

# Total serum IgE and eosinophil count in children with and without a history of asthma, wheezing, or atopy in an urban community in Indonesia

Cissy B. Kartasamita, MD, PhD,<sup>a</sup> Oma Rosmayudi, MD,<sup>a</sup>  
Maurits Demedts, MD, PhD,<sup>b</sup> and The Respiratory Disease Working Group<sup>a</sup>  
Bandung, Indonesia, and Leuven, Belgium

**Aim:** The objectives of the study were to assess total serum IgE and eosinophil count in a random sample of 20% of the children between 12 and 54 months old in a suburban community of Bandung, Indonesia, and to investigate a possible relationship between these values and atopy, asthma or wheezing and parasite infestation.

**Methods:** Two hundred sixty-nine children were examined at the Integrated Primary Health Care Unit, and the parents or guardians were interviewed with the use of a standardized questionnaire.

**Results:** The overall median value of IgE was 436 IU/ml (range, 18 to 9707 IU/ml); almost 94% of the children showed an IgE value of more than 100 IU/ml, and 29% showed a value of more than 1000 IU/ml. The median value for eosinophils was 580/mm<sup>3</sup> (range, 70 to 5090/mm<sup>3</sup>); only 31% of the children had less than 400 eosinophils/mm<sup>3</sup>. IgE levels and eosinophilia were not related to age but showed a significant, although not high, correlation with each other ( $p < 0.05$ ). In about 36% of the children parasites were demonstrated in a single stool sample; in those subjects eosinophilia and IgE values tended to be greater, but the difference was not significant. About 7% of the children had asthma, and in those subjects the eosinophil counts and IgE levels were much more increased ( $p < 0.001$  and  $p \approx 0.01$ , respectively). No difference was found in IgE or eosinophil count in relation to other forms of atopy in the child (milk-induced dermatitis, urticaria, eczema, rhinitis) or in relation to a history of asthma or atopy in other family members. Yet, the occurrence of asthma in the child was significantly related to a history of asthma in other family members.

**Conclusions:** IgE values and eosinophilia are markedly increased in these children under 5 years of age in Bandung, Indonesia, and the highest values are found in the 7% with asthma. (*J ALLERGY CLIN IMMUNOL* 1994;94:981-8.)

**Key words:** Serum IgE, eosinophil count, parasite, atopy, asthma

From <sup>a</sup>Medical Faculty, Padjadjaran University, Bandung, Indonesia; and <sup>b</sup>Laboratory for Pneumology, Medical Faculty, Catholic University of Leuven, Belgium.

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Reprint requests: Maurits Demedts, MD, PhD, University Hospital, Pulmonary Division, Herestraat 49, B-3000 Leuven, Belgium.

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## Abbreviation used

ARI: Acute respiratory infection

For the eosinophil count, 400/mm<sup>3</sup> is often considered the upper limit of normality.<sup>1</sup> The normal limits for serum IgE vary with age, and there is no clear-cut upper limit of normality,<sup>2</sup> especially not in developing countries. In developed countries values below 50 IU/ml are generally considered normal up to 3 years of age and below 100 IU/ml up to 5 years of age.<sup>1</sup> Serum IgE

**TABLE I.** Summary characteristics of the 269 children

| Characteristic                           | Percent of group |
|------------------------------------------|------------------|
| Breast-fed in infancy                    | 94               |
| Malnutrition                             |                  |
| Mild (Z-score <sup>19</sup> below -1 SD) | 36               |
| Moderate (Z-score below -2 SD)           | 23               |
| Severe (Z-score below -3 SD)             | 3                |
| Hb concentration <11 gm/dl               | 5                |
| Tuberculin skin test (Mantoux) >10 mm    | 17               |
| Vaccinations                             |                  |
| BCG                                      | 91               |
| DPT                                      | 90               |
| Polio                                    | 87               |
| Parents smoke                            | 85               |
| Family income                            |                  |
| <25 U.S. dollars/mo                      | 24               |
| 25-125 U.S. dollars/mo                   | 73               |
| Parents' education                       |                  |
| Father, less than 12 yr                  | 64               |
| Mother, less than 12 yr                  | 78               |

Hb, Hemoglobin; SD, standard deviation; BCG, bacille Calmette-Guérin; DPT, diphtheria-pertussis-tetanus.

level and eosinophil count may be increased because of several factors, such as atopy<sup>3</sup> and parasite infestation.<sup>4</sup> Yet we are unaware of systematic studies on normal values of IgE and eosinophil count in children in developing countries. Also, data on prevalence of childhood asthma in these countries are scarce.

