Book Reviews

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This book aims to describe ‘the role played by antioxidant nutrients in the prevention of chronic degenerative diseases and conditions’. More specifically the author states that the book provides an exhaustive description of the biochemistry of antioxidation and antioxidants, as well as of the pro-oxidants that generate oxidative stress, and a thorough discussion of the most important epidemiological studies carried out over the past two decades. The first three chapters provide a background for the biochemistry of reactive oxygen and nitrogen species, endogenous and exogenous antioxidant systems, and discuss potential pro-oxidant activities of vitamins C and E. I found these chapters informative, but as a non-biochemist I would have liked some stronger links between the different sections and the three chapters, more figures of the biological pathways, and some of the information that is provided in the appendices included in the body of these three chapters.

Chapters 5–8 in turn present epidemiological evidence for the role of vitamins C and E, and β-carotene in the aetiology of cardiovascular disease, cancer, cataracts, and aging. I found the selection of studies and their critique somewhat one-sided. In general results from observational studies conducted in the 1980s and early 1990s that suggested protective effects are emphasized whereas more recent studies, in particular randomized controlled trials, that question the role of antioxidants in the prevention of cardiovascular disease and cancer are either ignored or disregarded. For example, the results of the ATBC trial are overlooked on the basis that ‘Gey criticizes the lack of data on vitamin C (and other vitamins) consumption in the cohorts of interventional studies such as ATBC.’ (page 53). Such criticism fails to acknowledge that if randomization is adequate there should be no difference in vitamin C levels between the randomized groups.

Some of the comments made in general about epidemiological studies and the presentation and discussion of results of some studies showed a surprising lack of epidemiological knowledge. For example, in the discussion of types of epidemiological study and their potential limitations there is no mention at all of confounding. The discussion on randomized controlled trials does not mention their important advantages in terms of avoiding confounding and selection bias, nor their limitations, such as potential lack of generalizability, lack of power and loss to follow-up. Interestingly the author’s conclusion, largely based on the Nurses’ Health Study, is that large dose supplementation with vitamin E is protective against cardiovascular disease. One of the issues that has dogged this area of work has been the debate and uncertainty around the dose and the mode of delivery of antioxidant vitamins that are required for protection. Here the author is making a very definite statement about both the dose and mode of delivery of vitamin E for cardiovascular disease prevention. Unlike the difficulties of randomizing individuals to certain diets, randomization to a particular drug—whether it is a high dose vitamin E supplement, hormone replacement therapy or a new antihypertensive—is more straightforward and a randomized controlled trial would be a valuable way to test the author’s hypothesis. A recent meta-analysis identified seven large-scale well-conducted randomized trials of the effectiveness of vitamin E supplementation in the treatment and prevention of cardiovascular disease. Of the seven trials, six showed no effect of vitamin E on cardiovascular disease. The pooled estimate of effect from these trials suggested that vitamin E had neither a statistically significant nor a clinically important effect on any important cardiovascular event (odds ratio 0.98 (95% confidence interval (CI) 0.94–1.03) all events combined) or its components (non-fatal myocardial infarction 1.00 (95% CI 0.92–1.09); non-fatal stroke 1.03 (95% CI 0.93–1.14); or cardiovascular death 1.00 (95% CI 0.94–1.05)).

I was also concerned by the way in which results from studies reviewed by the author were presented and interpreted. Relative risks and odds ratios were frequently presented with no definition of the reference group. This was often not obvious. For example, on page 55 a table of three relative risks (with no CIs) from the Nurses’ Health Study—0.56, 0.56, and 0.58—are presented for doses of 100–250, 300–500, and >600 IU/d of vitamin E respectively, with no indication of the group to which these are compared (it should be noted that the Nurses’ Health Study do produce clear tables with reference groups and 95% CIs in their papers). The author seemed to misunderstand the meaning of 95% CIs and implied that there was a high level of certainty for the results he presented when in fact inspection of the original papers frequently shows this to be far from the truth. For example, on page 51 with reference to a case–control study conducted in Edinburgh in the 1980s it is stated that ‘The results showed that the risk of angina pectoris was multiplied by a factor 2.68 (with a confidence level of 95%)’. The meaning of this is unclear, and a naive reader might consider that it means we can be confident that there is a large effect. In fact, if one actually refers to the paper in question one finds that this result refers to the adjusted odds ratio for angina between the lowest and highest quintiles of vitamin E concentrations that was reported as 2.68, with a wide 95% CI—from 1.07 to 6.70.

