Bacteria Associated with Acute Exacerbations of Chronic Obstructive Pulmonary Disease Requiring Mechanical Ventilation and Antimicrobial Management in Respiratory Care Unit of Central Chest Institute of Thailand

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Objective: *To investigate the role of bacterial infection, antimicrobial sensitivity and antibiotics usage in severe acute exacerbations of COPD requiring mechanical ventilation in the respiratory care unit of the central chest institute of Thailand.*
Material and Method: *All data were analyzed from medical records of 38 patients admitted in RCU of CCIT during 1 November 2008-31 August 2011 with severe acute exacerbations of COPD requiring mechanical ventilation. The tracheobronchial aspirates specimens were collected for Gram stain, quantitative culture and sensitivities testing. The sera were tested for antibodies to Chlamydophila pneumoniae and Mycoplasma pneumoniae with the immunofluorescence test.*
Results: *Bacterial pathogens were isolated by quantitative culture from 18 of 38 patients (47.3%). Gram-negative bacilli were the predominant organisms. K. pneumoniae was the predominant isolates 7 cases (18.4%) followed by H. influenzae 3 cases and P. aeruginosa 3 cases (7.9% each). A single pathogen was isolated from 12 patients (31.6%), two pathogens were isolated from 5 patients (13.2%) and three pathogens from 1 patient (2.6%). Serological samples were positive for Chlamydophila pneumoniae in 5 (13.2%) cases. 1 of these patients had coinfection with Acinetobacter baumannii. In the RCU, 33 (86.8%) patients were empirically treated with antibiotic. Ceftriaxone was the most commonly used antibiotic.*
Conclusion: *57.8% (22/38 cases) of the patients with severe exacerbations in COPD requiring mechanical ventilation caused by bacterial infection, Gram-negative bacilli were the predominant organism with a resistance to commonly used antibiotics of K.pneumoniae, P. aeruginosa, S. aureus, E. coli, A. baumannii, P. mirabilis, S. dysgalactiae and S. pneumoniae. 13.2% of the patients had serological evidence of Chlamydophila pneumoniae infection.*

Keywords: *Acute exacerbation, Chronic obstructive pulmonary disease, Bacteriology, Infection, Atypical pathogens*

J Med Assoc Thai 2012; 95 (Suppl. 8): S11-S18
Full text. e-Journal: *http://jmat.mat.or.th*

Acute exacerbations in COPD are defined as a worsening in baseline dyspnea, increased sputum volume, sputum purulence[1]. Exacerbations are associated with reductions in quality of life and deterioration in lung function. Bacterial infections have been considered as the leading cause of exacerbations[2]. *Haemophilus influenzae* is the most frequent pathogen isolated in the previous studies followed by *Streptococcus pneumonia* and *Moraxella catarrhalis*. Gram-negative bacteria were more frequently isolated in more severe exacerbations[2-8]. Bacteriologic etiology is correlated with severity of disease. Eller et al found that *Enterobacteriaceae and pseudomonas spp* were the predominant bacteria in patients with an FEV_1 < 35% of predicted value[9]. The role of atypical pathogen (*Mycoplasma pneumoniae, Chlamydophila pneumoniae*) remains unclear. Serological studies suggest that these pathogens may play an important role in exacerbations of COPD[1,10-16]. Variability in the results of serological assays existed. In order to determine the bacterial infections during severe exacerbations of COPD requiring mechanical

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ventilation, the present study was designed to collect the tracheobronchial aspirates using a sputum suction strap (TBAS) specimens for gram stain, quantitative culture and sensitivity testing. Serological studies were included to look for evidence of infections with *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*. The findings provide further insights in the role of bacterial infections during severe exacerbations of COPD in Thailand.

