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Epidemiology of Lower Respiratory Tract Infections

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Summary

The aim of this review is to focus on the epidemiology of lower respiratory tract infections, the etiology, prognosis and risk factors, dividing these problems into the following issues: global impact of these afflictions, community-acquired pneumonia, hospital acquired pneumonia, respiratory infections in surgery, acute bronchitis and exacerbations of chronic bronchitis. Every year about 5 million people die of acute respiratory infections. Among these, pneumonia represents the most frequent cause of mortality, hospitalization and medical consultation. Several factors (age, underlying disease, environment) influence mortality, morbidity and also microbial etiology. The authors also refer to recent data on the most frequently identified antibiotic resistance of respiratory pathogens. The knowledge of such different clinico-epidemiological situations is essential to physicians for an effective approach to treatment of pneumonia and bronchitis.

Key words: pneumonia, bronchitis, respiratory tract infections.

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INTRODUCTION

Only 100 years ago, in 1886, Weichselbaum proved for the first time that the etiologic agent of pneumonia is pneumococcus, successively called *Streptococcus pneumoniae.*

50 years ago, in 1944, Arthur Fleming discovered penicillin, which seemed to change the prognosis of this infection, formerly responsible for high mortality (200 deaths per 100,000 per year); so that physicians hoped the use of antibiotics would solve the problem of respiratory infections. An example of such opinion is this sentence which appeared in 1956 in a famous pneumological review, in regard to successful penicillin treatment of respiratory infections: "In cases of pneumonia in the age group 15-60 without significant coexistent disease, it is felt that routine bacteriologic studies are unnecessary" [1].

Following epidemiologic remarks clearly showed that pneumonia still required evaluation because of the high morbidity and new clinical features. In the last 15 years, in fact, etiological changes have occurred because of the differing incidence of "old" pathogens and the appearance of "new" pathogens, frequent selection of bacteria resistant to most utilized antibiotics (penicillin, ampicillin, macrolides), changes in host/infection challenge, due to both the increase in the number of old people and higher incidence of disease impairing host defense against infections [2,3,4].

The aim of this study is to focus on the epidemiology of lower respiratory tract infections, the etiology, prognosis, and risk factors, dividing the problems into the following issues:

1. Impact of problem

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2. Community-acquired pneumonia
3. Hospital-acquired pneumonia
4. Respiratory infections in surgery
5. Lower respiratory tract infections (bronchitis).

IMPACT OF PROBLEM

It is hard to report the exact incidence of pneumonia, because physicians are not obliged to declare it, and some patients prefer to avoid hospital admission. However, there are many sources to examine, in order to define the impact of the problem. In 1994, WHO published results of a demographic report about world mortality up to 1990 by Murray and Lopez [5], showing that every year about 50 million people die, among which 39 million are from Developing Countries.

Respiratory infections are responsible for about 10% of total mortality *(Table 1)*. Two parameters, age and country of origin, are particularly interesting: mortality in Developed Countries has the highest incidence in patients over 60, whereas in Developing Countries it is between 0 and 4 years of age. Such a difference depends on a higher mean age of people living in Developed than in Developing Countries, and on a very high peri- and neonatal mortality in these, due to insufficient hygienic and socio-economic conditions *(Table 2)*.

TABLE 1 - *Estimated deaths from respiratory infections* 1990 [5].*

	Respiratory infections		All causes of death
World	4,314,400	(8.6%)	49,971,100
Developed regions	330,000	(3%)	10,883,100
Developing regions	3,984,400	(10.2%)	39,088,000

* tuberculosis excluded

These data are supported by recent studies, performed in the US, UK and Scandinavia. The National Health Survey estimates that more than 200 million acute respiratory infections occur every year [6], among which there are 4 million community-acquired pneumonias

TABLE 2 - *Estimated deaths (in thousands) from respiratory infections* by age and sex, 1990 [5].*

		Males							Females						
Regions	Both sexes	0-4	5-14	15-29	30-44	45-59	60-69	70+	All ages	0-4	5-14	15-29	30-44	45-59	60-69	70+	All ages
World	4,314.4	1,383.6	120.7	42.0	31.7	49.8	164.3	364.5	2,156.6	1,348.4	124.3	43.1	32.2	43.2	140.5	426.0	2,157.6
Developed regions	330.0	12.4	---	1.8	4.7	11.0	17.1	115.3	163.1	9.3	---	1.2	2.1	4.3	9.4	139.9	166.9
Developing regions	3,984.4	1,371.2	119.9	40.2	26.9	38.9	147.1	249.3	1,993.5	1,339.1	123.6	42.0	30.1	38.9	131.1	286.1	1,990.9

* tuberculosis excluded

(CAP) with an incidence of 1.5 episodes for every 100 persons per year.