The aims of this study were to assess in children under 5 years of age in a tropical developing country: (1) serum IgE level and eosinophil count, (2) incidence of asthma and atopy, and (3) the relationships of IgE level, eosinophil count, and asthma or atopy.

## METHODS

This study is part of a larger epidemiologic survey of all children under 5 years of age in Cikutra, a suburban village of Bandung, Indonesia, in which the frequency and risk versus protective factors for acute respiratory infections (ARIs) were assessed.<sup>5</sup> First, a cross-sectional door-to-door census of the total group of 1961 children under 5 years of age was performed by trained health care workers under the supervision of the medical team of the Health Center (Puskemas). Second, a prospective follow-up and intervention study was carried out in 269 children from 12 to 54 months of age, who were selected by stratified sampling (i.e., from

each of the 15 subcommunities of Cikutra 20% of the children were retained at random). These children were investigated every month by a medical team in the Integrated Primary Health Care Units (Posyandu) of the corresponding subcommunity.

This study is based on data obtained from these 269 children at the start of the prospective study. The group consisted of 51.7% boys and 48.3% girls with a mean age of  $33 \pm 10$  months, (range, 12 to 54 months). The relevant characteristics of the children are presented in Table I.

Data on wheezing and asthma and other forms of atopy (allergic rhinitis, urticaria, eczema, and milk-induced dermatitis) in the 269 children and in the other family members were obtained by interviewing the mothers or adult guardians by using a standardized questionnaire adapted from the epidemiologic children's questionnaire from the ATS/DLD-78-C.<sup>6</sup> Questions were related to the presence of cough, congestion and/or phlegm, wheezing, chest illness, ARI, and immunization in the child; to atopy in the family; to parental smoking, education, and income; and to the housing conditions (crowdedness, indoor pollution).<sup>5</sup>

Venous blood was drawn from an antecubital vein and was analyzed for total serum IgE level by enzyme immunoassay and for blood eosinophil count by microscopy. IgE level could be assessed in 224 children and eosinophilia in 209.

Parasite examination of single stool samples could be carried out for 151 children.

All the data were stored and analyzed by the SPSS-PC+ version 3.0. statistical program (SPSS Inc., Chicago, Ill.). The statistical analyses involved nonparametric methods: Mann-Whitney U test, Kruskal-Wallis one-way analysis of variance, Pearson's correlation coefficients, and chi square tests.

## RESULTS

Serum IgE level and blood eosinophil count were not related to age but were significantly related to each other ( $p \approx 0.03$ ), although the correlation was not high ( $r = 0.15$ ) (Figs. 1 to 3).

The levels of IgE and eosinophilia and the types of stool parasites are shown in Table II. The median value of IgE was 436 IU/ml (mean  $\pm$  SD:  $864 \pm 1079$  IU/ml, ranging from 18 to 9707 IU/ml). Almost 94% of the children showed a value greater than 100 IU/ml, which is the normal upper limit according to the laboratory kit; and 29% showed values greater than 1000 IU/ml. The median blood eosinophil count was  $580/\text{mm}^3$  (mean  $\pm$  SD:  $703 \pm 620/\text{mm}^3$ , ranging from 70 to  $5090/\text{mm}^3$ ), and only 31% of the children showed less than 400 eosinophils/ $\text{mm}^3$ , which was the cutoff point of normal values. In 35.8% of the children (54/151) parasites were found, mostly *Ascaris lumbricoides* and *Trichuris trichiura*.

