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Technical bases for the WHO recommendations on the management of pneumonia in children at first-level health facilities

Programme for the Control of Acute Respiratory Infections

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TECHNICAL BASES FOR THE WHO RECOMMENDATIONS ON THE MANAGEMENT OF PNEUMONIA IN CHILDREN AT FIRST-LEVEL HEALTH FACILITIES

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1. INTRODUCTION

About 13 million children under 5 years of age die every year in the world, 95% of them in developing countries. Pneumonia is one of the leading causes, accounting for about 4 million of these deaths.

Despite this fact, for a combination of technical and operational reasons, pneumonia has been a neglected problem until very recently. Clinicians and epidemiologists thought that the control of respiratory infections did not deserve high priority because of the difficulties involved in preventing and managing these infections; it was said that antibiotics might not be an effective treatment against pneumonia because patients are often weakened by conditions such as chronic malnutrition and parasitic infections, and that a wide variety of viruses and bacteria are associated with pulmonary infections making it impossible to identify the specific etiological agent in each patient (1). On the other hand, some public health experts felt that a programme aimed at preventing mortality from pneumonia could not succeed because it would be difficult to deliver the available technology (antibiotics) through peripheral health units and community-based health workers.

At most, one quarter of the pneumonia cases in children can be prevented by the measles and pertussis vaccines included in the immunization schedule of the Expanded Programme on Immunization. There is a clear need for research to develop and test vaccines against the most frequent agents of pneumonia in children. Such research has been pursued by WHO, notably within the Programe for the Control of Acute Respiratory Infections (ARI) and the Vaccine Development Programme; however, WHO has simultaneously been utilizing current clinical knowledge to formulate a case management strategy to reduce the high mortality from pneumonia in children.

The present document is not intended to provide detailed case management guidelines. These are to be found in the manual "Acute respiratory infections in children: Case management in small hospitals in developing countries. A manual for doctors and other senior health workers", document WHO/ARI/90.5 (1990).

2. TECHNICAL BASES FOR STANDARDIZED CASE MANAGEMENT OF ACUTE RESPIRATORY INFECTIONS

2.1 Importance of bacterial pneumonia

Present evidence indicates that in the developing countries bacteria play a far greater role as causes of pneumonia in children than they do in developed countries. Two kinds of data lend support to this evidence: etiological studies of pneumonia and information on the prevalence of nasopharyngeal carriers of pathogenic bacteria.

Etiological studies of pneumonia. The etiological diagnosis of pneumonia in infants and young children is very difficult to establish because sputum is usually not available (2). Rapid immunological techniques such as counter immunoelectrophoresis,

ELISA, latex agglutination, or coagglutination are not yet entirely satisfactory for determining the role of bacteria in the etiology of pneumonia in children (3). Only cultures of lung aspirates and blood cultures can produce a reliable bacteriological diagnosis (4).

Lung puncture is the most sensitive method for recovery and identification of the bacterial agents of pneumonia in children. Cultures of lung aspirates yield a very low false-positive rate (a positive result is strong evidence of bacterial infection if common contaminating skin organisms, like *Staphylococcus epidermidis,* are excluded). In the 1970s and early 1980s they were used in 13 studies in developing countries in children with pneumonia who had not received previous antimicrobial treatment (5-8). When the results of these studies were pooled, bacteria were isolated in 456 (55%) of the 835 aspirates examined (Table 1); they were found in at least 50% of the children in all but three studies. In fact, a high proportion of the negative results were probably false-negatives because of the many factors that mask the presence of bacteria: for example, the appropriate lung lesion may not be reached with the needle, the material collected may be scanty, or the laboratory methods may be inadequate to isolate all the possible bacterial

TABLE 1

POSITIVITY OF BACTERIOLOGICAL CULTURES OF LUNG ASPIRATES FROM CHILDREN WITH PNEUMONIA WHO HAD NO PREVIOUS ANTIBIOTIC TREATMENT

Place	Year of publication	N° of children	Age in years	Bacterial cultures (+) Number	%
Brazil: Recife	1978	60	0- 4	34	60.0
São Paulo	1974	37	0- 7	20	54.1
Chile: Santiago (Mimica)	1971	160	0- 2	91	56.8
Santiago (Schuster)	1966	125	0-10	67	53.6
Colombia: Cali	1976	71	0-14	15	21.1
Gambia: Fajara*	1986	51	0- 9	33	64.6
India: Pune	1981	50	0-11	30	60.0
Nigeria: Benin	1981	46	0-12	34	73.9
Zaira	1977	88	0- 8	54	61.3
Papua New Guinea: Goroka	1984	71	0- 5	48	67.6
Tari	1983	18	0- 9	8	44.0
Philippines: Manila	1979	18	0-14	9	50.0
Zimbabwe: Bulawayo	1988	40	0-11	13	32.5
TOTAL		835		456	54.6

* including the results of blood cultures.

