

Quantitative assessment of allergic shiners in children with allergic rhinitis

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Background: The knowledge on allergic shiners is extremely limited. A conceivable tool able to quantify allergic shiners has not been established.

Objectives: We sought to determine the significance and changeability of allergic shiners through our newly developed computerized method.

Methods: We developed a novel computerized method to measure allergic shiners and enrolled a cohort of children with or without allergic rhinitis. Children with allergic rhinitis were prospectively assessed. A standardized digital photograph was taken during each visit, and a modified Pediatric Rhinoconjunctivitis Quality of Life Questionnaire was completed. Subject global assessment for nose symptoms and subject global assessment for eye symptoms (SGAE) were self-recorded daily.

Results: We included 126 children with allergic rhinitis and 123 healthy control subjects. One hundred three (82%) participants with allergic rhinitis completed at least 4 prospective assessments. Shiners were darker ($P < .001$) and larger ($P < .001$) in children with allergic rhinitis. Darkness and sizes of allergic shiners were paradoxically inversely correlated ($P = .02$). Darkness of allergic shiners positively correlated with the duration of allergic rhinitis, practical problem scores, and SGAE values ($P = .02$, $P = .004$, and $P = .002$, respectively), but sizes of allergic shiners did not. Shiners were found to be darker in children with scores of eye symptoms of greater than 6, scores of practical problems of greater than 5, and SGAE values of greater than 0 ($P = .02$, $P < .001$, and $P = .003$, respectively), whereas shiners were larger in children with scores of other symptoms of greater than 9 and activity limitations of greater than 4 ($P = .02$ and $P = .002$, respectively).

Conclusion: Computer-analyzed allergic shiners correlate with the chronicity and severity of allergic rhinitis. (*J Allergy Clin Immunol* 2009;123:665-71.)

Key words: Allergic shiners, digital photograph, darkness, area, allergic rhinitis

Shiners are caused when blood and other fluids accumulate in the infraorbital groove. The causes in children include nasal congestion, inflammatory diseases of the conjunctiva, trauma to the forehead or nose, face surgery, and malignancy.¹⁻⁴

In children with allergic rhinitis, the blue-gray to purple discoloration beneath the lower eyelids is referred to as *allergic shiners*, which are believed to be caused by venous stasis resulting from nasal congestion.^{1,4} According to Duke's description in 1930,⁵ nasal disease must be established at least 1 year before infraorbital changes occur.

The term allergic shiners was coined by Marks^{6,7} in 1954. He found that dark eye shadows could be observed bilaterally in most children with perennial allergic rhinitis. In 1963, he further stated that many of the allergic shiners resulted from long-standing perennial allergic rhinitis.⁸ Since then, allergic shiners have been widely considered important signs of allergic rhinitis.^{4,9-11} However, there was no objective or quantitative tool to verify these clinical observations. In addition, whether shiners fluctuated according to the symptoms of allergic rhinitis remained unclear.

In this study we developed a novel computerized method to make a quantification of allergic shiners possible and enrolled a cohort of children aged 6 to 12 years with or without perennial allergic rhinitis. We determined the extent to which allergic rhinitis affected the formation of shiners and investigated whether allergic shiners were changeable.

METHODS

Study design

This study was conducted at the National Taiwan University Hospital and the nearby Dong-Menn Elementary School between June and November 2005. The general data of all of the volunteers were collected and recorded, including age, sex, body weight, body height, and a comprehensive medical history. Children aged 6 to 12 years were classified into allergic rhinitis and healthy control groups. Atopy was documented by positive results on serum total IgE or allergen-specific IgE measurement at the beginning of the study. Inclusion criteria for the allergic rhinitis group included a history consistent with perennial allergic rhinitis, absence of any underlying disease other than allergy, nasal mucosa consistent with allergic rhinitis, and presence of atopy. Volunteers were enrolled as healthy control subjects if they had never been given a diagnosis of allergy, had never presented with any allergic symptom, and had no underlying disease. Those with respiratory tract infections within the week before beginning the study were excluded.

A standardized digital photograph of every participant was taken at the beginning of the study. Children with documented allergic rhinitis were further

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Abbreviations used

- SGA: Subject global assessment
 SGAE: Subject global assessment for eye symptoms
 T_a : Threshold between the control and allergic rhinitis groups of first visit based on the area values
 T_d : Threshold between the control and allergic rhinitis groups of first visit based on the darkness

assessed prospectively in our clinics at least 4 times, either on scheduled monthly visits or when they had aggravated symptoms. A standardized digital photograph was taken on each visit, and frequencies and levels of both of allergic symptoms were evaluated by using a modified version¹² of the Pediatric Rhinoconjunctivitis Quality of Life Questionnaire.¹³

After the first visit, daily symptoms were also monitored by using subject global assessment (SGA) for nose symptoms and SGA for eye symptoms (SGAE) self-recorded every night before sleeping, with scores from 0 (no symptoms) to 4 (severe symptoms).

The study was approved by the ethics committee of the National Taiwan University Hospital. Informed consent was obtained from the parents of all participants.

Standardized digital photography

A rectangular color checker, approximately 4.3 cm in width, was placed in front of the chin of the participants as a reference to standardize both the size and color of the photographs (for details, see the **Methods** section and Fig E1 in this article's Online Repository at www.jacionline.org).

