THE MAGNITUDE OF MORTALITY FROM ACUTE RESPIRATORY INFECTIONS IN CHILDREN UNDER 5 YEARS IN DEVELOPING COUNTRIES

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The most widespread and fatal of all acute diseases, pneumonia, is now Captain of the Men of Death.
Sir William Osler, 1901.

Introduction

In developed countries, during the last hundred years, the evolution of mortality due to acute respiratory infections (ARI) has been dramatic *(1)*. At high levels of mortality, such as XIXth century Europe, ARI was the category of diseases making the largest contribution to shortening of life expectancy. Diseases due to ARI represented a loss of 7.5 years of life, more than all other infectious diseases (4.8 years) and diarrhoeal diseases (2.9 years). Among infants and children, ARI was the first cause of death outside the neonatal period. When life expectancy was below 45 years, 25% of all deaths in the age group 0-4 years were due to ARI, compared to only 4% when life expectancy was higher than 70 years.

Recognition of pneumonia and other ARI as an important public health problem in developing countries is recent. The magnitude of mortality from ARI in childhood in developing countries was documented and published for the first time in the early 1960s *(2)*.

More recently, the World Health Organization (WHO) and other international agencies have made ARI one of their priorities for intervention. Increased concern about the important contribution of ARI deaths to overall mortality was raised at the World Health Assembly in 1976.[d] In 1983, a Technical Advisory Group on ARI was established by WHO in Geneva *(3)*. The global programme for the control of acute respiratory infections was officially initiated in 1984 as a distinct programme under Disease Prevention and Control in WHO's Seventh General Programme of Work, covering the period 1984-1989. The central objective of the programme is to reduce mortality from ARI, in particular pneumonia. This objective is endorsed in the Declaration of the World Summit for Children, New York, 30 September 1991, which established the goal of reducing by one-third the deaths due to ARI in children under 5 years of age during the period 1990-2000.

The most recent WHO estimates (for 1990) indicate that out of nearly 12.9 million children under 5 who die each year in developing countries, about 4.3 million die of ARI. Of these, it is estimated that 0.8 million (18.6% of all ARI deaths) occur in the first month of life. Other estimates have indicated that about two-thirds of ARI deaths occur in the first year of life *(4)*. The WHO estimates further state that the ARI complications of measles accounted for 0.48 million deaths (11% of ARI deaths and 55% of all measles deaths) and that the ARI complications of pertussis accounted for 0.26 million deaths (6% of ARI deaths and 72% of all pertussis deaths). Thus, ARI was estimated to be the single largest cause of death in young children, being associated with 33% of all childhood deaths in developing countries.[e]

These estimates are based on various sources. The main sources of information have been analyses based on national cause-of-death statistics notified to WHO and extrapolations from these data to those countries which do not record cause-of-death data but have similar levels of child mortality. The aim of this article is to review and discuss the available data on mortality from ARI among children under 5 in developing countries. For this purpose, 25 studies with data on ARI deaths were reviewed. They were compared with historical data from developed countries before 1965.

Data and method

To evaluate the relationship between proportion of ARI deaths and level of mortality in historical populations, the study by Preston et al. *(5)* was used. The authors analysed the causes of death by age and sex in 180 data sets from 43 national populations before 1965 (a complete review of the data will be published in a separate paper: Garenne et al. forthcoming).[f] Causes of death from ARI were coded according to the International Classification of Diseases (ICD), Sixth and Seventh Revisions.

To estimate the magnitude of mortality from ARI in developing countries, a search of the MEDLINE data base from January 1980 to December 1991 was performed. The search focused on community studies of mortality from all causes and from ARI in children under 5 years in developing countries. Results from 2 unpublished studies were provided by the authors *(6, f)*. The data base revealed 21 community-based longitudinal studies in 13 countries *(6-26, f)*: only the studies with detailed causes of death for children aged < 5 years were kept for the final analysis. In 12 studies, the ascertainment of ARI deaths was part of an overall assessment of cause-specific mortality (5 in Bangladesh, 1 in Kenya, 1 in Morocco, 1 in Nigeria, 2 in Senegal, 1 in The Gambia and 1 in Guinea-Bissau). In the 9 remaining studies, the longitudinal surveillance was aimed specifically at ascertaining deaths due to ARI. The latter studies were undertaken to assess the impact on ARI-

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[e] World Health Organization. *Implementation of the Global Strategy for Health for All by the Year 2000, second evaluation: and eighth report on the world health situation.* Geneva, WHO, 1992. (Document A45/3).

[f] Garenne, M. et al. *ARI mortality in a rural area of Senegal.* Draft paper, 1992.

mortality of a community-based ARI intervention project (2 in India, 2 in Nepal, 1 in Pakistan and 1 in the United Republic of Tanzania); to assess the impact of a pneumococcal vaccine (2 in Papua New Guinea); to identify the etiological agents responsible for acute lower respiratory infections (ALRI) and to determine risk factors for ARI morbidity (1 in the Philippines).

In addition, 2 studies based on national death registration systems were included. Puffer & Serrano investigated causes of death in children from 13 regions in 8 countries in Latin America during the period 1968-1971 *(27)*. They used the Eighth Revision of the ICD for classification of ARI deaths *(28)*. Von Schirnding reviewed national data on mortality from ARI in South Africa for the period 1968-1985 *(29)*. Data on ARI in children from "coloured race" were included in our analysis. Data on black children were excluded because of underreporting of deaths in this group. Causes of death were classified according to the Ninth Revision of the ICD *(30)*. Data from these studies were compared to the historical data.

Definition of ARI deaths

Classification of ARI deaths

The International Classification of Diseases and Causes of Death (ICD) classifies diseases according to the biological etiology of the causes of death or, where etiology is not apparent, the anatomical localization. The ARI classified under "diseases of the respiratory system" in the Ninth Revison are presented in *Table 1*. Acute bronchitis and bronchiolitis are coded under the acute respiratory infections (code 466). Influenza and pneumonia are grouped under the same subtitle (code 480-487). In addition, the fourth digit of the ICD makes it possible to specify pneumonia occurring after certain diseases, such as measles (code 484.0), whooping cough (code 484.3) and varicella (484.8). Earlier revisions of the ICD differ slightly from the Ninth Revision *(28, 31)*. For instance, in the Eighth Revision pneumonia (480-486) was classified separately from influenza (470-474) and pneumonia after measles, varicella or pertussis was not included in the diseases of the respiratory system.

In the community studies reviewed, the lack of consistency in the inclusion of the diseases causing death from ARI was striking. In 10 studies, deaths due to ARI were not further differentiated into upper or lower respiratory infections. ALRI, where specified, mostly referred to deaths from pneumonia. ARI deaths following measles were addressed separately in 7 studies. Pertussis was considered as an ARI death in 2 studies *(9, 11)*, while 4 studies listed pertussis as a separate cause *(6, 12, 23, [f])*. Deaths due to laryngitis and influenza were listed in 2 studies only *(6, [f])*. Varicella was mentioned in the sole Senegal study.[f] One study classified ARI under the heading "symptoms, signs and ill-defined diseases" *(13)*.

