory flow rates (PEF), symptoms, asthma medication use and time spent at home for a two-week period. Participants were provided with peak expiratory flow (PEF) meters (Allersearch, Melbourne) and trained to record the highest of three peak expiratory flows twice a day on waking each morning and at bedtime. The frequency of the use of inhaled medications was recorded as number of puffs per day. Symptoms of asthma, i.e. wheeze, cough, sleep disturbance and restriction of activities were recorded on a scale from 0 (asymptomatic) to 3 (severe). These scores were added to derive the daily total symptom score for each day for each individual. Daily peak flow variability (PFV) was defined as the difference between morning and evening PEF on each day expressed as a percentage of the higher figure [16]. Peak flow variability indicated airflow obstruction which was variable spontaneously or with treatment. Daily peak flow variability of 6–10% was considered consistent with mild asthma [17].

Six clinical indices were calculated for each 14-day period from the information extracted from the diary cards: the average night and day symptom scores, total daily symptom score, the average daily frequency of the use of preventer (anti-inflammatory) and reliever (bronchodilator) medication, and the average PFV.

#### Blinding

The participants and investigators performing the tests and analysis were blinded at all times to the type of covers used by the participant to avoid misclassification bias. It was not necessary to prematurely 'crack the code' for clinical reasons for any individual.

#### Sample Size and Analysis

The sample size was calculated to detect a reduction in Der p 1 down to 6  $\mu\text{g/g}$  of fine dust, which was the mid point between the threshold for sensitization (2  $\mu\text{g/g}$  of fine dust) and for symptoms (10  $\mu\text{g/g}$  of fine dust) [18]. The geometric mean of the Der p 1 level for 485 homes in Melbourne was 20.0  $\mu\text{g/g}$  of fine dust with a geometric standard deviation of 3.0 [19]. To have 80% power to detect a reduction from 20.0 to 6.0  $\mu\text{g/g}$  as statistically significant (two-sided  $p < 0.05$ ) required 15 homes per group. This number also provided 80% power to detect a reduction in bronchial hyper-reactivity (doubling dose of  $\text{PD}_{20}$ ). Therefore, a parallel group design with 16 in each group was planned to allow for a 5% drop out over the study period.

The Statistical Analytical System package [20] was used to analyse the data. The statistical significance of the difference in the baseline characteristics between the two groups was examined using either two-sample parametric or non-parametric tests depending on the distribution of the data. Repeated-measures analysis of variance was carried out to assess the significance of reduction in the allergen levels and the change in the clinical indicators of asthma within as well as between groups. The conventional cut-off value of  $p < 0.05$  was considered as the level of statistical significance.

#### Ethics

Informed consent was obtained from all participants at the commencement of the study. Ethical approval was granted by the Ethics Committees at the Alfred Hospital and Monash Medical Centre in Melbourne.

## Results

Thirty-two participants had their bedding encased and a total of 30 completed the study. One participant in the intervention arm withdrew from the study after the second visit due to excessive night sweating following encasement of the bedding. Another participant in the control arm withdrew just after encasement as she moved out of the house. Among the 30 participants who completed the study, 24 had fitted carpets (12 active, 12 placebo) and 6 had floorboards (3 active and 3 placebo).

Information on sociodemographic variables, Der p 1 levels, measurements of asthma and other potential confounding variables were compared between active and placebo groups at baseline (table 1). The age of the participants in the active group ranged from 18 to 43 years and in the placebo group from 19 to 47 years. Only the difference in the peak flow variability, which was higher in the control group (10%) than in the active group (8%), was marginally statistically significant ( $p = 0.05$ ). A majority of the participants in both groups had severe BHR ( $\text{PD}_{20} < 0.1$  mg of MCh). In contrast, all the participants in both groups except one in the active group had a baseline  $\text{FEV}_1$  of more than 80% predicted. Thirteen of fifteen in each group had taken a puffer or inhaler within 24 h prior to lung function testing. Fourteen in the active group and 10 in the placebo group had taken a reliever within this period.

A statistically significant reduction in geometric mean Der p 1 levels was observed in the active group from 19.2 to 6.7  $\mu\text{g/g}$  of dust by the second visit and this reduction was sustained until the third visit (7.3  $\mu\text{g/g}$  of dust) (fig. 1) ( $p < 0.05$ ). In contrast, there was no significant change in the Der p 1 levels in the placebo group (i.e. 18.9, 16.2, 21.2  $\mu\text{g/g}$  of dust, respectively). The difference in the reduction in Der p 1 levels between the two groups was statistically significant ( $p < 0.05$ ).

