# SPECIAL ARTICLE

# Risk Factors for Acute Respiratory Infections in Underfive Children\*

Cissy B Kartasasmita\*\*, Maurits Demedts\*\*\*

(\*Department of Child Health, Medical School, Padjadjaran University, Bandung, \*\*Catholic University of Leuven, Belgium)

ABSTRACT A longitudinal study on acute respiratory infections was conducted from April 1988 until June 1990, in Cikutra, an urban community in the municipality of Bandung, Indonesia. The study consisted of 3 parts: a presurvey, a cross sectional study, and a one-year prospective study. All children aged less than five years in Cikutra were included in the presurvey. A simple questionnaire was used for collecting data. In the cross sectional study 500 children were selected by stratified random sampling. Field investigators visited the children's homes and interviewed mothers using a standardized questionnaire. For the prospective study 269 children of less than 48 months of age were enrolled, and followed for one year. The prevalence of all ARI was 57-58%, mild-moderate ARI 55-56%, and severe ARI 5%. On average the children suffered from 6.7 episodes of ARI per child per year, with a mean duration of episode of 5.3 days. Several factors showed significant relationship with the prevalence, incidence, severity of duration of ARI. [Paediatr Indones 1995; 35:65-77]

## Introduction

Acute respiratory infections (ARI) still constitutes a major health problem in developing countries such as Indonesia. The high mortality and morbidity has been shown in many studies. According to WHO a child suffers on average from 5 to 8 episodes of ARI per year when he or she lives in an urban area.<sup>1</sup>

The mortality of ARI in developing countries is also high. According to Miller (1985)<sup>2</sup> six million underfive children died every year due to ARI, and most of them lived in developing countries.

Several risk factors have been consid-

A review article of thesis. \*\*Medical School of Padjadjaran University, Bandung, Indonesia\*\*\* Catholic University of Leuven, Belgium. Author's address: Department of Child Health, Medical School, Padjadjaran Univeersity, Jalan Pasteur, Bandung, Indonesia.

mortality. Many studies were done on those factors; however, some of them showed conflicting results.<sup>3</sup>

Several records on ARI mortality and morbidity have been published in Indonesia. However, most of them came from university hospitals, and thus might contain very selective cases, and might not representative for the whole population. It is reported that the prevalence of ARI ranged from 12 to 45%; yet we do not know the incidence of ARI, and neither the possible risk factors for it. Therefore, we decided to study the prevalence, incidence, duration and risk, or beneficial factors for ARI.

#### **Methods**

Our study consisted of 3 parts: a presurvey, a cross sectional study, and a one-year prospective study.

The presurvey. All underfive children in Cikutra were enrolled. There were 3225 households in Cikutra with 1967 underfive children; however, in 6 children the exact age was not known, thus only 1961 children were included for the analysis. The aim of the presurvey was to obtain baseline data on underfive children, to know the prevalence of ARI. and to investigate several possible risk factors. Data were collected by trained primary health care workers, who interviewed the mothers or adult guardians using a simple questionnaire. For this study ARI was classified into two classes: mild-moderate and severe.

The cross sectional study. Six hundred underfive children were selected by stratified sampling from the 1961

children of the presurvey. However, only in 500 children could the questionnaires be analyzed. The aim of this study was to obtain detailed data on possible risk or beneficial factors. Data were collected by nurses from the local health center, who had been trained before as field investigators. They interviewed the mothers or adult guardians using questionnaires which were modified from the epidemiologic children's questionnaire of the American Thoracic Society. For this study ARI was also classified into mild-moderate and severe, similar as in the presurvey.

The prospective study. All the children from the cross sectional study with age of less than 48 months were planned to be included. However, the prospective study was postponed due to some technical difficulties in the field. Thus, at the beginning of the prospective study. only 269 children could be enrolled. The aims of the prospective study were to know the incidence, severity and duration of ARI; to investigate several technical data such as plasma retinol level. IgE, eosinophil, hemoglobin, parasite in stool, chest X-ray and tuberculin test, and to know the influence of vitamin A supplementation. In this study the children were subdivided at random into 2 groups according to those who received vitamin A or placebo.