Role of pneumonia

Among the diseases listed in *Table 1*, it is generally agreed that in developing countries, most ARI

TABLE 1. ARI IN THE INTERNATIONAL CLASSIFICATION OF DISEASES, NINTH REVISION (ICD-9)
TABLEAU 1. LES IRA DANS LA CLASSIFICATION INTERNATIONALE DES MALADIES, NEUVIÈME RÉVISION (CIM-9)

Diseases of the respiratory system — Maladies de l'appareil respiratoire	
ACUTE RESPIRATORY INFECTIONS (codes 460-466) — AFFECTIONS AIGUËS DES VOIES RESPIRATOIRES (codes 460-466):	
(460)	— common cold — rhume banal
(461)	— acute sinusitis — sinusite aiguë
(462)	— acute pharyngitis — pharyngite aiguë
(463)	— acute tonsillitis — amygdalite aiguë
(464)	— acute laryngitis and tracheitis — laryngite et trachéite aiguës
(465)	— acute upper respiratory infections of multiple or unspecified sites — infection aiguë des voies respiratoires supérieures, à localisations multiples ou non précisées
(466)	— acute bronchitis and bronchiolitis — bronchite et bronchiolite aiguës
PNEUMONIA AND INFLUENZA (codes 480-487) — PNEUMONIE ET GRIPPE (codes 480-487):	
(480)	— viral pneumonia — pneumonie à virus
(481)	— pneumoccocal pneumonia — pneumonie à pneumocoque
(482-483)	— pneumonia due to other bacteria and other organisms — pneumonies dues à d'autres bactéries ou d'autres organismes
(484)	— pneumonia in infectious diseases classified elsewhere — pneumonie au cours d'autres maladies infectieuses classées ailleurs
484.0	• measles (055.1) — rougeole (055.1)
484.3	• whooping cough (033) — coqueluche (033)
484.8	• varicella (052) — varicelle (052)
484.*	• other infectious diseases — autres maladies infectieuses
(485)	— bronchopneumonia, organism unspecified — bronchopneumonie, micro-organisme non précisé
(486)	— pneumonia, organism unspecified — pneumonie, micro-organisme non précisé
(487)	— influenza — grippe

Notes. Codes 470-478 include other URI diseases and chronic conditions (deviated septum and polyps and chronic upper respiratory). Codes 490-496 include chronic obstructive pulmonary disease and allied conditions (chronic bronchitis, emphysema, asthma). Codes 010-018 cover tuberculosis, including respiratory tuberculosis. — Les codes 470 à 478 couvrent d'autres maladies des voies respiratoires supérieures (déviation de la cloison, polypes, affections chroniques). Les codes 490 à 496 couvrent des maladies pulmonaires obstructives chroniques et affections connexes (bronchite chronique, emphysème, asthme). Les codes 010 à 018 couvrent la tuberculose, y compris celle de l'appareil respiratoire.

deaths among infants and children may be ascribed to pneumonia, bronchiolitis and acute obstructive laryngitis *(32)*. However, the similarity in clinical symptoms of pneumonia and bronchiolitis have often hampered the distinction of these syndromes in developing countries and the magnitude of mortality due to viral bronchiolitis is not well documented in populations. Indirect evidence from hospital studies suggests that pneumonia is the leading cause of death from ARI in developing countries. Pneumonia is the primary cause of hospitalization for ARI, before bronchiolitis and laryngitis *(33-37)*. Hospital-based data on case-fatality rates (CFR) by clinical syndrome vary widely. Rahman reported similar CFRs for pneumonia and bronchiolitis (CFR = 8%) among children under 5 years old in Bangladesh *(33)*. In the United Republic of Tanzania, Mtango observed the highest CFRs in children with laryngotracheitis (CFR = 28%) and bronchiolitis (CFR = 6%), while children with pneumonia had a CFR of 3% *(34)*. Weissenbacher observed higher CFRs for pneumonia than for other infections (CFR 5.8 vs. 2.1) *(35)*. In addition, the risk of death is higher in children when a bacterial pathogen is identified *(33, 35)*.

Results from national registration data confirm these findings. Von Schirnding *(29)* found that among 3 774 "coloured" infants aged 0-11 months who died from ARI, 96.3% had a diagnosis of pneumonia recorded on the death certificate. Puffer & Serrano *(27)* also reported a majority of deaths due to pneumonia in Latin America: among neonatal deaths from ARI, 95.1% (1 092/1 148) had pneumonia; this proportion was 77% (2 591/3 359) among infants (1-11 months) and 69.8% (489/701) among children aged 12-59 months. In Ecuador, pneumonia accounted for 59% and bronchiolitis for 28% of the 1 304 ARI deaths reported in infants in 1987 *(37)*.

Bronchiolitis may be misclassified as an upper respiratory tract infection (URTI), as has been suggested by Bulla & Hitze *(38)*. The authors suggest that the high proportion of deaths due to URTI reported in 9 African countries (64% of all ARI), may have been in part due to misclassification of lower respiratory tract infections (LRTI), e.g. bronchiolitis classified as URTI. In addition, bronchiolitis is often complicated with pneumonia in developing countries.

Diagnosis of ARI

The validity of causes of death depends first on the validity of the diagnosis. In the case of ARI, the clinical distinction between the various syndromes remains a difficult undertaking. Inter-observer variation in auscultation of the chest is frequent and ideally, definitive clinical diagnosis should be based on X-ray findings, culture of lung aspirates and measurement of blood oxygen levels *(39-41)*. The distinction between pneumonia and bronchiolitis is particularly difficult. Clinical signs for both syndromes include signs of respiratory distress such as tachypnea, nasal flaring and intercostal retractions. The presence of diffuse wheezing characteristic of bronchiolitis may be difficult to recognize for non-trained observers. Wheeze can also be found in children with pneumonia.

Specific problems of verbal autopsies

The ICD classification scheme normally requires a physician or a laboratory diagnosis. Its application to developing countries raises specific difficulties since most deaths of children occur outside hospitals. Investigators have therefore developed methods for interviewing relatives of the deceased person and have attemped to translate this information into a medical diagnosis. These procedures, called "verbal autopsies", have been reviewed recently *(42)*. In community studies, verbal autopsies have been used systematically for more than three decades for assessing causes of death *(42, 43)*.