NOTE: Gambia study, reference (6); Zimbabwe study, reference (7); the other studies, reference (5).

pathogens. Cases that have received previous antibiotic therapy may also have been included in these series since it is not always possible to determine with accuracy the treatment background of young children. Thus, the actual proportion of positive bacterial cultures was probably higher than that reported.

Published evidence from lung aspirate studies performed in the pre-antibiotic era indicates that the bacteriology of pneumonia in developed countries used to be similar to that observed in many developing countries today (5). Nowadays, however, it is accepted that most episodes of pneumonia in children in developed countries are of viral origin, the most important organisms being respiratory syncytial virus, parainfluenza, influenza, and adenoviruses. In a lung aspirate study conducted in Newark, USA, a bacterial etiology was demonstrated in only 11% of untreated cases of community-acquired pneumonia (9). Nevertheless, recent studies using antigen detection techniques have concluded that bacterial infections may be more common in developed countries than has generally been recognized (2,10,11).

Since lung puncture is an invasive method that exposes the child to serious risks, there have been strong ethical objections to its use in clinical research. In recent years, the best information on the bacterial etiology of pneumonia in young children has been obtained through blood cultures, despite the fact that the sensitivity of this method is somewhat lower. In studies in three countries supported by BOSTID (Board on Science and Technology for International Development, US National Research Council), cultures were made on blood samples taken from children with acute lower respiratory infections, mostly pneumonia, diagnosed by hospital services (Table 2). The positivity of the bacterial cultures was 26.1% in Pakistan (12), 26.8% in Papua New Guinea (13), and 13.4% in the Philippines (14). These results represent a fraction of the real rates of bacterial lung infection, because it is generally admitted that blood cultures yield positive results in one quarter to one third of bacterial pneumonia cases.

TABLE 2

POSITIVITY OF BLOOD CULTURES FROM CHILDREN 0-4 YEARS OLD WITH PNEUMONIA WHO HAD NO PREVIOUS ANTIBIOTIC TREATMENT

Place	Reference	N° of children	Bacterial cultures (+)	
			Number	%
Pakistan: Islamabad (BOSTID Study*)	10	1331	347	26.1
Papua New Guinea: Goroka	11	253	68	26.8
Philippines: Manila	12	537	72	13.4

* includes children with any of the following signs: fast breathing, chest retractions, cyanosis, wheezing or rales upon auscultation.

Although the evidence from lung aspirate and blood culture studies relates to hospitalized children with pneumonia, these are the children who die if they are left untreated.

These studies also have consistently demonstrated that *Streptococcus pneumoniae* and *Haemophilus influenzae* are the most frequently isolated bacteria. Table 3 summarizes the findings from the studies that provided this information. These two bacteria accounted for more than two thirds of all bacterial isolates, 73.9% of lung aspirate isolates, and 69.1% of blood isolates.

TABLE 3

DISTRIBUTION OF BACTERIA ISOLATED FROM LUNG ASPIRATES AND BLOOD CULTURES

Place	*Strepto-coccus pneumoniae*	*Haemophilus influenzae*	*Staphy-lococcus aureus*	Other bacteria	Total isolates
I. LUNG ASPIRATES					
Brazil: Recife	25	13	0	0	38
São Paulo	15	3	1	1	20
Chile: Santiago (Schuster)	26	19	15	13	73
Colombia: Cali	4	4	5	2	15
Gambia: Fajara	26	12	1	2	41
Nigeria: Zaira	31	9	8	20	68
Papua New Guinea: Goroka	27	41	1	23	92
Tari	7	1	0	0	8
Zimbabwe: Bulawayo	7	3	4	1	15
Subtotal	168	105	35	62	370
Percent	45.5	28.4	9.4	16.7	100.0
II. BLOOD CULTURES					
Pakistan: Islamabad	132	144	25	87	388
Papua New Guinea: Goroka	29	30	0	9	68
Philippines: Manila	11	19	11	31	72
Subtotal	172	193	36	127	528
Percent	32.6	36.5	6.8	24.1	100.0
TOTAL	340	298	71	189	898
PERCENT	37.9	33.2	7.9	21.0	100.0

