



CONTROL OF ACUTE RESPIRATORY INFECTIONS IN CHILDREN BETWEEN 2 MONTHS AND 5 YEARS OF AGE

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I. OVERVIEW

Of the 15 million annual deaths worldwide among children under 5 years of age, one-third are due to acute respiratory infections (ARI), especially pneumonia. Studies conducted in several developing countries have shown that early recognition and treatment of pneumonia are the most effective action to reduce ARI-related mortality (1).

Normally, a child presents between 7 and 10 episodes of ARI a year, the majority of which are mild and self-limiting. The number of cases, however, represents an enormous job for health services, and children with risk factors, in particular, can develop pneumonia or a more severe disease that increases the risk of death and requires inpatient attention. Of the entire population in the Region of the Americas, approximately 713 million inhabitants, 11% of the population is under 5 years of age. The level of sociocultural and economic development varies widely throughout the Region, and health, as one of its basic components, reveals exceedingly high infant morbidity and mortality in countries where resources are fewer, birth rates are higher, and mortality declines very slowly. This situation contrasts with that of countries that enjoy high levels of economic development, where infant mortality rates not only are low but continue to decrease at a sustained pace. These conditions show an extreme inequality in infant health conditions (2).

II. ETIOLOGY AND PHYSIOPATHOGENY

There are predisposing factors or risk factors for ARI, such as poor socioeconomic conditions, multiple births, low birth weight, absence of breast feeding, malnutrition and specific nutritional deficiencies (e.g., vitamin A deficiency), exposure to cold, especially in nursing infants, overcrowding, and pollution in the home and elsewhere.

The pathogens vary with the patient ages, their immune condition, and surrounding environment. The great majority of ARI episodes at all ages are brought on by viruses, such as respiratory syncytial virus (RSV), parainfluenza virus, influenza virus, and adenovirus. These pathogens tend to present clinical manifestations in patients between 2 months and 5 years of age, bronchiolitis (RSV), laryngeal tracheitis (RSV and parainfluenza virus), and pneumonitis (influenza virus and adenovirus). The distribution by age of some of these viruses may be very broad, but the pathologies they tend to produce are more or less circumscribed within specific age groups. The same phenomenon occurs with other germs such as *Chlamydia trachomatis*, which is prevalent from birth to 6 months of age.

In children between 1 month and 5 years of age, the bacteria most frequently causing pneumonia are *Streptococcus pneumoniae* and group B *Haemophilus influenzae*, which is found especially in children between 4 months and 2 years of age. *Staphylococcus aureus* is also a frequent cause of pneumonia in children under 5 years of age. *S. pneumoniae* and *H. influenzae* colonize the upper airways early on in nursing infants and children, especially in developing countries, in which nasopharyngeal transmission rates of 76 to 97% for *S. pneumoniae* have been found in children up to 4 years of age, as compared with rates of 30 to 50% in developed countries. Between 6 and 10% of type B *H. influenzae* has been found in a carrier stage in pediatric communities in developing countries as compared with 2% of the infant population in industrialized countries. This phenomenon, in conjunction with precipitating viral infections and multiple risk factors, can help to explain the high frequency of bacterial acute lower respiratory infections in poor communities (3).

Different series studied in developing countries have yielded positive cultures of bacteria from samples taken by pulmonary puncture in up to 62% of the cases in children without prior antibiotic therapy. This finding is a firm indication of the high frequency of bacterial pneumonia in economically depressed communities.

On some occasions, ARI may be caused by germs other than those described, but their sporadic presentation corresponds to more specific conditions, such as underlying pathology (e.g. cystic fibrosis, *Pseudomonas A pneumoniae*); endemic incidence (tuberculosis and some mycosis); an immunosuppressed state (in the case of *Pneumocystis carinii* and tuberculosis); exposure to fowl (*Chlamydia psittaci*); or nosocomial pneumonia, associated with gastrointestinal flora or the hospital environment, such as *Pseudomonas* spp., *Klebsiella* spp., *Escherichia coli*, and fungi of the *Candida albicans* type.

A precise determination must be made of each patient's risk factors on the basis of epidemiological, environmental, and personal characteristics; but it is essential to keep in mind that the

most important prevalent bacteria causing pneumonia in children 1 month to 5 years of age are *S. pneumoniae* and *H. influenzae* (1, 3-7).