We can presume that such an incidence is 2-4 times smaller than reality, because patients do not always consult a physician and frequently chest X-ray is not performed. These data are in line with the Washington Group Health Cooperative Study (1963-75), which reports an annual pneumonia incidence of 1-2% cases per year out of all diseases [7]. A high number of pneumonia cases requires hospitalization: more than 500,000 patients suffering from pneumonia are admitted to hospital in the US every year; the highest hospitalization index (11.5%) is reported on patients of more than 65 years of age *(Table 3)*[8]. Mortality is around 24.1 per 100,000, reaching 5th place after cardio-vascular, neoplastic, cerebro-vascular and chronic bronchitis disease. There is a similar trend in the UK, where 60,000 people die every year because of pneumonia [9]. Studies performed in hospital have generally shown a mortality of around 10-15%, although the BTS multicenter study recorded a surprisingly lower mortality of 5.7% [10]. Although pneumonia occurs very frequently in the last decades of life, deaths from pneumonia for patients under 65 exceed other infectious causes of death. In the UK the impact of such disease in the National Health Service has been established: acute pneumonia represents the most frequent cause of medical consultations (25 million prescriptions/year of antibiotics). Besides, these infections cause 9 million lost working days/year, and are responsible for thousands of admissions to the hospital.

In Sweden, nowadays mortality is around 60 per 100,000, with a morbidity of 4%, one of the lowest in the world [11].

TABLE 3 - *Hospitalization due to pneumonia* [8].

Age (year)	Number (thousands)	Rate per 1,000 population	Average length of hospital stay (days)
15	229	4.4	5.2
15-44	107	1.0	6.6
45-64	130	2.9	9.4
65	302	11.5	11.5
Total	768	3.4	8.6

Obviously, these data allow just a rough assessment of the epidemiology of pneumonia, because of various criteria considered in different studies, and several factors (age, underlying disease, environment) influencing mortality [12].

COMMUNITY-ACQUIRED PNEUMONIA (CAP)

Several negative factors impede the process of making a correct etiological diagnosis of CAP: difficulty of obtaining patients' sputum, especially if valuable according to Bartlett criteria; low sensitivity of routine bacteriological assays on sputum; difficulty of performing routine serological tests concerning viruses, Mycoplasma, Legionella, Chlamydia; unsuitable samples for anareobic assays.

However, there are some prospective controlled studies, performed on a large number of patients, which are very useful for evaluating the incidence of different pathogens of pneumonia. These epidemiological data are very important for the correct evaluation of the "ab initio" pneumonia patient because treatment is often empiric, since clinical and radiological features are not always specific, and it is not easy to perform, outside the hospital, diagnostic tests to identify pathogens [13].

Formerly, indeed, different authors [8,9] have said that clinico-radiological features alone allow us to make an etiological diagnosis of CAP. Recently, on the contrary, it is felt that microbial etiology can be correctly predicted by discriminate multivariate analysis only in 42% of pneumonia cases. Among 4 groups of classified pneumonia (*Mycoplasma pneumoniae*, *Streptococcus pneumoniae*, other bacteria unidentified), only Mycoplasma cases have been diagnosed in a high ratio of cases (77%).

So, therapeutic planning for CAP cannot be based only on clinico-radiological features, as formerly. Two meaningful factors influencing microbial etiology, and consequently initial treatment, are disease severity, old age and underlying afflictions [14]. In regard to these factors, the American Thoracic Society in 1993 formulated guidelines for the initial management of adults with CAP [15], based on identification of 4 groups of pneumonia *(Table 4)*. For each group, it is possible to foresee the incidence of most frequent pathogens, considering

the results of prospective studies carried out in the USA and Europe.

1. Out-patient pneumonia without concomitant disease and <=60 years of age

In this group the pathogens responsible for pneumonia include: *S. pneumoniae, M. pneumoniae*, viruses, *Chlamydia pneumoniae* and *Haemophilus influenzae (Figure 1).*

TABLE 4 - *Guidelines for community-acquired pneumonia (American Thoracic Society, 1993).*

1. Community-acquired pneumonia occurring in patients 60 years of age or younger who have no evidence of comorbidity and who can be treated in outpatient setting.
2. Community-acquired pneumonia occurring in patients with evidence of comorbidity and/or who are 60 yr of age or older who can be treated in an outpatient setting.
3. Community-acquired pneumonia requiring hospitalization but not admission to an intensive care unit.
4. Severe community-acquired penumonia, generally requiring ICU care.

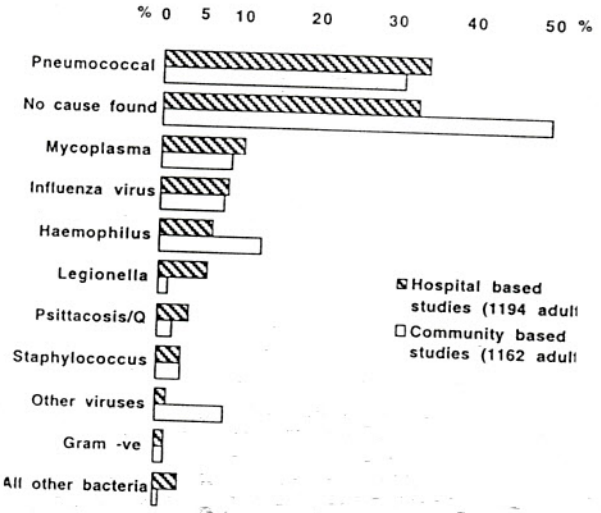

FIGURE 1 - Pathogens implicated in recent studies of adult community-acquired pneumonia conducted both in hospital and in the community [9].