Before the study started, physical and laboratory examinations were performed by a medical team. Every two weeks the *kader* who had been trained before as field interviewers visited the children's homes, interviewed mothers or adult guardians on respiratory symptoms during the previous two weeks, using a

questionnaire. Every month the doctor re-examined the children and rechecked the filled-in bi-weekly questionnaires. Two hundred thousand IU vitamin A or placebo were given on the first and sixth month of the study. Plasma retinol levels were assayed three times: before the study started, at the third, and sixth month of the study. For this study ARI was classified into three classes: mild, moderate, and severe.

## Definitions and classification

ARI was defined as any infections of acute onset (<14 days) apparently due to microorganisms, in any area of the respiratory tract including the nose, ear, pharynx, larynx, trachea, bronchi, bronchioles, or lung. For this study we use the classification of ARI according to the degree of severity as proposed by WHO in 1982: mild, moderate and severe. 6

### **Results and Discussion**

Characteristics of the subjects is shown in Table 1.

# Morbidity and duration of ARI

The overall prevalence of ARI during one month before the study ranged between 57-58%, for mild-moderate ARI 55% and for severe ARI 5%. The prevalence of ARI in our study is higher than in other studies conducted in Indonesia. This may be caused by the fact that our study was conducted in the rainy season, where the prevalence of ARI was higher. From our prospective study we found indeed, an incidence of ARI of 43% during

the dry season and 56% during the rainy season.

However, as also mentioned by Hadiwinoto and Prihatini<sup>9</sup> a different environment may cause a difference in the morbidity of ARI. Our study showed that the overall incidence ARI was 6.7 episodes per child per year. Two children never experienced ARI during the whole year, thus the cumulative incidence during the observation period was 99%. One child had experiences with 20 episodes of ARI during the one year observation; however, most of the children (i.e., almost 50% of subjects) suffered from 5-8 episodes of ARI.

Several community-based studies conducted in several urban and rural areas in developing countries showed that the incidence of ARI in an urban area ranged from 5 to 7 episodes per child/ year. 10,11 This is similar with our study, except for the study from Thailand12 which showed higher episodes. The duration of ARI is also important because the longer the child suffers from ARI the higher the chance to compromise her / his growth and development. From the prospective study we found that on the average each child suffered from ARI for 36 days per year, and the mean duration of ARI episodes was 5.3 days. Our finding was shorter than that mentioned by the WHO1 which stated a duration of ARI of 7-9 days, or Lang et all3 who reported a mean duration of 8.5 days, however, Lang's study was undertaken in Burkina Faso, a rural area in West Africa, and our study was done in an urban area where the sick child can easily seek medical help. Furthermore, in our prospective study in fact, there

