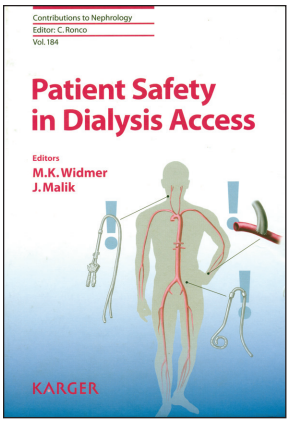
Book Reviews

Patient Safety in Dialysis Access. M.K. Widmer, J. Malik (eds). Karger, Basel, 2015. *270 pp, prince not mentioned*. ISBN 978–3–318–02705–1.



This book is aimed at the principal precept of bioethics: *primum non nocere* that means 'first, do no harm'. Chronic kidney disease (CKD) is now recognized as a public health problem and its burden is rising worldwide. End-stage renal disease (ESRD) is the natural culmination of progression of CKD, and maintenance dialysis is the main life-saving therapy for ESRD. An analysis revealed that in 2010 approximately 2 million patients were on dialysis around the world and the numbers are expected to more than double in the next two decades. Dialysis is an intense procedure in terms of resources, associated risks and morbidity. The performance of dialysis is essentially dependent on long-term functional dialysis access (vascular or peritoneal). With so many stakeholders in the care of ESRD patients, not limited to the dialysis nurse and nephrologist, the issue of patient safety is of paramount importance to save lives, and prevent unnecessary morbidity and mortality.

The book is organized succinctly in the form of various chapters addressing all aspects of planning, conceptualization, execution, monitoring and management of specific complications of dialysis access. The biggest success of the book lies in converging the reader's focus to the issues related to patient safety or more specifically errors in healthcare delivery. The first chapter 'Patient safety: What is it all about' is a fine elaboration of various aspects and definitions of medical errors, slips, lapses, omissions, adverse events, etc. This informs readers on the nuances of approaching the subject. It emphasizes that knowing right is not a guarantee of doing the right thing especially with the care of patients with ESRD being so fragmented. The other stimulating chapter on 'Simulation in vascular access surgery' introduces with examples the utility of simulation. The best part of this chapter is the observation that the healthcare industry can learn a lot from the commercial aviation industry with their unprecedented safety record facilitated by simulation. This chapter seamlessly gels with the next chapter on 'Team training to establish a safety culture in dialysis access surgery'. Herein the concept of checklists and their utility is brought up elegantly with good tables and sample checklists. This chapter places in perspective the human and organizational factors and 'error chain' analysis. These chapters are ably complemented by the well-written section on 'The patient's role in patient safety and importance of a dedicated vascular access team' placing the emphasis on patient-centric communications and the patient's proactive involvement. It also introduces various aspects of communication barriers that are often the cause of medical errors.

If these chapters are set aside, the other sections are informative pieces on various technical and operational aspects of dialysis access with discussions on the usual complications, their prevention and management. Some sections are devoted substantially to the definition of CKD or aspects of pharmacology in CKD, which seem unnecessary. In fact, many chapters blur the perceived gap a reader expects between medical errors and medical complications of procedures. The avoidance of complications is within the broad ambit of patient safety. But, the title and theme of 'patient safety' induces thinking on the lines of errors and various unexpected situations beyond the realms of known complications or adverse events. A more apt title for the book could have been 'Improving outcomes and safety of patients on dialysis'.

Nevertheless, the book presents a vast amount of information and advice on many aspects of dialysis access making it a good repository of information. However, the shifting focus between patient safety and standard medical information thwarts it from being a comprehensive book on the latter part as well.

It is a lucid read with many fine pictures and illustrations. Some case studies would have added more spice to it. Also, a multimedia link or CD-ROM with the book would have added a fillip.

Overall, a readable and informative book but leaves the reader wanting for more depth and incisiveness.

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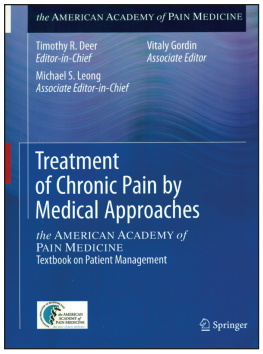
Treatment of Chronic Pain by Medical Approaches. Timothy R. Deer, Vitaly Gordin, Michael S. Leong (eds). Springer, New York, 2015. *219 pp, price not mentioned.* ISBN 978–1–4939–1817–1.



