ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Effect of Limestone Dust Exposure on Lung Physiology Decline and Increase of Interleukin6 Level of Blood Serum of Limestone Processing Workers in Kesamben Village, Plumpang Sub-district of Tuban Regency.

Inne Ariane Gobel[1]*, J Mukono[1], and R Endro Sukmono[2].

[1]Department of Environmental Health, Airlangga University, Surabaya, Indonesia.
[2]Dr. Soetomo General Hospital, Surabaya, Indonesia.

ABSTRACT

Limestone produces silica dust long time exposure with dust exposure size as big as 3-5mg/m^3 can cause inflammatory reactions due to increase of IL-6 serum level and decline in lung function. The approach used in this research was across sectional. Measurement of lung function and IL-6 level of serum performed after they worked (case group) and district officers (control group). The total sample was 18 respondents divided into 9 sample case group that works in the processing of limestone and 9 samples of the control group who work in health centers. The sample was taken randomly and based on the inclusion criteria. The measurements used PDS for limestone dust exposure, lung function measurement (FVC and FEV1) used aspirometer (SpirolabIII), and measurement ofIL-6 levels of blood serum used ELISA technique. Characteristics of respondents include, age and length of work. The results of regression test analysis showed that limestone dust exposure significantly affected the increase inIL-6 levels of serum ($p < 0.05$) but not for the decline in lung function. Physical activity and the immune system of each individual were a factor that could affect the respiratory symptoms due to increased levels of IL-6 serum so the decrease of lung function after working 6 was not happened. The use of personal protective equipment such as Air Purifying Respirator Non-power types (NAPR) is important to prevent ingress of dust resulting from the processing of limestone.

Keywords: Limestone dust, IL-6 of blood serum, Lung function, Limestone Processing Workers

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Limestone is a sedimentary rock formed by special manifold of small animal's skeleton in ocean. Limestone occurred on several ways with organic, mechanical or chemical. The most of limestone found in nature occurred on organically process, this kind of stones comes from the deposition of shell / shells of snails, foraminifera or algae, or derived from an animal skeleton shells /coral. Limestone can be creamy white, light gray, dark gray, brown and even black, depending with the presence of mineral impurities [19].

The most limestone contained iron oxide, alumina magnesium, and sulfur with CaO (22-56%), and MgO (21%) as the main component. Limestone using was often found in industrial rubber, tires, paper and become impurities, etc. The characteristics of limestone that when heated will turn into calcium oxide lime (CaO) as a process of decarbonization or CO2 release gas. There are several kinds of limestone combustion [21].

1. Quick Lime. That is a direct result of limestone burning in form of oxides from calcium and magnesium.
2. Hydrate lime / slake lime. That is form oxides of magnesium or calcium are made of hard limestone and given water to react and produce heat. Typically used in the installation of brick buildings.
3. Hydraulic lime. There were CaO and MgO chemically combined with fouling. Hydrated lime oxide with easily by adding water or leave with air, this reaction will occur thermal. Hydraulic lime sell as Hydrat lime contain some impurities (impurities) consisting of silica, iron oxide and other, so pure of hydraulic lime may only contain 10-35% lime clear.

Limestone processing has produces such CO_2, Ca, and dust particles that can damage for health likes pneumoconiosis disease , shortness of breath and cough. The direct impact is felt when inhale smoke such eye irritation , shortness of breath and if touches our skin it feels like burning [23]. Lime dust dust particles are irritants and its main effect is acute or chronic lung disorders. Its effects on the respiratory tract are respiratory tract irritation, increased of mucus production, airway narrowing , loss of cilia and mucous membranes of cell layer and difficulty for breathing. Early detection of lung function limestone industry workers should be done to early so as not be a pulmonary diseases such as an obstruction and restriction of lungs [14].

Lung defense mechanism against inhaled dust exposure are consists of three interrelated system are mechanical filtration of air, fluid mucus and lung-specific defense. Therefore, pulmonary function tests are needs in supporting the diagnosis to observe abnormalities ventilation in pulmonary like obstruction and restriction. In additionally, the inflammatory for response a lime dust is inhaled can involve inflammatory cells and the release of certain cytokines [21]. Healthy workers without respiratory disorders such as asthmaafter inhaling dust, they will decrease a flow air in the lungs (FEV_1decreased are 10-40%) and increase of pro-inflammatory cytokines, namely IL - 8 and IL – 6 [12].Cytokines released in interstial lung TNF - α as well as pro-inflammatory cytokines such as IL - 8 and IL - 6 that can cause pulmonary fibrosis resulting in pulmonary restriction [28]. Cytokines released in interstial of lungs likes TNF - α cytokines such as IL-8 and IL-6 that will cause pulmonary fibrosis resulting in pulmonary restriction [28].