The importance of simultaneous viral and bacterial infections has been fully described, and it is accepted that an initial viral infection, after denuding the epithelial respiratory cover during replication of the virus, facilitates the adherence of bacteria and their consequent invasion in the respiratory system, beginning with the upper respiratory tract. The coexistence of two or more pathogenic bacteria in pulmonary culture, especially *S. pneumoniae* and *H. influenzae* (5), has been shown.

After analyzing the interaction between the host, the environment, and the infectious agent, it should be remembered that the distribution of the different germs by age group, is quite even in all latitudes. However, with a specific bacterium, a child from a developing country is at a biological disadvantage and, due to his situation, is predisposed to at least several risk factors such as malnutrition, lack of immunizations, pollution, delayed medical consultation, and lack of access to health services. These factors largely explain the much greater vulnerability of an underprivileged child to the same germ and the child's increased risk of dying from pneumonia.

Under normal conditions, the respiratory system is highly competent in avoiding infection, since it possesses anatomical, physical, physiological, and immunological processes and defense mechanisms against a vast number of infectious viral and bacterial agents, as well as parasites, that are present in human habitats. Pulmonary infection occurs when one or more of these defenses is overcome, and germs from an inhaled contaminant reach the peripheral air passages and alveoli or enter through the blood system. This phenomenon causes edema in the bronchia, bronchioles, and alveoli, along with leukocyte infiltration and posterior phagocytosis of the cellular remains by the macrophages (8, 9). This process may be circumscribed within a single segment or lobe or may extend to other lung segments, the pleura, or extrapulmonary organs. As consolidation takes place, the respiratory function alters and the vital capacity and distensibility of the airways diminishes. Moreover, the blood flow and ventilation of the involved areas is affected, which alters the ventilation/perfusion relationship and results in hypoxia and an increase in the respiratory and cardiac workload.

III. CLINICAL MANIFESTATIONS

The symptoms and signs of lower respiratory infections in children 2 months to 5 years of age vary depending on the pathogenic microorganism, the immunological state of the host, and in particular the severity of the infection. A child this age may present general, respiratory, pleural, and extrapulmonary manifestations. General findings may include rhinorrhea, discomfort, fever, chills, listlessness, headache, and sore throat, as well as occasional gastrointestinal symptomatology such as vomiting, diarrhea, and painful and distended abdomen, especially in older children (10). The most obvious respiratory manifestations are coughing and the various degrees of respiratory distress, which include nasal flaring, cyanosis, tachypnea, use of the accessory respiratory muscles, and subcostal indrawing. Respiratory frequency is the most

sensitive and reliable index for evaluating the presence and severity of an acute respiratory infection (11, 12) and should be measured when the child is at rest.

The percussive signs are reduction of the vesicular murmur and the finding of stertors upon auscultation. They are important, even though they vary with different clinical manifestations and with age and therefore are not always specific for a given infectious pathology. Other findings, such as dullness to percussion, limited motility of the hemithorax, or reference to pleural pain, depend on the size of the thorax, the degree of pathologic involvement, and the child's capacity to express his or her perceptions.

The extrapulmonary spread of respiratory infections observed in some cases presents clinical manifestations that may be quite useful for etiologic diagnosis. For example, cellulitis or abscesses of the skin or soft tissues raises the likelihood of *S. aureus*; the presence of media otitis, conjunctivitis, sinusitis, or meningitis concomitant to ARI suggests *H. influenzae*; myringitis bullosa simultaneous with pneumonia indicates an etiology of *Mycoplasma pneumoniae*.

Traditional classifications based on the type of anatomical, functional, radiological, etiological, and physiopathogenic involvement continue to be fully valid and are an ideal complement to diagnosis of ARI in children. The proper performance of these procedures requires medical and technological resources that are often lacking in many countries. For this and other reasons, classification based on the severity of the process benefits from being simple and geared toward immediate, appropriate, and progressive action and treatment of children. It is also the basis for primary care that is clearly demonstrated to have scientific validity and effective results in reducing mortality.

Given that the basic strategy for reducing mortality from ARI and especially pneumonia is adequate and timely treatment, international health organizations such WHO/PAHO and UNICEF have outlined recommendations on identifying and classifying ARI according to severity, which are based on numerous studies carried out in different parts of the world. These studies determined the most sensitive and specific parameters for diagnosing ARI and ensuring that they would be readily recognizable by primary health care workers.