Material and Method

Overall 38 patients admitted to the Respiratory Care Unit (RCU) of central chest hospital with severe exacerbations of COPD and acute respiratory failure using mechanical ventilation were studied during a 34-months period. Inclusion criteria were; clinical diagnosis of COPD, acute exacerbations of COPD using mechanical ventilation and intubation within 24 hours of admission. Exclusion criteria were; bronchiectasis and pneumonia (chest x-ray no infiltrate), severe immunosuppression (chronic renal failure or liver disease, long-term systemic corticosteroids or other immunosuppressant drugs used), malignancies and coagulopathies.

The patients data on admission were recorded: age, gender, smoking habits, comorbidity, previous glucocorticoid therapy, number of hospitalizations within the last year, influenza vaccination, sputum appearance, antibiotic treatment during the last 24 h, pulmonary function test, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, arterial blood gases and oxygenation index (PaO_2/FiO_2). The hospital Medical Ethical Committee approved the proposal and the process of the present study along with the consent of all patients.

All patients were obtained TBAS within the first 24 h of mechanical ventilation. The specimens were stained with Gram (Hucker modification method). Homogenized, undiluted and serially diluted secretions (10^{-3}, 10^{-4}, 10^{-5}, 10^{-6}) were plated on blood, MacConkey and chocolate agar[17]. Cultures were evaluated for growth after 24 and 72 h. Negative bacterial cultures were discarded after 3 days. Identification of microorganisms was performed by standard technique[18]. Susceptibility testing was done by using the standard for antimicrobial susceptibility method[19,20]. Results of quantitative cultures were reported as colony-forming units per milliliter (cfu/ml).

The sera were tested for antibodies to *Chlamydophila pneumoniae* and *Mycoplasma pneumoniae* with the indirect immunofluorescence test using Anti-*Chlamydophila pneumoniae* IIFT (IgA, IgG or IgM) and *Mycoplasma pneumoniae* IIFT (IgA, IgG or IgM) (EUROIMMUN Medizinische Labordiagnostika AG, Lubeck, Germany). Serological titers of immumoglobulinG (IgG) and immunoglobulin M (IgM) for *Mycoplasma pneumoniae* was considered as diagnostic in case of seroconversion (at least a fourfold rise in titer)[21]. A fourfold increased in titer of IgG or IgM or IgG titer of $\geq$ 1: 512 or an IgM titer $\geq$ 1: 16 were considered diagnostic for *Chlamydophila pneumoniae*[22]. Descriptive statistics were needed to summarize all patient characteristics.

Results

Patient population

The 38 study patients (35 males and 3 females) had a mean age of 71 $\pm$ 8.5 years (range 50-86). Patient characteristics on admission are summarized in Table 1.

Microbiology

Bacterial pathogens were isolated from 18 of the 38 cases (47.3%). A single organism was isolated from 12 (31.6%) patients, two organisms were isolated from 5 (13.2%) patients and three were one patient (2.6%). Gram-negative bacilli were the predominant organisms as shown in Table 2. *K. pneumoniae* was the predominant isolates (18.4%) followed by *H. influenzae* and *P. aeruginosa* (7.9% each), *C. koseri, E. coli, A. baumannii* and *S. aureus* (5.3% each), *P. mirabilis, S. maltophilia, S. pneumoniae* and *S. dysgalactiae* (2.6% each).

The acute and convalescent-phase serum specimens collected from 14 of 38 patients. Serological samples were positive for *Chlamydophila pneumoniae* in 5 of 38 (13.2%) cases. All of these patients had serum IgG titer $\geq$ 1: 512 (3 cases IgG titer 1: 1,600 and 2 cases IgG titer 1: 800), but negative IgM titer (titer < 1: 10). One patient had concomitant pathogens (*Acinetobacter baumannii*). Serological samples for *Mycoplasma pneumoniae* IgM were positive in 1 case (titer 1: 20) and IgG *were* positive in 11 cases (titer $\geq$ 1: 8), none of these had fourfold rise in convalescent serum.