Serum IgE antibodies

The Pharmacia CAP system (Pharmacia, Uppsala, Sweden)¹⁴ was used to detect serum total IgE and allergen-specific IgE for 8 common inhaled allergens, including *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Blomia tropicalis*, cat dander, dog dander, cockroach, Bermuda grass, and ragweed. Total IgE levels of 150 IU/mL or greater or allergen-specific IgE levels of 0.7 IU/mL or greater were considered positive.

Digital image analysis

Each element of a digital image is called a *pixel*. The intensity value of each pixel is called the *gray level*. The darker a pixel appeared, the smaller the gray-level value was.¹⁵

In this analysis the very first step was *preprocess*, which automatically standardized all of our images according to the appearance of the color checker in each photograph. Its purpose was to reduce the possible influence of imaging environments that might cause different color intensities and image sizes (for details, see the **Methods** section in this article's Online Repository).

Every image completing preprocess was sampled for darkness and area value measurements. Darkness was measured by means of 2 different methods performed by 2 separate investigators blind to the symptom severities. The first method was called the *semiautomatic method* (Fig 1, A and B). It was started by clicking 3 times on the outer margin of the cornea: once on the nasal side, once on the temporal side, and once on the lowest point of the cornea. Once the location of the cornea was determined, the computer program would automatically place a block (242 × 132 pixels) closely beneath it to circumscribe a measuring region. The gray-level mean values in the infraorbital groove (S_m) and cheek (C_m) were then computed in the upper and lower slanted triangle regions, respectively.

The other method, the *manual method* (Fig 1, C and D), was designed to evaluate the validity of the semiautomatic method. We used 2 mobile blocks (54 × 66 pixels) to locate regions for analysis on either side of each image. The upper block was manually placed on the site that appeared darkest in the infraorbital groove and the lower block on the brightest site on the cheek. After the upper and lower blocks were located manually, we

computed the gray-level mean values in their respective slanted triangle regions.

Darkness (D) was defined as follows: $D = C_m - S_m$. It could greatly reduce the influence of different skin colors on the darkness grade of shiners. Moreover, the darker a shiner looked, the larger the darkness value.

To measure a shiner's area value, we sampled the curve of each lower eyelid. In Fig 2 we sketched the red curve in line segments using a computer mouse to approximate the lower eyelid line. After that, 242 pixels from the lowest point of the red curve were extended automatically to circumscribe the regions to be analyzed. Then an optimal demarcation separating the shiner from the cheek area was plotted automatically according to the entropy theorem,¹⁶ which helped understand the probability distribution of an event. Hence we could estimate the area value of each shiner in pixels and translate it to square centimeters, which was represented by the area value of shiners, where 1 pixel was around 0.01 cm. Every area value of shiner's value (in square centimeters) was normalized by body surface area to obtain another parameter (in square centimeters per square meter).

By using the method composed of histogram transformation^{17,18} and curve fitting (for details, see the **Methods** section in this article's Online Repository),^{19,20} a threshold²¹⁻²³ between the control and allergic rhinitis groups at the first visit based either on the darkness (T_d) or the area values (T_a) was established. Shiners darker than T_d and larger than T_a were classified as shiners with significant darkness and shiners with significant size, respectively.

Dark shiners and large shiners were respectively defined as shiners darker and larger than two third of shiners in patients with allergic rhinitis during their first visit.

Retesting performed by another investigator for the same digital photographs from the compiled allergic rhinitis (first visit) and normal control groups was carried out 2 years after the initial test to determine the reliability of the computerized method.

Statistical analysis

The differences in darkness and area values between the 2 groups were analyzed by using the Mann-Whitney test. Correlation analyses were performed with the Spearman test. Differences in categorical variables were assessed by using the Fisher 2-tailed exact test. Test-retest reliability was assessed by means of Spearman correlations, and interrater reliability was estimated by using intraclass correlations. A P value of less than .05 was considered to be statistically significant.

RESULTS

Study populations

A total of 126 volunteers were enrolled in the allergic rhinitis group (first visit) and 123 in the control group. Background data, including age, body weight, and body height, did not differ between these 2 groups (Table I). The male/female ratio was 3:2 in the allergic rhinitis group and 2:3 in the control group.

One hundred three (82%) participants with allergic rhinitis completed at least 4 visits (approximately 4-7 visits), accounting for a total of 503 visits. From the second to the final visit of these 103 patients, daily SGA between visits was recorded without a loss in 326 (82%) visits. The mean follow-up period (first to final visit) was 3.7 ± 0.6 months, and the average duration between each visit was 1.0 ± 0.1 months.