There were statistically significant improvements among both groups in total quality of life ( $p < 0.05$ ), but there was no significant difference in the improvement between the two groups (fig. 2). There was a statistically significant improvement in the quality of life subscores in the domains of social disruption and concern for health in the active group ( $p < 0.05$ ), but not in the placebo

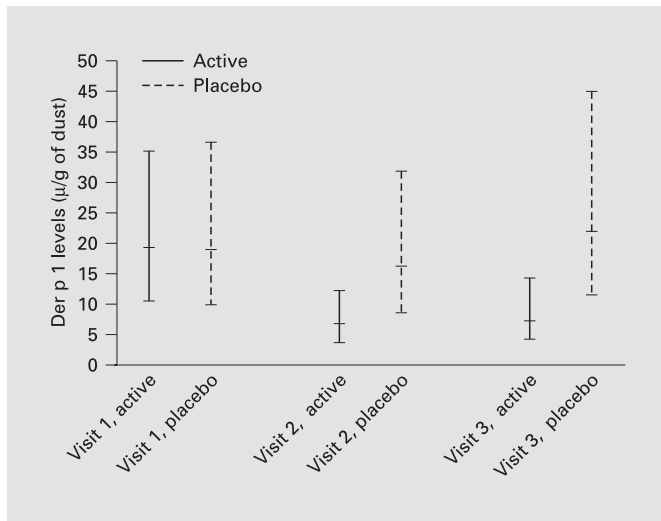


**Fig. 1.** Geometric mean and 95% CI for the mean of the Der p 1 levels by the visit and the group over the study period.

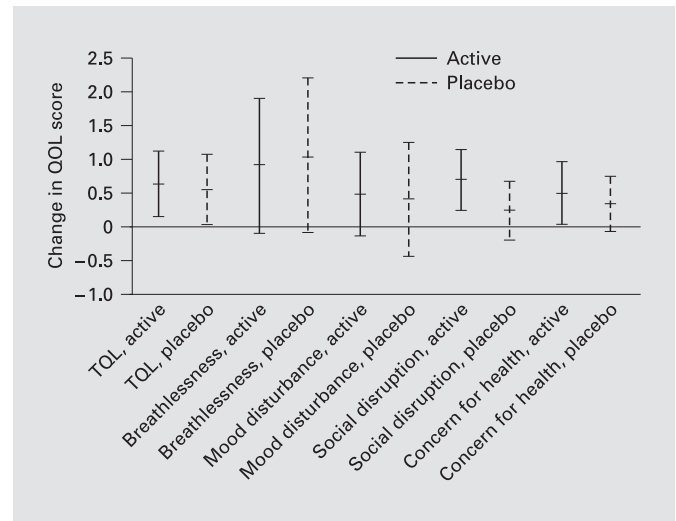


**Fig. 2.** Change (visit 1–visit 2) in quality of life (QOL) over the study period by the group; mean and 95% CI for the mean.

**Table 1.** Comparison of baseline characteristics between the intervention and placebo groups

| Baseline characteristics               | Active group   | Placebo group   |
|----------------------------------------|----------------|-----------------|
| Age, mean $\pm$ SD, years              | 29.8 $\pm$ 5.3 | 33.2 $\pm$ 7.2  |
| Male                                   | 7 (47%)        | 5 (31%)         |
| PFV, %, mean $\pm$ SD                  | 8.3 $\pm$ 4.6  | 10 $\pm$ 5.4    |
| FEV <sub>1</sub> , % predicted         |                |                 |
| <80%                                   | 1              | 0               |
| 80–90%                                 | 5              | 3               |
| >90%                                   | 9              | 12              |
| log PD <sub>20</sub> , mean $\pm$ SD   | –1.9 $\pm$ 1.0 | –2.25 $\pm$ 1.1 |
| PD <sub>20</sub>                       |                |                 |
| <0.1 mg                                | 10             | 11              |
| 0.1–1 mg                               | 4              | 4               |
| >2 mg                                  | 1              | 0               |
| log dose-response slope, mean $\pm$ SD | 5.8 $\pm$ 1.5  | 6.0 $\pm$ 1.7   |
| TQL, median and range                  | 1.8 (0.8–3.2)  | 1.8 (1.1–4.0)   |
| Day symptom score, median and range    | 0 (0.0–0.6)    | 0.7 (0–0.6)     |
| Night symptom score, median and range  | 1.1 (0.07–2.0) | 1.3 (0.4–1.7)   |
| log Der p 1, mean $\pm$ SD             | 3.0 $\pm$ 1.2  | 2.9 $\pm$ 1.3   |
| Use of preventers, median and range,   |                |                 |
| average number of puffs per day        | 2 (0–6)        | 1 (0–4)         |
| Use of relievers, median and range,    |                |                 |
| average number of puffs per day        | 0.7 (0.7–7.9)  | 1.1 (0.1–2.7)   |
| SPT wheal size, median and range, mm   |                |                 |
| HDM                                    | 12 (6–26)      | 12 (6–26)       |
| Cat                                    | 9 (0–17)       | 6 (0–17)        |
| Rye grass                              | 7 (0–24)       | 9 (0–24)        |
| Houses with cats                       | 3 (20%)        | 4 (26%)         |
| Cat sensitization among cat owners     | 2 (66%)        | 3 (75%)         |
| Houses with mouldy patches             | 3 (20%)        | 5 (33%)         |

