CORRESPONDENCE

Shift Work and Cancer: The Evidence and the Challenge

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Further Potentially Carcinogenic Effects of Chronodisruption

In addition to the suppression of melatonin production and circadian disruption with deregulation of peripheral growth control functions as discussed in the article, we would like to mention further pathophysiological mechanisms that are fundamental to chronodisruption and may therefore promote the development of cancer (1).

- Sleep disruption as a consequence of shift work can result in disruption of the hypothalamic-pituitary gland axis, which in turn triggers an increased release of glucocorticoids. A resulting chronic suppression of immune response after years of exposure may increase the susceptibility to developing cancer.
- In addition to changes to activity periods and dietary habits, night work can cause further lifestyle changes, for example with regard to alcohol and tobacco consumption, and may thus indirectly affect the pathogenesis of cancer.
- Even though the evidence is inconclusive regarding the cancer-protective effects of vitamin D (2), night work may result in lower exposure to UV light and therefore reduced production of vitamin D, which, for example, may facilitate the development of colorectal cancer.

How molecular-biological mechanisms in nocturnal exposure to light and chronodisruption influence the risk of disease is an important research field in occupational epidemiology. In the future it will be importance to study which shift roster triggers relevant chronodisruption. The increasing use of longitudinal study designs with prospective assessment of shift-work systems-as it would be possible for example in the context of the national cohort-can make a valuable contribution to this important research field.

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In Reply:

Dr Behrens and colleagues mention further pathophysiological mechanisms that may contribute to the development of cancer via chronodisruption. The complements are appropriate. Following a reviewer's suggestion, we focused on epidemiology in our review. However, mechanistic details are included in the cited publications.

IARC places considerable weight on biological plausibility in their preamble to the „IARC Monographs on the Evaluation of Carcinogenic Risks to Humans" (1). Ultimately, however, epidemiological studies will have to show whether what appears biologically plausible is indeed relevant for female and male shift workers. Methodologically, the plethora of mechanistic ideas offers a unique situation with regard to considerations of causality such as undertaken by IARC in October of 2007. Indeed, in this important research area one can refer to „white-box" epidemiology (2): a multitude of mechanisms of action are "waiting to be considered" to interpret associations, possibly observed in epidemiological studies in coming years, as being causal and relevant (3).

We agree with our colleagues' expectations: shift work and chronodisruption will be an important research field for occupational epidemiology and occupational science. The National Cohort Study appears to be an appropriate means to provide insights into chronodisruption, due to different shift regimens, and possible links with cancer.

Overall, it is our expectation that coming years will bring numerous epidemiological studies regarding shift work, chronodisruption and cancer which also consider the pathophysiological mechanisms mentioned by Dr. Behrens et al. The primary objective must be to have high quality observational studies; it must be avoided that qualitatively inferior studies will be published by invoking the suggestive biological plausibility of the investigated relationships.

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Conflict of interest statement
The authors of both contributions declare that no conflict of interest exists according to the guidelines of the International Committee of Medical Journal Editors.