Antibiotic susceptibility pattern of all bacterial pathogens is shown in Table 2. In 100% (7/7) of *K. pneumoniae*, resistance was observed to ampicillin and 14% (1/7) resisted to amoxycillin-clavulanic acid, quinolones and co-trimoxazole. The patient characteristics of typical and atypical pathogens shown in Table 3.

Table 1. Patient characteristics on admission in 38 cases

	Number (%)
Age, yr (mean ± SD)	71 ± 8.5
Gender (male/female)	35/3
Smoking history, pack-yr (mean ± SD)	29.89 ± 31.78
Prior hospitalizations within the last year, n (%)	24 (63.2 %)
Number of hospitalizations for AECOPD in previous year, (mean ± SD)	1.79 ± 1.98
Influenza vaccination within the last year, n (%)	4 (10.5 %)
Comorbidity* present, n (%)	28 (73.7%)
Diabetes mellitus	6 (15.8 %)
Hypertension	17 (44.7%)
Cardiovascular disorder	9 (23.7%)
Old tuberculosis	12 (31.6 %)
Dyslipidemia	8 (21.1 %)
Benign prostatic hypertrophy	4 (10.5 %)
Miscellaneous (gout, pulmonary hypertension)	3 (8 %)
FEV_1 % predicted, (mean ± SD)	52.04 ± 21.50
FEV_1/FVC ratio %, (mean ± SD)	48.82 ± 21.44
PaO_2/FiO_2, (mean ± SD)	337.93 ± 118.08
APACHE II, (mean ± SD)	19.4 ± 4.2
Antimicrobial treatment within the last 24 h, n (%)	6 (15.8 %)
Antimicrobial treatment within 2-4 week, n (%)	4 (10.5 %)
Previous glucocorticoid therapy within 2 week, n (%)	5 (13.2 %)
Sputum appearance, n (%) : Colourless, mucoid	11 (28.9 %)
Purulent	27 (71.1 %)
Days of treatment in RCU, (mean ± SD)	5.1 ± 2.9
Days of in-hospital treatment, (mean ± SD)	12.6 ± 11.2
Days of mechanical ventilation, (mean ± SD)	3.7 ± 2.9
Mortality, n (%)	2 (5.3%)

* More than 1 comorbidity can be presented

Antibiotic therapy

Six Patients had received antibiotic therapy during the last 24 h prior to the admission to the RCU. Antibiotic treatment in 3 out of 6 patients was changed after admission to the RCU. In the RCU, 33 (86.8%) patients were empirically treated with intravenous antibiotic in 17 (44.7%) oral antibiotic in 7 (18.4%) and combination intravenous plus oral antibiotic in 9 (23.6%). Ceftriaxone was the most commonly used antibiotic in RCU 7 (18.4%), followed by the combination of clarithromycin and ceftriaxone (13.2%) and roxithromycin, oral levofloxacin and intravenous levofloxacin (5.3% each), but other broad spectrum antibiotics were also used as shown in Table 4.

Four patients who had positive serology for *Chlamydophila pneumoniae* received appropriate antibiotic therapy, 1 patient recovered without antibiotic to cover this pathogen. 11 patients' isolated bacterial pathogens sensitive to antibiotics therapy in RCU. Five patients had organisms' resistance to antibiotics therapy in RCU (*P. aeruginosa, A. baumannii, E. coli, S. maltophilia)*, whereas 2 patients recovered *without* antibiotic treatment (*S. dysgalactiae* and *S. aureus*).

Outcome

The overall outcome was satisfactory though a mortality rate 5.3% (2/38 cases). One patient passed away because of sepsis and upper gastrointestinal bleeding. Another patient died because of acute renal failure and upper gastrointestinal bleeding.

