

BOOK REVIEWS

Annual Review of Medicine, 2020. Mary E. Klotman, Michael S. Parmacek and Howard A. Rockman (eds). Annual Reviews, El Camino Way, P.O. Box 10139, Palo Alto, California 94303-0139, USA. Vol. 71. viii + 392 pages. Price: US\$ 118.00. ISBN 978-0-8243-0571-0.

The wonderful aspect about reading the latest research in the *Annual Review of Medicine* is that it overturns many of one's cherished views and opinions – some of which, of course, have been 'established truths' in medicine. This volume is no different. There are 26 articles spread over 377 pages and the topics include a spectrum, right from cancer and cardiovascular disease (always the most common topics) to osteoarthritis, asthma, HIV and others.

The first chapter is a good example to justify the first statement in this review. I must admit to having been a little sceptical about the very concept of bariatric surgery, a little over a decade ago, when it was relatively new. However, after interacting with my surgical colleagues and seeing their experience, I began to realize that I was wrong. This chapter illustrates how very wrong I was. Use of data over two decades and more than hundreds of thousands of patients has shown us that diabetes mellitus is indeed a 'surgical disease' as well and not just a 'medical disease' like we have believed for a century. Using various procedures, with sleeve gastrectomy being the most common, patients have managed to have long-term weight loss, better glycated haemoglobin (HbA1c) levels and reduced cardiovascular risk factors. Microvascular and macrovascular events are reduced (compared to those with respect to medical management of diabetes) and thus complications like retinopathy and nephropathy are also reduced. In fact, at the time of writing this review (September 2022), it has now been shown that bariatric surgery is also strongly associated with reduced incidence of different cancers.

Another area where I learned unexpected truths was in the field of atherosclerosis, until recently believed to be irreversible, but now known to be reversible. As the authors' state, atherosclerosis (and our understanding of it) is now making a U-turn. Of course, reversal of atherosclerosis has been known for half a century now. Regression of atherosclerotic plaques has been documented by angiography, intravascular ultrasound, optical coherence tomography, coronary computed tomography angiography, magnetic resonance imaging, etc. How-

ever, surprisingly – and happily – we now know that reversal of lifestyle and usage of lipid-lowering medicines results in greater reduction of cardiac events than would have been expected from the change in size of the atherosclerotic lesion. This is because of the stabilization of vulnerable plaques (lipid-rich, thin-cap atheroma) rather than merely a reduction in the size of the atheroma.

Likewise, cardiac amyloidosis (CA) we learn, is overlooked, underappreciated and (somewhat) treatable – and not rare and untreatable as is commonly believed. There are two types of CA – transthyretin CA (ATTR-CA) (which itself is of two subtypes, viz. wild type transthyretin (ATTR) and variant transthyretin) and immunoglobulin light chain CA (AL-CA). That diagnosis of CA is difficult is obvious when you learn that in one study, more than 30% of patients needed more than one year and had seen at least five physicians for an accurate diagnosis. ATTR-CA can be diagnosed (with a sensitivity and specificity percentage in the 90s) by bone nuclear scan, while AL-CA needs an endomyocardial biopsy. Endomyocardial biopsy offers the best material for diagnosis, but is, of course, a difficult procedure. Alternative methods such as anterior abdominal fat pad biopsy are only about 70% sensitive in advanced disease.

Yet another subject that took me by some surprise was on male hormonal contraception. The options in female contraception are many, but have various side-effects and varying failure rates. For males, vasectomy is an invasive procedure with poor rates of reversal while condoms have high failure rates. Thus, there has been ongoing research in male contraception for some decades too. However, as is well known, we have not made great advances. The block in progress is because hormonal methods – which aim to suppress the rate of sperm formation – result in far too many side-effects such as pain, acne, weight gain, mood changes, etc. Besides, there are racial variations in the rate of sperm suppression. Asians are more susceptible to the effects of the exogenous hormone: in studies where almost all Asians have achieved azoospermia, only about half the number of Caucasian males had achieved this effect. Further, studies have not been performed on Latinos and Africans/African-Americans. All of this and more reasons suggest that testosterone-based contraception is still some time away. Hence, hormonal methods without testosterone are now being considered. Gonadotropin-releasing hormone antagonists, novel androgens such as MENT (7-alpha-Methyl-19-norte-

stosterone) and a 'male pill' are among them.