S. pneumoniae is still the most frequent bacterium (30%), although less than formerly, followed by *M. pneumoniae* with a varying incidence in the different studies, as seen with recurrent epidemics of this disease. This concept is proved by the results of an important prospective study, performed in Nottingham in 1987 on 236 outpatients suffering from community-acquired pneumonias [16]. As shown in *Table 5*, the results are in agreement with other studies but with a lower incidence of *M. pneumonia* due to no epidemics during the study period. In comparing the results of a study carried out by the same authors some years before [17], the marked decrease in incidence of *S. pneumoniae* becomes clear (from 76% to 36%).

TABLE 5 - *Pathogens detected in patients with CAP in two studies (1980 and 1987) in Nottingham* [16,17].

Pathogen	1982 number (%) 127 cases	1987 number (%) 236 cases
S. pneumoniae	96 (76)	85 (36)
Legionella spp.	19 (15)	1 (0.5)
H. influenzae	4 (3)	24 (10)
St. aureus	3 (2.4)	2 (1)
E. coli	1 (0.8)	2 (1)
Mycoplasma pneumoniae	3 (2.4)	3 (1)
Chlamydia psittaci	7 (5.5)	3 (1)
Influenza virus (A e B)	7 (5.5)	19 (8)
Respiratory syncytial virus	2 (1.5)	2 (2)
Adenovirus	1 (0.8)	5 (2)
Varicella virus	1 (0.8)	
Parainfluenza virus		1 (0.5)
Cytomegalovirus		1 (0.5)
N. pathogens	4 (3)	107 (45)

H. influenzae is the third pathogen, in order of frequence, followed by respiratory viruses; Rickettsiae and Chlamydiae occur respectively in 2% and 5% of total cases.

According to some authors, in this group of patients, the highest incidence seems to be that of pathogens causing so-called "Atypical Pneumonia Syndrome" including viruses, Mycoplasma, Rickettsiae and Chlamydiae. In a recent study performed in Spain [18], 50% of pneumonias observed outside hospital were caused by these pathogens, while only 21% showed a bacterial etiology.

Although there is continuous improvement of laboratory methods for diagnosis of *Legionella* spp., the incidence of this infection

is still not well defined. The most mentioned studies indicating an incidence of Legionella in the USA of about 25,000-50,000 cases/year, have several limitations. A critical review of the most important published studies on this topic shows results ranging from <1% to <30% [19]. Such differing evaluations could be explained by the variability of methods used, size of the studied population and real geographic differences [20]. A similar pattern is remarkable for *C. pneumoniae,* considered responsible for 2-5% of CAP, although some reports show a higher incidence, up to 15% [21,22].

Results of studies mentioned above, as a whole, suggest a progressive reduction in the etiological role of *S. pneumoniae,* once considered responsible for 70%-80% of CAP, while the spectrum of other pathogens is going to become larger, including new species.

Acute respiratory infections present, as is well known, marked seasonal variations, strongly increasing in the first 2-3 months of the year. The influenza virus peak occurs from January to March: in the same period the incidence of causative Pneumococcus and *Staphylococcus pneumoniae* markedly increases [23], reaching the highest mortality rate for such infections.

Although Mycoplasma infections are more frequent in autumn, they generally have a longer cycle, with epidemic courses every 3-4 years. During such epidemics, Mycoplasma infection represents a frequent cause of community pneumonia (colleges, barracks), whereas, except during epidemics, it occurs sporadically. *Legionella pneumophila* and parainfluenza virus infections are more common in summer and early autumn, while those caused by rhinoviruses and syncytial respiratory virus are frequent at the beginning of winter. Even if these are a typical trend, respiratory infections can sporadically occur in any period of the year or have an epidemic course, according to environmental conditions. In addition, infrequently observed pneumonia such as that caused by Psittacosis and Q-Fever can occur [24].

2. *Outpatient pneumonia with concomitant disease and/or >60 years of age*

CAP course and prognosis undergo marked variations in the presence of another chronic disease, promoting the appearance and progression of infection. Among these, respiratory and cardiovascular diseases are the most frequent *(Table 6).*

Another risk factor, often concomitant with the previous, is represented by old age [25]. The incidence of respiratory infections in the elderly *(Table 7)* is much higher than in young adult subjects, so it represents an important epidemiologic and therapeutic problem, because of the increasing number of old people. The pneumonia mortality rate in elderly patients reaches a high value, much more than for other infectious diseases *(Table 8).* About 80% of geriatric patients affected by pneumonia need hospitalization, and 70% of pneumonia deaths occur in elderly subjects [26]. The mean hospitalization period for these patients is twice as high as in younger patients; the therapy cost has been calculated (1985) as about 550 million dollars. Estimated demographic changes will lead to a worsening of the problem: in 1980 11% of Americans (about 22 million) were over 65 years, in 2030 this number will increase to 17% (about 48 million).

