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Title: Comorbidity by smokers – A cumulative effect of exogenic and endogenic factors?

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Body: This work is an analysis of our studies and literary data about a cumulative effect of tobacco smoke and another risk factors and comorbidity. There is investigated the connection between COPD and COPD and lung cancer (COPD + Ca): A. Clinically. There are follow up 120 smokers with COPD + Ca, 181 smokers with COPD, 50 with lung cancer and 50 health smokers (control group). We proved that: The number of smoked cigarettes ($p = 0.009$) and air pollution at work environment (exogenic factors) are more risky about COPD + Ca than early beginning of tobacco smoke ($p = 0.821$). Predisposition about Ca is more risky than another diseases in family (14.17 %). Smokers with COPD + Ca and COPD more often have cardiovascular and metabolic diseases than this with lung cancer and control group. Predisposition in family about cardiovascular and metabolic diseases exceed the interval – 2 – 4 %, established with the control group and the group with lung cancer. B. Experimental. There is investigated lung and bone marrow in rats, treated with tobacco smoke for 30 days. We found a centroacinar emphysema with predominant destruction by massive exposition and bronchiolitis. The micronuclei (erythrocytes with nuclear chromatin) in bone marrow are significant higher compared with the control group ($4.35 \pm 0.5 / 1.58 \pm 0.33$). This results showed that in conjunction with local lung changes occur systemic effects (clastogenesis as a result of cytotoxic effect). Conclusion: The comorbidity in relationship with tobacco smoke is related with a cumulative effect of exogenic and endogenic factors. There are necessary profound analysis to prove of related with the cumulative effect of exogenic and endogenic factors comorbidity.