General references in medical literature and the results of the studies mentioned indicate respiratory frequency as a valuable indicator in predicting the presence of pneumonia. Since respiratory frequency changes with the child's growth, the validity of different ranges for each age group has been demonstrated, and basic parameters of normality have been established. Thus, the normal respiratory frequency in children 2 months to 5 years of age may be classified as follows:

From 2 to 11 months: less than 50 breaths per minute

From 1 year to 5 years: less than 40 breaths per minute

Breathing patterns should always be recorded when the child is still, preferably at rest in the mother's arms for an entire minute. Respiratory frequency is a sensitive parameter and allows the recognition of pneumonia in the greatest number of children so that they can be adequately treated. It is also specific in differentiating pneumonia from nonpneumonia cases. It can be easily detected by the mother or caretaker ("the child breathes fast") and can be evaluated by

health personnel, whatever their level of training in efficient case management, according to the parameters reviewed below.

As pneumonia progresses and the respiratory function becomes more affected, pulmonary and thoracic distention decreases and the effort to inhale increases, leading to subcostal indrawing, i.e., a retraction of the lower part of the thorax upon inhalation. The child's rib cage is elastic and distention due to difficult breathing causes a perceptible horizontal extension of the ribs. Even in normal conditions, a certain highly variable intracostal or supraclavicular indrawing may take place, which makes it inconsistent as a parameter for evaluating the severity of the case. However, inspirational subcostal indrawing is a reliable sign of a severe restriction of the pulmonary parenchyma; i.e., of severe pneumonia. A child with subcostal indrawing has a greater risk of dying from pneumonia (because it would be a very severe one) than one who has only fast breathing (12).

The use of a small specific number of diagnostic criteria in the management protocols recommended by PAHO/WHO has been planned to facilitate the recognition of patients and the use of standards at the primary level. The admission criteria for these patients under the Program for Acute Respiratory Infections are coughing and difficult breathing for the child, which are the most frequent and obvious signs in children with probable ARI. Even though stridor, a sign related to the upper respiratory tract, is included in the parameters for severe lower ARI ("danger signs"), it implies severity and indicates the need for speedy transfer to a hospital for treatment. Other entry criteria are earache and sore throat, which are the most frequent basis for children's consultation. (See Chapter 10.)

The most frequent complications in lower respiratory infections in children from 2 months to 5 years of age are pleural empyema, pulmonary abscesses, and extrapulmonary infections such as meningitis or sepsis. The common denominator in these pathologies is the combination of several risk factors, such as malnutrition and the lack of breast feeding and of immunizations, late consultation and inadequate case management, especially in the early stages where lack of knowledge of basic precepts leads to the indiscriminate use of antibiotics, thereby delaying referral and timely treatment of the child.

The majority of patients with complications arrive at the hospital in the advanced stages of their disease, with evident signs of difficult breathing, and in a septic state or even in the throes of multisystem failure. They usually have not had prior treatment. The etiology of these complicated respiratory infections, especially empyema and pulmonary abscesses, coincides with ARI in general, and usually is caused by *S. aureus*, *S. pneumoniae*, and *H. influenzae*. In other words, carelessness or improper treatment allows incipient or simple ARI to develop into more severe forms (13, 14). Other complications are shock, pneumothorax, especially in the course of an empyema, pericardial effusion, cardiac insufficiency, and remote incipient infections such as meningitis and infections of the ears and joints. Some patients reveal inadequate secretion of antidiuretic hormone.

There has been an attempt to define some clinical signs that would help to identify children at high risk of dying from severe pneumonia and who should thus receive intensive therapy.

Some of these signs are prolonged acute disease, extreme changes in patient x-rays, cyanosis, leukocytosis, or leukopenia, hepatomegaly, inability to eat, and severe indrawing. Malnourished and feverish children have high mortality (15).

IV. PARACLINICAL DIAGNOSIS

The radiological study of a child with ARI often affords a confirmation of the clinical diagnosis and a determination of the degree of impairment. In some instances, it allows differentiation to see whether the picture is consistent with the virus. In such cases there may be findings of air blockage, diffuse peribronchial, multilobar, poorly defined, parahilar infiltrate, microatelectasis, and interstitial infiltrate. In a bacterial situation, however, there is a finding of lobar, segmentary, subsegmentary, single or multiple, well-defined infiltrate, spreading hyperlucid lesions, adenomegaly, and other manifestations.