TABLE 6 - *Adult community-acquired pneumonia coexisting with chronic diseases (153 diseases in 108 patients)* [17].

System	N. of patients
Respiratory	74
Cardiovascular	32
Diabetes mellitus	10
Neurological	9
Neoplastic	1
Renal	1
Steroid therapy	5
Others	21

TABLE 7 - *Incidence of community-acquired LRTI by age* [61].

Age (yr)	No. of cases/ no. in practice	Cases per 1,000 population per year
16-19	8/812	8.1
20-29	53/1512	30.0
30-39	75/1772	36.3
40-49	78/2065	32.4
50-59	65/1241	44.9
60-69	85/1100	66.2
70-79	111/783	121.5

TABLE 8 - *Mortality in community-acquired pneumonia requiring hospitalization* [31].

Category	CAP	Nursing home	All
No. patients	588	131	719
Mean age	60	76.9	63.2
No. died (%)	100 (17)	52 (40)	152 (21)
Mortality	8.5% < 60 yr	28.6% > 60 yr	

The specific pathogen(s) causing the disease is strongly correlated with the setting in which it occurs *(Table 9)* [27] and the physician must be guided by this knowledge to ensure that appropriate empiric therapy is promptly instituted. CAP in the elderly is characterized by a high degree of pathogenic diversity, but approximately 50% of all CAP in geriatric patients is caused by *S.pneumoniae* [28]. *H. influenzae* is also important in the etiology of pneumonia in the aged, and although the exact figure is difficult to determine, it is estimated that it causes 2 to 20% of cases.

The elderly are much more susceptible to community-acquired gram-negative pneumonia than are younger persons. Approximately 5 to 15% of cases in patients >65 years may be due to gram-negative organisms, which are particularly virulent once they infect the lower respiratory tract, especially in the very old.

Anaerobic pneumonia due to mixed flora is probably common in the elderly, but its incidence is only conjectural because transtracheal aspiration is required for accurate diagnosis. *Legionella pneumophila, Staphyloccus aureus*, and *Branhamella catarrhalis*, an aerobic gram-negative Diplococcus, can also be important community-acquired pathogens in the elderly.

Chlamydia pneumoniae has been identified in CAP in the elderly, but its role as a pathogen in this population has not yet been defined.

TABLE 9 - *Percentage of bacterial pneumonias in elderly persons in three settings* [28].

	Community	Institution	Hospital
Streptococcus pneumoniae	55%	35%	20%
Haemophilus influenzae and other *Haemophilus* spp.	10%	5%	5%
Staphylococcus aureus	1%	1%	5%
Gram-negative bacilli	5%	15%	35%
Mixed flora	25%	40%	30%
Other	4%	4%	5%

The characteristics of pneumonia acquired in extended-care facilities are similar to those acquired in the hospital. Bacterial pneumonia is the most common infection of the lower respiratory tract initiated by aspiration. *Klebsiella* spp and *S. aureus* are frequent isolates and are associated with methicillin-resistance [29]. Fortunately, *P.aeruginosa* is not often isolated in nursing home-acquired pneumonia. The etiological difference between subjects <65 and >65 is the rare incidence of so-called "atypical infection" in the second group *(Table 10)*. The

TABLE 10 - *Pathogens causing community-acquired pneumonia in Nottingham studies after stratification for age (from Venkatesan et al.* [25]*: modified).*

	Age range 12-64y (n=239): No. (%) of cases		Age range 65-79y (n=124): No. (%) of cases		Age range 65-97y (n=73): No. (%) of cases	
Streptococcus pneumoniae	117	(49)	67	(54)	22	(30)
Haemophilus influenzae	17	(7)	19	(15)	5	(7)
Legionella spp.	16	(6.7)	4	(3.2)	2	(3)
Staphylococcus aureus	4	(1.6)	1	(0.8)	—	
Gram negative bacilli	2	(0.8)	2	(1.6)	—	
Atypical infections*	15	(6.3)	2	(1.6)	—	
Influenza virus	15	(6.3)	11	(8.8)	5	(7)
Other viruses	12	(5)	4	(3.2)	1	(1.4)
Other pathogens	3	(1)	1	(0.8)	—	
No pathogen found	66	(28)	43	(34.7)	31	(43)

**Mycoplasma pneumoniae, Chlamydia psittaci, Coxiella burnetti*

mortality rate in this group of patients varies from 5 to 8%; about 25% need admission to hospital [28].