The quality of verbal autopsies depends upon many conditions: the design of the interview (structured, semi-structured or open interview), the time elapsed since death, the person answering the questions, the quality of the interviewer and the qualification of the persons who review and code the interviews.[9] Sensitivity and specificity of the criteria used in verbal autopsies depend not only on their own characteristics but also on the capacity of the family to notice and report the symptoms. Clinical case definitions of ALRI have been validated against confirmed diagnoses of pneumonia, whether they were fatal or not, and may not be accurate for identifying death due to ARI. Few studies have attempted to validate clinical criteria against death from ALRI. Kalter *(44)* validated clinical signs reported by the mother after the death of the child in 100 children under 2 years who died from ALRI as diagnosed by a physician. Reports of cough and dyspnea before death had a sensitivity of 86% and a specificity of 47%. Including duration of symptoms improved the specificity but sensitivity decreased to 41%. Navarro *(45)* found that in 71 children under 5 with autopsy-proven pneumonia, 50 (70%) had clinical signs of severe or complicated pneumonia at admission. Shann *(46)* evaluated clinical signs among children 1-59 months of age, admitted with cough and chest in-drawing and compared those who died with those who survived. Among the clinical signs evaluated, highest specificity was achieved through identifying the severity of the chest in-drawing.

Standard criteria for post-mortem diagnosis of ARI have not yet been developed. In the community studies reviewed, 7 authors provided no criteria for classifying ARI deaths. Pandey *(20)* defined an algorithm for classification of cases, but not for deaths. The ICD classification was utilized in 5 studies. Criteria for inclusion in the specific ARI categories and lists of ARI codes, however, were not provided. In Matlab (Bangladesh), 3 physicians independently assigned the ICD code after reading the post-mortem interview and an additional interview was undertaken if no consensus could be reached *(9, 10)*.

ARI in multiple causes of death

Often, ARI do not occur alone, but in association with other infections or conditions, such as malnutrition, diarrhoea and chronic conditions. The coding of multiple causes has been discussed extensively in other documents *(47)* and in particular in the ICD. Investigators usually include in causes of death diseases where ARI is an underlying (principal, primary) or precipitating (immediate, coprimary) cause. In the studies reviewed, some authors only considered single causes of death *(19, 22)* while others assumed that deaths from ALRI were always the primary or coprimary cause of death *(11)*. Some authors include

[9] Garenne, M. & Fontaine, O. *Assessing probable causes of deaths using a standardized questionnaire — a study in rural Senegal.* Proceedings of the IUSSP seminar on morbidity and mortality, Sienna, 7-10 July 1986.

or distinguish ARI as a contributing (associated) cause *(7, 21, 25, f)* although the criteria used for detemining when ALRI contributes to — rather than directly causes — the death are not provided.

In summary, the accuracy of available data on ARI deaths can be seriously questioned. The apparent validity of the data on ARI as underlying cause of death is probably due to the fact that pneumonia and bronchiolitis are the most common causes of death from ARI, that their clinical diagnosis has a relatively high sensitivity and specificity, and that mothers can easily recognize and accurately recall the symptoms. A more complete discussion on the validity of classification of ARI deaths will be published separately (Ronsmans et al., forthcoming).

Results

Most of the data available refer to underlying causes of death. These are first analysed, both for developed countries and for developing countries. ARI deaths after measles and pertussis are analysed separately.

ARI mortality in European populations prior to 1965

In his analysis, Preston *(1)* found that the proportion of ARI deaths declined with the level of mortality, that the proportion of ARI deaths was slightly higher among children 1-4 than among infants, and that there was no difference by sex outside of infancy *(Table 2)*.

The analysis of the proportion of ARI deaths was pursued separately for children <1 and 1-4 in the European populations prior to 1965. The relationship of the percentage of ARI deaths with the level of mortality was investigated using a log-linear regression, where the dependent variable was the logarithm of the age-specific death rate (ASDR). The logarithmic scale was utilized to better fit the marked decline of the proportion of ARI deaths at low levels of mortality. Results were highly significant and are summarized in the following equations:

Age 0-11 months:
%ARI = −4.446 + 4.823*LN (ASDR_0-11)

Age 12-59 months:
%ARI = 14.928 + 3.387*LN (ASDR_12-59)

A multivariate analysis was designed to investigate the statistical effect of four variables: level of mortality, regional patterns (West, North, East and South) *(48)*, time and level of economic development (Garenne et al., forthcoming). The level of mortality was significant for both infant and child mortality. There were differences according to regional pattern, with higher proportions of ARI deaths in the East regional pattern. The proportion of ARI deaths was significantly lower after 1950 among children aged 1-4 years. This could be interpreted as the effect of antibiotics on ARI mortality. The proportion of ARI deaths was significantly lower in the more developed countries at ages 1-4, but not in infancy. This again suggests a probable role of case management, which is likely to be better in more developed countries.

Comparison with developing countries

The data from the community studies and from the vital registrations were compared to the European experience by combining the two age groups: <1 and 1-4 years. Values of (q) and (m), the quotient of mortality (probability of dying between age 0 and 5 years per 1 000 live births), and the age-specific death rates (deaths at ages 0-4 years per 1 000 person-years at risk), are provided to allow easier comparisons of mortality levels. The expected proportion of deaths from ARI was computed using the regression equation from the European data. To calculate the expected proportion of ARI deaths in the age group 0-59 months, the expected proportion of ARI deaths for the age groups 0-11 months and 12-59 months were weighted by the proportion of children dying in each age group.[h]

[h] $\% (E_{0-59}) = [({}_1q_0 * \%(E_{0-11})) + ((1-{}_1q_0) * {}_1q_4 * (E_{12-59}))] / {}_5q_0$ where ${}_nq_x$ = probability of dying between ages x and x+n, and $\% (E_{x-x+n})$ expected proportion of ARI deaths in age group x to x+n based on historical population.

TABLE 2. ARI MORTALITY IN EUROPEAN POPULATIONS PRIOR TO 1965: AVERAGE OF EMPIRICAL LIFE TABLES, ACCORDING TO LEVEL OF MORTALITY

TABLEAU 2. MORTALITÉ IRA DANS DES POPULATIONS EUROPÉENNES AVANT 1965: MOYENNE DES TABLES DE MORTALITÉ EMPIRIQUES, SELON LE NIVEAU DE MORTALITÉ

Level of mortality (e°)[a] Niveau de mortalité (e°)[a]	Average e° (years) e° moyenne (en années)	Age-specific death rates — Taux de décès par âge: Total/1 000	ARI/1 000 IRA/1000	Percentage ARI/100 Pourcentage IRA/100	Sex ratio/100 Taux de masculinité /100
Age 0-11 months — 0 à 11 mois					
<45	38.6	223.10	45.41	20.4	117.6
45-54	49.5	146.95	26.58	18.1	116.8
55-64	60.7	71.09	12.31	17.3	121.8
65-69	67.5	39.48	5.71	14.6	117.2
70-74	71.2	23.68	2.53	10.7	118.1
Age 12-59 months — 12 à 59 mois					
<45	38.6	36.13	9.62	26.6	97.7
45-54	49.5	20.95	4.73	22.6	100.5
55-64	60.7	6.65	1.46	22.0	102.3
65-69	67.5	2.39	0.49	20.6	98.2
70-74	71.2	1.16	0.15	13.2	100.7

[a] e° is the life expectancy at birth in years — e° représente l'espérance de vie à la naissance, en années.
Source: Reference *(1)*, Table 5.1 — Référence *(1)*, tableau 5.1.