Interleukin 6 function on nonspecific and specific immunity that produced by monocular phagocytes, endothelial cells vaskula, fibrolast and other cells as response against microbes and other cytokines. Non-specific immune IL-6 stimulates hepotosit to produce APP (acute phase proteins) and along the CSF (cerebrospinal fluid) stimulates progenitors in bone marrow to produce neutrophils. In specific immunity, IL-6 stimulates the growth and differentiation of B cells into antibody which producing plasma cells [4,7,1]

According with Susanto (2011), a lung disease caused by silica dust exposure involves a complex interactions between inflammatory cells, mediators of inflammation and tissue on airway [23]. The main of inflammatory cells as a main role were mast cells, and lymphocytes. Meanwhile the main inflammatory mediators which involved are histamine, leukotrienes, eosinophil chemotactic factors, and cytokines IL-3, IL-4, IL-6, IL-13. Cells were involved in inflammation in airways, among others:

1. Mast cells, activated by an allergens through with IgE binding (immunoglobulin E), which has been attached to its receptor on surface of mast cells. This bond has triggers of intracellular

biochemical events that cause the outbreak Mastocyte mast cells or mast cells which causes the release of various inflammatory mediators.

2. Lymphocyte cells, consist of lymphocytes T and lymphocytes B, lymphocytes T are divided in two, namely the T-helper 1 (Th1) and T-helper 2 (Th2). Th2 lymphocytes produced a various kinds of cytokines IL-3, IL-4, IL-6, IL-9, IL-13 as main a role on inflammatory reactions. For cytokine IL-3 and IL-4 can activate the lymphocytes B to produce IgE (immunoglobulin E) which will then be attached to inflammatory cells and will trigger of inflammatory mediatorsrelease.
3. Inflammatory Mediators, is a network of local inflammatory reaction for infection or injury which involving multiple inflammatory mediators. One of the cytokines areinvolved on inflammation that when IL-6 derived from Th2 which more specific with allergic inflammation [6].

Changes amount of inflammatory mediators such as TNF-α, IL-6 are found in the form of increased levels of acute phase proteins to patients with stable COPD though. TNF-α regulate the inflammatory processes on multicellular level by stimulating increase of expression to leukocyte adhesion molecules and also endothelial cells in additionally to improve setting of another proinflammatory cytokines (IL-8 and IL-6), and induces angiogenesis. TNF-α stimulates the formation of IL-6 in proinflammatory cytokines increase on lungs[10].

In Indonesian pneumoconiosis prevalence data are available bythe result of small-scale research in a variety of industries has a risk of pneumoconiosis. Data by the research in Bandung in 1990 on stone quarry workers founda cases of pneumoconiosis by 3.1 %. Research by Wijayain 1998 on stone mining in Bandung found cases of pneumoconiosis by 9.8 % [25]. Research by OSHA in 2002 on ceramic workers found silicosis by 1.5 % [23]. Looking at the data description can be concluded that Indonesia has not a nationally data about the prevalence of pneumoconiosis.

Kesamben village, sub-district Plumpang of Tuban Regency has a limestone processing that much because the type of soil is a red mediterranean yellow derived from limestone sediment. According to the Central Statistics Agency of Tuban Regency about that minerals were exploited in Tuban Regency in 2012 include limestone, clay, marshal, dolomite, quartz sand, and phosphate but the most minerals exploitation was limestone is reached 13,729,788 tons per years [16].

SUBJECTS AND METHODS

This research was analytical research with aims to analyzed a difference between of research groups. Based on this research time approach was case-control study that comparing lime dust exposed population groups (study) and population groups are unexposed with lime dust (control).

Research location in Kesamben village, sub-district Plumpang of Tuban Regency, with five month long study during the month of June to October 2014.