Correlation between right and left

Measured by using either the semiautomatic method ($R = 0.87$, $P < .001$) or manual method ($R = 0.83$, $P < .001$), the darkness of shiners between the right and left sides from the allergic rhinitis group (first visit) was highly correlated (see Fig E2, A and B, in this article's Online Repository at www.jacionline.org). This

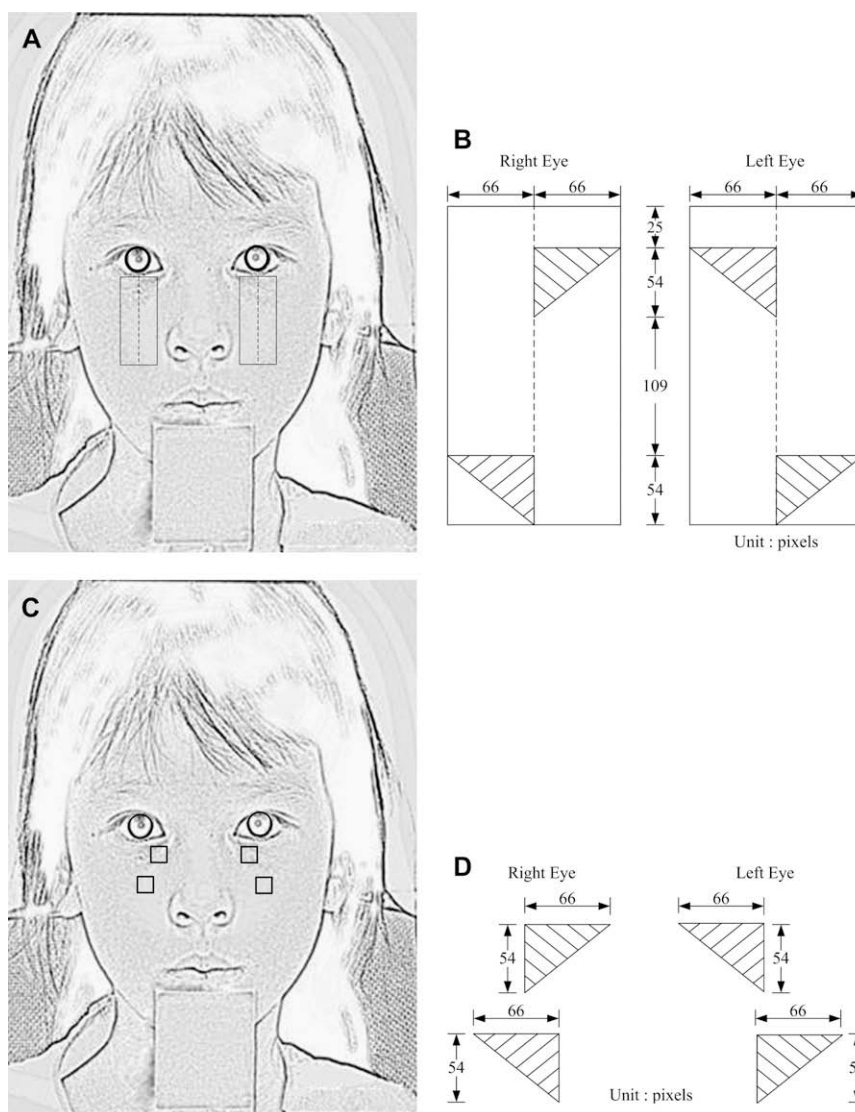


FIG 1. Measurement of darkness of shiners. Darkness of shiners was measured by using the semiautomatic method (**A and B**) and the manual method (**C and D**). The gray-level mean values in the infraorbital groove and cheek were computed in the upper and lower slanted triangle regions, respectively, in both of the 2 methods.

high correlation was also noted in the area values ($R = 0.91$, $P < .001$; see Fig E2, D). The means of both darkness (semiautomatic method: 44.9 ± 12.2 vs 46.7 ± 12.7 , $P = .25$; manual method: 46.8 ± 12.1 vs 48.4 ± 12.5 , $P = .30$) and areas of shiners (2.1 ± 1.1 vs 2.2 ± 1.2 cm²/m², $P = .24$) did not differ between the right and left sides. Based on their high correlations and similarities, we used the average right and left values (average of darkness of shiners on the left and right sides and average of area value of shiners normalized by body surface area [in square centimeters per square meter] on the left and right sides) to represent the darkness and area of shiners.

Morphology of shiners

In our photographs we noticed shiners were darker nasally and faded away temporally. They could be crescents or triangular in shape.

Validity of the semiautomatic method

The validity of the semiautomatic method was assayed based on its correlation with the manual method. The results were highly correlated ($R = 0.94$, $P < .001$; see Fig E2, C), and their mean values were not statistically different (45.8 ± 12.0 vs 47.6 ± 11.8 , $P = .24$), which verified the representative role of the semiautomatic method.

Reliability

The reliabilities for both measurements of darkness by using the semiautomatic method ($R = 0.99$, $P < .001$; intraclass correlation coefficient = 0.99 , $P < .001$) and the area values of shiners ($R = 0.98$, $P < .001$; intraclass correlation coefficient = 0.99 , $P < .001$) were excellent (see Fig E3 in this article's Online Repository at www.jacionline.org). The means of both darkness with the semiautomatic method (38.0 ± 13.2 vs $38.0 \pm$