The comparison is based on slightly different definitions of underlying causes of death. However, the consistency of the data from developing countries with the experience of developed countries was striking *(Table 3, Fig. 1)*. The mean proportion of ARI deaths was 18.8% and the mean of the predicted values was 17.5%. In half of the cases, the proportion of deaths could be predicted by the level of mortality with a maximum relative difference of 25%. Major discrepancies between observed and expected values could be explained either by the definitions used, by the proportion of unknown causes of death or by atypical regional patterns of mortality, with the exception of South Africa's coloured population, for which the observed values were much higher than expected. In studies aimed at evaluating the effect of community-based interventions on ARI mortality, data from the control areas consistently reported the highest proportional mortality from ARI *(Fig. 1)*. At the other extreme, the very low proportional mortality from ARI reported by Chen et al. in Bangladesh *(8)* probably reflects the lack of standardization for coding ARI deaths.

Age pattern of mortality

The proportion of deaths occurring in each age group gives a picture of the age pattern of mortality. Three age groups were selected: neonatal (0-27

TABLE 3. COMPARISON OF OBSERVED PROPORTION OF ARI DEATHS AMONG CHILDREN UNDER 5 YEARS IN DEVELOPING COUNTRIES WITH EXPECTED VALUES FROM HISTORICAL EXPERIENCE (9 community studies and 14 registration systems)

TABLEAU 3. COMPARAISON DE LA PROPORTION DE DÉCÈS IRA OBSERVÉE CHEZ LES ENFANTS DE MOINS DE 5 ANS DANS LES PAYS EN DÉVELOPPEMENT ET LES VALEURS ATTENDUES PAR EXPÉRIENCE HISTORIQUE (9 études communautaires et 14 systèmes d'enregistrement)

Study — Etude	Number of deaths Nombre de décès	Mortality[a] (all causes) Mortalité[a] (toutes causes) q/1 000	m/1 000	Observed % ARI deaths % décès IRA observés	Expected % ARI deaths % décès IRA attendus	Ratio observed/expected Rapport observés/attendus
Community studies — Etudes communautaires						
Bangladesh	7 858	251.0	62.8	6.2	23.0	0.27
India — Inde						
control — témoin	161	159.5	36.6	26.2	20.2	1.30
intervention	176	118.5	26.2	18.8	18.7	1.01
Kenya	557	75.2	16.0	19.5	16.9	1.15
Morocco — Maroc	382	101.9	22.2	11.4	17.7	0.64
Nepal — Népal						
surveillance	64	258.0	65.0	31.2	23.1	1.35
intervention[b]	74	172.3	40.0	18.8	21.2	0.89
Nepal — Népal	2 101	341.5	94.0	22.4	24.7	0.91
Pakistan						
control[c] — témoin[c]	130	136.8	30.7	33.1	20.2	1.64
intervention	378	100.0	21.7	20.8	18.3	1.13
Senegal — Sénégal	1 593	256.3	64.5	15.8	23.8	0.66
U.-R. of Tanzania[d] — R.-U. de Tanzanie[d]						
control — témoin	325	182.2	40.1	35.7		
intervention	873	149.4	32.3	34.9		
Registration systems — Systèmes d'enregistrement						
South Africa — Afrique du Sud						
1968-1973	13 810	19.5	4.0	18.6	10.5	1.76
1974-1979	11 079	16.5	3.4	18.6	10.0	1.86
1980-1985	4 647	7.1	1.4	18.5	5.6	3.29
Argentina — Argentine						
Chaco	1 701	96.7	21.0	16.4	17.6	0.93
San Juan	2 558	88.2	19.0	16.8	17.1	0.98
Bolivia — Bolivie	4 276	138.2	31.1	32.6	19.6	1.66
Brazil — Brésil						
Recife	3 635	121.3	26.9	12.4	18.8	0.66
Ribeirão	1 126	63.1	13.3	10.7	15.5	0.69
São Paulo	4 312	74.5	15.8	16.6	16.3	1.02
Chile — Chili	2 714	65.6	13.8	20.0	15.6	1.28
Colombia — Colombie						
Cali	1 627	75.9	16.2	12.5	16.7	0.75
Cartagena — Carthagène	1 255	69.0	14.6	9.8	16.4	0.59
Medellín	1 348	68.4	14.5	11.5	16.4	0.70
El Salvador	2 210	126.3	28.1	11.7	19.2	0.61
Jamaica — Jamaïque	1 903	46.9	9.7	8.8	14.1	0.63
Mexico — Mexique	3 953	75.9	16.2	16.2	16.5	0.98
Mean — Moyenne	2 649	115.7	27.6	18.8	17.5	1.07

[a] q = probability of dying between birth and age 5 per 1 000 live births; m = age-specific death rate among children 0-4 years old (deaths per 1 000 person-years at risk) — *q = probabilité de décès entre la naissance et l'âge de 5 ans, par 1 000 naissances vivantes; m = taux de mortalité par âge chez les enfants de 0 à 4 ans (décès pour 1 000 années/personnes à risque).*

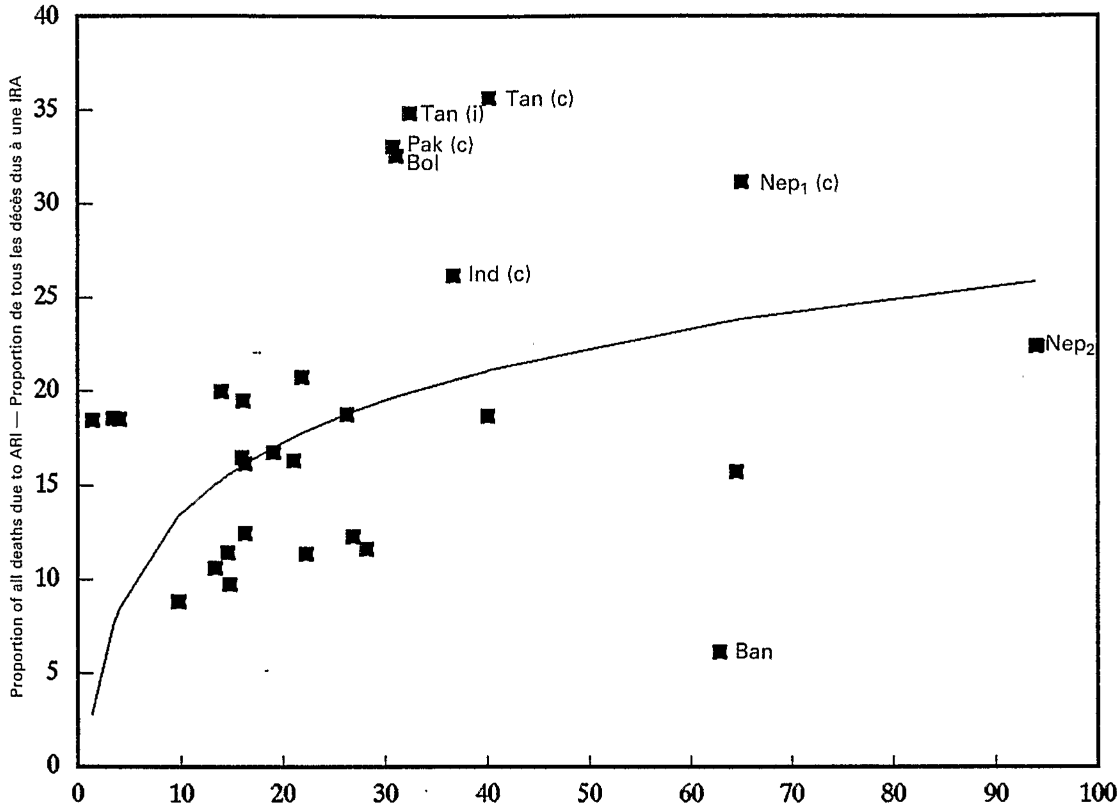
[b] Results from first and second intervention year combined — *Résultats pour les deux premières années d'intervention ensemble.*