Nevertheless, radiological findings alone are not specific or pathognomonic of any particular germ (16). An X-ray should be interpreted by first comparing it with the clinical findings, but its high cost in developing countries dictates priority for complicated ARI cases and those with access to hospitals or clinics where the resources are available.

The customary laboratory methods may be useful for detecting the presence of infection (e.g., hematological picture, with leukocytosis and neutrophilia in the case of bacteria, or leukopenia in the case of virus), but these methods are not very specific and cannot be analyzed in isolation. The same holds true in determining the globular sedimentation velocity and C-reactive protein, since these are nonspecific indicators of inflammation. A hemoculture may boast greater specificity, but its accuracy is barely 15 to 20% in pneumonia caused by *H. influenzae*, *S. aureus*, and *S. pneumoniae*.

Culture from children's pharyngeal secretions is of only limited value, because its interpretation requires more than 25 polymorphonuclears and less than 25 epithelial cells per field to be considered true sputum. When performed correctly these tests can be correlated to the causal agent, but the samples are hard to obtain, especially in small children, due to their inability to expectorate. On the other hand, positive nasopharyngeal and pharyngeal cultures may simply indicate a carrier status and not coincide with the bacteria causing an acute lower respiratory infection (17).

The culture of material obtained by thoracentesis or pulmonary puncture has been used for determining ARI etiology in several studies and has a good index for testing positive, up to 80%, but in routine practice it is indicated only for patients with pleural effusion or under certain specific parameters not applicable to all ARI patients. Transtracheal puncture is not indicated in pediatrics, because the procedure is so traumatic and carries a high risk for hematomas, the danger of a false passage, and cardiac arrhythmia.

There are now advanced technological methods for determining viruses, such as cultures, immunofluorescence to detect viral antigens, and the enzyme-linked immunoadsorbent assay (ELISA). Other tests include the culture growth and hybridization of nucleic acids and poly-

merase chain reactions (18), as well as counterimmunoelectrophoresis (CIE), latex agglutination for type B *H. influenzae*, *S. pneumoniae*, *Neisseria meningitidis*, and type B β -hemolytic *Streptococcus*. The sensitivity of immunofluorescence, coagglutination, and other immune tests (6) depends on the germ studied and the body fluid used. These tests have very limited application due to their high cost and the laboratory infrastructure and human resources they require, particularly in countries with few economic resources.

V. ARI CONTROL

Along with case severity, pneumonia deaths increase in number due to delays in receiving medical attention, lack of training among personnel, and the indiscriminate use of antibiotics. The fundamental objective of the ARI Program in children 2 months to 5 years of age is to reduce severity and mortality from ARI and especially from pneumonia in this age group. One of the objectives of the program activities is to increase the population's access to health services where personnel are trained to treat pediatric pneumonia cases correctly. Another is to increase the ability of parents to identify clinical signs and encourage them to seek attention when their children may have ARI.

Among the most effective means for rapid and substantial reduction in mortality from pneumonia in developing countries is recognition of simple clinical signs for classification and appropriate case management; permanent provision of appropriate antibiotics to the community through primary care institutions; sufficient personnel trained in the ARI Program; and the use of complementary and preventive measures.

The most appropriate procedure for treating a child with ARI, after diagnosis preferably performed at the initial stage, is to determine accurately which germ is causing the disease, using the most accurate and current microbiological technology, and then to start the specific antibiotic therapy immediately. This approach is ideal but utopian; it assumes that using all the attention and technological resources, which are not available in most of the communities in the countries of the Region, will be brought to bear.

On the other hand, the broad spectrum of etiologic and clinical possibilities are not only very costly and complex, they may themselves present risks and fail to be sufficiently accurate. Even in industrialized countries, one-fourth of hospitalized children, and even more outpatient cases, are diagnosed incorrectly (12). In any case, a deep and broad knowledge of all the clinical and paraclinical methods for diagnosing ARI and their routine application by physicians are not incompatible with the methods used in primary care at the broadest community level.