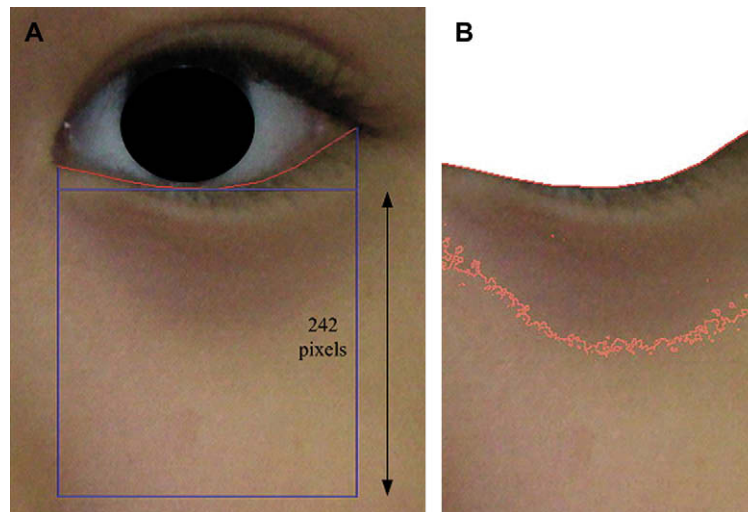


FIG 2. Eyelid sampling and measurement of area values of shiners. The lower eyelid curve (A) was sketched with automatic downward extension of 242 pixels from the lowest point of the red curve to mark a boundary. This region was examined with the entropy theorem, and a line of demarcation was plotted automatically to circumscribe the area of shiners (B).

TABLE I. Background data in the healthy control and allergic rhinitis groups

	Healthy control group (n = 123)	Allergic rhinitis group (n = 126)	P value
Age (y)	8.6 (1.5)	8.7 (1.8)	.81
Body weight (kg)	30.4 (9.0)	32.1 (8.8)	.14
Body height (cm)	130.9 (17.3)	133.3 (10.5)	.18

Values are presented as the mean (SD).

13.2, $P = 1.0$) and areas of shiners (1.6 ± 1.1 vs 1.8 ± 1.3 cm²/m², $P = .13$) between test and retest did not differ. The average time spent on processing each digital image was approximately 0.5 to 1 minute.

Inverse correlation between darkness and area

Correlation analysis for shiners from the 503 visits revealed that darkness and area values were inversely correlated ($R = -0.18$, $P = .02$).

Effect of allergic rhinitis on the formation of shiners

The skin below the lower eyelids was significantly darker (52.5% increase, $P < .001$) and the areas of shiners were significantly larger (111.7% increase, $P < .001$) in the allergic rhinitis group (first visit) than those in the control group (Fig 3). T_d and T_a values between the control and allergic rhinitis groups on their first visit were 36.9 and 1.62 cm²/m², respectively (see Fig E4 in this article's Online Repository at www.jacionline.org). One third of first-visit children with allergic rhinitis had shiners darker than 49.9 cm²/m², larger than 2.36 cm²/m², or both.

The prevalences of shiners with significant darkness, dark shiners, shiners with significant sizes, and large shiners were all much higher in the allergic rhinitis group than in the control group (all $P < .001$, see Table E1 in this article's Online Repository at www.jacionline.org).

Allergic shiner as a marker to identify allergic rhinitis

We compiled and analyzed data from the control and allergic rhinitis groups (first visit). As shown in Table II, different definitions for shiners led to different sensitivities and specificities for allergic diseases. Dark shiners had an excellently high specificity for allergic rhinitis (100%), whereas the sensitivity was low.

Factors modifying the severity of allergic shiners

To investigate which factors in children with allergic rhinitis could modify the severity of allergic shiners, we first obtained data from the allergic rhinitis group (first visit) and analyzed the correlation of allergic shiners with several possible factors, including age; durations (from disease onset to present) of allergic rhinitis, allergic conjunctivitis, asthma, and atopic dermatitis; current eosinophil count; serum total IgE level; and specific IgE level. The result showed the duration of allergic rhinitis was the only factor positively correlated with the darkness of shiners ($R = 0.21$, $P = .02$). None was found to be statistically correlated with the area values.

Next we obtained data from children with allergic rhinitis completing at least 4 visits and investigated whether there were any threshold values of symptoms associated with increased severities of shiners. The results showed that children with scores (frequencies) of eye symptoms of greater than 6 (9.0% increase, $P = .02$) and of practical problems of greater than 5 (8.9% increase, $P < .001$) had significantly darker shiners (Fig 4, A and B) and that children with scores (frequencies) of other symptoms of greater than 9 (16.2% increase, $P = .02$) and of activity limitation of greater than 4 (15.8% increase, $P = .002$) had significantly larger shiners (Fig 4, C and D). Children with SGAE values of greater than 0, either recorded on the day before visits (7.5% increase, $P = .003$), summed from daily scores in the past 1 week (8.5% increase, $P < .001$; Fig 4, E and F), or obtained from averaged weekly summation of SGAE values from prior

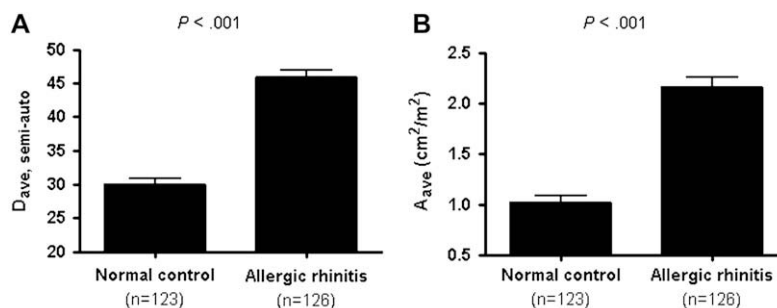


FIG 3. The effect of allergic rhinitis on the formation of allergic shiners. **A**, D_{ave} , Average of darkness of shiners on the left and right sides. **B**, A_{ave} , average of area values of body surface area on the left and right sides.