Discussion

The present study findings are as follows: 22 of 38 (57.8%) of patients with severe exacerbations requiring mechanical ventilation had positive bacterial findings determined by TBAS sampling culture and/or positive serology. Sethi and Murphy estimated that 40-60 % of acute exacerbations of COPD are bacterial in origin[2]. Panchit et al[8] obtained growth in 60% of cases where as Alberto et al[12] obtained growth in

Table 2. Microorganisms isolated from quantitative sputum cultures and antimicrobial sensitivity patterns from 38 patients

Pathogen	n (%)	Colony count (cfu/ml)				Antimicrobial resistant pattern, n (%)										
		10^2, n (%)	10^3, n (%)	10^4, n (%)	10^5, n (%)	Ampicillin	Amoxycillin-clavulanic acid	Third generation cefalosporin	Forth generation efalosporin	Aminoglycoside	Quinolones	Piperacilin-tazobactam	Carbapenem	Extended-spectrum Beta-lactamases producing	Vancomycin	Co-trimoxazole
K. pneumoniae	7 (18.4)	-	5 (13.2)	1 (2.6)	-	7 (100)	1 (14)	-	-	-	1 (14)	-	-	-	-	1 (14)
P. aeruginosa	3 (7.9)	-	1 (2.6)	1 (2.6)	1 (2.6)	2 (66)	1 (33)	2 (66)	-	-	1 (33)	-	-	-	-	2 (66)
E. coli	2 (5.3)	1 (2.6)	-	1 (2.6)	-	2 (100)	1 (50)	1 (50)	1 (50)	-	2 (100)	1 (50)	-	1 (50)	-	2 (100)
A. baumannii	2 (5.3)	-	1 (2.6)	-	1 (2.6)	2 (100)	2 (100)	2 (100)	1 (50)	2 (100)	2 (100)	2 (100)	2 (100)	-	-	2 (100)
P. mirabilis	1 (2.6)	-	1 (2.6)	-	-	-	-	-	-	-	-	-	-	-	-	-
C. koseri	2 (5.3)	-	2 (5.3)	-	-	-	-	-	-	-	-	-	-	-	-	-
H. influenza	3 (7.9)	-	-	-	3 (7.9)	-	-	-	-	-	-	-	-	-	-	-
S. maltophilia	1 (2.6)	-	1 (2.6)	-	-	-	-	-	-	-	-	-	-	-	-	-
S. aureus	2 (5.3)	-	1 (2.6)	-	1 (2.6)	-	-	-	-	-	-	-	-	-	1 (50)	-
S. pneumoniae	1 (2.6)	1 (2.6)	-	-	-	-	-	-	-	1 (100)	-	-	-	-	-	1 (100)
S. dysgalactiae	1 (2.6)	-	1 (2.6)	-	-	-	-	-	-	-	-	-	-	-	-	-

Table 3. Patient characteristics of typical and atypical pathogens

Patient characteristics	Typical pathogens (18 cases*)	Atypical pathogens (5 cases)	Total (38 cases)
Age, yr (mean ± SD)	72.7 ± 10.2	74.2 ± 7.1	71 ± 8.5
Number of hospitalizations for AECOPD in previous year, (mean ± SD)	1.67 ± 1.75	3.20 ± 1.78	1.79 ± 1.98
Comorbidity present, n (%)	13 (72.2%)	5 (100%)	24 (63.2%)
FEV_1 % predicted, (mean ± SD)	50.90 ± 21.90	46.33 ± 10.06	52.04 ± 21.50
APACHE II, (mean ± SD)	19.8 ± 4.8	20.0 ± 0.7	19.4 ± 4.2
Sputum appearance, n (%): Colourless, mucoid	5 (27.8 %)	2 (40%)	11 (28.9%)
Purulent	13 (72.2 %)	3 (60%)	27 (71.1%)
Days of treatment in RCU, (mean ± SD)	5.7 ± 2.8	6 ± 4	5.1 ± 2.9
Days of in-hospital treatment, (mean ± SD)	15.3 ± 14.9	21.8 ± 12.1	12.6 ± 11.2
Days of mechanical ventilation, (mean ± SD)	4.1 ± 2.9	4.8 ± 4.0	3.7 ± 2.9
Mortality, n (%)	2 (11.1%)	0 (0%)	2 (5.3%)
Antibiotics in RCU**, n (%)			
None	2 (11.1%)	0 (0%)	5 (13.2 %)
Azithromycin	2 (11.1%)	0 (0%)	3 (7.9 %)
Amoxycillin-clavulanic acid	4 (22.2%)	0 (0%)	4 (10.5 %)
Ciprofloxacin	1 (5.6%)	0 (0%)	3 (7.9 %)
Ceftriaxone	8 (44.4%)	1 (20%)	15 (39.5 %)
Roxithromycin	1 (5.6%)	0 (0%)	3 (7.9 %)
Clarithromycin	5 (27.8%)	2 (40%)	9 (23.7 %)
Levofloxacin	1 (5.6%)	2 (40%)	5 (13.2 %)
Cefoparazone-sulbactam	0 (0%)	1 (20%)	1 (2.6 %)
Piperacillin-tazobactam	2 (11.1%)	0 (0%)	2 (5.3 %)
Ceftazidime	2 (11.1%)	0 (0%)	2 (5.3 %)
Ertapenem	1 (5.6%)	0 (0%)	1 (2.6 %)

