

## **Phagocytic Ability of Granulocytes and Monocytes in Elderly Patients with Community Acquired Pneumonia**

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### **Abstract**

In the elderly, pneumonia has higher risk of fast progression and mortality. The reason for this fact is unclear, one explanation could be the altered immune functions in senior subjects. Due to age-related changes of the immune system, elderly people tend to be more susceptible to infections. It is well known that the immune response declines with senescence. The mechanisms underlying age-related changes in immune function are not fully understood but are likely to be multifactorial. The objective of this study is to investigate the phagocytic ability of elderly cases having serious lung infections.

The study population consisted of pneumonia patients older than 65 year of age who were admitted to the hospital. The phagocytic ability of neutrophils and monocytes is measured by using Phagotest flow cytometry method.

The study was conducted in a group of 53 patients (41 men and 12 women) with a mean age of 74.04 (65 - 90). The mean phagocytic activity was  $85.90 \pm 24.45$  for granulocytes and  $68.28 \pm 29.04$  for monocytes. The phagocytic activity of granulocytes and monocytes showed no significant difference between subjects under and above 70 years of age. Phagocytic activity was not found to be correlated with neutrophil count, procalcitonin, CRP, Ig levels and PSI.

Study failed to show a correlation between phagocytic activity and severity of pneumonia in elderly subjects. According to our findings, the severity and prognosis of lung infections in elderly is not dependent on phagocytic activity.

**Keywords:** *Phagocytic Ability; Granulocytes; Monocytes; Community Acquired Pneumonia*

### **Introduction**

Pulmonary infections are a significant cause of morbidity and mortality in the population, especially in the elderly. The severity of the disease ranges from mild to severe and in some cases it leads to serious organ failure and even death. In the elderly, pneumonia has higher risk of fast progression and mortality. The reason for this fact is unclear, one explanation could be the altered immune functions in senior subjects. Due to age-related changes of the immune system, elderly people tend to be more susceptible to infections [1,2]. Bacterial, fungal and viral infections are an important cause of morbidity and mortality amongst elderly subjects, and once infection is established, the aged cases have a diminished capacity to prevent its spread. A variety of changes are observed in the immune system with increasing age. It is well known that the immune response declines with senescence. The mechanisms underlying age-related changes in immune function are not fully understood but are likely to be multifactorial [1-3].

## Objective of the Study

The objective of this study is to investigate the phagocytic ability of elderly cases having serious lung infections.

## Methods

The study population consisted of community acquired pneumonia patients older than 65 year of age who were admitted to the hospital. All cases had symptoms of pneumonia, associated physical findings and infiltration on chest radiograph. The symptoms, detailed physical examination findings including body temperature, respiratory rate, heart rate and blood pressure, comorbidities, smoking and alcohol consumption history were noted. The laboratory tests included complete blood count, CRP, procalcitonin, biochemical analyses, antiHIV and arterial blood gases. Sputum cultures (if possible) and blood cultures were taken.

The phagocytic ability of neutrophils and monocytes is measured by using Phagotest flow cytometry method. It measures the overall percentage of monocytes and granulocytes showing phagocytosis and the individual cellular phagocytic activity (the number of bacteria per cell). The phagocytosis test kit contains fluorescein-labelled opsonized *Escherichia coli* and other necessary reagents. Bacteria are ingested by phagocytes generating a green fluorescence signal, quantified by flow cytometry. Heparinized whole blood is incubated with reagent B (FITC-labelled *E. coli*) at 37°C, a negative control sample remains on ice. The phagocytosis is stopped by placing the samples on ice and adding quenching solution. This solution allows the discrimination between attachment and internalization of bacteria by quenching the FITC fluorescence of surface bound bacteria leaving the fluorescence of internalized particles unaltered. After two washing steps with washing solution erythrocytes are then removed by addition of lysing solution. The DANN staining solution, which is added just prior flow cytometric analysis, excludes aggregation artifacts of bacteria or cells. The percentage of cells having performed phagocytosis are then analyzed as well as their mean fluorescence intensity (number of ingested bacteria).

The *E. coli* bacteria are opsonized with immunoglobulin and complement of pooled sera. Cells of the phagocytic system (monocytes, polymorphonuclear neutrophils) have receptors for a complement component (C3b) and for the constant part of the immunoglobulin molecule (Fc) mediating the adhesion of the bacteria to the cell surface. By utilizing both opsonized and nonopsonized bacteria, which are also available, both opsonic capacity and phagocytosis can be measured at the same time. Thus, it can be determined whether abnormal phagocytosis is due to a failure in the opsonization process or to a defect in the ingestion capability of the phagocyte.

All statistical analyses were performed with SPSS 17.0 software (SPSS, Chicago, IL, USA). Values were expressed as mean with standard deviation. Data analyses were performed by applying parametric and non-parametric tests, as appropriate. The comparisons were made by t test and Mann-Whitney test. The correlation analyses were made by Spearman correlation test. P value of < 0.05 was considered significant.

## Results

The study was conducted in a group of 53 community acquired pneumonia patients (41 men and 12 women) with a mean age of 74.04 (65 - 90). Of the group, 36 were over 70 and 14 were over 80 years of age. History of aspiration was present in 14 subjects (20.8%). Fourteen patients had no history of smoking (26.4%). History of alcohol consumption was present in 5 cases (9.4%). Seven (13.2%) cases were nursing home residents.

Most frequent symptoms were cough (n = 40, 75.5%), dyspnea (n = 39, 73.6%), sputum production (n = 36, 67.9%), fever (n = 36, 67.9%) and confusion (n = 19, 35.8%).