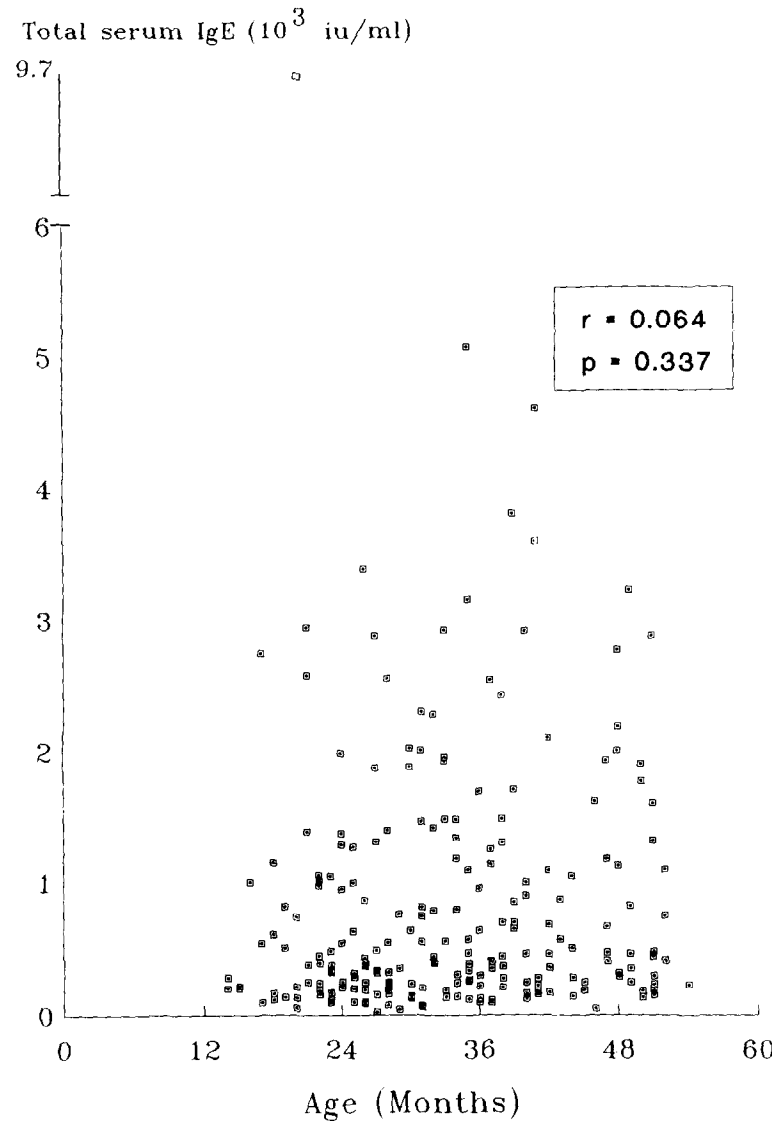


FIG. 1. Relationship between serum IgE level and age.

TABLE II. Distribution of total serum IgE, blood eosinophil count, and parasites in single stool samples

| IgE           |                  | Eosinophil count          |                  | Parasites                                      |                  |
|---------------|------------------|---------------------------|------------------|------------------------------------------------|------------------|
| Level (IU/ml) | Children No. (%) | Level (/mm <sup>3</sup> ) | Children No. (%) | Type                                           | Children No. (%) |
| <100          | 14 (6.3)         | <350                      | 56 (26.8)        | None                                           | 97 (64.2)        |
| 100 to <150   | 16 (7.1)         | 350 to <500               | 33 (15.8)        | <i>A. lumbricoides</i>                         | 24 (15.9)        |
| 150 to <300   | 53 (23.7)        | 500 to <1000              | 82 (39.2)        | <i>T. trichiura</i>                            | 17 (11.3)        |
| 300 to <500   | 40 (17.9)        | 1000 to <2000             | 31 (14.8)        | <i>A. lumbricoides</i> and <i>T. trichiura</i> | 7 (4.6)          |
| 500 to <1000  | 36 (16.1)        | 2000 to <4000             | 5 (2.4)          | Other*                                         | 6 (4.0)          |
| 1000 to <3000 | 57 (25.4)        | ≥4000                     |                  |                                                |                  |
| ≥3000         | 8 (3.6)          |                           |                  |                                                |                  |

\*Included: *E. vermicularis*, *H. nana*.