Fundamental changes in the field of medicine keep taking place and one of them involves the replacement of surgical therapy by medical management or, at the very least, by non-surgical management. Transcatheter mitral valve replacement is a perfect example of the latter. The mitral valve in the left heart may be impaired and result in mitral regurgitation. This may be because of mitral valve degeneration of various aetiologies or due to cardiomyopathies. Surgical repair, in cases where it is indicated, has been effective. However, the use of a transcatheter approach avoids open surgery, which has a greater than 5% mortality, with the benefits of also avoiding cardiopulmonary bypass (and its many possible complications). The procedure is, of course, technically complex and can be applied only to a select group of patients based on specific anatomic or clinical reasons. MitraClip is the only device in use currently, but there are more than 30 devices under development.

Irritable bowel disease provides an example of an ailment that we know very little about, especially its aetiology and pathogenesis. Patients with irritable bowel disease present themselves with diarrhoea or occasionally constipation. Investigations, including endoscopy and biopsies, yield no useful information. Yet, this condition, that patients and doctors are uncomfortable dealing with, we now know, may have some solutions. Patients are recommended to go on a low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diet. For instance, foods which have a high FODMAP content (and which should be avoided) include wheat, mangos, apples, dates, onions, mushrooms, cauliflower, milk, yogurt, most beans, processed meats, rum, etc. To those of you who are wondering what indeed is left for one to then survive on, here is a partial list of foods with low FODMAP – potatoes, rice, grapes, lemons, papayas, pineapples, carrots, cucumber, spinach, tomatoes, most cheeses, lentils, chicken, eggs, fish, coffee, beer, etc. An obvious drawback with this diet is the resultant nutritional deficiencies that may develop, as well as change in the gut microbiome (about which, I discuss later).

About a decade ago, researchers made the discovery that the hitherto term of 'non-small cell carcinoma' (NSCLC) of the lung, which clubbed squamous carcinoma and adenocarcinoma would need further categorization, because drugs specific for the

subtypes of NSCLC had been developed. Targeted therapy, for example, exists for adenocarcinomas of the lung which express EGFR mutation, ALK and ROS-1 rearrangements, BRAF V600E mutation and NTRK fusion genes.

Another significant advance – which resulted in a Nobel Prize in 2018 – is that of immune checkpoint inhibitors. Tumour cells evade the cells of the immune system by expressing immune checkpoints to disrupt the function of cytotoxic T cells, which then undergo apoptosis. Monoclonal antibodies against PD-1 and PDL-1 block these immune checkpoints and help sustain the activity of T cells, and thus fight the cancer. The presence or absence of driver mutations as well as geographic variations (according to the data available on East Asians and Caucasians) in the mutations and gene arrangements mentioned above illustrate how medicine in the near future will necessarily have to be personalized.

The human microbiome which consists of commensal bacteria – and now considered by some to be an organ by itself – has been in the news for about a decade now and two chapters are devoted to specific aspects of the microbiome. Changes in the microbiome are associated with various diseases. One chapter deals with the microbiome anomalies in allogeneic haematopoietic cell transplantation, while the other is on the role of diet in the relationship between gut microbiota and cardiometabolic disease.

Allogeneic haematopoietic stem-cell transplant affects the diversity of the microbiome because of the effects of chemotherapy, radiation and donor haematopoietic cells. Antibiotics which are used to prevent and treat infections also impact the composition of the microbiome. Remarkably, even the timing of the treatment matters. Patients who have received the antibiotics prior to transplant have poorer outcomes than those who have received them post-transplant. Besides, *Clostridium difficile* infection which manifests as diarrhoea in the peri-transplant period is also exacerbated by the change in the gut flora caused by the antibiotics. Finally, graft-versus-host disease is another serious complication of the transplant and is related to the host microbiome. Whether the donor's microbiome also has an effect on graft versus host disease is yet to be resolved. It has been hypothesized that damage to the intestinal microbiome can be reduced and can result in better patient outcomes. This attractive hypothesis needs to be tested; but it has limitations, prime among them being methodological

ones which are related to determining the exact composition of a person's microbiome. Strategies to modify the microbiome also include modification in the diet, use of prebiotics and probiotics as well as faecal microbiota transplantation.

