CORRESPONDENCE

E-Cigarettes—Prevention, Pulmonary Health, and Addiction

by Prof. Dr. med. Dennis Nowak, PD Dr. rer. nat. Rudolf A. Jörres, Dr. med. Tobias Rüther in issue 20/2014

Tumor-Promoting Activities of Nicotine not Addressed

In their review (1), the authors have discussed the pros and cons of e-cigarettes from the perspectives of preventive and respiratory medicine. The authors arrive at the conclusion that e-cigarettes may to some extent be useful as an aid to smoking cessation and that the toxicological dangers are some orders of magnitude less than those of tobacco smoking. However, the tumor-triggering effects of nicotine is not mentioned at all (2). For about ten years it is known that almost all cells of the human body express nicotinic receptors (3). Nicotine and its metabolites cotinine and N-nitrosonornicotine activate these receptors and are thus capable of promoting tumor growth and even carcinogenicity. Nicotine may have a mutagenic effect on epithelial cells (2). In animal studies with mice, the administration of a dose of 2.1 mg nicotine/kg (5 days per week over a period of 24 months) resulted in the development of leiomyo- and rhabdomyosarcomas in 78% of the exposed animals (2). Abnormal cell growth, telomerase activation, apoptosis inhibition, and promotion of tumor cell spread were demonstrated (2); thus today various tumors are thought to be associated with nicotine consumption (non-small cell and small cell lung cancer, head and neck tumors, gallbladder tumors, urinary bladder, and stomach, as well as kidney, breast and colorectal cancers). These new insights should be taken into consideration when the use of e-cigarettes (as well as other carrier systems for the systemic administration of nicotine) is evaluated, especially since genetic-based differences seem to have an individual impact on the nicotine toxicity described above (2).

DOI: 10.3238/arztebl.2014.0682a

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Conflict of interest statement
The author declares that no conflict of interest exists.

In Reply:

Many thanks for this comment which adds yet another aspect to the discussion of the issue of e-cigarettes. However, for the following reasons we believe that it does not have a major impact on the overall evaluation: First, not all consumed liquids contain nicotine. Second, the risk should be seen in relation to the known carcinogenic substances in cigarette smoke, especially when a smoker changes from conventional cigarettes to e-cigarettes. In addition, it is important to note that we have a very clear and comprehensive appreciation of the risks associated with carcinogenic hydrocarbons. This is not the case with nicotine. Data are mainly derived from experimental models; however, these findings are not supported by epidemiological data, e.g. by an increased cancer risk with nicotine replacement therapy. Modelling the effect of nicotine in humans is complicated by the fact that the expressed receptors are acetylcholine receptors of the nicotinic type and not nicotinic receptors as such; therefore particular care is required when choosing suitable control experiments.

In addition, the available data suggest that the route of application (subcutaneous versus inhalation) may play an important role with regard to adverse reactions. Furthermore, tumor induction and promotion of tumor progression have different implications on such risk, depending on predispositions. Thus the available data do not allow to draw clear conclusion with regard to extrapolation to humans.

Although we believe that primarily the long-term risks of e-cigarettes are not known, the overall risk associated with e-cigarettes – including the nicotine-related risk – should always be seen in relation to known potent carcinogenic substances and inflammation-inducing pollutants in cigarette smoke. From a clinical perspective, it is always beneficial to stop or at least reduce smoking, especially since there is no known other intervention that matches the effectiveness of this measure when it comes to the prevention of lung cancer and chronic obstructive pulmonary disease (COPD).

DOI: 10.3238/arztebl.2014.0682b

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Conflict of interest statement
Prof. Nowak has received consultancy fees (Advisory Board) from Pfizer (a manufacturer of smoking cessation aids). He has received lecture fees from GSK. Prof. Nowak is a member of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (Senatskommission zur Prüfung gesundheitsschädlicher Arbeitsstoffe) of the German Research Foundation (DFG, Deutsche Forschungsgemeinschaft) and of the Scientific Advisory Board of the German Federal Institute for Risk Assessment (Wissenschaftlicher Beirat des Bundesinstituts für Risikobewertung).

PD Dr. Jörres has given lectures (on areas of pulmonology unrelated to tobacco cessation) for GSK, AstraZeneca, Boehringer, Novartis, and Mundipharma and has received reimbursement of travel expenses and fees in return. He is a member of the Executive Committee of Germany's national COPD network, COSYCONET.

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