Table 1. Characteristic of subjects

Characteristics	Children (%) Characteristics		0111	
Breast feeding in infants:	- The second of		Children (%	
Yes	93.6	Parent's education:		
No	5.4	Father		
Nutritional status:	5.4	< 12 years	64.4	
< -3 SD	2.0	>= 12 years	35,6	
< -2 SD	3.2	Mother		
< -1 SD	23.1	< 12 years	78.1	
	36.2	>= 12 years	21.9	
> -1 SD	37.4	Parent's occupation:	21.5	
Crowding:	8.58	Father		
Family size		Working	98.7	
< 5	30.6	Not working	2.3	
≥ 5	69.4	Mother	2.3	
Room occupancy:		Working		
< 3	54.4	Not working	18.0	
> 3	45.6	Indoor sin polyticary	82.0	
Square meters per person	40.0	Indoor air polution:		
=> 10 m2	19.8	Smoking pollution		
< 10 m2		Smoking parents	84.9	
Family income:	80.2	/- Non	15.1	
< 25 USD		Bedroom pollution		
	24.0	Coils: Yes	75.0	
> 25 USD	76.0	No	25.0	
Family possession:		Smoking: Yes	38.2	
House		No	61.8	
Cwn house	38.5	Kitchen pollution	01.0	
No house	61.5	Yes	00.0	
Car		No	96.2	
Yes	4.6	Asthma and atopy in children	3.8	
No	95.6	Asthma Asthma		
Motorcycle	30.0	ASUIIIId	6.0	
Yes	14.8	Wheezing	12.4	
No		Atopy	28.0	
Television	85.2	Asthma in the family:		
Yes		Father	3.5	
No	54.0	Mother	5.0	
	46.0	Sibling	2.7	
Maid		Atopy in the family:		
Yes	7.2	Father	19.3	
No	92.8	Mother	28.3	
Tuberculin test >10 mm	16.8	Sibling	26.3 19.0	
mmunization status:		Technical data:	19.0	
BCG	91.0	PRL (μg/dl) < 10	7.0	
DPT	90.0	10 - 20	7.8	
Polio	87.0		53.2	
Measles	64.0	> 20	47.0	
(erophthalmia:		Hemoglobin (g/dl):		
Parasite (s) :	0	< 11	4.9	
	35.8	≥ 11	95.1	
Abnormal chest X-ray:	20.4	Median IgE (IU/ml):	436.0	
15		< 100	6.3	
		Median eosinophil (μl)	580.0	
		< 400	31.1	

was also intervention on ARI management.

## Risk factors

Several risk factors have been considered to influence ARI morbidity, mortality and degree of severity. We investigated several possible risk factors, however, not all factors showed interesting results. Several factors that seemed important from our study were the followings:

Age. Our study showed that the prevalence of ARI was lower in infants of less than 1 year old compared to the other age groups. Our study revealed that the incidence and duration of ARI decreased with increasing age. We found that significantly the incidence of ARI was higher, and the duration longer in younger children. However, no children of less than one year were included. Several studies showed that the incidence of ARI was higher in infants of less than one year old which decreased with increasing age. 14,15

Nutritional factor. We assessed the nutritional status of the children according to weight for age, and compared it to the median weight for age of the reference population of the National Center for Health Statistics. Sixty-three percent of the children showed weight for age below-1 SD of the median weight for age of the reference population of the NCHS, and 25% showed less than -2 SD below the median. This study clearly showed a tendency toward a higher prevalence of mild-moderate and severe ARI and a higher incidence of severe ARI. however, this was not significant. Several

studies showed malnutrition to be one of the important risk factors for ARI. <sup>12,17</sup> In chronic and severe malnutrition, more lower respiratory tract infections were found. <sup>11</sup> It is also reported that duration and mortality rate of lower respiratory tract infections (LRTI) were higher in severely malnourished children. <sup>13</sup> However, Cruz et al <sup>10</sup> similar with us, failed to find the relationship between malnutrition and ARI.

Breast-feeding. In our study almost all infants (95%) were still breast-fed. Our study failed to show any protective effects of breast-feeding; the prevalence of mild-moderate and severe ARI was similar in breastfed or non breastfed infants. However, the number of non breastfed infants in our study was too small (5%) for a meaningful analysis. From our prospective study we could not analyze the role of breast feeding because there were no more infants included. It is mentioned that breast feeding can protect infants against infections such as ARI.18 Several studies showed the prevalence of ARI to be higher in non breast-fed infants. However, Launer et al 19 found in their study in Indonesia that in adequately breast-fed infants only the duration of the respiratory tract illnesses was shorter.

Vitamin A. Great attention was paid to vitamin A because of studies conducted in Indonesia, especially on the role of vitamin A supplementation on ARI. <sup>20,21</sup> Several recent studies were conducted to know the effect of vitamin A supplementation on ARI morbidity, mortality and duration of illness. <sup>12,23-32</sup> Among the studies in communities not all show that vitamin A supplementation

shows a favorable effect. <sup>22,27,30</sup> At the moment the only widely accepted practice, as also proposed by the WHO, is to give vitamin A supplementation in children with measles in population where the case fatality rate of measles is more than 1%.