**Table 2.** Change (visit 1 – visit 2) in clinical indicators of asthma over the study period by the group: mean and 95% CI for the mean

| Clinical indicators of asthma                      | Change in the intervention group: mean (95% CI) | Change in the placebo group: mean (95% CI) |
|----------------------------------------------------|-------------------------------------------------|--------------------------------------------|
| log DRS                                            | 0.41 (–0.12 to 0.94)                            | 0.38 (–0.18 to 0.94)                       |
| log PD <sub>20</sub>                               | –0.18 (–0.56 to 0.21)                           | –0.17 (–0.79 to 0.46)                      |
| Peak flow variability, %                           | 1.95 (–0.05 to 3.9)                             | 0.5 (–1.5 to 2.5)                          |
| Day symptom score                                  | 0.02 (–0.03 to 0.07)                            | 0.04 (–0.02 to 0.10)                       |
| Night symptom score                                | 0.2 (–0.08 to 0.49)                             | 0.14 (–0.17 to 0.45)                       |
| Use of preventers: average number of puffs per day | 0.15 (–0.02 to 0.37)                            | 0.05 (–0.26 to 0.38)                       |
| Use of relievers: average number of puffs per day  | 0.36 (–0.14 to 0.85)                            | 0.2 (–0.02 to 0.43)                        |

group. However, the differences in the change of the scores between the two groups were not statistically significant (fig. 2). There were improvements in quality of life related to the other three domains in both groups, but the differences within or between the two groups were not statistically significant (fig. 2).

There was a reduction in bronchial reactivity in both active and placebo groups as evidenced by the reduction in the log dose response slope and the increase in the PD<sub>20</sub>, but the differences within or between the two groups were not statistically significant (table 2). Also, there was no significant impact of the intervention on FEV<sub>1</sub>. Similarly, asthma symptoms improved and use of medication fell in both groups as evidenced by the reduction in the symptom severity scores and dose of asthma medications, but the differences within or between the two groups were not statistically significant (table 2).

## Discussion

In this study, encasement of bedding with HDM impermeable covers reduced the allergen levels almost 3-fold. While this was below the proposed threshold dose for induction of asthma symptoms, it is acknowledged that the confidence intervals of these levels did overlap the 10 µg/g threshold. However, the relevance of an absolute allergen threshold is controversial as discussed further below. Furthermore, the reduction was sustained over a 3- to 6-month period, although this reduction did not have a significant impact on indicators of asthma severity. Asthma-related quality of life significantly improved in both active and placebo groups reflecting placebo and/or Hawthorne effects [21]. However, there was no difference in the improvement between the two groups,

suggesting that allergen reduction had no significant impact on the patients' quality of life.

There are a number of ways of defining clinical activity in asthma, such as with symptoms, lung function and BHR. The latter has come to be regarded as a gold standard of the surrogate markers of underlying disease, but it is important that a comprehensive approach to the assessment of asthma is made in any intervention study. This study assessed different clinical asthma outcomes comprehensively by both questionnaires and extensive laboratory testing. Furthermore, this study used very stringent criteria to include subjects who would have been highly likely to benefit from the intervention. A majority of the participants in both groups had severe BHR. In contrast, all but one participant had normal lung function, which may be related to their use of medication. Therefore, the results of this study are relevant evidence to guide clinical practice in such patients.