[c] 3 years combined for the control and intervention area respectively — *Résultats de trois années pour les zones témoin et d'intervention respectivement.*

[d] Control = first year in the control area. Expected values of % ARI deaths were not calculated since age-specific death rates were not provided — *Témoin = première année dans la zone témoin. Les valeurs attendues du % de décès IRA n'ont pas été calculées, car les taux de mortalité par groupe d'âge n'étaient pas disponibles.*

FIG. 1

OBSERVED AND PREDICTED PERCENTAGE OF ARI DEATHS BY LEVEL OF MORTALITY[a]
(8 community studies and 14 registration systems)
POURCENTAGE DE DÉCÈS IRA OBSERVÉS ET PRÉVUS PAR NIVEAU DE MORTALITÉ[a]
(8 études communautaires et 14 systèmes d'enregistrement)



[a] (c) refers to the control area, (i) to the intervention area — (c) indique une zone témoin, (i) une zone d'intervention.

Study codes — Codes étude

Ban: Bangladesh	Nep: Nepal — Népal
Bol: Bolivia — Bolivie	Pak: Pakistan
Ind: India — Inde	Tan: U.R. of Tanzania — R.U. de Tanzanie

days), post-neonatal (28 days-first birthday) and early childhood (1-4 years). ARI deaths in children under 5 are usually concentrated in the age group 1-11 months *(Table 4, Fig. 2)*. For all studies combined, 20.8% of ARI deaths occurred before age 1 month, 57.8% at 1-11 months and 21.5% at 12-59 months. There was a marked gradient of deaths at ages 12-59 months, ranging from low values in East regional patterns to high values in extreme South regional patterns such as Senegal. The share of neonatal mortality was more mixed, probably reflecting inconsistencies in definitions more than real differences. In particular, in the Indian study *(18)*, neonatal mortality from ARI seems to have been largely overestimated.

Contribution of measles to ARI mortality

As reported by various authors, a high proportion of measles deaths seem to be associated with ARI *(Table 5)*. Proportions range from 100% in Guinea-Bissau and the Philippines to 25% in Bangladesh. Few authors, however, define in detail "measles associated with ARI". It is possible that the upper respiratory symptoms accompanying measles have been misclassified as pneumonia after measles. In Senegal, where an in-depth analysis of complications of measles cases was conducted, pneumonia usually occurring in the second and third week after the onset of the symptoms accounted for 30% of measles deaths, and acute laryngitis, usually occurring in the third or fourth week, for about 2%. Other measles deaths were due mainly to diarrhoea, sometimes with an accompanying pneumonia.

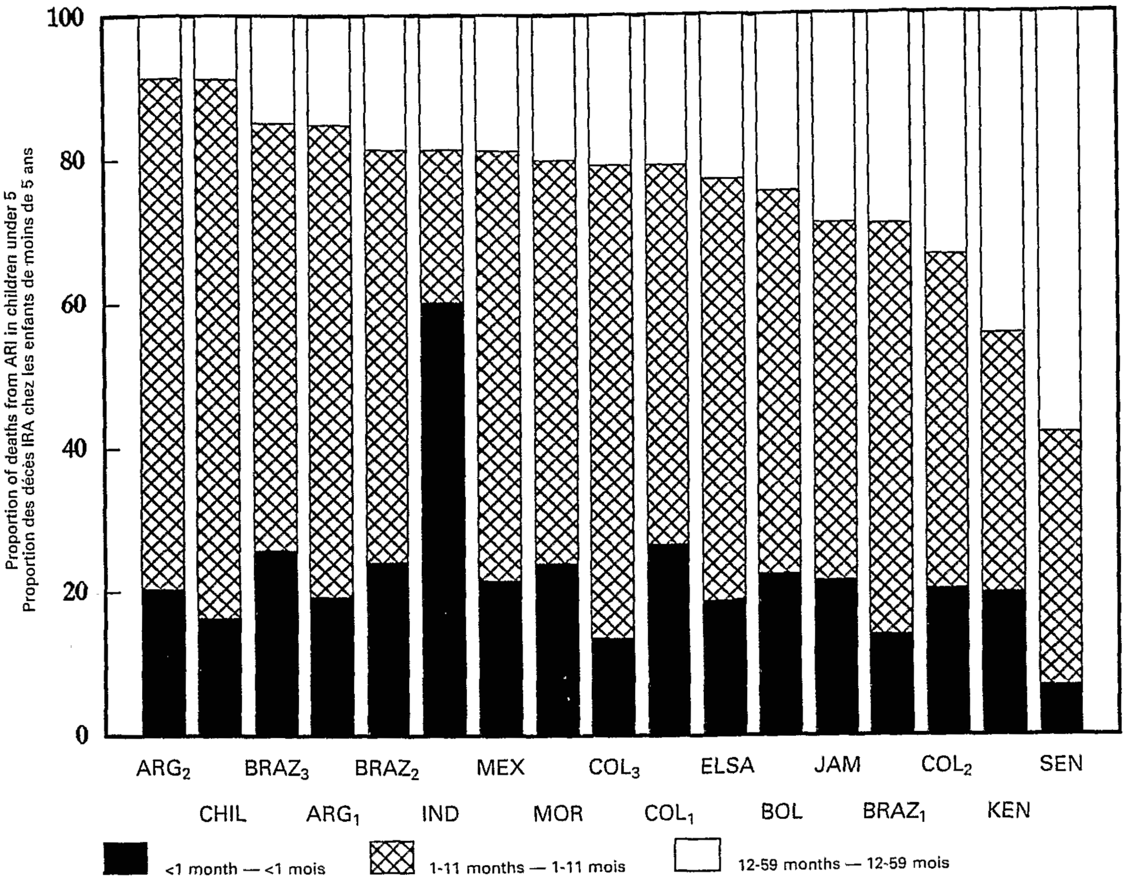
Measles also represents an important proportion of all ARI mortality. This proportion ranges from 1.5% in Chile to 92.5% in Guinea-Bissau, and the mean for all studies is 18.6%. This proportion depends very much on the incidence of measles and the measles immunization coverage over the period considered. In Chile, measles immunization coverage was high and few measles deaths were registered. In Guinea-Bissau, Smedman *(16)* reported a massive outbreak of measles in the year of the study. The two studies describing an unusually high contribution of measles to ARI *(16, 25)* assumed that all measles deaths were associated with ARI, which is not agreed by other authors.