TABLE II. Sensitivities and specificities of shiners for allergic diseases

	Shiners with significant darkness ($D_{ave, semi-auto} \geq 36.9$)		Dark shiners ($D_{ave, semi-auto} \geq 49.9$)		Shiners with significant sizes ($A_{ave} \geq 1.62$)		Large shiners ($A_{ave} \geq 2.36$)	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
Allergic rhinitis	76	76	33	100	61	85	33	94
Allergic conjunctivitis	77	67	35	95	61	76	36	91
Asthma	82	61	38	91	61	69	32	85
Atopic dermatitis	77	59	39	90	49	65	23	81

$D_{ave, semi-auto}$, Average values of right and left differences of darkness between cheeks and infraorbital grooves evaluated by using the semiautomatic method; A_{ave} , average of right and left shiner area values normalized by body surface area.

visits (8.5% increase, $P = .02$), presented with significantly darker shiners. Levels of bother had no similar association.

Also, we assessed the linear correlation between the severities of allergic rhinitis and the darkness/size of allergic shiners. Darkness of allergic shiners positively correlated with the practical problem scores ($R = 0.13$, $P = .004$), SGAE values recorded on the day before visits ($R = 0.14$, $P = .01$), SGAE values summed from daily scores in the past 1 week ($R = 0.18$, $P = .002$), and SGAE values obtained from averaged weekly summation of SGAE values from prior visits ($R = 0.22$, $P < .001$), but sizes did not.

DISCUSSION

Through this newly developed computerized method, objective measurement of allergic shiners can be properly done for the first time. We proved that shiners were indeed much more common and prominent in children with allergic rhinitis than in healthy subjects. Darkness and sizes of allergic shiners were paradoxically inversely related. Dark shiners had an excellent specificity for allergic rhinitis. Darkness of allergic shiners positively correlated with the chronicity of allergic rhinitis, practical problem scores, and SGAE values, but sizes of allergic shiners did not. Moreover, frequent symptoms above certain thresholds were associated with increased severities of shiners.

This is the first attempt to generate a conceivable tool that will quantify allergic shiners. The resolution of hyperpigmentation-related black eyes in adults has once been evaluated by using a quartile rating scale,²⁴ the results of which depended solely on ocular inspection of traditional photographs. This is not suitable for

the delicate measurement in our study. Our novel computerized method can avoid biases of human ocular inspection, and the results are reproducible. This is a considerable breakthrough and might be used in the future to clarify possible but undetermined causes of shiners, such as inheritance, sleeplessness, or racial difference.

That shiners were more common in children with allergic rhinitis^{6,8} than in healthy children was an unverified belief. Allergic shiners were mostly recognized subjectively. Lacking an objective morphologic definition made determining the percentages of shiners very difficult and unreliable. In this study we proposed preliminary boundaries (T_d and T_a) to separate shiners with significant darkness/size from those without. By using this definition, allergic shiners were indeed more common in children with allergic rhinitis.

Knowledge on the morphologic characteristics of allergic shiners is extremely limited. Our data showed that shiners between the right and left sides were highly correlated and similar. However, the darkness and size of shiners were inversely correlated. We proposed that the morphologies of allergic shiners constituted a wide spectrum. On one end, shiners looked narrow and deep, whereas on the other end, shiners appeared wide and shallow. Which direction a specific condition might go depended on the extensibility of the skin below the lower eyelids. Moreover, different allergic inflammations might contribute to different features of allergic shiners, especially because our data showed that thresholds of symptoms reflecting enhanced darkness of shiners were not associated with an increased size and *vice versa*.

Physical signs, including facial grimaces, nasal creases, allergic shiners, and Dennie-Morgan lines, are suggestive but not