* 1 case had *A. Baumannii and Chlamydophila pneumoniae* coinfection.
** More than 1 antibiotics used

54.7% of patients, De Serres et al 49%[23] and Larsen et al 50%, that is corresponding with the present study[24].

Gram-negative bacilli was the most common isolated organism and *K. pneumoniae* (18.4%) was the predominant organism, which correlated with the study results of Panchit et al[8] (5/12 cases) and Sheng-Hsiang Lin et al[25] (19.6%). In the prior studies, the predominant organisms were *H. influenza*e (Nester et al[10] (33%), Alberto et al[12] (9/35 cases), Levent et al[13] (30%) and L. Davies et al[26] (18/34 cases)). These differences may due to difference in age, severity of the disease and environmental conditions.

In the present study, the authors found evidence of *Chlamydophila pneumoniae* infection in 5 cases (13.2%). Nestor et al[10] and Levent et al found a higher incidence (18% and 17%)[13]. The lower incidence of the present study results may be due to fewer numbers of pair serum specimens and the difference in criteria for diagnostic titer. But the lower incidence found in the study of Blasi et al[14] (4%), Miyashita et al[15] (7.8%) and Beauty et al (5%)[16]. The authors did not find evidence of *Mycoplasma pneumoniae* by serological test, correlated with the study results of Nestor et al[10], may be due to this pathogen mainly infected in young adults, but had less incidence in the elderly. Mandira Varma-Basil et al found 16% of the patients had evidence of *Mycoplasma pneumoniae* infection by serology and antigen assay[27]. The number of hospitalizations for AECOPD in a previous year, comorbidity, severity of COPD, days of treatment in RCU, days of in-hospital treatment and days of mechanical ventilation were higher among patients found with atypical pathogens infection (Table 3).

33 of 38 (86.8%) patients' admission to the RCU were empirically treated with antibiotics and ceftriaxone was the most commonly used. These results were similar to the findings of L. Davies et al[25] that 151 of 167 patients (90%) received antibiotic therapy at the time of admission but the commonest antibiotic used

Table 4. Antibiotic therapy in 38 patients

Antibiotic	Start within 24 h of admission, n (%)	During RCU admission, n (%)	Home medication, n (%)
None	32 (84.2)	5 (13.2)	31 (81.58)
Intravenous	-	17 (44.7)	-
Intravenous plus oral	2 (5.3)	9 (23.6)	-
Oral	4 (10.5)	7 (18.4)	6 (15.8)
Antibiotics administered*			
Azithromycin	-	3 (7.9)	-
Amoxycillin-clavulanic acid	-	4 (10.5)	2 (5.3)
Ciprofloxacin	-	3 (7.9)	-
Ceftriaxone	2 (5.3)	15 (39.5)	-
Roxithromycin	4 (10.5)	3 (7.9)	-
Clarithromycin	2 (5.3)	9 (23.7)	2 (5.3)
Levofloxacin	-	5 (13.2)	2 (5.3)
Cefoparazone-sulbactam	-	1 (2.6)	-
Piperacillin-tazobactam	-	2 (5.3)	-
Ceftazidime	-	2 (5.3)	-
Ertapenem	-	1 (2.6)	-