Thus, antimicrobial therapy covering the most frequent etiologic agents of pneumonia in children 2 months to 5 years of age (whose sensitivity to those antibiotics is widely recognized) has been accepted in practice. In choosing antibiotics, it is necessary to take into account the most probable etiology, sensitivity to the medication, bioavailability and capacity to penetrate the different respiratory tissues, the pharmacokinetics of the drugs, the clinical spectrum,

adverse effects, cost, and the possibility of having them available at all times in the community health services. In children 2 months to 5 years old the chosen antibiotic must be effective against *H. influenzae* and *S. pneumoniae*. In developing countries, the majority of strains of these bacteria are sensitive to trimethoprim-sulfamethoxazole (TMP-SMX), amoxicillin, ampicillin, and penicillin.

Antibiotic treatment of severely ill patients does not substitute for the need for adequate oxygenation, good nutrition, hydration, and other general support measures. The health impact of the use and abuse of antibiotics should always be taken into account (19). An antibiotic failure may be attributed to an inappropriate indication, insufficient dose, insufficient duration, inappropriate administration, resistance, superinfection, or immune deficiency.

From a public health program perspective, classification of ARI according to the severity as defined by the patient's clinical signs is required to decide whether antibiotics are needed and if treatment will be given at home or in the hospital. Three separate groups of children with ARI between 2 months and 5 years of age should be identified:

- a) Those with pneumonia or a very severe disease requiring antibiotics and hospitalization;
- b) Those with nonsevere pneumonia who require antibiotics at home. Children with acute otitis or throat infection, such as from streptococcus, also belong to this group; and
- c) Those who do not have pneumonia but a common cold and need only support measures provided at home.

The most effective technology for the control of ARI in developing countries is based on three principles:

- a) Preventive measures: immunizations, especially DPT, measles, and BCG; control and improvement of the environment, prenatal control, breast feeding, appropriate nutrition, and protection against cold.
- b) Health education: to increase the family's ability to recognize simple respiratory signs and to apply therapeutic support measures, such as avoiding as far as possible, contact with other sick children.
- c) Case management: using entry criteria such as "cough or difficult breathing," a direct evaluation of the child is initiated with questions to the mother or caretaker about the symptoms and an examination of the patient to classify the disease correctly. For obvious operational reasons, the patient cannot be classified other than in a single category. There are four categories of classification for children 2 months to 5 years of age:

c.1) Very Severe Disease

Children who show danger signs such as an inability to drink, convulsions, abnormal sleepiness, or difficult to wake, stridor, or severe malnutrition shall be classified

in this category. The child who has any of these signs is classified as having a very severe disease. In these instances it is not as important to determine the exact cause of the severe disease (at least initially); rather, it is imperative that the child be sent with urgency to the hospital for immediate treatment and to prevent an unnecessary death. If conditions demand it, a first dose of antibiotics should be administered.

c.2) Severe pneumonia

It can be assumed that the child suffers from serious pneumonia if chest indrawing is observed, as this implies intense compromise of the pulmonary parenchyma; on the other hand, chest indrawing is the best clinical manifestation predictive of serious pneumonia. Obviously, there could be some other signs of serious illness, as cyanosis, moaning, and nasal flaring, but these can be very diverse. If the child has wheezing, this will be treated according to the recommendations stated in the pertinent chapter. If the child is classified in this category, he has to be referred urgently to the hospital to ensure appropriate treatment. If it is necessary and possible a first dose of antibiotic should be given.

c.3) Nonsevere pneumonia

If the patient has no danger signs or subcostal indrawing but has fast breathing, pneumonia may be present. It is considered fast breathing if the frequency is higher than normally expected for the child's age: for example, more than 50 times per minute between 2 and 11 months, or more than 40 times per minute between 1 and 5 years. A child with fast breathing but without indrawing may have nonsevere pneumonia, possibly incipient, and should receive antibiotics on an outpatient basis to avoid pneumonia death or complications.

The mother should be instructed how to administer the antibiotic and a return control visit should be scheduled in 48 hours or earlier if the child's condition worsens. At home, the mother should also follow through with support measures, such as continuing to breast feed, or feeding the child, removing nasal obstructions, and safeguarding against her child catching cold. If the patient presents fever, safe antipyretic physical measures should be applied, or acetaminophen is indicated if the fever goes over 38.5o C. If the child has wheezing, treatment is recommended. If the fever or wheezing continues, referral is indicated to ensure better study of diagnostic possibilities, such as tuberculosis and asthma.

c.4) Non-pneumonia (simple cough or cold)

The majority of children with ARI do not present the above mentioned danger signs, subcostal indrawing, or increased respiratory frequency; i.e., they do not fit in the above classifications, because they simply have a common cold. Obviously, this group

of patients does not require antibiotics but needs attention at home. Instructions should be given to the mother on pneumonia danger signs and indications on the need to return for attention if the child worsens. Every opportunity should be used to educate the parents on different aspects of the child's care; immunization, nutrition, and hygiene, which are all essential for family development and short- and long-term health promotion in the community (22).