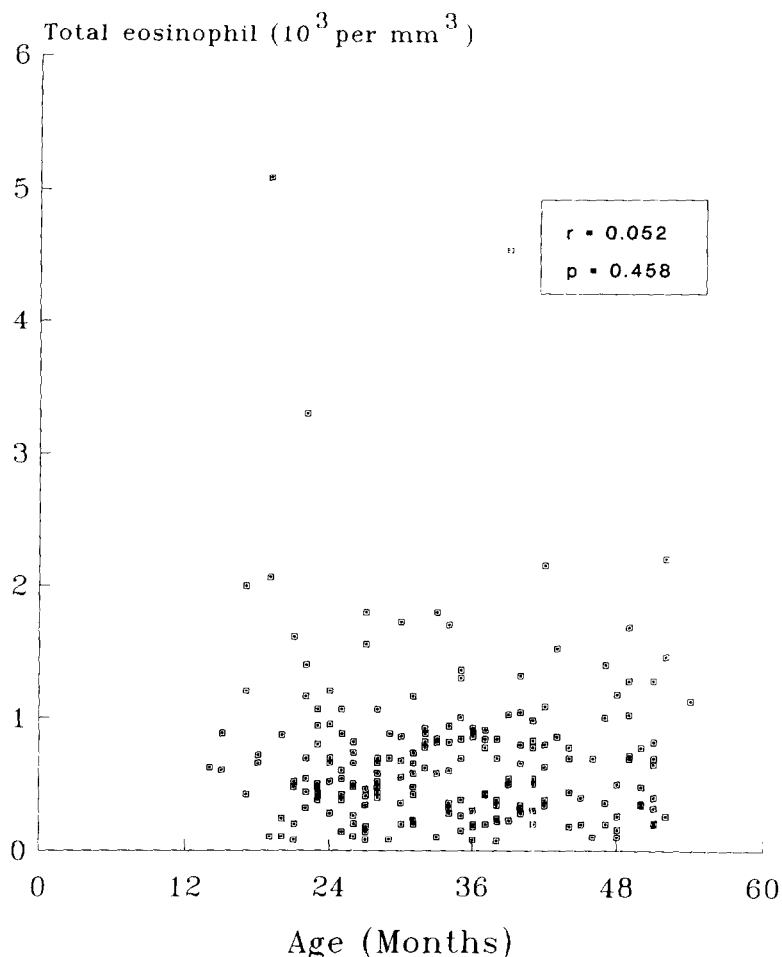


FIG. 2. Relationship between blood eosinophil count and age.

Table III shows the relationships among parasite infestation, asthma, wheezing, or atopy and IgE or eosinophils. The IgE level and eosinophil count tended to be higher in children with parasite infestation than in those without, but the difference was not significant. Both values were also not significantly different between the children with and without atopy. IgE level and eosinophil count were, however, markedly and significantly different between the children with asthma and those without ( $p \approx 0.01$  and  $p < 0.001$ , respectively). IgE level and eosinophil count were also higher in the children with wheezing than in those without, but this was only significant for IgE ( $p < 0.01$ ). Neither in the subgroups with asthma, nor those with wheezing, nor those with atopy were IgE or eosinophilia higher in those with parasites than in those without parasites.

We also analyzed whether there was an asso-

ciation between a history of asthma, wheezing, or atopy and parasite infestation (Table IV). No significant associations were found.

Finally, we determined whether there was a relationship with atopy or asthma in the family (father, mother, or siblings) (Table V). Atopy in at least one of the other family members was present in 47% of the families and in at least one of all members including the child under 5 years of age in 55% of the families. Asthma in at least one of the other family members was present in 13% of the families and in at least one of all members including the child under 5 years of age in 16%. For both atopy and asthma, there was a significant correlation between a positive history in the child and a positive history in the family ( $p < 0.000$  and  $p < 0.01$ , respectively). We found no significant relationship between atopy or asthma in the family and the values of IgE or eosinophils in the child ( $p > 0.05$ ).