Chronic pain is one of the most prevalent and costly problems in both the developed and the developing world today. For this condition patients seek care from various healthcare providers irrespective of their specialty. This type of pain causes much suffering and disability and is frequently mistreated or undertreated. As we learn more about the complex issues of pain, it is becoming important to have physicians with specialized knowledge and skills to treat patients with these problems. An in-depth knowledge of the physiology of pain, the ability to evaluate patients with complicated pain problems, understanding of specialized tests for diagnosing painful conditions are all used by a healthcare provider to treat pain. With an increasing number of new and complex drugs becoming available every year for the treatment of pain, the specialist physician has to be adequately trained to use this new knowledge safely and effectively to help her/his patients.

The American Academy of Pain Medicine (AAPM) has a strong scientific presence in medicine and, in particular, pain medicine, and this has been well reflected by the compilation of *Comprehensive treatment of chronic pain by medical, interventional and integrative approaches: The American Academy of Pain Medicine textbook on pain management*. The book under review covers a spectrum of medical approaches used in management of pain.

It is a clinically focused resource on pain management and is designed as a practical and comprehensive primary reference for busy physicians. Each chapter starts with a highlighted 'Key points' preview, which sums up the contents of that chapter and simplifies the subject. The book starts with a recap of the neurophysiology of pain, beginning at the periphery and its receptors and moving on to a detailed discourse of central pain pathways and complex neuroanatomical and neurophysiological relationships. The authors then approach the taxonomy of analgesics with exemplary clarity. There are tables that provide clear information and compare the different existing taxonomies. On reading further, it is apparent why all of us are confused with such classifications—there appears to be no consensus on the correct one to use in everyday practice, or indeed when teaching.

The next chapter explores specific pharmacological pain targets in detail: the cannabinoid system, the cyclo-oxygenase pathway, opioid pathways and the 5-HT receptor system. The authors provide a commendable delineation of the exact modes of action of drugs, at both the receptor–effector and microcellular levels. It is clear while going through the references that a vast amount of work has gone into this section.

Further chapters focus on special topics within pain pharmacology such as description of addiction and tolerance, from a theoretical and evidence-based perspective. The neurophysiological pathways concerned are discussed revealing that things are far more complicated than we presumed.

Currently, opioids are regarded as among the most effective drugs for the treatment of pain. Their use in the management of acute severe pain and chronic pain related to advanced medical illness is considered the standard of care in most of the world. In contrast, the long-term administration of an opioid for the treatment of chronic non-cancer pain continues to be controversial. Concerns related to effectiveness, safety and abuse liability have evolved over decades, sometimes driving a more restrictive perspective and sometimes leading to a greater willingness to endorse this treatment. Six chapters (i.e. 10–15) are devoted to the clinical use of opioids in the management of chronic pain and their adverse effects. These chapters discuss very well the issues of opioid dependence, opioids and the law, and toxicology screening of opioids.

Patients who seem to lie outside the 'norm' are described well in the chapter on pharmacogenetics of pain. This gives us some idea as to why one patient in recovery seems to have emptied the cupboard of analgesics, while the next patient is 'narcotized' after a minute quantity. The reasons are complex, particularly when the list of genes identified extends well into double digits.

The book ends with a chapter on polypharmacy and drug interactions which gives an in-depth coverage of interactions of commonly prescribed drugs. Also, the chapter on future of pain pharmacology gives a good insight into newer drugs and research and development.

Overall, the book provides a good clinical approach to the pharmacology of pain, including in obstetrics, paediatrics, the elderly, obesity and palliative care.

In summary, this is a fabulous book from the beginning till the end. It offers a wide and experienced knowledge base, backed up by a vast array of clinical and non-clinical research. We would recommend it to those interested in this ever-expanding field of pain management.