* More than 1 antibiotics used

was co-amoxiclav. 15 of 22 patients' isolated bacterial pathogens in the present study had appropriated antibiotics therapy in RCU. 7 patients recovered with antibiotic treatment that did not cover pathogens isolated by TBAS and serology.

The limitations of the present study were: (1) small patients' population; (2) interlaboratory variation and lack of standardized criteria in the interpretation of serological test; (3) not distinguished colonization from infection. The authors recommended a larger study to establish the role of bacterial infection in severe exacerbations of COPD by culture and detection by PCR.

Conclusion

Bacterial infection in patients with severe exacerbations of COPD requiring mechanical ventilation is high (57.8%). Gram-negative bacilli were the predominant organism with high resistance to commonly used antibiotics. *Chlamydophila pneumoniae* is involved in a few cases. The authors recommended that the studies results should be considered when choosing an antimicrobial agent in severe exacerbations of COPD.

Acknowledgement

The authors wish to thank all participating nurses, medical technologist and physicians from the Medicine Department for their cooperation with the present study.

Potential conflicts of interest

None.

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การศึกษาเชื้อแบคทีเรียที่เป็นสาเหตุของการกำเริบรุนแรงของอาการของโรคหลอดลมอุดกั้นเรื้อรังในผู้ป่วยที่ต้องใช้เครื่องช่วยหายใจและเข้ารับการรักษาตัวในหอผู้ป่วยหนักโรคปอดและการใช้ยาปฏิชีวนะของสถาบันโรคทรวงอก

สุดารัตน์ สิริภัทรวณิช, รังสิยา ไผ่เจริญ, สุมล เติมเศรษฐเจริญ, นุชรา กลางประพันธ์

***วัตถุประสงค์**: เพื่อศึกษาเชื้อแบคทีเรียและแบบแผนการดื้อยารวมถึงการใช้ยาปฏิชีวนะในการรักษาผู้ป่วยที่มีการกำเริบของโรคหลอดลมอุดกั้นเรื้อรังรุนแรงจนต้องใช้เครื่องช่วยหายใจ*

***วัสดุและวิธีการ**: ศึกษาโดยเก็บข้อมูลการรักษาจากเวชระเบียนของผู้ป่วย 38 ราย ที่มีการกำเริบของโรคหลอดลมอุดกั้นเรื้อรังที่รุนแรงจนต้องใช้เครื่องช่วยหายใจและรับเข้ารักษาในหอผู้ป่วยหนักโรคปอดของสถาบันโรคทรวงอกตั้งแต่วันที่ 1 พฤศจิกายน พ.ศ. 2551 ถึงวันที่ 31 สิงหาคม พ.ศ. 2554 เก็บเสมหะส่งตรวจย้อมแกรมและเพาะเชื้อแบคทีเรียแบบ Quantitative culture รวมถึงทดสอบความไวของเชื้อ ตรวจทาง serology เพื่อดูการติดเชื้อ Chlamydophila Pneumoniae และ Mycoplasma pneumoniae ด้วยวิธี Immunofluorescence*