Our findings on the efficacy of encasement in reducing HDM allergen levels support some studies carried out in the past. In a cross-sectional study conducted in Melbourne (Australia), the average allergen level in the beds with impermeable covers was below the threshold for sensitization (<2 µg/g of fine dust) compared to other beds where the average was above the threshold for induction of asthma (>10 µg/g of fine dust) [8]. Three clinical trials provide some evidence for the efficacy of impermeable covers in reducing HDM allergen levels [6, 7, 9], but the results were not conclusive due to the absence of placebo interventions. A recent randomized placebo-controlled trial conducted in an area with low ambient HDM allergen levels demonstrated a significant reduction in allergen levels in the intervention group over a 6-month period, but not over a 12-month period [12]. However, similar studies conducted in areas with high indoor HDM

allergen levels, such as in Australia, have shown that the encasement of bedding with impermeable covers leads to a significant reduction in HDM allergen levels [10, 22] even after 12 months. The reduction of allergen levels in one of these studies [22] has been associated with a reduction in the required dose of inhaled corticosteroid in asthmatic children, suggesting that such an intervention can have a positive impact.

Marks et al. [23] investigated the efficacy of the combination of encasement of bedding with impermeable covers plus the use of a surface chemical treatment of bedding in a randomized controlled trial. Their control group had a placebo spray, but no placebo cover. The difference in allergen levels between the two groups after 2 weeks was significant, but no difference was observed after 3 months. These negative results may have been due to an interaction between the two interventions. The dampness created on the cover by the spray, which may have encouraged HDM growth, may have masked any beneficial effects of the cover.

In our study, the reduction of HDM allergen levels to 6.7 µg/g of dust by encasement of bedding as a single intervention was not associated with a significant improvement in clinical asthma. It should be noted that the figure of 6 µg/g of dust used in the power calculations was arbitrary. In contrast, a before and after trial on encasement of bedding reported a significant improvement in BHR in children with asthma [9]. However, this effect could be confounded by seasonal changes in symptoms, which cannot be excluded without a control group.

The lack of association between reduction in allergen levels below the presumed threshold and clinical asthma may indicate that the true clinical threshold level is well below this proposed threshold. Although rather approximate, and still debated [24], this threshold has been widely accepted. However, the correlation between threshold allergen levels and induction of symptoms is far more complex than the originally proposed direct dose-response relationship. Data from primary prevention of allergy studies suggest complex and dynamic gene-environment interactions which are different for different populations studied, resulting in apparently inconsistent and conflicting results [25]. It is possible that such interactions are also relevant in secondary disease prevention studies.

Also, it could be argued that the contribution of mite allergens originating from other sources, especially carpets, could have confounded the results. However, as a result of the stratified sampling, both groups had equal numbers of carpeted rooms and we have observed a good correlation of HDM allergen levels between the carpets

and bedding [3]. Another important issue that needs to be considered in interpreting these results is whether the follow-up time was sufficient to consider the progression of the disease [26]. Perhaps the reduction may need to be sustained longer than 6 months to have an impact on clinical asthma, quality of life and BHR, as suggested in some studies [27]. However, a randomized controlled trial reported a significant improvement in BHR within 6 months after the intervention when the encasement of bedding was combined with air cleaners in the house, but not when encasement was used alone [7].

It also should be noted that HDM-sensitive asthmatic patients are usually sensitive to other allergens, so that successful elimination of only one allergen may have limited benefits [28]. There may of course be a subset of patients highly sensitive to mites who would benefit from the reduction in HDM allergen levels achieved in this study.

Our study showed that encasement of bedding as a single intervention was effective in reducing HDM allergen levels well below the accepted threshold for induction of asthma. This finding has implications for public health, as it is a relatively inexpensive and a very simple method that could be widely used to reduce HDM allergen levels in the community. However, this reduction was not sufficient to have a significant impact on asthma disease activity among patients whose HDM allergy played a clinically significant role in their asthma, and consequently we cannot recommend encasement of bedding with impermeable covers alone as a secondary preventive method of asthma in this subgroup of asthmatics. However, it is likely that the intervention need to be sustained longer than 6 months, given that there were some non-significant improvements in clinical indicators and therefore, conducting a longer-term study on this subgroup of patients is recommended.

## Acknowledgments

We would like to thank the Victorian Health Promotion Foundation and Department of Human Services for funding this study. We acknowledge the assistance received in data collection from Trina Vincent and John Elliot and laboratory analysis from Anna Cheng and Diana Cao.

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