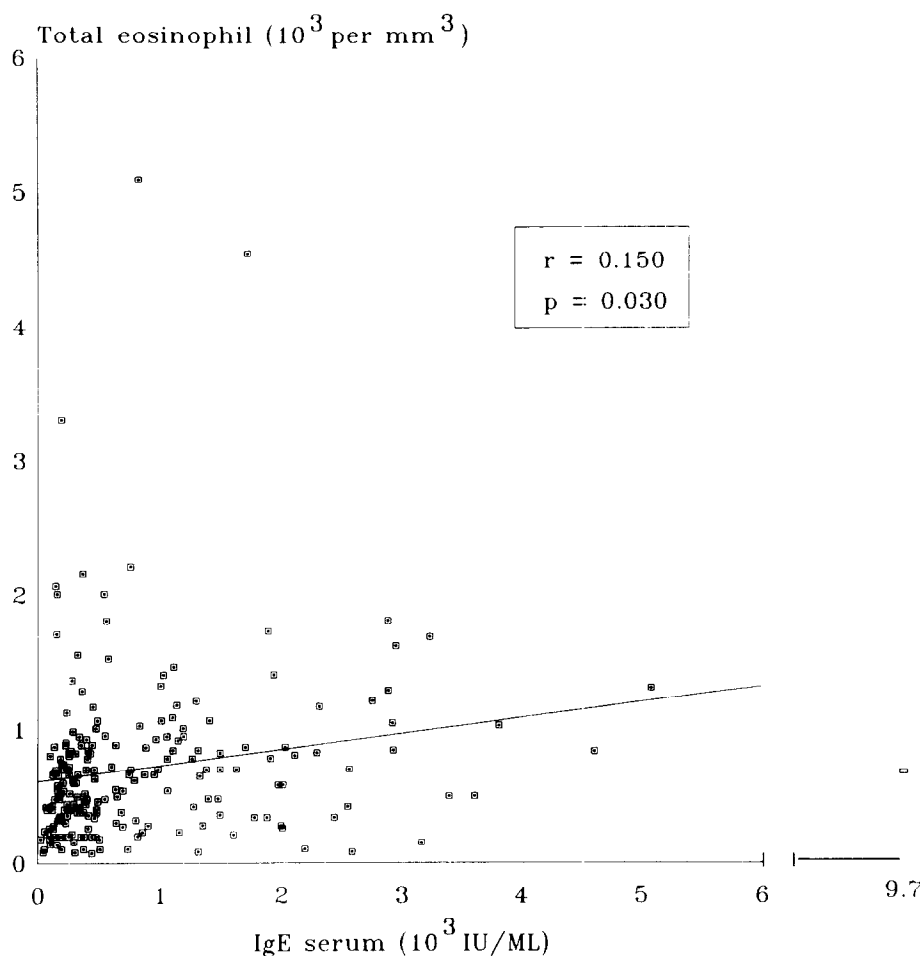


FIG. 3. Relationship between serum IgE level and blood eosinophil count.

## DISCUSSION

In this study we found in a stratified random sample of 269 children under 5 years of age (ages, 12 to 54 months) in a suburban area of Bandung, Indonesia, high values of IgE (median, 436 IU/ml) and of eosinophilia (median, 580/mm<sup>3</sup>). The interindividual ranges were very large and not related to age; however, there was a significant correlation between IgE level and eosinophil count ( $p = 0.03$ ).

We found clearly higher values of IgE and eosinophil count in children with asthma ( $p \approx 0.01$  and  $p < 0.001$ , respectively) or with wheezing ( $p < 0.01$  for IgE,  $p = \text{NS}$  for eosinophil count). We did not examine the correlation with the severity of asthma. Sears et al.<sup>7</sup> reported that in Canada, 36% of 11-year-old children with a serum IgE level greater than 1000 IU/ml had asthma. It is well known from studies in developed countries that asthma is associated with an increase in eosinophilia and IgE levels and that

there is a correlation between the clinical severity of asthma and the degree of hypereosinophilia<sup>8,9</sup> and the increase in IgE.<sup>3,7,10,11</sup>

An important issue in this study is that IgE level and eosinophil count were also very much increased in the children without asthma and that these markers of asthma thus cannot be used in these settings. Therefore specific markers (results of RASTs or skin tests) should be considered. Wilson and Hamburger<sup>12</sup> thus proved cow's milk allergy in infants by RAST or skin testing. The diagnosis of asthma should, however, be primarily based on clinical grounds.