From the laboratory examination before the study we found that the mean plasma retinol level (PRL) among the children was 20 µg/dl which is the lower limit of normal value, and 53% of the children showed a PRL of less than 20 μg/dl, 8% of them showed a deficient level. However, no xerophthalmia was found on the eye examination before the study started. From the prospective study (Table 2) no difference was found in the incidence and of ARI between vitamin A supplemented and unsupplemented children; also no difference was found before and after supplementation. However, the duration of ARI was longer in unsupplemented vitamin A children.

Family income. Twenty one percent of the children came from low income families (<25 USD/month), 73% from middle income (25-125 USD/month) and only 5% from high income families (>125 USD/month). The prevalence of mild-moderate ARI was significantly higher in children of lower income families. Nevertheless, no influence of income on the incidence, severity and duration of ARI was found. Social economic status was considered as an important risk factor in developed countries.3,6 According to Miller more ARI was found in less privileged children. However, Lang et al 13 also failed to show a positive effect of socio-economic status.

Crowding. We defined crowding as

the number of persons in the household, family size of more than 5 persons, the square meter space per person of less than 10 m² and the number of persons sleeping in the same room of more than 3 persons per bedroom. In our study the prevalence of ARI was higher in more crowded conditions; however, no influence of crowding on the incidence, severity or duration of ARI was found, except, a higher incidence of severe ARI in children with a family size of more than 5 persons in the households. Our study confirmed the study of Turner et al³³ but it was different, again, from those of Lang et al.¹³

Atopy. Recently airway hyperactivity was identified as one of the important risk factors for ARI. However, not many studies were done on the role of atopy and airway hyperactivity on ARI. The prevalence of atopy and asthma in the subjects and family was ranging between 19-28%, and 3-6%, respectively; and the prevalence of wheezing in children was 12% No influence of these factors on the prevalence or duration of ARI was found. However, the incidence of moderate ARI was higher in the presence of a history of atopy in the family, and in children with a history of atopy, wheezing and asthma. Cogswell et al also found a similar result, more respiratory infections in atopic children. A recent publication from IUATLD also mentioned that airway hy- perreactivity is one of the endogenous risk factors for ARI.35 Nevertheless, the relationship between atopy and ARI in developing countries has remained unrecognized. We therefore consider our findings important.

The serum IgE and blood eosinophil

the number of persons in the household, family size of more than 5 persons ments in 269 children

Categories retinol level (µg/dl)	Vitamin A suppl.	Number of children		Plasma retinol (μg/dl)	Incidence of ARI/year	Duration (days/year
		N	%	mean (SD)	mean (SD)	mean (SD)
< 10 < 10 10 - 20 10 - 20	Yes	7	3.5	7.8 (1.5)	6.4 (1.6)	29.3 (12.2
	No	9	4.4	7.8 (1.9)	6.8 (2.9)	33.1 (14.6
	Yes	42	20.5	15.2 (2.8)	7.3 (3.9)	39.5 (24.2
	No	50	24.5	15.9 (2.7)	7.2 (3.2)	42.5 (25.7
> 20	Yes	54	26.5	26.7 (5.9)	6.5 (3.4)	22.9 (19.3
> 20	No	42	20.6	25.5 (5.4)	7.1 (4.0)	36.6 (22.8

p > 0.05 for each of the categories of retinol levels

count were also measured before the prospective study started. The median values of IgE and eosinophil before the study were high, 436 IU/mL and 580/µl with a large range (18-9707 IU/µl and 70-5090/µl), respectively. The normal limit of IgE is 100 IU/ml, only 6.3% of the children showed IgE of less than 100 IU/µl and the normal limit for eosinophil is 400/µl, 31.1% of the children showed eosinophil count of less than 400/µl. Figure 1 and 2 show the association between incidence and duration of ARI and serum IgE and blood eosinophil count. We found no relationship between these two data and ARI.