In all of these situations it is of key importance to provide instructions to the mother with regard to support measures such as continuation of feeding, whether it is breast feeding or the child's normal diet, ensuring that it be increased after the ARI episode; the provision of liquids to maintain sufficient hydration; protection against catching cold (without over-covering); nasal de-obstruction, cleaning the nasal cavities and if necessary using drops of saline solution or clean warm water to rinse out the secretions.

The classification parameters and therapeutic standards proposed by PAHO/WHO have been widely disseminated in all countries. The majority of community care organizations have posters, which should be consulted and followed by all health teams. The posters contain all the information and decisions presented in sketches and are simple to follow.

When an antibiotic is indicated, such as for pneumonia, it should cover *H. influenzae* and *S. pneumoniae* (23). Among the options are injectable procaine penicillin and two oral antimicrobials such as trimethoprim-sulfamethoxazole (TMP-SMX) and amoxicillin, which is preferable to ampicillin because of its easy absorption and fewer doses and gastrointestinal effects. In the majority of cases, SMX-TMP is fully indicated because of its efficacy, broad spectrum, easy administration (only two doses a day), low cost, and few side effects.

For the treatment of pneumonia itself, oral phenoxymethyl penicillin or benzathine penicillin is not recommended; they affect only low blood levels and have little effect against *H. influenzae* and *S. pneumoniae*. Erythromycin has little effect on *H. influenzae*, and so is not indicated for pneumonia.

A child admitted to the hospital should be treated with all appropriate ARI case management therapies tailored to the needs of each case. These include oxygen therapy or ventilation assistance if necessary, nasal de-obstruction, nutrition, hydration if required, antibiotic therapy, or other medication such as bronchodilators and antipyretics.

Crystalline penicillin is among the antibiotics to be considered in the treatment of a hospitalized child. If the child is very severely ill, chloramphenicol should also be considered because of its effectiveness against *H. influenzae*, *S. pneumoniae*, and some Gram-negative microorganisms. On some occasions it is necessary to use other antibiotics (23-25), such as oxacillin, methacycline, cephalosporins, or gentamicin-type aminoglycosides. However, this depends on analysis of the peculiarities of the patient and drug availability.

Indicating oxygen for a child with severe pneumonia is based on the need to improve the hypoxia secondary to parenchymal involvement. The recommended parameters of the ARI Program for administering oxygen are central cyanosis, inability to drink, restlessness that

improves with oxygen, intense indrawing, and more than 70 breaths per minute in children 2 months to 5 years of age (26).

Work is being carried out on the production of both viral vaccines (RSV, parainfluenza, adenovirus, and influenza) and bacterial vaccines (*H. influenzae* and *S. pneumoniae*). However, the evaluation period for the viral vaccine and the high cost of the bacterial vaccines have prevented their mass distribution.

The WHO protocol is geared mostly to primary level personnel and community doctors to help them to identify pneumonia cases among children who present with cough or difficult breathing to ensure that they receive an appropriate antibiotic. This strategy should be accessible to all children.

VI. WHAT TO AVOID IN ARI TREATMENT

No medications exist that improve the rheological properties (physical-chemical) of mucus, ciliary clearance, or phagocyte capacity, or that specifically counteract the alteration produced by virus and bacteria. Nor has it been demonstrated that decongestants, cough suppressants, expectorants, or mucolytics are of benefit or are risk free in the normal course of an acute lower respiratory infection, which is why they should not be used in the integrated case management of children with ARI. The deeply rooted habit in our communities of administering all sorts of products (such as bird or shark oils or fats, alcohol, petrolatum, mentholated products) to children with acute respiratory infections should be discouraged whether in oral form, nasal plugs, or even rubs, due to the danger of increasing the irritation of the air passages and, above all, the possibility of severe bronchial inhalation.

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