***ผลการศึกษา**: พบเชื้อแบคทีเรียจากการเพาะเชื้อ 18/38 ราย (47.3 %) ส่วนใหญ่เป็นเชื้อแกรมลบได้แก่ Klebsiella pneumoniae 7 ราย (18.4 %) รองลงมาคือ Pseudomonas aeruginosa และ Haemophilus influenzae อย่างละ 3 ราย (7.9 %) จากการเพาะเชื้อพบเชื้อ 1เชื้อในผู้ป่วย 12 ราย (31.6%) พบเชื้อ 2 เชื้อในผู้ป่วย 5 ราย (13.2%) และพบ 3 เชื้อในผู้ป่วย 1 ราย (2.6 %) ผู้ป่วย 5 ราย (13.2 %) พบการติดเชื้อ Chlamydophila Pneumoniae ซึ่งในจำนวนนี้ 1 รายพบการติดเชื้อ Acinetobacter baumanii ร่วมด้วย ขณะเข้ารับการรักษาในหอผู้ป่วยหนักผู้ป่วยจำนวน 33 ราย (86.8 %) ได้รับยาปฏิชีวนะ และยาที่ใช้มากที่สุดคือ ceftriaxone*

***สรุป**: ผู้ป่วยที่มีการกำเริบของโรคหลอดลมอุดกั้นเรื้อรังรุนแรงที่ต้องใช้เครื่องช่วยหายใจของสถาบันโรคทรวงอกพบสาเหตุจากเชื้อแบคทีเรียและเชื้อในกลุ่ม Atypical pathogen ได้ถึง 57.8 % (22/38 ราย) ส่วนใหญ่เป็นเชื้อแกรมลบ พบการดื้อต่อยาปฏิชีวนะของเชื้อ K. pneumoniae, P. aeruginosa, S. aureus, E. coli, A. baumannii, Proteus mirabilis, S. dysgalactiae และ S. pneumoniae มีการติดเชื้อ Chlamydophila Pneumoniae 13.2 %*

Instrumental diagnostics of pulmonary diseases. Radiologic diagnostics. Rontgenologic methods play important role in pulmonary diseases diagnostics to confirm diagnostic suppositions arisen on previous stages of patient examination.Â Chronic cough without visible reason. Delayed pneumonia resolution. Atelectasis Cancer of lung Abscess.Â Congestive pulmonary phenomena in heart failure, chronic and acute illnesses of upper respiratory tract, avitaminous promote a pneumonia development. Considerable overwork apparently just as predisposes to crupous pneumonia. Finally, it may be pointed relatively high rate of pneumonias in the past in patients with crupous pneumonia. Chronic obstructive pulmonary disease (COPD) is a debilitating disease with rising worldwide prevalence. Exacerbations of COPD cause significant morbidity and become more common with advancing age.Â Exacerbations of COPD cause significant morbidity and become more common with advancing age. Healthcare providers caring for elderly patients should therefore be familiar with effective treatments for exacerbations of COPD.Â Non-invasive ventilation reduces the morbidity and mortality associated with acute exacerbations complicated by hypercapnic respiratory failure. Strategies to prevent COPD exacerbations include smoking cessation, long-acting inhaled beta-adrenoceptor agonists, inhaled long-acting anticholinergics, inhaled corticosteroids and vaccination. Background: Patients with chronic obstructive pulmonary disease (COPD) often present with severe acute exacerbations requiring hospital treatment. However, little is known about the prognostic consequences of these exacerbations. A study was undertaken to investigate whether severe acute exacerbations of COPD exert a direct effect on mortality.Â A severe acute exacerbation of COPD was defined as any sustained increase in respiratory symptomatology compared with the baseline situation requiring modification of regular medication and hospital treatment.26 A prospective registry was made of all exacerbation episodes requiring hospital management during the year of the study. Acute exacerbation of COPD is a sudden worsening of COPD symptoms (shortness of breath, quantity and color of phlegm) that typically lasts for several days. It may be triggered by an infection with bacteria or viruses or by environmental pollutants.Â Severe exacerbations can require hospital care where treatments such as oxygen and mechanical ventilation may be required.[19] Mechanical ventilation can be invasive (endotracheal intubation) or non-invasive forms of ventilation such as continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP).Â "Management of acute exacerbations of chronic obstructive pulmonary disease: a summary and appraisal of published evidence". Ann. Intern.