**Season.** We found the incidence of all mild, moderate and severe ARI to be significantly higher during the rainy season. It was mentioned that in the tropics more ARI occurred during the rainy season. However, Lang et al found more ARI during the dry season, they attributed this low humidity as the cause for the decreasing defense mechanism.

In this study we also investigated other factors such as sex, indoor air pollution, parents education and occupation, family goods, and immunization status of the children. Also se-veral other technical data such as hemoglobin concentration, parasite in the stool, chest X-ray and tuberculin test. However, we failed to show a significant effect of those factors.

#### **Conclusions**

Our study showed that the prevalence of ARI in the area of study was high, 57 to 58%, for mild-moderate ARI 55 to 56% and 5% for severe ARI. These findings were higher than those of other studies done in Indonesia. However, these were similar with the studies from other developing countries. The incidence of ARI was 6.7 episodes per child per year. It is similar with that reported from developed or developing countries. The dur-

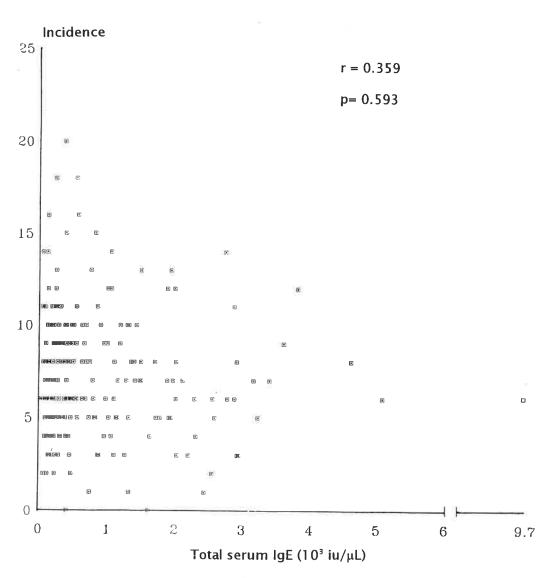


Figure 1

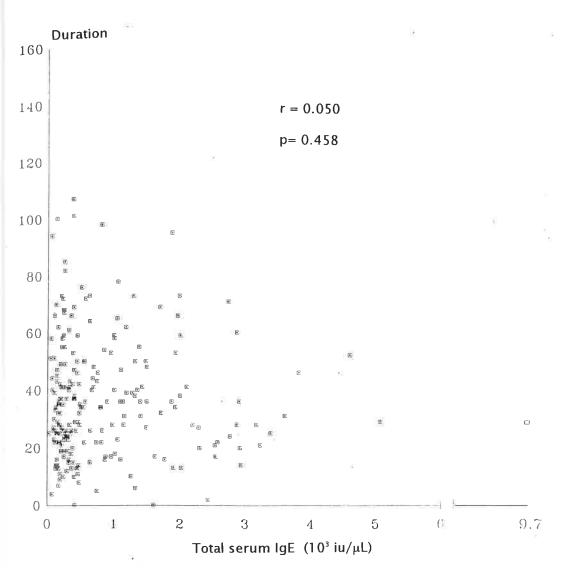
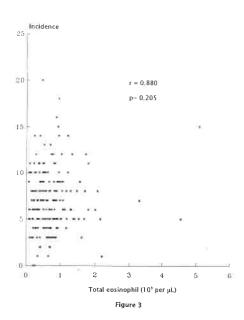
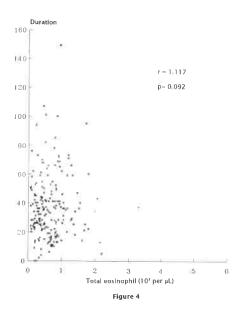


Figure 2





ation of ARI of 5.3 days was shorter than in other studies in developing countries. Furthermore, our study revealed that several risk factors showed a significant association with ARI such as: age, crowding, history of atopy in the family, and history atopy, asthma and wheezing in the children. Our study failed to show a beneficial effect of vitamin A supplementation on ARI incidence; however, we found that the duration of ARI in unsupplemented children seemed longer. We also found that airway hyper-reactivity and atopy were important risk factors for ARI. However, even though a significant relationship was found, it does not mean that the factor has a very important influence. In the presurvey, a discriminant analysis on several risk facwas analyzed together. All those factors, family income, vitamin A supple- mentation and age, however, only influenced 18% of ARI in infants, the rest might be caused by another factors, and in children of 1 to 5 years even much more less (0.4-1.8%).

