Aspergillosis spores and medical marijuana

Thank you for the article[1] on the rare but catastrophic risk of inhaling aspergillosis spores, and for the warning, particularly for our immunocompromised patients, that this risk may rise with the inhalation of cannabis.

Part of Health Canada's responsibility is to assure consumers that the dried cannabis they purchase from our licensed commercial producers is safe and free from such contaminants. Some of these producers irradiate their cannabis specifically for immunocompromised patients, eliminating the risk of spore inhalation. As a doctor who prescribes medical cannabis over narcotics, primarily for harm reduction, this case report highlights the importance of getting our patients to switch to the safer irradiated cannabis now available to them.

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Clinical trial transparency

In a *CMAJ* news article,[1] Goldacre overlooks the estimated 30% to 50% of clinical trials that are submitted to the US Food and Drug Administration (FDA) in support of new drug approvals. These trials remain unpublished and have been available on the agency's website free of charge since 1998.[2–4] These documents are called "approval packages" and are detailed analyses conducted by FDA scientists. These packages must be made available to the public under the US Freedom of Information Act.

Regrettably, approval packages are infrequently used, throwing into question the validity of review articles based on the published literature, including meta-analyses, economic analyses and clinical practice guidelines.

Approval packages are much more than simple reviews of data submitted by manufacturers. They contain the number of events, benefits and harms, which is critical in assessing the therapeutic value of new drugs.

It remains to be seen what effect the Protecting Canadians from Unsafe Drugs Act will have on clinical trial transparency in the near term. In the interim, Canadians can access much of the information the AllTrials campaign is advocating for on the FDA website.

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An epidemiological paradox

I read with interest the *CMAJ* editorial on radon, this neglected known human carcinogen.[1] The majority of lung cancer deaths attributable to radon occur following relatively small exposure.[2] This is explained by a nonthreshold dose–response relationship and the fact that the great majority of homes have radon concentrations lower than the cut-off point for mandatory corrective measures.

This epidemiological paradox reminds us that integrating prevention measures into building codes should be the keystone of all interventions planned with a population approach, all other interventions being oriented toward high-risk individuals, with an efficacy and an efficiency at a population scale that are debatable.[3] In order to achieve any substantial impact, we would need a high radon screening rate of the highest at-risk population: smokers. In Quebec, we have estimated that 90% of radon-related deaths involve "ever-smokers."[4] Such observations have led some experts to state that "the public health problem of radon is, for the most part, a problem of radon and smoking."[5] Some experts have even recommended that smoking cessation campaigns incorporate advice regarding radon risk, screening and remediation.[6]

Such recommendations bring us to the frontier of a new, uncomfortable paradigm: promoting safe environments for smokers. One can legitimately question whether it is ethical to give smokers a false sense of security by intervening on radon while patients continue to smoke, however, the extraordinarily high cancer risks implied cannot be ignored. At 800 Bq/m^3 (the former Canadian Guideline for residential radon), the lifetime cumulative risk of lung cancer for a smoker is one in three, 10 000 to 100 000 times higher than the levels usually tolerated by environmental regulation. This exceptional situation could justify adopting a pragmatic risk reduction perspective. Such strategies have been put forward for other public health problems (e.g., illicit drug injections). Are we ready to move in that direction for radon?

Who knows, perhaps the most effective radon screening strategies are those no one is yet willing to talk about?

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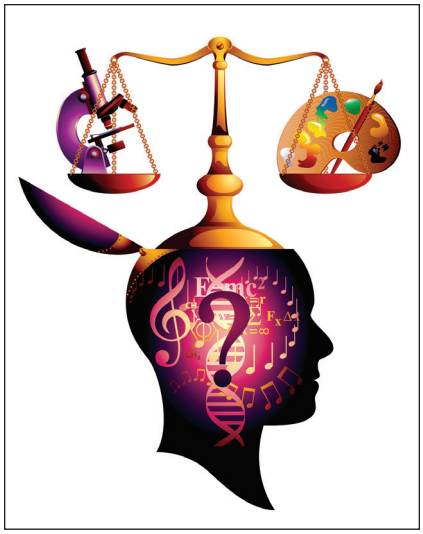
The art of medicine

In their *CMAJ* essay, Whitehead and Kuper[1] rightly note that dichotomizing medical teaching and practice into "science" and "art" is unhelpful and misleading. Montgomery[2] compares the science–art dichotomy to the wave-particle duality of light and argues that the term "art" is used to capture that which seems to defy scientific study, such as clinical judgment and bedside manner.

If we compare the art and science of medicine to the wave-particle duality of light, the science of medicine perhaps seems like the particle: solid, tangible, weighty, circumscribed. Meanwhile, the art seems like the wave: ethereal, intangible, elusive and ineffable. Ethereal things seem less real, like the luminiferous ether at the root of the word. When, near the end of the 19th century, Michelson and Morley set out to measure the ether, they discovered that it wasn't really there.[3] The ethereal image of clinical judgment is reinforced by voluminous research concluding that "mechanical predictions" (made using scientific rules or algorithms) consistently outcompete "clinical predictions" (made on the basis of clinical judgment).[4]



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On the other hand, the conception that the art of medicine is intangible, elusive and ineffable is reinforced by the presumption that it is unresearchable and unteachable. Art is creative genius, not to be disturbed. Such an attitude adopts a narrow view of scientific research as consisting in basic science and clinical epidemiology. As a philosophy graduate student and a medical student, I've learned that clinical judgment involves formal and informal reasoning, values, intuition and assumptions. All these components fall under the purview of philosophical study as well as scientific study, broadly construed to include not only basic science and clinical epidemiology, but also logic and the social sciences and humanities (including psychology, history and sociology).

Rather than denigrate clinical judgment and other components of the art of medicine as unscientific or exalt them as creative genius, we must teach them rigorously, and just as importantly, research them rigorously. Otherwise, like a light wave they will dissipate before our eyes.

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Long-term use of diphenhydramine

The review article in *CMAJ* by McMillan and colleagues concluded that there is a paucity of long-term safety and efficacy data for the use of non-benzodiazepine sedative-hypnotics such as diphenhydramine.[1]

A recently published prospective cohort study reveals a higher cumulative strong anticholinergic use is associated with an increased risk for dementia.[2] Anticholinergics include tricyclic antidepressants, bladder antimuscarinics and first generation antihistamines.

Harvard Health Blog brings attention to this study linking the common anticholinergic drug Benadryl to increased dementia risk.[3]

In addition to being a non-benzodiazepine sedative-hypnotic, Benadryl is also used as an antihistamine.

Benadryl may contain different antihistamines. In Vancouver, it is diphenhydramine; in London, United Kingdom, it is cetirizine; in Cophenhagen, Denmark, it is acrivastine.[4,5]

Benadryl-containing diphenhydramine is available in a number of countries worldwide including the United States, Canada, Singapore, Taiwan, Italy, Hong Kong and others. However, diphenhydramine is a banned substance in Zambia.

Patients should check the ingredients instead of relying on the brand name. Caution should be exercised for long-term use of Benadryl (diphenhydramine), an antihistamine and a non-benzodiazepine sedative-hypnotic, because of the association of increased risk for dementia.

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Letters to the editor

Letters have been abbreviated for print. See www.cmaj.ca for full versions and competing interests.