The population of this research was all female workers who work in limestone processing plant and employees of district office with the inclusion criteria was a requirement that must be order for the respondent has been sample research, which consist of:

1. Woman
2. Has been work at least one year continuously
3. Has age 20-50 Years
4. Has not a history of previous work which may lead to increased respiratory disease eg cement and asbestos factories, and others.
5. Has not a history of bleeding was difficult to stop as hemophilia
6. Has not smoker behavior
7. Willing to be a respondent

ISSN: 0975-8585

The sample size calculated with formula hypothesis of sample test based on average [17].

$$n = \frac{2\sigma^2(Z\alpha + Z\beta)^2}{(\mu_1 - \mu_2)^2}$$

n = The minimum of sample size
Zα = Adjusted of standard deviation for α test on 2 directions (1.96)
Zβ = Adjusted standard deviation for β (β = 0,20 Z = 0,84)
σ = SD for response control group / conventional (σ = 0, 22) [13]
μ_1 = The mean of response from expected group one (μ1 = 3.71) [13]
μ_2 = The mean of response from expected group two (μ1 = 4.00) [13]

$$n = \frac{2(0.22)^2(1.96 + 0.84)^2}{(3.71 - 4.00)^2} = 8.96$$

Sampling method was by simple random sampling technique after the sample inclusion criteria did. For the non-exposed group were taken with the same amount as many as 9 people adjust with exposed group (study).

RESULTS

Characteristics of Respondents

Age

Based on the questionnaire results were obtain exposed group 66.7% were aged 45-49 years and age group unexposed 11.1% was age 30-34 years. The lowest age group 40 years and the exposure is the lowest age group unexposed 20 years.

Table 1: Age Distribution of Respondents in Kesamben Village Sub-District Plumpang of Tuban Regency

Age	Respondents				Total	
	Exposed Group		Unexposed Group			
	n	%	n	%	n	%
20 – 24	0	0	2	22,2	2	11,1
25 – 29	0	0	0	0	0	0
30 – 34	0	0	1	11,1	1	5,5
35 – 39	0	0	2	22,2	2	11,1
40 – 44	3	33,3	2	22,2	5	27,8
45 – 49	6	66,7	2	22,2	8	44,4
Total	9	100	9	100	18	100
Mean (SD)	45,11 (2,67)		36,67 (9,38)			

Table 1 shows determine of average respondent's age from exposed group were 45.11 years, while for unexposed group were average 36.67 years.

Working Period

Based on the questionnaire results were obtain working period on exposed group 44.4% and worked for 1-3 years and non-exposed group 33.3% worked for 10-13 years. The fastest working period in the exposed

group and unexposed group were 1 year and while the longest of working period exposed group was 10 years and the unexposed group was 24 years.

Table 2: Distribution Working Period of Respondents in Kesamben Village Sub-District Plumpang of Tuban Regency

Working Period (Years)	Respondents				Total	
	Exposed Group		Unexposed Group			
	n	%	n	%	n	%
1 – 3	4	44,4	2	22,2	6	33,3
4 – 6	1	11,1	0	0	1	5,5
7 – 9	2	22,2	1	11,1	3	16,7
10 – 13	2	22,2	3	33,3	5	27,8
14 – 16	0	0	1	11,1	1	5,5
17 – 19	0	0	0	0	0	0
20 – 23	0	0	1	11,1	1	5,5
24 – 26	0	0	1	11,1	1	5,5
Total	9	100	9	100	18	100
Mean (SD)	5,44 (3,57)		12,11 (7,75)			

Table 2 shows the average working periode of exposed group was 5.44 years and while working period unexposed group was 12.11 years.

Lungs Function

Lung function measurements of respondents used spirometer that can be known air volume in and out of the lungs. Parameters measured include FVC, FEV1, % FVC, FEV 1%.

Table 3: Distribution Values of Lungs Function of Respondents

Lungs Function Parameters	Respondents		p
	Exposed Group	Unexposed Group	
FVC	2,06 (0,35)	2,33 (0,31)	0,106
FEV_1	1,82 (0,31)	2,06 (0,31)	0,116
% FVC	89,62 (16,85)	96,50 (13,26	0,351
% FEV_1	94,52 (17,18)	99,01 (15,08)	0,565

Table 3 shows that in group exposed has average value of FVC (2.06), FEV1 (1.82),% FVC (89.62), % FEV1 (94.52). While unexposed group FVC (2.33), FEV1 (2.06),% FVC (96.50),% FEV1 (99.01).

Levels of IL-6 Serum

Levels of IL-6 in serum were analyzed by ELISA (Enzyme Linked immunosorbent Assay) method. The results measurements of levels IL-6 serum in exposed group and unexposed groups can be seen in table 4.