# **Acknowledgments**

We express my sincere thanks and gratefulness to all colleagues from the Respiratory Diseases Working Group for their cooperation. We also thank the doctor and health center staffs, and the kaders for their cooperative and invaluable work. This study was undertaken within the framework of the Interuniversity Programme Cooperation between the Medical School of Padjadjaran University, Bandung, Indonesia and the Flemish Interuniversitaire Council (VLIR)

Belgium, and was also supported by the Belgian Ministry of Development Cooperation (ABOS) and the Ford Foundation.

#### References

- WHO/UNICEF. Basic principles for control of acute respiratory infections in children in developing countries. WHO/ UNICEF. Geneva, 1986: 5-18.
- Miller DL. Issues for the future of ARI control. In: Douglas RM, Kerby-Eaton, Eds, Proceeding Intern Workshop on "Acute respiratory infections in childhood". Sydney 1984, Univ Press, Adelaide 1985; 100-3.
- Graham NMH. The epidemiology of acute respiratory infections in underfive children and adults: A global perspective. Epidemiol Rev 1990; 12:149-78.
- DepKes RI. Prosiding Lokakarya Infeksi Saluran Pernapasan Akut (ISPA) II, Ciloto, 1988. DepKes RI 1989:27-108.
- Ferris BG Jr. Epidemiology standardization project. Am Rev Respir Dis, 1978; 118 (Suppl):36-53.
- Stansfield SK. Acute respiratory infections in developing world: Strategies for prevention, treatment and control. Pediatr Infect Dis J 1987; 6:662-9.
- Budiarso RL. Pola kematian. Prosiding seminar survai kesehatan rumah tangga 1986. Badan Penelitian dan Pengembangan Kesehatan Pusat Penelitian Ekologi Kesehatan. DepKes RI, 1987; 113-24.
- Ismail R, Djamil H, Anwar Z, Pardede N, Arifin F. Acute respiratory tract infections. Prevalence, mortality and case management in the community in eleven villages of rural South Sumatra, Indonesia. Paediatr Indones 1987;27:61-7.
- Hadiwinoto W, Prihatini SB. Pengamatan hasil uji coba Program Penanggulangan Penyakit ISPA di Kabupaten Lamongan. Prosiding Lokakarya Infeksi Saluran Pernapasan Akut II, Ciloto, 1988. DepKes RI

- 1989; 176-85.
- 10. Cruz JR, Pareja G, de Fernandez A, Peralta F. Careres P, Cano F. Epidemiology of acute respiratory tract infections among Guetemalan ambulatory preschool children. Rev Infect Dis 1990: 12 (Suppl 8): S1029-34.
- 11. Tupasi TE, Leon LE, Lupisan S, Torres CU. Leonor ZA. Patterns of acute respiratory tract infection in children: A longitudinal study in a depressed community in Metro Manila. Rev Infect Dis 1990:12 (Suppl. 8):S940-9.
- 12. Vatanophas K, Sangchai R, Raktham S et al. A community based study of acute respiratory infection in Thai children. Rev Infect Dis 1990; 12 (Suppl. 8):S957-65.
- 13. Lang T, Lafaix C, Fassin D et al. Acute respiratory infections: A longitudinal study of 151 children in Burkina-Faso. Int J Epidemiol 1986; 15:553-60.
- 14. Dertny FW. Acute respiratory infections in children: Etiology and epidemiology. Pediatr Rev 1987; 9: 135-46.
- 15. Wafula EM, Onyango FE, Mirza WM et al. Epidemiology of acute respiratory infections among young children in Kenya. Rev Infect Dis 1990, 12 (Suppl): S1035-8.
- 16. WHO. Measuring change in nutritional status, guidelines for assessing the nutritional impact of supplementary feeding programmes for vulnerable group. Geneva: WHO, 1983.
- 17. Hortal M. Benitez A, Contera M, Etorena P. Montano A. Meny M. A communitybased study of acute respiratory tract infetions in children in Uruguay. Rev Infect Dis 1990; 12 (Suppl. 8): S966-73.
- 18. Howie PW, Forsyth JS, Ogston SA, Clark 28. West KP Jr, Pokhrel RP, Katz J, et al. Effi-A, Florey C du V. Protective effect of breast feeding against infection. Br Med J 1990; 300: 11-6.
- 19. Launer JL, Habicht JP, Kardjati S. 29. Coutsoudis A, Broughton M, Coovadia Breast-feeding protects infants in Indonesia against illness and weight loss due to illness. Am J Epidemiol 1990; 131: 322-31.