Pneumonia is often caused by multiple microbial agents. Concurrent bacterial infection is quite frequent in children who have an acute viral infection. Viral infections may alter the host defense factors and reduce the efficiency of the antibacterial activities of the lungs, creating suitable conditions for invasion by the pathogenic bacteria that are commonly present in the upper respiratory tract (15). In about 20% of confirmed cases of viral acute lower respiratory infection (pneumonia or wheeze) a bacterial superinfection was also demonstrated by culture of blood or lung aspirates (Table 4). In view of the number of false-negative results that are expected with these isolation techniques, the true positivity should be higher. Mixed bacterial and viral infections in children are also being recognized more frequently in developed countries (2,16). Therefore, the presence of a viral infection does not exclude concomitant bacterial infection.

TABLE 4

CONCOMITANT BACTERIAL INFECTION IN CHILDREN WITH VIRAL ACUTE LOWER RESPIRATORY INFECTIONS

Place	Reference	(+) Viral cases		(+) Bacterial cases		
		Type	Number	Diagn. method*	Number	%
Colombia: Cali	16	Pneumonia	27	LA	5	18.5
Pakistan: Islamabad	10	Pneumonia/ Wheeze	553	BC	135	24.4
Papua New Guinea: Goroka	5	Pneumonia	62	LA/BC	12	19.4
Philippines: Manila	12	Pneumonia/ Wheeze	180	BC	17	9.4
TOTAL			822		169	20.6

* BC - Blood culture
LA - Lung aspirate culture

Similarly, multiple bacterial isolates were often found in lung aspirates. Table 5 presents the information on multiple bacterial isolates from the nine studies listed in the upper part of Table 3. Multiple isolates were reported by six studies. Pooling all the results, two bacteria were identified in 14.5% of cases, and more than two in 4.4% of cases.

Nasopharyngeal carriage of bacteria. Pneumonia in children is probably often caused by inhalation of infected nasopharyngeal secretions into the lungs. The pneumococcus and *H. influenzae* are components of the normal flora of the upper respiratory tract. Aspiration of secretions is a common event in normal individuals, particularly during sleep. Because upper respiratory secretions may contain large numbers of potential pathogens that have colonized the nasopharynx, the aspiration of a very small amount

could deliver a large enough inoculum to cause bacterial pneumonia, especially if the local defenses of the lower respiratory tract are impaired because of malnutrition, a viral infection, or other factors. The close association between the nasopharyngeal acquisition of pneumococcus strains and the incidence of invasive disease has been documented in epidemiological studies (17). A recent study conducted in Islamabad, Pakistan, showed that 98% of children with clinical pneumonia and bacteraemia carried the same pneumococcus serotypes with the same drug sensitivity in the blood and in the nasopharynx (18). This finding was confirmed in a subsequent study in Islamabad, Pakistan, in which the prevalence of antimicrobial resistance was similar for invasive isolates of pneumococcus and *H. influenzae* and isolates carried by children with clinical pneumonia for all the antimicrobials tested.

TABLE 5

SINGLE AND MULTIPLE BACTERIAL ISOLATES FROM LUNG ASPIRATE CULTURES

Place	N° of patients with (+) culture	Bacterial isolates			Total bacterial isolates
		1	2	>2	
Brazil: Recife	34	30	4	0	38
São Paulo	20	20	0	0	20
Chile: Santiago (Schuster)	67	61	6	0	73
Colombia: Cali	15	15	0	0	15
Gambia: Fajara	33	29	2	2	41
Nigeria: Zaira	54	36	14	4	76
Papua New Guinea: Goroka	48	27	14	7	76
Tari	8	8	0	0	8
Zimbabwe: Bulawayo	13	11	2	0	15
TOTAL	292	237	42	13	362
PERCENT	100.0	81.1	14.5	4.4	