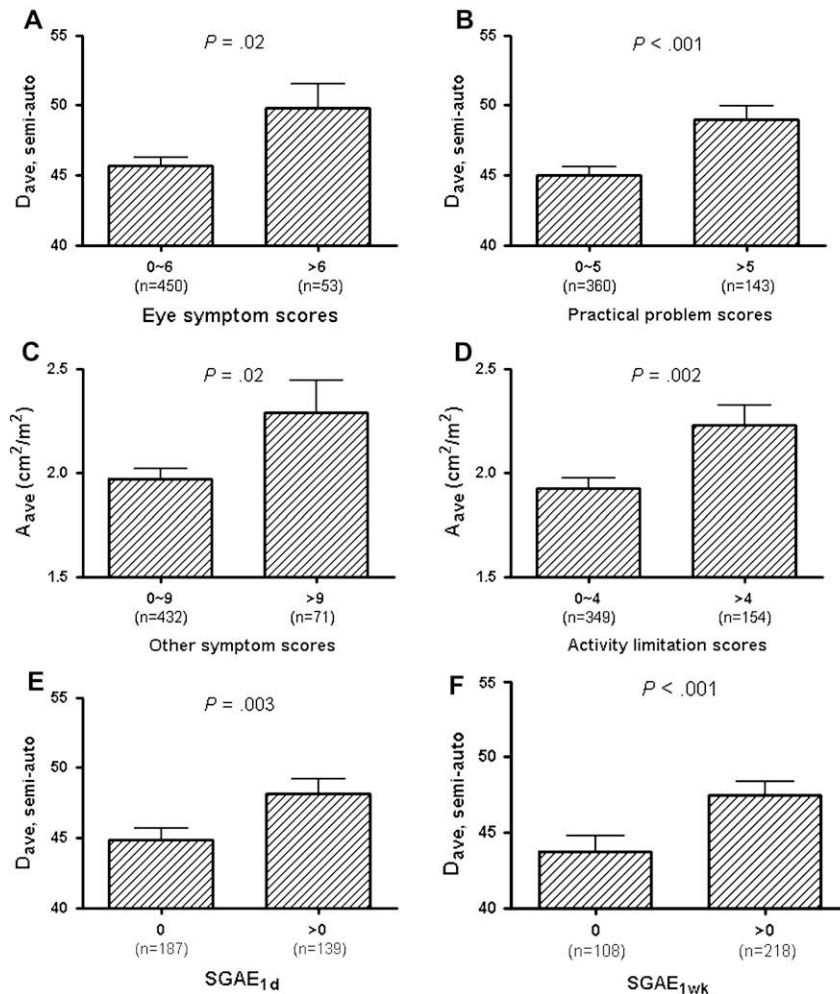


FIG 4. The thresholds of symptoms associated with enhanced darkness (**A**, **B**, **E**, and **F**) or increased sizes (**C** and **D**) of shiners on different visits. D_{ave} , Average of darkness of shiners on the left and right sides; A_{ave} , average of area values of body surface area on the left and right sides; SGAE_{1d}, SGAE recorded on the day before visits; SGAE_{1wk}, SGAE summed from daily scores in the past week.

pathognomonic of allergic rhinitis.⁸⁻¹¹ Because the dark shiner defined in our study had an excellent specificity for allergic rhinitis, a dark shiner can be recognized as a symbol of allergic rhinitis in children.

The possible correlation between allergic shiners and the duration of allergic rhinitis was originally described by Marks.⁸ He found that the nasal disorder was of long duration when blue-black shadows were deep and wide. In our study we documented that the darkness of shiners indeed positively correlated with the duration of allergic rhinitis. However, the size of shiners did not. This might be reasonable because the darkness and size of shiners were 2 different entities that were even inversely associated.

Whether allergic shiners correlated with the severities of symptoms of allergic rhinitis has never been investigated. This relationship seems to be logical because the pathogenesis of allergic shiners is believed to be related to venous stasis resulting from nasal congestion.^{1,4} To solve this puzzle, we designed this study and found in the prospective follow-up visits that frequent allergic rhinitis symptoms above certain thresholds were associated with either darker or larger allergic shiners. Among these

symptoms, practical problem scores (including rubbing eyes/nose, and blowing nose) and SGAE values further had linear correlations with the darkness of allergic shiners. For the first time, these correlations showed that allergic shiners could fluctuate accordingly.

However, sizes of allergic shiners did not correlate linearly with symptoms. A possible explanation was that the infraorbital areas might be less adjustable than the depth. Moreover, our data showed that eye symptoms correlated with allergic shiners much better than nasal symptoms. Allergic shiners are present in children with allergic conjunctivitis as a result of localized venous congestion caused by mast cell mediators surrounding eye tissues.²⁵ Therefore it is rational that allergic nasal inflammations extending upward to affect ocular structures probably leads to more severe venous stasis than those restricted to the nose. Visible darker shiners might indicate more frequent eye symptoms, reminding parents and physicians that children might require more medical help.

In summary, we have developed a novel computerized method to quantify allergic shiners. This method is an important breakthrough for the study of shiners. Through it, basic characteristics

and the clinical significance of allergic shiners have been disclosed for the first time. Allergic shiners are changeable and might get worse if symptoms of allergic rhinitis are not controlled. Detailed mechanisms require further investigations.

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Clinical implications: This newly developed method makes a quantification of shiners possible. Darker or larger allergic shiners might indicate more frequent allergic symptoms.

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METHODS

Standardized digital photography

All of the photographs were taken indoors. The same digital camera was used by the same investigator with identical camera settings, lighting, and participant positioning. A flash light was used for every child. The height of the chair every participant sat on was 42 cm. The distance from the participant to the camera was 110 cm. A rectangular color checker, approximately 4.3 cm in width (see Fig E1), was placed in front of the chin of the participants as a reference to standardize both the size and the color of the photographs.

Digital image analysis: Fundamentals

For a color digital image, each pixel includes 3 color values red (R), green (G), and blue (B). The range of each color value is ranked between 0 and 255. We can obtain the gray-level value as follows: $Gray\ level = (R+G+B)/3$.