Yet, asthma is often not considered in developing countries and probably even wrongly interpreted as ARI. On the basis of standardized questionnaire, adapted from the ATS/DLD 78-C epidemiologic questionnaire,<sup>6</sup> we found asthma in 7%, wheezing in 11%, and atopy in 30% of children under 5 years of age in this study. In 6- to 11-year-old Hawaiian children a similar asthma

**TABLE III.** Serum IgE and eosinophil count in relation to parasite infestation and a history of atopy, asthma, and wheezing

|                                    | Parasites |        | Asthma |        | Wheezing |        | Atopy |        |
|------------------------------------|-----------|--------|--------|--------|----------|--------|-------|--------|
|                                    | Pos       | Neg    | Pos    | Neg    | Pos      | Neg    | Pos   | Neg    |
| No.                                | 54        | 97     | 14     | 203    | 24       | 200    | 67    | 157    |
| Percent                            | 35.8      | 64.2   | 6.5    | 93.5   | 10.7     | 89.3   | 29.9  | 70.1   |
| IgE (IU/ml)                        |           |        |        |        |          |        |       |        |
| Median                             | 477       | 407    | 1262   | 435    | 922      | 402    | 541   | 406    |
| Mean                               | 975       | 781    | 1513   | 835    | 1408     | 799    | 981   | 814    |
| SD                                 | 1023      | 925    | 1207   | 1074   | 1301     | 1304   | 1017  | 1104   |
| Z score                            |           | 1.2587 |        | 2.4558 |          | 2.7038 |       | 1.5447 |
| p Value                            |           | 0.2081 |        | 0.0141 |          | 0.0068 |       | 0.1224 |
| No.                                | 54        | 97     | 14     | 188    | 23       | 186    | 63    | 146    |
| Percent                            | 35.8      | 64.2   | 6.9    | 93.1   | 11.0     | 89.0   | 30.1  | 69.9   |
| Eosinophils (per mm <sup>3</sup> ) |           |        |        |        |          |        |       |        |
| Median                             | 590       | 550    | 920    | 520    | 700      | 580    | 580   | 590    |
| Mean                               | 722       | 707    | 1247   | 656    | 925      | 676    | 660   | 723    |
| SD                                 | 583       | 741    | 1005   | 558    | 935      | 567    | 405   | 693    |
| Z score                            |           | 0.4581 |        | 3.2331 |          | 1.2814 |       | 0.3341 |
| p Value                            |           | 0.6469 |        | 0.0012 |          | 0.2001 |       | 0.7383 |

Pos, Positive; Neg, negative.

**TABLE IV.** Relationship between asthma, wheezing, or atopy and parasite infestation (number of children)

|           | Asthma* |     |       | Wheezing† |     |       | Atopy‡ |     |       |
|-----------|---------|-----|-------|-----------|-----|-------|--------|-----|-------|
|           | Pos     | Neg | Total | Pos       | Neg | Total | Pos    | Neg | Total |
| Parasites |         |     |       |           |     |       |        |     |       |
| Pos       | 3       | 47  | 50    | 7         | 46  | 53    | 18     | 35  | 53    |
| Neg       | 5       | 85  | 90    | 8         | 86  | 94    | 25     | 69  | 94    |
| Total     | 8       | 132 | 140   | 15        | 132 | 147   | 43     | 104 | 147   |

Pos, Positive; Neg, negative.

\*Chi square = 0.07; *p* = 0.79.†Chi square = 0.38; *p* = 0.54.‡Chi square = 0.57; *p* = 0.45.

prevalence of 6.7% was noted.<sup>13</sup> These numbers are somewhat lower than those reported in developed countries. Ninan and Russell<sup>14</sup> found a prevalence of asthma and wheezing in 10.2% and 19.8% of primary school children, respectively, in the United Kingdom; and Mutius et al.<sup>15</sup> found a prevalence of asthma and wheezing in 7.3% to 9.3% and 17% to 20%, of primary school children, respectively, in Germany.