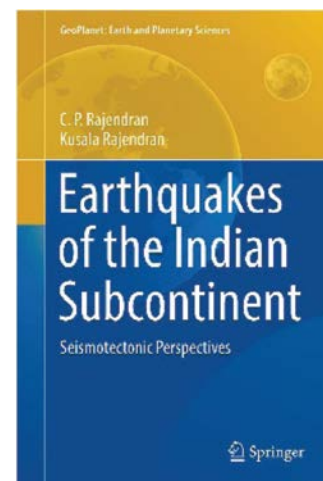
That diet is linked intimately to the microbiome also indicates that another disease that is intricately linked to the diet is also affected by the microbiome – the disease in question, of course, being cardiometabolic disease. The problems of interpreting dietary studies is clear when one realizes that there exists a substitution effect: when we compare a high-protein and a low-protein diet, we are also simultaneously comparing a low-carbohydrate/low-fat and a high-carbohydrate/high-fat diet.

Even in this age of omics, brilliant discoveries can be made from routine tests which have been around for more than a century. The chapter on asthma gives us one such example. We have known for decades that the sputum in asthma contains eosinophils. Yet, in the early part of this century, it was realized that sputum count could be used to adjust treatment doses. Based on this finding, those with high eosinophil counts in the blood and sputum are treated with the monoclonal antibody mepolizumab. In fact, a new subtype of asthma has now been defined, called severe eosinophilic asthma. Cutting-edge therapy also exists for asthma. While bronchodilators and steroids have been the mainstay for the past half century, we now have new options like monoclonal antibodies. Besides mepolizumab, there are others too – omalizumab (which inhibits the activity of IgE), benralizumab (which inhibits the actions of IL-5 receptor) and dupilumab (which inhibits the actions IL-4 and IL-13). The latest approach for the treatment of this 'medical' disease is to anatomically alter the airway. Patients with severe asthma may now undergo bronchial thermoplasty, which consists of delivering radiofrequency energy via catheters in the bronchial tree. This results in reducing the mass of the smooth muscle, which is hyperplastic, hyper-reactive and hypertrophied in asthma.

As I stated at the beginning the *Annual Review of Medicine* makes you question your cherished ideas.

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Earthquakes of the Indian Subcontinent: Seismotectonic Perspectives. C. P. Rajendran and Kusala Rajendran. Geo-Planet: Earth and Planetary Sciences. Springer Nature Singapore Pte Ltd, 152 Beach Road, #21-01/04 Gateway East, Singapore 189721. 2020. 253 pages. Price: €29.99. doi.org/10.1007/978-981-16-4748-2.

In the Preface of this book, the authors pose a question, 'Why another book on this topic'? This is a question commonly posed whenever a new book comes out. The answer to this question (according to one of my teachers) is 'because there are so many books on the topic, here is yet another one' (which brings more clarity and comprehensiveness).

Albeit a plethora of scientific literature on earthquakes of the Indian subcontinent, most of it exists in the form of focused research papers. Thus, for a geoscientist interested in comprehending the genesis of Indian earthquakes and understanding their diversity and common characteristics, it is highly desirable to access this information at one place. This book serves the purpose since the authors succeed in synthesizing all the information on recent and historical earthquakes from a seismotectonic perspective. Rajendran and Kusala Rajendran have pioneered earthquake studies over the past three decades, and have extensively investigated almost all the prominent earthquakes in India and adjoining regions. With increasing instrumentation and our understanding on earthquake occurrence, the amount of data to describe an earthquake and its rupture process, keeps increasing with each new one, thereby populating the number of articles. At the same time, lack of instrumental data resulting mostly in qualitative information on historical and prehistoric earthquakes, poses non-uniqueness