Nonrespiratory Effects of Smoking

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Smoking is an addictive, chronic disease and the subject of numerous studies that have significantly deepened our scientific understanding of this condition. Smoking is the major single cause of preventible disease and premature death in developed countries[1] and its relationship with chronic diseases, such as cancer and cardiovascular and respiratory diseases, among others, has been well demonstrated.[2]

Tobacco is a highly toxic product whose known ingredients include many dangerous chemical compounds collected from environmental pollution (ammonia, pyridine, tars, polycyclic aromatic hydrocarbons, nitrosamines, cadmium, cyanide, polonium-210, radon, acetal dehydrates, and others), and when tobacco burns, more than 4000 toxic substances are released, 60 of them known to be carcinogenic.[3]

Normal body functions can be seriously affected and the organism's survival compromised as a consequence of direct inhalation of tobacco smoke (active smoking) or of exposure to the contaminants present in environmental smoke (passive smoking).

In the last 20 years a direct association has been found between smoking and more than 25 diseases.[1] It would be too lengthy to go into the many recent studies on the nonrespiratory effects of smoking tobacco. Such effects have an impact on practically all human biological systems (the cardiovascular, immune, digestive, and metabolic systems) and involve branches of medicine dealing with most other systems (obstetrics and gynecology, stomatology, otorhinolaryngology, psychiatry, ophthalmology, geriatrics, and many more). Given the obvious importance of the nonrespiratory effects of tobacco, it may be of interest to look closely at only a few recent studies since they may play a decisive role in shaping future strategies in smoking prevention and treatment.

1. Tobacco and cancer. There is now sufficient scientific evidence to demonstrate that smoking is associated with cancers at diverse locations other than the respiratory tract, specifically the ear, nose and throat (mouth, sinuses, nasopharynges); the digestive tract (stomach, esophagus, liver, pancreas); kidneys (renal pelvis); reproductive organs (uterine cervix); urinary tract; and blood (myeloid leukemia).[4] Smoking is known to be a major risk factor for squamous cell cancers although only a small percentage of the exposed population actually develop the disease. The hypothesis is that abnormalities in regulatory processes predispose the organism to tumorigenesis. Such regulatory processes that can be affected by tobacco components are: *a)* xenobiotic metabolism; *b)* mechanisms supporting genetic stability (DNA repair, cell cycle—apoptosis in particular); and *c)* control of microenvironmental factors (matrix metalloproteinase, inflammation, growth factors). Furthermore, it is believed that genetic susceptibility favors the interference of tobacco smoke in these regulatory mechanisms and predisposes a person to the onset of cancer[5] For example:

– Genetic polymorphisms of the slow acetylator phenotype N-acetiltransferase-2 is associated with higher risk of colorectal adenoma in smokers[6] and predisposes postmenopausal women smokers to breast cancer[7]

– Certain cytochrome P450 polymorphisms (*CYP1B13/3*) are associated with greater susceptibility to breast, urogenital (*CYP1B1-4B1*), and head and neck (*CYP1B3/3*) cancers[8]

– Tobacco interferes in the immune response to papillomavirus (serotypes 16 and 18) and thereby increases the risk of cancer of the female reproductive system[9]

2. Tobacco and cardiovascular disease. Epidemiological evidence continues to support the relationship between smoking, including passive smoking, and cardiovascular disease in all its manifestations:

– The Interheart study,[10] recently carried out in 52 countries, showed that patients who are smokers run the risk of a second heart attack (odds ratio, 1.87) for 3 years after quitting, and remain at high risk for 20 years after quitting

– Certain genetic polymorphisms of the cytochrome P450 (*CYP1A1-CC*) and homozygote variants of endothelial nitric oxide synthase increase smokers' susceptibility to severe coronary disease[11]

– Periods of passive smoking give rise to anatomical abnormalities in the vascular endothelium similar to those observed in active smokers, thereby increasing the risk of heart disease by as much as 35%[12]

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3. Tobacco and other diseases.

– *Infertility*. Male infertility: studies of the last 15 years have shown that the toxic components of tobacco smoke can pass through the testicular barrier and impair sperm quality, an event which is associated with infertility.[13] Female infertility: absorption of certain components of tobacco smoke (cadmium, nicotine, etc) can give rise to intrafollicular abnormalities, explaining decreased fertility[14]

– *Erectile disfunction*. Apart from being a risk factor for the onset of type 2 diabetes, tobacco smoke produces abnormalities in the microvasculature of the corpora cavernosa of the penis, thereby leading to erectile disfunction and sexual impotence in males[15]

– *Blood-borne diseases*. Meta-analysis has shown that inhaling tobacco smoke can be a risk factor for the onset of follicular non-Hodgkin lymphoma, especially in individuals with a high level of consumption (>36 pack-years).[16] The biological mechanisms underlying this association are still unclear. Furthermore, some studies have reported that benzopyrene and certain radioactive substances in tobacco smoke are related to the onset of severe myeloid leukemia and an evident decrease in the survival of individuals who continue to smoke[17]

– *Infections*. Smoking favors the risk of infection as a consequence of immune system structural changes that compromise response. For example, *a)* the risk of invasive pneumococcic disease can increase by as much as 4-fold in smokers, *b)* the risk of infection by *Haemophilus influenzae* is higher in smokers, *c)* passive smoking among children is associated with a greater tendency to develop meningococcal disease and middle ear infection, and *d)* the containment of passive smoking among adults is associated with a lower risk of meningococcal disease and flu infection.[18] Infection clearly puts smokers at high risk of disease and death

– *Other associations*. Some studies have reported the association of smoking with other types of abnormalities: *a)* psychiatric disorders (depressive syndrome, posttraumatic stress syndrome); *b)* slow healing of wounds; *c)* metabolic bone disorders; *b)* periodontal disease; and *e)* ophthalmologic disease[19]

In conclusion, it would be excessive to enumerate all the reported nonrespiratory effects of smoking tobacco that contribute to reducing quality of life and compromising survival in smokers. However, such effects should reinforce the application of preventive and therapeutic interventions for smoking by all health care professionals regardless of our specialty.

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