We did not examine the pathogenesis of asthma in these children except for possible familial predisposition. We found, indeed, that asthma was significantly more frequent in children under the age of 5 years when a parent or sibling also had

asthma or atopy. We found no relationship to parasite infestation. Furthermore, in a previously published study, we found that children with asthma had more moderate and severe ARIs (and less mild ARIs) than those without asthma.<sup>5</sup>

Many factors, besides asthma and atopy, are known to increase IgE levels and/or eosinophilia, especially parasite infestation but also fungal or other infections, collagen vascular disease, hematologic disorders, immune disease, and paraneoplastic syndromes. The children in this study were followed up for 1 year in the framework of a prospective survey on ARIs,<sup>5</sup> and there was no correlation between IgE level or eosinophil count

**TABLE V.** Relationship between a history of asthma or atopy in the child and in other family members (number of children)

|        | Child with asthma* |     |       | Child with atopy† |     |       |
|--------|--------------------|-----|-------|-------------------|-----|-------|
|        | Yes                | No  | Total | Yes               | No  | Total |
| Family |                    |     |       |                   |     |       |
| Yes    | 6                  | 28  | 34    | 55                | 58  | 113   |
| No     | 8                  | 219 | 227   | 20                | 111 | 131   |
| Total  | 14                 | 247 | 261   | 75                | 169 | 244   |

\*Chi square = 11.6;  $p < 0.01$ .†Chi square = 31.7;  $p < 0.000$ .

and the incidence and duration of ARI. Other major diseases were also excluded.

The values of IgE and eosinophil count tended to be slightly higher in the 35.8% children with parasites in a single stool sample than in those without, but the difference was not significant. It should be noted that in the children who had no parasites in the stool, the eosinophil count and IgE level were still high. We must, however, be aware of the fact that the finding of parasites in the stool of only 35.8% of the children is an underestimation. Studies conducted in Indonesia by Lubis et al.<sup>16</sup> and by Chaerulfatah<sup>17</sup> showed that the prevalence of parasite infestations in children was 85% to 100%. Santoso et al.,<sup>18</sup> in addition, demonstrated that more than 50% of the children with no *Ascaris* organisms in a stool sample had a positive RAST result for *Ascaris* species, thus indicating a persisting immunologic reaction after a past infection. Similarly, in children in developed countries, high levels of IgE and eosinophils may be found for extended periods after, for instance, infestation with *Toxocara canis* (which provokes visceral larva migrans). Indeed, a positive RAST result and thus a high IgE level may persist for years in the apparent absence of further allergenic exposure.<sup>10</sup> This could be an explanation for our finding that there was no significant difference in IgE level nor in eosinophilia between those with and those without proven parasite infestation. In addition, Santoso et al.<sup>18</sup> found, in Indonesian children with a negative RAST result, an IgE level 10 times lower than that in our study.

The results emphasize the problem in defining "normal limits" for serum IgE<sup>2</sup> and for eosinophilia in a random group of apparently healthy children. In developed countries mean normal values for IgE of about 70 IU/ml (160  $\mu$ g/ml) with an upper limit of 120 IU/ml are generally re-

ported in adults, and somewhat lower values are generally reported in children.<sup>1, 4, 7</sup> In developing countries the "normal" values reported in "healthy" children are generally much higher. Johansson et al.<sup>4</sup> found, in Ethiopian children with a stool sample negative for *A. lumbricoides*, values that were five times higher. Normal values for serum eosinophil count in developed countries are between 40 and 400/mm<sup>3</sup>.<sup>1</sup> In developing countries higher values are often reported, but we are unaware of systematic studies on this phenomenon, at least in Indonesia.

In conclusion, the majority of "healthy children" in Cikutra, Indonesia, had markedly increased values of IgE and blood eosinophil count. A significant correlation with asthma and wheezing was found. An influence of parasite infestation could not be proven, probably because of technical factors.

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