Four patients were ECOG 1 (7.5%), 20 were ECOG 2 (37.7%), 12 were ECOG 3 (22.6%) and 17 were ECOG 4 (32.1%).

The comorbidities of the subjects are as follows: Hypertension (n = 30, 56.6%), diabetes mellitus (n = 25, 47.2%), chronic obstructive pulmonary diseases (COPD) (n = 20, 37.7%), congestive heart failure (CHF) (n = 14, 26.4%), neurological disorders (n = 18, 34%), coronary artery disease (n = 11, 20.8%), cancer (n = 6, 11.3%), tuberculosis sequela (n = 6, 11.3%), chronic renal failure (n = 5, 9.4%) and asthma (n = 4, 7.5%).

Chest radiography was repeated 7 - 10 days after initiation of the treatment; 9 patients showed full regression, 23 regressed more than 50%, 19 had no regression and 2 progressed despite treatment.

The mean phagocytic activity was  $85.90 \pm 24.45$  for granulocytes and  $68.28 \pm 29.04$  for monocytes. The phagocytic activity of granulocytes and monocytes were  $91.27 \pm 14.40$  and  $84.06 \pm 27.00$  for subjects under 70 and  $80.20 \pm 20.08$  and  $64.44 \pm 30.68$  above 70 years of age, respectively (p = 0.27 ve p = 0.07) (Table 1).

	%phagocytic activity of granulocytes	%phagocytic activity of monocytes
All cases	$85.90 \pm 24.45$	$68.28 \pm 29.04$
Cases under 70 years of age	$91.27 \pm 14.40$	$80.20 \pm 20.08$
Cases above 70 years of age	$84.06 \pm 27.00$	$64.44 \pm 30.68$

**Table 1:** The results of phagocytic activity tests for granulocytes and monocytes in cases under and above 70 years of age.

Phagocytic activity was not found to be correlated with neutrophil count (p = 0.19 for granulocytes and 0.20 for monocytes); procalcitonin (p = 0.51 for granulocytes and 0.80 for monocytes); CRP (p = 0.59 for granulocytes and 0.99 for monocytes) Ig levels and PSI. (p values for IgA, IgG and IgM were 0.64, 0.49, 0.72 for granulocytes and 0.24, 0.37, 0.36 for monocytes, respectively).

Phagocytic activity was not related to response to treatment or accompanying diseases.

Smoking history was not correlated to phagocytic activity, whereas in case of alcohol use activity of granulocytes (p = 0.013) and monocytes (p = 0.03) were statistically significantly lower.

**Discussion**

Our study reveals no changes in phagocytic activity of elderly subjects having pneumonia with respect to age, performance status, comorbidities or severity of the pneumonia. The phagocyte functions were not correlated with other immune system components such as total count of neutrophils or immunoglobulins. Immunosenescence is an important factor considered to play role in both defensive role of the immune system and response to vaccination in the elderly population. According to our findings aging of phagocytic activity may not be a component of immunosenescence in this subset.

Humans live in close contact with various microorganisms and presence of effective defenses is crucial. Adequately functioning immune system is required to prevent microbial invasion. The antimicrobial activity of phagocytes is important in the host innate defense against infections. Neutrophils, monocytes and macrophages are critical phagocytes. They migrate to site of inflammation to engulf and destroy pathogenic organisms [4,5].

It may be assumed that disturbances in antimicrobial activity contribute to increased morbidity and mortality rates in the elderly. Phagocytes constitute a vital part of defense against infectious agents. The effect of aging on remodeling of the immune system is not fully clarified. Pneumonia is among the top etiologies of mortality in the geriatric population. With aging, vulnerability to infections increases and immune response to vaccinations decreases [6].

As subjects get older, they are more prone to serious diseases, mainly infections. Prcina, *et al.* have studied on the age-related defects in immune system, i.e. immunosenescence. They proposed that older people have accumulation of memory and non-functional immune cells, impaired signalling due to restricted repertoire of receptors, overall pro-inflammatory environment and complete dysregulation of the immune system, therefore they have decreased ability to respond to new stimuli, such as infections and vaccinations [7].

In a study, where phagocytotic capacity of monocyte and macrophages in smoker and non-smoker tuberculosis patients was investigated, monocytes and macrophages of tuberculosis patients who smoke had reduced phagocytic capacity compared to nonsmokers. Phagocytic capacity was inversely correlated with cigarette smoking as measured by pack years [8].

Several studies have been conducted on community acquired pneumonia in elderly, however most of them have focused on demographic, clinical, laboratory and radiological variables [9-11]. To our knowledge, this currency study is the first to assess phagocytic functions in elderly with community acquired pneumonia. It is proposed that immune response decreases with senescence, however the present study failed to show a correlation between phagocytic activity and severity of pneumonia in elderly subjects.

Our study has several limitations, the first being the fact that it includes a small population. The population is homogenous including elderly community acquired pneumonia cases and this limits us to give the data of this limited group. A comparison between our population and healthy elderly subjects or younger subjects could be helpful. The assessment of immune system was based only on phagocytic function, the functions of B and T cells, natural killer cells, dendritic cells were not studied.

### Conclusion

According to our findings, the severity and prognosis of lung infections in elderly is not solely dependent on phagocytic activity. More studies evaluating immune mechanisms in elderly should be conducted, thereby opening new avenues for enhancing vaccine efficiency in this population.

### Disclosure

No conflict of interest for any author. The paper is not published elsewhere or is under current evaluation for publication.

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