Several reasons explain the high incidence of respiratory infections in the elderly and their severity. Variations in biological, immunological and mechanical defense systems, such as cough and mucosal clearance, are involved. However, the exact meaning of the aging process on these host defense mechanisms is not completely understood, nor is the role of other concomitant diseases.

3. Hospitalized patients with CAP

This group includes 30 - 40% of CAP patients requiring hospital admission because of old age and/or the presence of underlying disease. Mortality has ranged from 4-24% in adult patients hospitalized because of CAP for various reasons *(Table 11)* [30].

TABLE 11 - *Mortality in community-acquired pneumonia requiring hospitalization.*

	No. patients	Mortality No.	%
MACFARLANE et al. [17]	127	19	15
BTS [10]	453	26	5.7
ORTQUIST et al. [11]	277	12	4
MARRIE [31]	588	152	24

However, there are only two studies in which the importance of different prognostic factors has been investigated with multivariate statistical methods: a British multicenter study [10] and a Canadian study [31]. In the British study the mortality was 5.7%, similar to that reported from Bristol [32], but patients over 74 were excluded. In a Swedish hospital this age group constituted a substantial part of the total admissions and deaths due to CAP: the overall case fatality rate was 4% (12 of out 277). In the Canadian study the overall mortality was 21%, but 18% of patients were admitted directly from nursing homes and their pneumonias cannot be considered to be community acquired.

As clearly shown in *Table 8*, most mortality is due to patients needing nursing-home care, who are very old. The British hospital study [10] with about 453 adults with a mortality of 5.7% showed that mortality correlated with age, absence of chest pain, absence of vomiting, previous treatment with digitalis, tachypnea, diastolic hypotension, confusion, leukopenia and increased blood urea levels. Patients had a 21-fold increased risk of death if they had two of the following parameters in addition to hospital admission: respiratory rate of >30, diastolic blood pressure of <60 mm Hg, or blood urea nitrogen level of >7 mmol/L .

In the Canadian study [31], the following variables were significant predictors of mortality: number of lobes involved in the pneumonic process, number of antibiotics used to treat the pneumonia, age at admission to a nursing home, ventilatory support, and the number of complications that occurred while the patient was in the hospital.

The most common pathogens in patients requiring hospitalization, but who are not critically ill, are: *S. pneumoniae, H. influenzae,* polymicrobial infection (including anaerobes), aerobic gram-negative bacilli, *Legionella* spp., *S.aureus, C. pneumoniae* and respiratory virus. This group differs from those with less severe pneumonia because it includes more patients with polymicrobial pathogens, which probably reflects coexisting processess leading to aspiration of colonized oropharyngeal secretions, and more patients with *Legionella* spp. because this infection results in more severe disease.

4. Hospitalized patients with severe CAP

Although there is no universally accepted definition of severe CAP, the presence of at least one of the following conditions justify defining the pneumonia as severe:

1. Respiratory frequency >30 breaths min at admission.
2. Severe respiratory failure defined by a PaO_2/ FiO_2 ratio <250mm Hg.
3. Mechanical ventilation required.
4. Chest radiography showing bilateral involvement of multiple lobes.
5. Shock (systolic blood pressure < 90mm Hg or diastolic blood pressure <60mm Hg).
6. Vasopressors required for more than 4 h.
7. Very low total urine output.

Patients with severe pneumonia must be recognized immediately so they can be separated from cases of less severe pneumonia requiring hospitalization because of the high mortality rate among patients with the former illness (between 25-50%) *(Table 12)*. The differences in mortality are difficult to explain as the populations included in most of these investigations seem to be similar. The only partial explanation may be the different number of patients needing mechanical ventilation included in each series, a finding strongly related to mortality [33].

Most series dealing with severe CAP show a distinct spectrum of etiologic agents: *S. pneumoniae* and *L. pneumophila* are the most common organisms responsible for these pneumonias (about 50%). Aerobic gram-negative bacilli *(K.pneumoniae, H. influenzae)* cause pneumonia only in those patients with concomitant coexisting illness, including COPD, diabetes mellitus and alcoholism (about 20%); *P. aeruginosa* (5%) was always associated with bronchiectasis and the highest mortality (100%).

The knowledge of such differing clinico-epidemiological situations (etiology, possibility of hospitalization) is essential to the physician for an effective approach to the treatment of CAP [34].

HOSPITAL-ACQUIRED PNEUMONIA (NOSOCOMIAL PNEUMONIA)

Nosocomial pneumonia (NP) is the second most frequent cause of hospital-acquired infection in the United States [35]. Its incidence ranges from 4 to 50 cases per 1000 admissions to general hospitals, and from 120 to 220 cases per 1000 admissions in some intensive care units (ICU). An Italian multicenter report shows that among nosocomial infections as a whole, NP represents 25% of the total, while when considering just ICU, 1 patient out of 6 suffers from NP [36]. Italian data differ from American studies in terms of mortality: in Italy, mortality reaches 73.9%, while in the USA it is 50% [37].