Table 4: Distribution Values of IL-6 Serum Levels of Respondents

Level of IL-6 Serum (pg/ml)	Responden	
	Exposed Group	Unexposed Group
Average of IL-6 Serum levels	17,16 (15,77)	4,49 (3,21)
p = 0,028		

Table 4 shows of average of IL-6 serum levels based on different locations. Levels of IL-6 serum average in exposed group was 17.16 pg / ml and unexposed group at 4.49 pg / ml.

ISSN: 0975-8585

Analysis of Dust Exposure Effect to Lungs function of Respondents

To determine the effect of dust exposure on lung function was analyze by multiple regression test. Analysis of effect dust exposure to lungs function can be seen in Table 5.

Table 5: Analysis of Dust Exposure Effect to Lungs function of Respondents

Variable	FVC		%FVC		FEV_1		$\%FEV_1$	
	β	p	β	p	β	p	β	p
Dust Exposed	0,308	0,381	0,297	0,424	0,460	0,160	0,462	0,207
Age	-0,183	0,575	0,064	0,853	-0,224	0,452	0,188	0,573
Working Period	-0,001	0,999	-0,067	0,856	-0,151	0,637	-0,207	0,566

P < 0,05 (Significant) ** P > 0,05 (not significant) *

Table 5 shows that there is no effect of lime dust exposure to lung function FVC (β = 0.308, p = 0.381) and % FVC (β = 0.297, p = 0.424). Age and working periode does not affect to respondent's pulmonary function (FVC and% FVC). β value was dominant negative and only dust exposure variable was positive, but its small effect to pulmonary function.

There is no effect of lime dust exposure to lungs function FEV1 (β = 0.460, p = 0.160) and% FEV1 (β = 0.462; p = 0.207). Age and working period does not affect to respondent's pulmonary function (FEV1 and FEV1). β value was positive but exposed with lime dust may not be able to affect lungs function of respondents.

Analysis of Dust Exposure Effects to IL-6 Serum levels of Respondents

Table 6: Analysis of Dust Exposure Effects to IL-6 Serum levels of Respondents

Variable	IL-6 Serum Levels	
	β	p
Dust Exposure	0,665	0,014
Age	0,080	0,725
Working Period	-0,149	0,546

From Table 6 shows that there is influence of dust exposure to serum levels of IL-6 (β = 0.665, p = 0.014). The value of β was positive, which means the highest of dust exposure can influence serum levels of IL-6 has been increased.

DISCUSSION

Characteristics Respondent

Age

The age of respondent by exposed group from this Study has a range 45-49 years old and age unexposed group has a ranged 30-34 years old with minimum of age from exposed group had 40 years old and from unexposed group had 20 years old. According with Budiono (2007), Age factor affects to physical conditions and associated with pulmonary function, the pulmonary function capacity will continues to increase with age increase and it will be reach on maximum values when 21 years old. After 21 years old a pulmonary function values will change with age increase [5]

Research by Yunus (2009) shows that same results volume of air exhaled from the maximum breathing was an indication of someone health associated with aging factor. Diffusion of lungs, ventilation of lungs, oxygen uptakes and all parameters of pulmonary function decreased in accordance with aging after

reach a maximum point for young adults [27]. Associated by the results of research by Kaidah (2012) on Lusno (2013) was declare that, there hasn't significant relationship between age and pulmonary function from workers of stone processing in awang village on western Bangkal which indicated by p value = 0.654 ($p > 0.05$). While from previous research has stated that, the stone processing workers on older age group than 40 years has not always working on the long time. Accordingly the age does not affect to pulmonary function [12].

In addition with factors of age, gender, race, body mass index, the other factors that can affect to lungs vital capacity are physical activities like exercise. Athletes can be their lung capacity has been increase 30-40% above normal when they do exercise with routine and regularly [8].

Working Period

Long working period can determine how long person's exposure with risk factor, the long of working period will be greater the risk factor. Variables that could be potentially problems to pulmonary function impairment were working period by some worker. The longs of working period by workers in place that could be potentially cause of respiratory problems such as a dusty place, so more dust has been inhaled and will accumulate in lungs of workers [22].