Contribution of pertussis to ARI mortality

According to the ICD, deaths from pertussis are classified under ARI if they are caused by pneu-

FIG. 2

AGE DISTRIBUTION OF DEATHS FROM ARI
(4 longitudinal studies, 13 registration systems)
RÉPARTITION PAR ÂGE DES DÉCÈS DUS AUX IRA
(4 études longitudinales, 13 systèmes d'enregistrement)



Study codes — Codes étude

ARG: Argentina — Argentine
BOL: Bolivia — Bolivie
BRAZ: Brazil — Brésil
CHIL: Chile — Chili
COL: Colombia — Colombie
ELSA: El Salvador
IND: India — Inde
JAM: Jamaica — Jamaïque
KEN: Kenya
MEX: Mexico — Mexique
MOR: Morocco — Maroc
SEN: Senegal — Sénégal

TABLE 4. PROPORTION OF ARI DEATHS BY AGE AND STUDY, CHILDREN AGED UNDER 5 YEARS[a]
TABLEAU 4. PROPORTION DES DÉCÈS IRA PAR ÂGE ET PAR ÉTUDE (ENFANTS DE MOINS DE 5 ANS)[a]

Country — Pays	Study code — Code étude	Age group — Groupe d'âge <1 month/mois	1-11 months/mois	12-59 months/mois
India — Inde	IND	46 (60.5)	16 (21.1)	14 (18.4)
Kenya	KEN	19 (19.8)	34 (35.9)	42 (44.3)
Morocco — Maroc	MOR	12 (24.0)	28 (56.0)	10 (20.0)
Senegal — Sénégal	SEN	17 (6.8)	88 (35.1)	146 (58.2)
Argentina — Argentine				
Chaco	ARG1	54 (19.4)	183 (65.6)	42 (15.1)
San Juan	ARG2	88 (20.4)	306 (71.0)	37 (8.6)
Bolivia — Bolivie	BOL	308 (22.5)	727 (53.1)	334 (24.4)
Brazil — Brésil				
Recife	BRAZ1	62 (14.0)	253 (57.0)	129 (29.0)
Ribeirão	BRAZ2	29 (24.2)	69 (57.4)	22 (18.4)
São Paulo	BRAZ3	184 (25.9)	421 (59.3)	105 (14.8)
Chile — Chili	CHIL	89 (16.4)	406 (74.9)	47 (8.7)
Colombia — Colombie				
Cali	COL1	54 (26.6)	107 (52.6)	42 (20.7)
Cartagena — Carthagène	COL2	25 (20.3)	57 (46.3)	41 (33.4)
Medellín	COL3	21 (13.5)	102 (65.9)	32 (20.6)
El Salvador	ELSA	69 (18.8)	214 (58.5)	83 (22.7)
Jamaica — Jamaïque	JAM	36 (21.7)	82 (49.4)	48 (28.9)
Mexico — Mexique	MEX	139 (21.7)	383 (59.8)	119 (18.6)
All studies — Toutes études		1 254 (20.8)	3 491 (57.8)	1 296 (21.5)

[a] The figures give number (percentage) of ARI deaths in each age group — Les chiffres indiquent le nombre (pourcentage) des décès IRA dans chaque groupe d'âge.

TABLE 5. CONTRIBUTION OF MEASLES TO ARI MORTALITY, SELECTED COUNTRIES, VARIOUS YEARS[a]

TABLEAU 5. CONTRIBUTION DE LA ROUGEOLE AUX DÉCÈS IRA, DANS UN CERTAIN NOMBRE DE PAYS ET POUR DIVERSES ANNÉES[a]

Author/year/area — Auteur/année/zone	Age group (months) Groupe d'âge (mois)	Number measles deaths Décès par rougeole	% measles deaths associated with ARI % de décès rougeole associés avec les IRA	Number ARI deaths Nombre de décès IRA	% ALRI[b] deaths due to measles % de décès IARI[b] dus à la rougeole
Spika, 1989	1-59	122	(25.4)	390	(7.9)
Riley, 1986	6-59	22	(63.6)	68	(20.6)
Fauveau, 1990 intervention	6-35	1	(100.0)	31	(3.2)
comparison — comparaison	6-35	13	(77.9)	73	(13.7)
Bhatia, 1989 intervention	1-11	12	(75.0)	88	(10.2)
comparison — comparaison	1-11	22	(77.3)	131	(13.0)
Smedman, 1986	0-83	62	(100.0)	31	(92.5)
Tupasi, 1990	0-59	11	(100.0)	18	(61.1)
Garenne, 1992	0-59	78	(30.0)	250	(9.2)
Mtango, 1986	0-59			421	(25.0)
Puffer, 1973 Argentina — Argentine					
Chaco	0-59	57	(49.1)	588	(4.8)
San Juan	0-59	102	(78.4)	1 072	(7.5)
Bolivia — Bolivie	0-59	564	(80.1)	2 512	(18.0)
Brazil — Brésil					
Recife	0-59	406	(84.0)	1 867	(18.3)
Ribeirão	0-59	47	(91.5)	429	(10.0)
São Paulo	0-59	162	(85.2)	2 026	(6.8)
Chile — Chili	0-59	23	(82.6)	1 249	(1.5)
Colombia — Colombie					
Cali	0-59	83	(87.9)	687	(10.6)
Cartagena — Carthagène	0-59	109	(61.5)	563	(11.9)
Medellín	0-59	92	(80.4)	603	(12.3)
El Salvador	0-59	181	(65.2)	1 534	(7.7)
Jamaica — Jamaïque	0-59	11	(45.4)	540	(9.0)
Mexico — Mexique	0-59	332	(75.6)	2 011	(12.5)

[a] Deaths from measles or ALRI as an underlying or associated cause. Pertussis deaths are not included in the ALRI deaths — Décès ayant pour cause immédiate ou associée la rougeole ou une IARI. *Les décès dus à la coqueluche ne sont pas comptés parmi les décès IARI.*

[b] ALRI: acute lower respiratory infection — IARI: infection aiguë des voies respiratoires inférieures.

monia. Only one study provided an indication of the magnitude of pneumonia among pertussis deaths. In Senegal, only 12% of all pertussis deaths were estimated to be due to pneumonia as an immediate cause. For the other studies, we computed the ratio of all pertussis deaths to all ARI and pertussis deaths. Percentages of pertussis deaths ranged from 0.5% in Medellín (Colombia) to 28.3% in Senegal *(Table 6)*. The studies reporting the highest proportions were studies where the epidemiology of pertussis was a major subject of research *(12, f)*. However, the ratio of pertussis deaths to ARI deaths in community studies depends very much upon the epidemiology of pertussis during the study period.