A Spanish report by Celis and coworkers shows that the overall fatality rate for patients who developed NP (general hospital and ICU) in 1987-1988 was 36.6% [38]. These authors, using multivariate analysis, have identified the following factors as responsible for a higher fatality rate: >60 years, place of hospitalization (medical ward or ICU), ultimately or rapidly fatal underlying conditions, "high-risk" microorganisms (*P. aeruginosa,* Enterobacteriaceae and other Gram-negative bacilli, *Streptococcus faecalis, S. aureus*, particularly polymicrobial episodes), roentgenographic bilateral pulmonary involvement, shock, respiratory failure, and inappropriate antibiotic therapy.

Niederman and coworkers focussed on the pathogenesis of NP [39] *(Table 13)*. Haley et al found that the risk of pneumonia was 21-fold higher in patients with continuous ventilatory support [40]. The percentage of NP caused by *Pseudomonas* sp. and other "high-risk" microorganisms can be decreased by avoiding or reducing the medical interventions able to modify the oropharyngeal microflora which is responsible for most cases of pneumonia through silent micro-aspirations [41]. Craven et al. noted that the utilization of respiratory care devices can account for two-thirds of NP cases [42].

TABLE 12 - *Mortality and etiology of severe community-acquired pneumonia.*

	Ortquist et al.	Woodhead et al.	Sorensen et al.	Feldman et al.	Pachon et al.	Torres et al.
Year	1985	1985	1986	1989	1990	1991
MV*, %	58	88	73	86	---	61
Mortality, %	25	54	47	53	21	22
Organism**	*S. pneumoniae* *M. pneumoniae*	*S. pneumoniae* *L. pneumophila*	*S. pneumoniae* *L. pneumophila*	*S. pneumoniae* *K. pneumoniae*	*S. pneumoniae* *L. pneumophile*	*S. pneumoniae* *L. pneumophila*

* mechanical ventilation
** first and second most frequent etiologic microorganism

(From Torres et al. [33]: modified)

TABLE 13 - *Factors that may increase the risk of nosocomial pneumonia by altering colonization, increasing the risk of aspiration, or impairing host defenses* [39].

- HOST FACTORS:
Age
Obesity
Coma
Underlying disease (diabetes mellitus, cancer, head trauma, uremia, systemic lupus)
- DRUGS:
Sedatives, antibiotics, antacids, steroids, cytotoxic drugs
- INVASIVE DEVICES:
Intubation, tracheostomy, mechanical ventilation, nasogastric tube

Regarding the incidence of different microorganisms causing NP, an important report from the National Nosocomial Infection Survey (NNIS) is shown in *Table 14* [43]; recently, epidemic infections caused by *L. pneumophila* and *Mycobacterium tuberculosis* have occurred in several countries. Pennington remarks that *H. influenzae* and *S.pneumoniae* are less frequent causes of NP [44]. *H. influenzae* pneumonia seems to be related to a previous oropharyngeal colonization [45], while viral episodes are estimated to occur in 5% of nosocomial infections, although it is very difficult to verify its role [46]. NP caused by fungi (particularly *Aspergillus* spp.), coming from dust or dampness, occurs frequently in immunocompromised patients (leukemia, transplantation) [47,48].

TABLE 14 - *Microbic prevalence in etiology of NP (NNIS, 1985-1988 = 15,499 patients).*

Pathogens	Rate %
- GRAM-NEGATIVE	
Pseudomonas aeruginosa	17.2
Enterobacter spp	10.4
Klebsiella pneumoniae	7.4
Escherichia coli	6.4
Haemophilus influenzae	6.4
Serratia marcescens	4.5
Proteus mirabilis	3.4
Acinetobacter	3.0
- GRAM-POSITIVE	
Staphylococcus aureus	14.6
Streptococcus pneumoniae	3.0
- FUNGI	
Candida albicans	3.7

(From Grassi [43]: modified)

Previous antibiotic treatment can cause bacterial colonization of the lower airways, but a real superinfection of the lungs occurs in just 0.4% of NP cases [49]. Recently, Cook et al. have noted that antacids, and particularly anti-H2 drugs, do not increase the risk of NP [50].

From a clinical point of view, NPs are, unlike CAP, not so easy to diagnose: in fact, these infections are not correctly recognized in 30% of cases [51]. Sometimes, only computerized tomography allows proper identification of pulmonary infiltrates, otherwise they are not recognized by conventional X-ray [52]. *Table 15* summarizes clinical criteria useful in NP diagnosis. Rarely is epidemic NP caused by *L. pneumophila, Aspergillus fumigatus,* VZ virus or by *M. tuberculosis* in HIV-positive patients [53].