Digital image analysis: Preprocess

First, we randomly picked 30 image samples to obtain parameters for image normalization. These parameters included the following. For red, green, and blue mean values, we used a block to catch a smooth place over the color checker (see Fig E1) and get those values. For the zooming mean, we computed the mean sizes (width and length) of the color checker in 30 images. Then we used these 2 parameters (color and size of color checker) as references to standardize all of our image samples automatically.

Digital image analysis: Histogram transformation and curve fitting

To find a threshold that could divide 2 partially overlapped but individually modeled distributions into 2 parts with minimal total average loss, we used a 3-step method. First, we obtained the histogram model from all samples.^{E1} Second, we used the "coordinate transformation"^{E1,E2} with proper bins to represent the distribution of the histogram model, which was denoted as HM_{ct} . The number of bins (N_B) was defined as follows: $(N_B)^2 = No. of\ all\ samples$. Third, we applied the "curve fitting (ie, polynomial regression)" method^{E3,E4} to represent the HM_{ct} with a mathematic function. The ideal threshold would be the crossover point of 2 curves transformed from 2 different groups.^{E5-E7}

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TABLE E1. Distributions of shiners (%)

	Shiners with significant darkness ($D_{ave,semi-auto} \geq 36.9$)	Dark shiners ($D_{ave,semi-auto} \geq 49.9$)	Shiners with significant sizes ($A_{ave} \geq 1.62$)	Large shiners ($A_{ave} \geq 2.36$)
Healthy control group	24	0	15	6
Allergic rhinitis group	76	33	61	33
<i>P</i> value	<.001	<.001	<.001	<.001

D_{ave,semi-auto}: Average of the right and left shiner darkness evaluated by using the semiautomatic method; *A_{ave}*: average of the right and left shiner area values normalized by body surface areas.

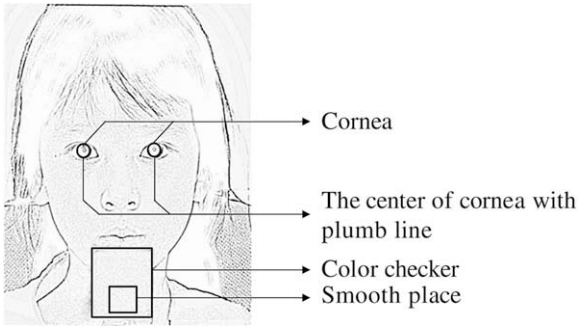


FIG E1. The position of the color checker.

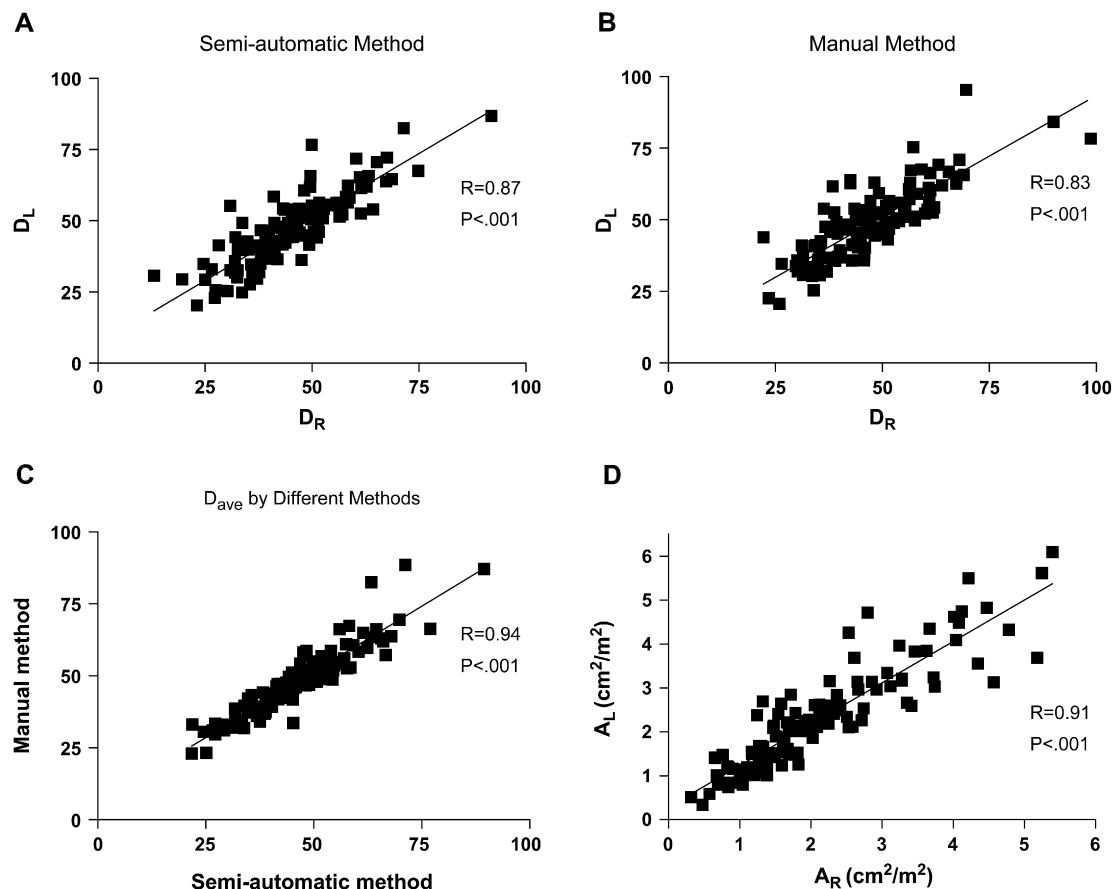


FIG E2. Correlations of shiners between 2 sides (**A**, **B**, and **D**) and between the semiautomatic and manual methods (**C**). D_L , Darkness of shiners on the left side; D_R , darkness of shiners on the right side; D_{ave} , average of darkness of shiners on the left and right sides; A_L , area value of shiners normalized by body surface area on the left side; A_R , area value of shiners normalized by body surface area on the right side.