The evidence for the role of antioxidant vitamins in the prevention of a number of adult chronic diseases remains unclear and confusing, which is why well-conducted systematic reviews of all of the evidence are required. In the area of cardiovascular disease and cancer meta-analyses of large randomized controlled trials suggest that there is no evidence that supplementation with these vitamins is beneficial. The authors of one review point out the importance of getting this message clearly across to the public since large amounts of
money are spent on vitamin supplements that are unlikely to be beneficial and the use of agents of proven lack of benefit, especially those easily available over the counter, may contribute to underuse of agents of proven benefit and failure to adopt healthy lifestyles. Unfortunately I did not find that this book provided a systematic and useful discussion or critique of the epidemiological evidence in this area.

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References


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Concerns that the MMR vaccine may increase the risk of autism—largely fuelled by a Lancet paper published in 1998—led to a fall in vaccine coverage to levels low enough for measles outbreaks to occur. Michael Fitzpatrick is a general practitioner and also the parent of a child with autism. Fortunately he is also a very good writer and has produced a readable, well-discussed book about the MMR–autism saga. The book is informative, detailed, and accurate. The objectives of the book are explicitly stated in the preface: to reassure parents about the safety of MMR; and to reassure the parents of children with autism that they have no reason to blame themselves over MMR.

A reviewer quoted on the cover states ‘Every health worker, parent, politician, and journalist concerned with these issues must read this brilliant book’. I would not go that far. For most parents, the preface and introduction are likely to be sufficient—between them presenting a convincing case that MMR does not increase the risk of autism. While for people with a lot of interest in the subject I would recommend the book, it is a somewhat relentless read on a single issue: there is no link between MMR and autism. However, it’s worth persevering, for there is a great deal of interest beyond this for the reader. There is a scary and fascinating chapter called Alternative autism. This includes, for example, a description of using lymphocyte extracts from donors to produce ‘immunity to autism’ in people affected by the illness. There are moving accounts of parents blaming themselves for their child’s autism, either because they had the MMR vaccine or simply because they feel guilty in some way. The long nights of guilt I felt as a mother, wondering what I done wrong to give him autism’, a quote from one parent. There are a few moments of light relief. The account of a study by Geier that reported a higher incidence of gait disturbance following MMR (given at age 1 year) than following DTP vaccine (given at several weeks of age) made me laugh out loud.

Fitzpatrick argues convincingly that the root of the problem lies with the media coverage. A rather strange sympathy for Wakefield and his theories among large sections of the media is clearly demonstrated. Why the MMR–autism link was such a major issue in the United Kingdom, but was largely ignored by much of the rest of the world, is the one issue the book does not really address. The book ends with the all too familiar call ‘more research is needed’. However, in this case, the call for more research into the causes of autism and interventions is clearly warranted to help the affected people and their families. If the MMR–autism scare produced anything good at all, it is an increased awareness of autism among the general public and greater interest in research in the area.

LIAM SMEETH


Statisticians have always used computational methods so perhaps there is no better way to start a 1070-page volume on computational statistics than with the truism ‘To do data analysis is to do computing’. The editors state in their introduction that the hallmarks of computational statistics are the use of complicated models, large datasets with both more observations and variables, and unstructured and heterogeneous datasets; heavy use of visualization, and, often extensive simulations: this handbook covers all of this.

One way to measure how much computational methods have both influenced statistics as well as been partially driven by it is to compare this handbook with two landmarks in computational statistics: Kennedy and Gentle’s Statistical Computing (1980) and Handbook of Statistics 9: Computational Statistics edited by C.R. Rao in 1993. Twenty five years ago there was no mention of resampling methods, density estimation, etc. The 1993 Handbook is much closer both in size (1066 pages) and in content to the present one, though it does not cover data mining procedures and MCMC, to mention two important...