TABLE 15 - *Clinical criteria useful for diagnosis of NP.*

- Sudden variation of clinical pattern, not referring to another disease (pulmonary embolism, myocardial infarction)
- Quick progression of a pulmonary infiltration
- Fever or variation of previous temperature
- Significant decrease of PA O_2
- Increase of volume and purulence of respiratory secretions

(From Esposito [78], 1993: modified)

RESPIRATORY INFECTIONS IN SURGERY

Respiratory tract infections are the most frequently found nosocomial surgical infections [54].

A study of 1 million people admitted to 388 American hospitals, shows that 42% were comprised of surgical patients among whom 71% developed a nosocomial infection [55]. This remark is confirmed by an NNIS study, pointing out that nosocomial infections occur most frequently in surgical divisions *(Table 16).* The most frequent seats of surgical infections are lung, urinary tract, veins used for parenteral treatment and surgical wound [56].

According to Alteimer's classification, the mean surgical infection incidence varies strongly from case to case [57]. In so-called "clean" surgery (thyroid, breast, etc...) it is low (1.8%); in "clean-contaminated" (lung, digestive system, genito-urinary tract) it increases (8.9%), reaching 21.5% in "contaminated" surgery (visceral contents or purulent process) [58]. There

TABLE 16 - *Nosocomial infections of the lower respiratory tract by service (NNIS data; July-December 1974)* [24].

Service	Number discharges	Infection rate/1000
Medicine	162,953	7.1
Surgery	216,773	7.5
Obstetrics	64,875	0.6
Gynecology	39,440	1.5
Pediatrics	32,665	1.8
Newborn nursery	56,450	1.5
Totals	573,156	5.3

are many factors causing a high frequency of respiratory infections in surgery: general surgical risk represented by rupture of skin and mucous membrane; decreasing host defense mechanisms, especially of the respiratory tract, of which the most important are: decreasing lung volume which begins on the first day and continues to the fourth day, and then goes down after two weeks for lower abdominal surgery, and after four weeks for thoracic surgery; superficial and frequent breathing leading to alveoli closure; hypoxemia due to right-left shunt, caused by ventilatory decrease and persistence of perfusion. These factors are responsible for collapse and bronchial secretion stagnation, followed by bacterial colonization, supported by lack of cough.

The problem of surgical infections has been investigated in a prospective study performed on 520 patients undergoing either thoracic or abdominal surgery, to identify risk factors. In 91 cases (17.5%) pulmonary infections occurred: their appearance seemed significantly related to low serum albumin concentrations and general condition, as evaluated by the American Society of Anesthesiologists, with a score from one to four *(Table 17)*. Other important risk factors were represented by duration and location of surgery, and variation of oropharyngeal flora according to duration of preoperating admission [59].

Information regarding microbial flora causing post surgery respiratory infections has great clinical and practical value *(Table 18)*. The high incidence of gram-negative bacteria, such as Enterobacteriaceae and *Pseudomonas* spp. are important as well as Staphylococcus (often methicillin-resistant strains) and *S. pneumoniae,* according to several authors [60]. Anaerobes are somewhat important, but they are difficult to

TABLE 18 - *Pathogens implicated in postoperative respiratory infections.*[79]

Pathogen	Incidence %
Klebsiella spp	12.0
Staphylococcus aureus	11.0
Pseudomonas aeruginosa	10.0
Escherichia coli	7.3
Enterobacter spp	7.0
Streptococcus pneumoniae	5.6
Serratia spp	4.0
Candida spp	3.0
Other	11.0
No cause found	25.0

TABLE 17 - *Relation between severity of underlying disease and incidence of postoperative pneumonia* [8].

		Number	Pneumonia*	
Serum albumin concentration on admission (mg/dl)	< 3.0	16	7 (44)	
	3.0-3.4	40	11 (28)	
	3.5-3.9	118	25 (22)	
	≥ 4.0	276	44 (16)	P < 0.005**
American Society of Anesthesiologists' (ASA) classification	1	136	8 (6)	
	2	179	33 (18)	
	3	164	41 (25)	
	4	28	8 (29)	P < 0.0001

* figures in parentheses give the incidence in percents
** Mantel-Haenszel chi square

identify, unless investigated by specific methods. In a good editorial (article) by R.C. Jones, entitled "Newer Antibiotics for the Surgeon" [55], the author emphasizes the importance of the matter mentioned above, concluding: "The surgeon must know the most likely organisms to contaminate the operative field in order to select an appropiate, non toxic antibiotic. The more potent antibiotics are reserved for established infections to attempt to prevent the emergence of resistant organisms".

LOWER RESPIRATORY TRACT INFECTIONS IN THE COMMUNITY (BRONCHITIS)

Lower respiratory tract infections (LRTI) include infections ranging from limited acute bronchitis to severe pnumonia. The overall incidence of these infections (pneumonia excluded) in Nottingham [61] was 44 cases per 1000 people per year; the incidence was 4 times higher in people over 60 than in those below 50. The term bronchitis covers a heterogeneous group of both infectious and non-infectious syndromes, which really differ regarding etiology, clinical and epidemiological characteristics: bronchitis in normal patients and bronchitis in patients with chronic obstructive pulmonary disease (COPD) [62].