- 20. Sommer A, Hussaini G, Tarwotio I, Susanto D. Increased mortality in children with mild vitamin A deficiency. Lancet 1983: (ii): 585-8.
- 21. Sommer A, Katz J, Tarwotjo I. Increased risk of respiratory in children with preexisting mild vitamin A deficiency. Am J Clin Nutr 1984; 40: 1090-5.
- 22. Barclay AJG, Foster A, Sommer A. Vitamin A supplements and mortality related to measles: A randomized clinical trial. Br Med J 1987; 294: 294-6.
- 23. Bloem MW, Wedel M, Egger RJ et al. Mild vitamin A deficiency and risk of respiratory tract diseases and diarrhea in preschool and school children in Northeastern Thailand. Am J Epidemiol 1990; 83: 31-40.
- 24. Vijayaraghavan K, Radhaiah G, Prakasam BS, Sarma KVR, Reddy V. Effect of massive dose vitamin A on morbidity and mortality in Indian children. Lancet 1990; 33 (ii): 1342-5.
- 25. Rahmatullah L, Underwood BA, thulasiraj RD et al. reduced mortality among children in Southern Indian receiving a small weekly dose of vitamin A. N Eng J Med 1990; 323: 929-35.
- 26. Hussey GD, Klein M. A randomized controlled trial of vitamin A in children with severe measles. N Eng J Med 1990; 232: 160-4.
- 27. Rahmatullah L, Underwood BA, Thulasiraj RD, Milton RC. Diarrhea, respiratory infections, and growth are not affected by a weekly low-dose vitamin A supplement: a masked, controlled field trial in children in southern India. Am J Clin Nutr 1991; 54: 568-77.
- cacy of vitamin A in reducing preschool child mortality in Nepal. Lancet 1991; 338 (ii): 67-70.
- HM. Vitamin A supplementation reduces measles morbidity in young African children: a randomized, placebo-controlled, double-blind trial. Am J Clin Nutr

- 1991; 54: 590-5.
- 30. Herrera MG, Nestel P, Amin AE, Fawzi WW, Mohamed KA, Weld L. Vitamin A supplementation and child survival. Lancet, 1992; 340 (ii): 267-71.
- 31. Daulaire NM, Starbuck ES, Houston RM, Church MS, Stukel TA and Pandey MR. Childhood mortality after a high dose of vitamin A in high risk population. Br Med J 1992; 304: 207-10.
- 32. Turner RB, Lande AE, Chase P, Hilton N,

- Weinberg D. Pneumonia in pediatric outpatients: Cause and clinical manifestation. J Pediatr 1987; 111: 194-200.
- 33. Cogswell JJ, Michell EB, Alexander J. Parental smoking, breast-feeding, and respiratory infection in development of allergic diseases. Arch Dis Child 1987; 62: 338-44.
- 34. IUATLD (Leading article): Acute respiratory infections: conclusion of an IUATLD workshop. Tubercle and lung disease 1993; 74:2-5.