Interventions

One way to indirectly validate the ascertainment of causes of death is to observe the changes in ARI-specific mortality rates after cause-specific interventions. The community-based treatment trials showed consistent declines in overall and ARI-specific mortality rates *(Fig. 3)*.

Discussion

The assessment of the magnitude of ARI mortality is hampered by several issues. Firstly, there is no standard definition of ARI. While there is a general agreement that most ARI deaths are due to pneumonia, bronchiolitis and laryngotracheitis, other causes such as influenza may have been overlooked. Influenza was a significant cause of death in XIXth century Europe. Since most of the definitions of deaths due to ARI refer to deaths from pneumonia, the reported data should be interpreted as representing primarily mortality from pneumonia.

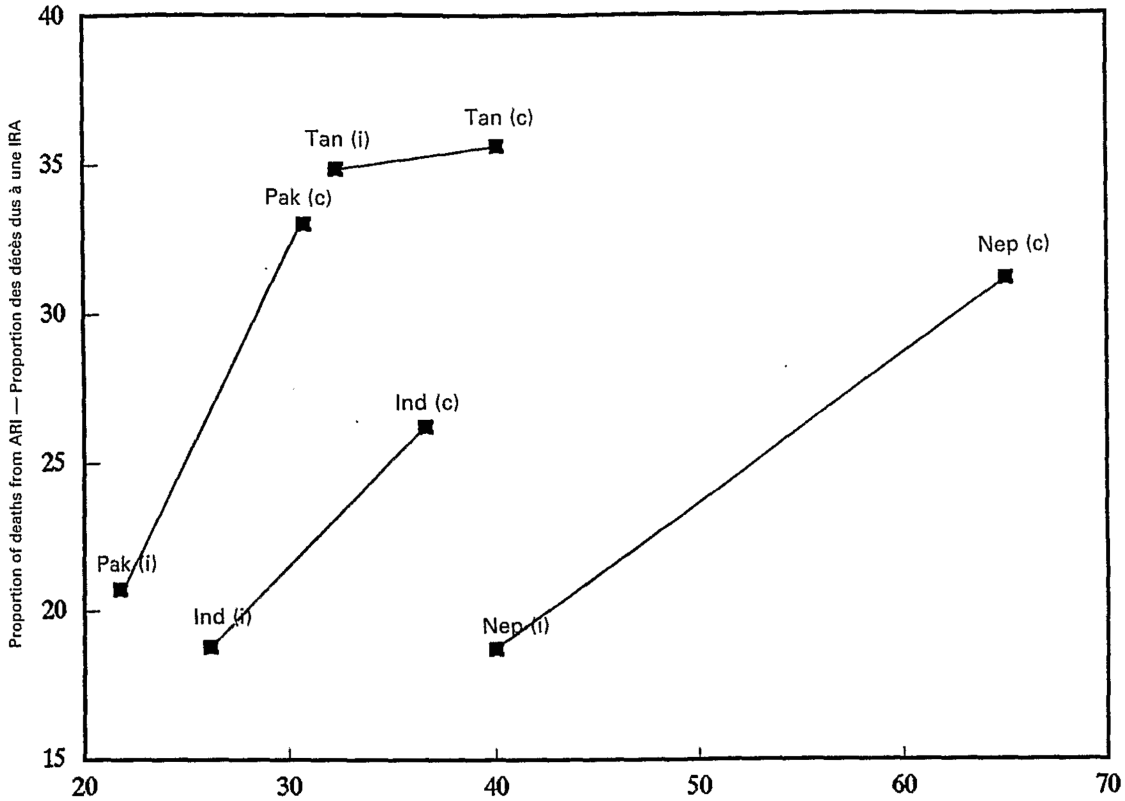
The lack of standardization for ascertaining causes of death is another major limitation for a proper evaluation of the magnitude of ARI in mortality among preschool children. This involves the methods of investigating causes of deaths, e.g. verbal autopsies, the lack of sensitivity and specificity of clinical diagnoses on which most cause-of-death data in developing countries are based, and the methods of recording and coding multiple causes of death. In particular, the role of ARI may be underestimated in considering only underlying causes of death. It is not surprising that the studies in which ARI was a major focus of research reported the highest proportional mortality from ARI. Whether these studies represent the true contribution of ARI to mortality, or whether the increased attention led to overestimation, is difficult to ascertain. Death is generally preceded by signs of respiratory distress. Unless specific criteria for a minimum duration of these symptoms before death are defined as a prerequisite for assigning ARI as the cause, inclusion of non-specific signs of respiratory distress may lead to overestimation of mortality from ARI. Few authors, however, defined a minimum duration of respiratory symptoms before death *(6, 18, f)*.

Associations of ARI with measles and pertussis deserve particular attention, since effective measures for the control of these infections are available. Pneumonia is one of the most important complications of measles and has been responsible for a large proportion of measles deaths in developing countries *(49, 50)*. Pneumonia typically occurs 2-3 weeks after the acute attack of measles and may be due to the direct effect of the measles virus or to the pulmonary superinfection following the depressive effect of the measles virus on the immune system *(51, 52)*. Despite the absence of clear definitions, and the often lacking information on levels of im-

FIG. 3

INTERVENTION EFFECTS ON MORTALITY FROM ALL CAUSES AND ARI IN CHILDREN UNDER 5 YEARS[a]
(4 community-based intervention studies)

EFFET DES INTERVENTIONS SUR LE NIVEAU DE MORTALITÉ ET LE POURCENTAGE DES DÉCÈS IRA CHEZ LES ENFANTS DE MOINS DE 5 ANS[a] (4 études d'intervention à base communautaire)



Age-specific death rate in children 0-5 years/1 000 years — Taux de décès par âge chez des enfants de 0 à 5 ans/1 000 années

[a] (c) refers to the control area, and (i) to the intervention area — (c) indique une zone témoin, et (i) une zone d'intervention.