Acute bronchitis in normal host mainly affects children and young adults and is most often caused by "respiratory viruses": influenza and parainfluenza viruses, rhinoviruses, coronaviruses, syncytial respiratory viruses. The only bacterial pathogens clearly recognized as causing acute bronchitis in normal patients are *M. pneumoniae, Bordetella pertussis* and *C. pneumoniae* [63]; rarely is infection caused by *S. pneumoniae* (5-10%) [64].

Unlike acute bronchitis in a normal host, *acute exacerbations of chronic bronchits* are more easily caused by bacterial pathogens. The most frequently isolated bacteria are *H.influenzae, S.pneumoniae, Moraxella catarrhalis* [65,66]. Other microorganisms, such as *K.pneumoniae, P. aeruginosa* and *Escherichia coli* are involved less frequently *(Table 19)*. A similar incidence is found in an Italian study *(Table 20)* [67].

According to such a trend, recent European Guidelines on care for acute exacerbation of chronic bronchitis have been drawn up [68].

TABLE 19 - *Etiology of acute bronchitis and acute exacerbations of chronic bronchitis* [62].

Acute bronchitis	Acute exacerbations of chronic bronchitis
Frequent[a] pathogens	**Frequent[a] pathogens**
Influenza virus	Non-typable
Parainfluenza virus	*H. influenzae* (35-50%)
Rhinovirus	*M. catarrhalis* (15-30%)
Coronavirus	*S. pneumoniae* (15-25%)
Respiratory syncytial virus	
Adenovirus	
M. pneumoniae	
Infrequent[b] pathogens	**Infrequent[b] pathogens**
B. pertussis	*P. aeruginosa* (10-15%)
C. pneumoniae	*S. aureus* (2%)
Enterovirus	*K. pneumoniae*
Propavirus	*E. coli*

[a] 90% [b] 10%

TABLE 20 - *Etiology of exacerbations of chronic bronchitis* [67].

Pathogens 230	%
Haemophilus parainfluenzae	54.4
Haemophilus influenzae	23.6
Haemophilus non typable	8.2
Branhamella catarrhalis	11.0
Streptococcus pneumoniae	11.0
Enterobacteriaceae	5.8
Pseudomonas spp	5.5
Pseudomonas aeruginosa	3.8
Staphylococcus aureus	2.2
Mycoplasma spp	1.1
Klebsiella oxytoca	1.6
Escherichia coli	1.6
Proteus vulgaris	1.1
Klebsiella pneumoniae	0.3
Enterobacter cloacae	0.3
Proteus mirabilis	0.3

BACTERIAL RESISTANCE

The wide and inadequate use of antibiotics has led to the appearance of bacteria resistant to the most commonly used antibiotics [69]. Such trends must be considered when choosing drugs for treatment of respiratory infection.

One of the most challenging problems related to control of pneumococcal disease concerns

changes in the susceptibility of pneumococci to various antimicrobial agents. Beyond a doubt, the incidence of antimicrobial resistant pneumococcal infections is increasing all over the world [70]. In the USA in 1987 the incidence of penicillin-resistant strains of pneumococci was about 5-8% [71]. In Spain this incidence has reached (15-20%) with a small percentage (2.5%) of third-generation cephalosporin-resistant strains too.

Penicillin-resistant *S. aureus* has increased since 1950 [72]. A study performed in London on outpatients shows that an incidence of resistance of 6% in 1950 became 81% in 1980 [73]. Methicillin-resistant *S. aureus* would be between 7% and 15%.

Since the mid- to late-1970s, when the first reports of ampicillin resistance for strains of *H.influenzae* emerged, the incidence of resistance has increase to 30% in some countries [74]. In a European study, there were higher rates of beta-lactamanase producing strains among type B strains in Spain (31.2%) and France (22.9%), in contrast to 10% beta-lactamase producing strains in Italy and 1.5% in Austria [75].

Although it was very rare to find a beta-lactamase producing *M. catarrhalis* strain prior to 1975, today 80-90% *M. catarrhalis* isolated produce beta-lactamase. These strains have increased from 25% in 1983 to 63% in 1988 in Denmark [76].

CONCLUSIONS

It is of utmost importance to know the epidemiology and incidence of various pathogens responsible for acute respiratory infections for the initial approach to these diseases. This knowledge, without microbiological data, together with information about the environment of the patient and the underlying afflictions are very important to the empirical management of community-acquired pneumonia [77].

Moreover, we must strive to identify the etiologic agents of infections, especially in old and immunocompromised patients, and to provide hospitalization when necessary.

Ongoing studies to define the changing epidemiology of pneumonia are necessary. Standardization of data collection and the battery of serologic tests used would make comparison of data from country to country easier. The difficulties of making an etiologic diagnosis of this illness remain formidable and research should focus on the development of methods whereby we can reliably detect, in serum or in urine, antigens of the agents that most commonly cause pneumonia.

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