On this study, working period of respondents from exposed group ranged between 1-3 years and working period of unexposed groups ranged between 10-13 years. However, by results of multiple regression test between working period and serum levels of IL-6 were not obtained a significant results. It was probably because everyone has a varying immunity, or everyone has a different susceptibility with exposure of pollutants in the work place. The other factors such as temperature, humidity, wind speed and wind direction can affect to amount of exposure materials by each workers to be different.

Lungs Function

Lungs function examination was using a spirometer. It was very useful to find the occurrence of respiratory disorders early on. The examination involves two parameters: forced expiratory volume on 1 second (FEV1) and forced capacity (FVC) [2].The measured parameters on this study were changes of FEV1, FVC, % FEV1 and % FVC.

Yulaekah (2007), had stating that lime dust are inhaled into the respiratory tract becomes ineffective, because of $CaCO_3$ and $MgCO_3$ contained on lime dust will reduce the lungs recoil at expiration. On normal conditions of expiration is a passive process that occurs as a result of lung's ability elastic return to original condition. In additionally, lime dust caused allergic reactions and impaired of pulmonary function. If connected with this research will caused damage of breath airways, which would decrease a pulmonary function [26]

Lung function tests such as FEV1, FVC, %FEV1 and %FVC aimed study of dust exposure effect on lungs volume [9]. Measurements did on after work for known the amount of lungs volume on each parameter. Lung function was measured one time, that after working on 8 hours. The average of value pulmonary function on limestone processing among others, FVC 2.06 (0.35), FEV1 1.82 (0.31), %FVC 89.62 (16.85), the percentage of FEV1 94.52 (17,18). While average of pulmonary function value on employee district office among others, FVC amounted 2.33 (0.31), FEV1 2.06 (0.31), % FVC 96.50 (13.26), and % FEV1 99, 01 (15.08). By results of two independent samples t-test obtained, no significant difference from value of pulmonary function on both groups of respondents.

Levels of IL-6 Serum

From statistical test results obtained levels of IL-6 serum on both groups of respondents after worked, there are significant differences. But more significant were group in limestone processing, it influenced by exposure with lime dust with high intensity in their work place.

IL-6 is a proinflammatory cytokine group that participates in inflammation process and tissue repair. IL-6 produced by variety of cells, including lymphocytes, neutrophils and T cells [15].

The increasing of IL-6 secretion which a proinflammatory media, it was influence by oxidant stress

that cause inflammatory cell recruitments and induction against oxidant stress mediators. Additionally there is a relationship between the characteristics of the respondents in such of age, weight and height with a disease caused by obesity [20]

Analysis of Dust Exposure Effect to Lungs function of Respondents

According with Widodo (2007), the workers who works in environments with high dust levels on a long time has a high risk of lungs disease and age can occur greater susceptibility with disease, especially respiratory distress in labor. But this study, was on results of multiple regression test states that there is no significant relationship between age, years of service and respirable dust exposure with pulmonary respondents. This is consist with research by Ansar 2005, which that there is no significant effect between dust exposure, age and working period with pulmonary function abnormalities on labor [3].

Analysis of Dust Exposure Effects to IL-6 Serum levels of Respondents

On this results of the regression test that lime dust exposure can reduce levels of IL-6 serum on respondents with p-value are 0.014. It because the components contained in lime dust has silica component and it's include on type of dust fibrosis so when exposed with high intensity can affect to levels of IL-6. According with Lee (2010), his research that IL-6 serum as a main role for respond amount levels of silica incoming and cause of inflammation on lungs tissue [11].

Therefore, respondent characteristics such as age and working period has not affect to accumulation levels of IL-6 serum because sensitivity enhancement its only acute [18].

REFERENCES

[1] Abbas A.K., (2010). Cellular and Molecular Immunology.San Fransisco California. Saunders Elsevier; p : 267-299

[2] AlsagaffH, and Mukty H.A.,(2010). Fundamentals Science of Pulmonary Disease. Surabaya. Airlangga University Press.

[3] Anshar, A.S., (2005).Relations of Limestone Dust Exposure With Forced Vital Capacity of Lungs Against Limestone Workers at UD. Forward effort Yogyakarta.Journal of Public Health Media Indonesia.http://www.perpus.fkik.uinjkt.ac.id (accessed on January 7, 2013).

[4] Baratawidjaja K.G., and Rengganis I., (2012).Basic of Immunology. 10th Ed, Jakarta: Publisher Agency Faculty of Medicine, University of Indonesia, p. 27-240.

[5] Budiono I., (2007). Risk Factors Impaired of Lung Function on Car Painting Workers, Thesis. Faculty of Public Health Diponegoro University of Semarang.

