cells may contain a polyclonal TR sequence of the EBV genome in NPC cell lines and tissues. Moreover, through IgA receptor-mediated endocytosis, EBV infection can be detected in NPC cell lines; and EBV-infected NPC cell lines also show increasing production of oncoproteins, such as epidermal growth factor receptor (EGFR), tumor growth factor-(TGF-α) and many cell proliferation-associated genes.

As a whole, above these extensive studies, we assume that EBV infection may play a role in the secondary effect during NPC progression, or EBV infection is not as a primary factor of NPC etiopathogenesis.

References


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Indoleamine 2,3-dioxygenase-expressing mature human monocyte-derived dendritic cells expand potent autologous regulatory T cells: Consideration of triamterene to treat lupus

Chung et al. [1] found that mature human monocyte-derived dendritic cells that express indoleamine 2,3-dioxygenase (IDO), can expand regulatory T lymphocytes, Tregs, which then significantly downregulate cytotoxic effector T cells. This is in accord with a large body of work (reviewed Ref. [2]) documenting Treg upregulation following increases in IDO. Tregs can suppress the self-antigen directed B cells in autoimmune diseases such as systemic lupus erythematosus [3]. We conclude that increases in IDO has potential to enhance Treg function and suppress manifestations of lupus and related diseases.

The weak potassium sparing diuretic triamterene (2,4,7-triamino-6-phenylpteridine) is FDA approved and has been marketed worldwide for decades. An old study, interestingly, showed triamterene enhancement of IDO activity [4]! We suggest therefore that triamterene has potential to diminish activity of the autoreactive B cells of lupus.

(There are reports of subcutaneous lupus as a side effect of patients taking triamterene in combination with hydrochlorothiazide (e.g., Ref. [5]). However, we think an allergic reaction to a thiazide moiety.)

In vitro testing of triamterene increases of Tregs or observational studies/chart review of lupus patients current on triamterene for hypertension may provide evidence to warrant a controlled trial of triamterene in lupus. Such a novel approach would be a most welcome addition to treatments currently available for lupus.

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Historical “evidence” that electrification caused the 20th century epidemic of diseases of civilization and the ecological fallacy

The hypothesis that electrification is the cause for increased rates of “diseases of civilization” since the early 1900s in the US has been put forward in an article recently published in this journal [1]. Although the author presented a very interesting hypothesis that, if true, could have an important impact on current society’s relationship with electrical technology, his interpretation regarding causality of electrification as the main risk factor for increased population rates of cancers, diabetes, heart disease, suicide, and motor vehicle accidents is fraught with problems. Hereby, we would like to take the opportunity to address some of the more important ones.

The author’s argument for causality in individual patients is based on data observed at an ecological level and as such is a
textbook example of a phenomenon widely recognized in epidemiology as the “ecologic fallacy” [2]. Ecological associations do not necessarily reflect associations at an individual level which is an artefact of heterogeneity of risk factors within groups that are compared [3]. Arguably, ecological bias in the analyses presented by Milham is likely to be large because EMF exposure levels presumably differed widely between individuals within partly electrified urban or rural communities. More likely, however, is that the associations observed by the author are a consequence of differences in age structure and socio-economic predictors between urban and rural areas and southern and northern US states.

A fundamental problem with the ecological design not recognized by the author is that different predictors are more highly correlated with each other at an ecological than at an individual level [3]. In the rapidly industrializing society which forms the background of the analyses by Milham, occupational and environmental exposures to a wide variety of other chemical and physical factors, accompanied by simultaneous changes in socio-economic and life-style factors (also addressed in a previous commentary to this article [4]), will change at the same time and, likely, at differing rates in urban and rural communities. As a result the individual effects of the different predictors on disease rates are difficult to separate statistically in the work of Milham due to the lack of individual data [3].

In developing a hypothesis, scientists in the public health arena rely not only on observational ecological data but must also consider the biological plausibility of what they propose. This matter is completely ignored by the author, despite extensive debate on it in the literature [5–8]. It should be noted that the “plausible electrical exposure agent” (high frequency voltage transients) [9] put forward by the author is in fact far from considered scientifically proven [10], nor does this concept include a description of a plausible biological mechanism of effect. Secondly, different latency times for different diseases are also ignored in the presented analyses. The fact that comparable associations were reported for heart disease and diabetes as well as for cancers, regardless of known differences in latency periods between exposure and clinical manifestation of a disease – which can vary from zero up to several decades depending on the disease [11] – suggests that the reported result are due to either bias or confounding.

The reported changes in disease rates at the ecological level can also plausibly be ascribed to the presence of diagnostic bias. Advances in technology signalled by electrification were paralleled by a rise in quality of medical care and advances in time of diagnoses of common illnesses. This would explain the increase in cause-specific mortality while the overall mortality rate declines, as seen in the data. It would have been helpful to see the numbers for unknown causes of death, but this would not ensure that death rate estimates are not biased by changes of quality of medical care and age at diagnosis. The example of melanoma (unreferenced discussion in the introduction) is rather instructive in this regard. It is a notoriously difficult tumour to study because most cases are not reported and access to care would be the major determinant of estimates of its rates.

In conclusion, although the author presents an intriguing hypothesis, there are several fatal flaws with the way the ecological analyses have been interpreted and how the argument in support of the hypothesis was constructed. Although the author has every right to put forward his ideas in a journal dedicated to the presentation of hypotheses the methods used to assess a hypothesis should adhere to commonly accepted scientific standards; as such, this data preclude testing of the hypothesis that electrification is causally related to increased disease rates in the early 20th century in the US.

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Earphone: A new approach to enhance mandibular growth in class II malocclusion

Mandibular retrognathia is the major aetiology of class II malocclusion [1]. The treatment effects of mandibular retrognathia with traditional functional appliances remain unsatisfactory.

Base on the theory that static magnetic field is clinically safe and has the chondrogenic and osteogenic effects, Li hypothesized that the combination of static magnetic field with functional appliances can enhance mandibular growth in adolescence and suggested placing a permanent magnet in front of each ear (the site of the condyle) when the patient wore the functional appliance at night [2].

The minimum time of wearing functional appliance considered necessary for successful treatment averages 12.8 h for functional appliances, and the longer wearing time the better effect will obtain [3]. But many patients refuse to wear the functional appliances in the daytime because of the interference with speech. We can infer that increasing the wearing time of the magnet