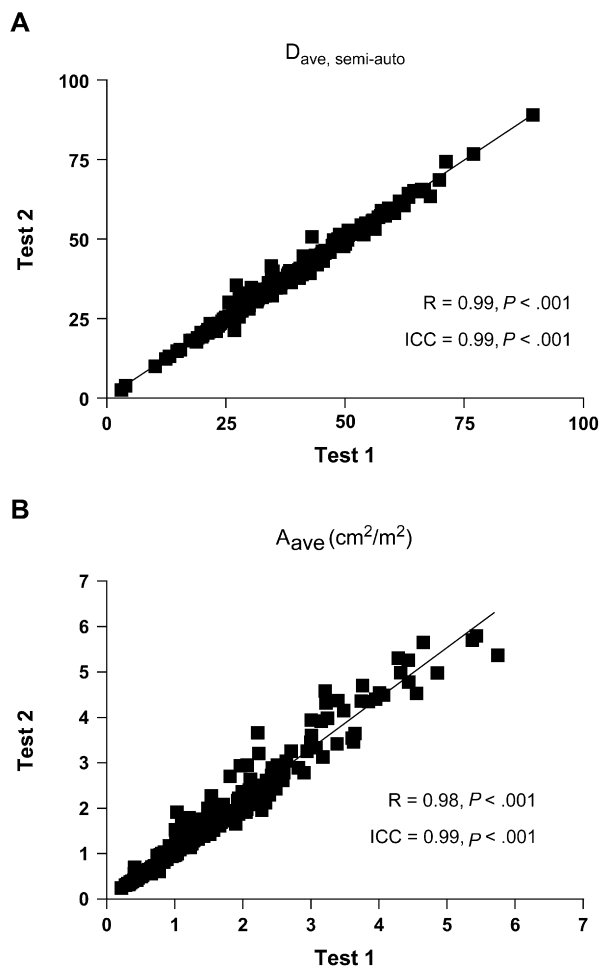


FIG E3. Reliabilities for measurement of darkness by using the semiauto-
matic method **(A)** and for measurement of area values **(B)** of shiners. Test 2
performed on the same digital photographs was carried out 2 years after
test 1. D_{aver} , Average of darkness of shiners on the left and right sides;
 ICC , intraclass correlation coefficient; A_{aver} , average of area values of body
surface area on the left and right sides.

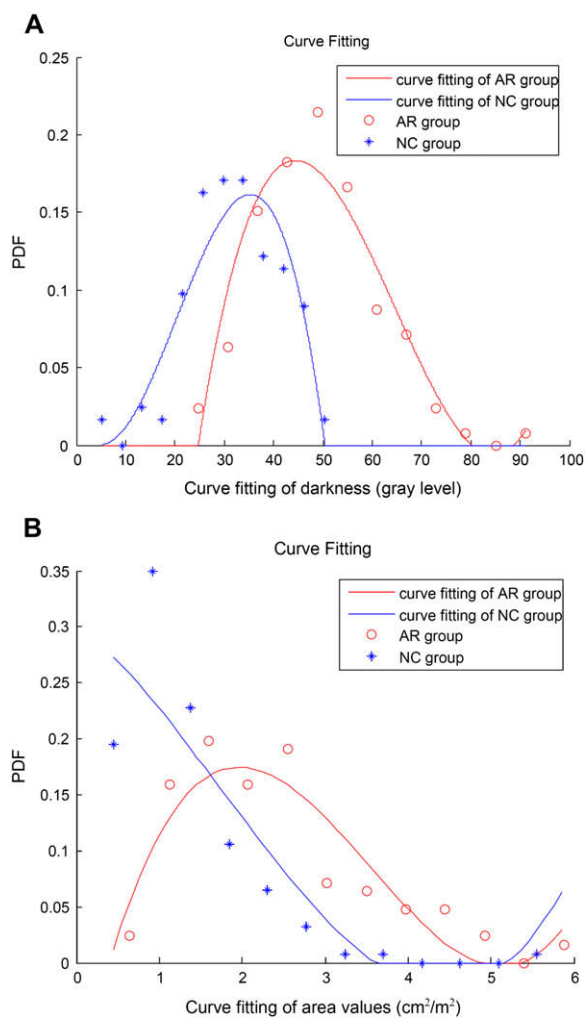


FIG E4. A and B. The thresholds between the control and allergic rhinitis groups at the first visit. *PDF*, Frequency count/numbers of all samples; *AR*, allergic rhinitis; *NC*, normal control.