[6] Dimitris A. (2011). In The Role of IL-6 Pathophysiology of Human Disease.Jurnal of Immunologi, p : 408-15

[7] Elgert K.D, (2009). Immunology Understanding the Immune System 2nd edition. New Jersey: John Wiley & Sons

[8] Guyton A.C., Hall J.E (2006) .Text Book Of Medical Physiology. 11th edition. International Edition, p. 1062-1065

[9] Ikhsan, (2009).Anthology of Occupational and Environmental Lung Diseases.1st edition. Jakarta: Hall of Publisher Medical Faculty of UI. p.27-47

[10] Jeremy, P.T., (2007). At a Glance Respiratory System 2nd Edition.ErlanggaMedical Series. Jakarta

[11] Lee, (2010).Serum level of interleukin 6 and Tumor Necrosis Factor alpha in coal workers: one year follow up study, vol 1, no 2, p : 69 - 79

[12] LusnoM.F. (2013). Increased Levels of Endotoxin LPS on Dust Rice Milling and Its Effect on Lungs Function Decline and Increased levels of IL-8 Blood Serum Operator. Thesis.Faculty of Public Health Airlangga University.

[13] Meo AS. 2006. Lung function in Pakistani wood workers. International journal of Environmental Health Research (Tailor and Francis Group). Vol. 3. No 16. p. 193 – 203

[14] Mukono, H.J. (2008). Air Pollution and It Effect on Respiratory Disorders. Surabaya: Airlangga University Press, p 10-69.

[15] Nijuis, (2003).Endothelial Cells are Main Producers of Interleukin 6 and Interleukin 8 through Toll – Like receptor 2 and 4 signaling during Bacterial Infection in Leukopenic Cancer Patients. Clinical and Diagnostic Laboratorium Immunology.Vol. 10. No. 4 p. 558-593

[16] Profile of Tuban Regency.(2013).Tuban in Figure.Tuban.The Central Bureau of Statistics Tuban Regency in East Java.

[17] Purnomo W and Bramantoro T., (2014).36 Practical Steps For Writing With Successfully of Scientific Papers. Surabaya: Petra Revka Media, p. 32-33

[18] Sekido, (1994).Essential Involvement of Interleukin 6 in Acute Inflamamation.Vol 56. No 5. p: 559 – 64

[19] Setiawan H.I, (2011). Influence of Limestone Processing Against Environement Pollution and Level of Public Health In Karangdawa Sub-District MargasaiDistric of TegalRegency. Undergraduate Thesis. Universitas Muhammadiyah Purwokerto.

[20] Sharabian, M.T.A, Vermeulen R, and Hosjineh F.S., 2011.Immunologic profile of excessive body weight.InformaHelath Care.Vol 16. No.3 p. 243-251

[21] Sucipto E, (2007).The relations of Dust Particle Exposure in Limestone Processing Against Lung Functions Decline. Thesis. Diponegoro University

[22] Suma'mur P.K., (2009). Hygiene and Health of Company (Occupational Health). CV. SetoAgung, Jakarta. p. 70-75.

[23] Susanto D.A. (2011). Pneumoconiosis.Department of Pulmonology and Respiratory, Faculty of Medicine, University of Indonesia.Journal of Medicine, Volume 61 number 12. Download 17 april 2014

[24] Tolinggi S. (2014). Effect Exposure of Lime Dust Inhalation to Increased Levels of IL-8 Blood Serum and Decrease of Pulmonary function on Lime Stone Mining Industry workers. Thesis.Faculty of Public Health.Airlangga University.

[25] Wijaya, (1998).Epidemiological Pneumoconiosis Analysis by X-ray of lungs classification of international labor standards organization (ILO) on workers' stone quarry in PT. A on West Java. Thesis. Faculty Of Engineering. University Of Indonesia.

[26] YulaekahS., (2007). Exposure of Inhalation Dust and Workers of Limestone Industry Impaired of Their Lung Function. Thesis.Diponegoro University.

[27] Yunus M, (2009). Impact of Industrial Dust on Worker's Lungs and Its Control, Mirror of World Medicine (online), 115 (http: library.usu.ac.id, accessed on December 20, 2014)

[28] Zhang, (2002).The Study on the interleukin-6 (IL-6), Journal of Biomedical Engineering. Vol.19. No. 4.p 699-702