Study codes — Codes étude

Ind: India — Inde
Nep: Nepal — Népal
Pak: Pakistan
Tan: U.R. of Tanzania — R.U. de Tanzanie

TABLE 6. CONTRIBUTION OF PERTUSSIS TO ARI MORTALITY, SELECTED COUNTRIES, VARIOUS YEARS[a]

TABLEAU 6. CONTRIBUTION DE LA COQUELUCHE AUX DÉCÈS IRA, DANS UN CERTAIN NOMBRE DE PAYS ET POUR DIVERSES ANNÉES[a]

Author/year/area — Auteur/année/zone	Age group (months) Groupe d'âge (mois)	Pertussis/ALRI[b] deaths Décès par coqueluche/IARI[b]	% Pertussis among ALRI[b] pertussis deaths % de coqueluche parmi les décès IARI[b] + coqueluche
Fauveau, 1990 intervention	1-35	4/96	(4.2)
comparison — comparaison	1-35	9/159	(5.7)
Omondi-Odhiambo, 1984	1-59	7/54	(13.0)
Darkaoui, 1989	1-59	3/41	(7.3)
Garenne, 1992	0-59	67/310	(21.6)
Mtango, 1986	0-59	10/431	(2.3)
Puffer, 1973 Argentina — Argentine			
Chaco	0-59	24/612	(3.9)
San Juan	0-59	21/1093	(1.9)
Bolivia — Bolivie	0-59	58/2570	(2.3)
Brazil — Brésil			
Recife	0-59	33/1900	(1.7)
Ribeirão	0-59	8/437	(1.8)
São Paulo	0-59	36/2062	(1.7)
Chile — Chili	0-59	7/1256	(0.6)
Colombia — Colombie			
Cali	0-59	12/699	(1.7)
Cartagena — Carthagène	0-59	21/584	(3.6)
Medellín	0-59	3/407	(0.5)
El Salvador	0-59	35/1569	(2.2)
Jamaica — Jamaïque	0-59	21/561	(3.7)
Mexico — Mexique	0-59	27/2038	(1.3)

[a] Death from pertussis or ALRI as an underlying or associated cause. Measles deaths are not included in the ALRI deaths — Décès ayant pour cause immédiate ou associée la coqueluche ou une IARI. Les décès dus à la rougeole ne sont pas comptés parmi les décès IARI.

[b] ALRI: acute lower respiratory infection — IARI: Affection aiguë des voies respiratoires inférieures.

munization coverage or the presence of major measles epidemics in the studies reviewed, the mean estimate of 16.8% of ARI deaths that can be ascribed to measles comes remarkably close to the commonly-used WHO estimate of 15%. With the current progress in world immunization against measles, this proportion has decreased to 10-12%.

Ascertainment of ARI deaths due to pertussis poses more problems. Before immunization was commonly practised in industrialized countries, major epidemics occurred every 4-6 years *(53)*. The epidemic pattern of pertussis makes difficult the establishment of its importance in short-term surveillance. In verbal autopsies, a history of the typical whoop will only be elicited if specific questions are asked. In addition, very young infants show a lower frequency of paroxysms and typical whoop, complicating the diagnosis in this age group. The high proportion of ARI deaths attributed to pertussis in the studies in Senegal and Kenya, where deaths from pertussis were addressed with particular attention, may merely reflect this fact, though the contribution of major epidemics during the study period cannot be excluded. Pertussis may also cause delayed mortality through its effect on the nutritional status of the child *(54)*. The epidemiology of pertussis has received less attention in developing countries than measles or ARI, and unless precise case definitions are developed and long-term surveillance carried out, its contribution to ARI will remain unknown.

Data based on underlying causes of death suggest that, in developing countries, approximately 1 out of 6 deaths of children aged 0-4 years are due to pneumonia. This estimate matches what is known from developed countries at similar levels of mortality in the past. To this major underlying cause of death, one should add other ARI deaths, ARI deaths after measles, pertussis or other infectious diseases as well as in association with acute malnutrition. Without more accurate data, it seems to be difficult to give a final estimate, but the WHO figure of 1 out of 3 deaths due to — or associated with — ARI may be close to the real range of ARI proportional mortality in children of developing countries.

ARI mortality has been declining steadily with improving living conditions in developed countries and has been declining very rapidly since 1950 when antibiotics became available. Perhaps the best way to estimate the current burden of ARI diseases in developing countries is to compare ARI mortality to the lowest values recorded in developed countries. This would provide a number of deaths that could be averted if the best medical technology were provided to every child. Such a comparison and the high values of ARI mortality found in many developing countries indicate that more efforts should be made to better control ARI.

SUMMARY

This article reviews the available evidence of mortality from acute respiratory infections (ARI) among children aged under 5 years in contemporary developing countries and compares the findings with European populations before 1965. In European populations before 1965, the level of mortality was found to be a determinant of the proportion of deaths due to ARI. There were marked differences according to regional patterns of mortality. Deaths from ARI played a smaller role after 1950, when the use of antibiotics became generalized.

In developing countries, the role of ARI mortality seems to be similar to the European experience. The age pattern is very marked. In absolute values, ARI mortality is highest in the neonatal period and decreases with age. In relative values, ARI mortality is highest in the postneonatal period.

ARI, mainly pneumonia, accounts for about 18% of underlying causes of death in developing countries. Pneumonia and other ARI are frequent complications of measles and pertussis; ARI is also commonly found after other infections and in association with severe malnutrition. Virtually no data are available in developing countries to provide final estimates of the role of ARI in mortality of children aged under 5 years. However, the WHO figure of 1 out of 3 deaths due to — or associated with — ARI may be close to the real range of the ARI-proportional mortality in children of developing countries.

Results are discussed in light of the definitions of ARI used in various studies, the difficulties in ascertaining and coding multiple causes of death and the quality of data from some sources.

RÉSUMÉ

Ampleur de la mortalité due aux affections aiguës des voies respiratoires chez les enfants de moins de 5 ans dans les pays en developpement

Cet article passe en revue les données disponibles concernant la mortalité actuelle par affection aiguë des voies respiratoires (ou infection respiratoire aiguë - IRA) chez les enfants de moins de 5 ans dans les pays en développement, et établit une comparaison avec la situation en Europe avant 1965. On avait constaté qu'avant cette date, dans les populations européennes, le niveau de mortalité était un déterminant de la proportion de décès dus aux IRA. Les tableaux de mortalité présentaient de très nettes différences selon les régions. Le rôle des décès par IRA a diminué à partir de 1950, avec la généralisation de l'usage des antibiotiques.

Dans les pays en développement, le rôle de la mortalité par IRA paraît similaire à ce qu'il était jadis en Europe. La répartition par âge est très nette. En valeur absolue, c'est au cours de la période néona-

tale que la mortalité par IRA est la plus forte; elle diminue ensuite avec l'âge. En valeur relative, cette mortalité est plus forte durant la période post-néonatale.

Les IRA, et en particulier les pneumonies, sont la cause initiale d'environ 18% des décès dans les pays en développement. Elles sont une complication fréquente de la rougeole et de la coqueluche; on les rencontre fréquemment aussi après d'autres infections, ou associées à la malnutrition grave. Il n'y a dans les pays en développement que très peu de données qui puissent fournir des estimations finales sur le rôle des IRA dans la mortalité des enfants de moins de 5 ans. Toutefois, le chiffre qu'indique l'OMS — 1 décès sur 3 dû ou associé aux IRA — doit être assez proche de la réalité, s'agissant de la mortalité proportionnelle par IRA chez les enfants des pays en développement.

L'analyse des résultats tient compte des définitions des IRA utilisées dans différentes études, des difficultés à déterminer les causes multiples de décès et à les coder, et de la qualité des données provenant de certaines sources.

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