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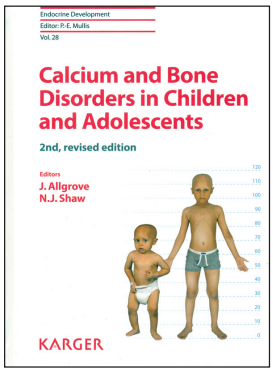
Calcium and Bone Disorders in Children and Adolescents. J. Allgrove, N. J. Shaw (eds). Karger, Basel, 2015. *433 pp, price not mentioned*. ISBN 978–3–318–05466–8.



This second, revised edition of the book is the 28th volume in the series on Endocrine Development published by Karger. Recent advances in understanding of the pathophysiology and genetic basis of diseases as a result of rapidly evolving genetic technologies inspired the editors, Jeremy Allgrove and Nick Shaw to come up with the second edition of the widely successful book by the same name published in 2009.

The layout of the chapters is largely the same as in the first edition. Chapters on skeletal dysplasia, genetics of osteoporosis, skeletal imaging and approach to a child with recurrent fractures are the important additions. The initial chapters dealing with physiology of bone, physiology of minerals and vitamin D and the dynamic endocrine control of bone and mineral metabolism provide sharp and clear concepts to help understand the various pathological states of metabolic bone disorders. The added chapter on radiology of important bone-related pathology further enhances the understanding of various disorders.

Characteristic features on imaging are also written in detail in the chapter on skeletal dysplasia. The chapter on bone mineral density provides a fair amount of information regarding interpretation of DXA (bone densitometry) and quantitative computed tomography. The clinical chapters which follow provide well-balanced knowledge regarding the pathophysiology, clinical approach, diagnostic tools and management. The authors have taken care to provide details regarding the molecular and genetic basis of bone and related metabolic disorders. The OMIM (Online Mendelian Inheritance in Man) entry number of the genetic disorders and the related genetic defect has been provided for further reference and reading. Disorders of magnesium and phosphate metabolism have been comprehensively discussed. The chapters on secondary osteoporosis and approach to recurrent fractures in children are important additions for a clinician. The chapter dealing with drugs used in bone and related metabolic disorders is up-to-date and provides a good insight on newer emerging drugs. The chapters on the classification of bone and

calcium disorders cover most of the related disorders. The unique case capsules series of this book has further extended its spectrum in the second edition and provides meticulously documented case details of 95 patients, covering most of the bone and related metabolic disorders. These case histories are comprehensive with adequate information on relevant investigation, management, progress of the patient on therapy, molecular genetics of the disorder and key learning points.

The book at its core is clinically oriented with great insight into genetic and molecular pathophysiology in a compact but easy-to-read manner. The rich content of the chapters will be useful and comprehensive for clinicians well-versed with background concepts of bone and mineral metabolism and its disorders. Endocrinologists, clinical geneticists and paediatric orthopaedicians would find this a concise reference for their routine academic and patient care needs. The chapters on approach to hypocalcaemia and hypercalcaemia, rickets, secondary osteoporosis and radiological imaging would be helpful to paediatricians for correctly evaluating and managing these commonly encountered disorders. However, a more detailed coverage of renal tubular acidosis would have been useful. Inclusion of reference data for bone density would have added to the utility of this information-rich book. Further, a more detailed section on long-term management of primary osteoporosis with bisphosphonates would have been helpful for clinicians treating cases of osteogenesis imperfecta.

This book is highly recommended as a concise and up-to-date reference for clinicians and teachers dealing with bone, calcium and other related metabolic disorders in the field of paediatrics, endocrinology, genetics and orthopaedics.

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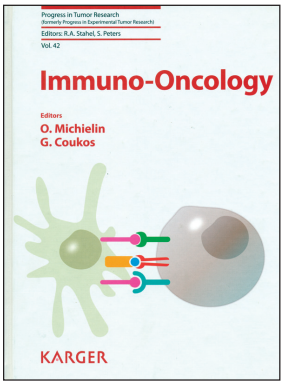
Immuno-Oncology. O. Michielin, G. Coukos (eds). Karger, Basel, 2015. *140 pp, CHF 198*. ISBN 978–3–318–05589–4.



Systemic therapy in oncology has been dominated by cytotoxic chemotherapy for the past several decades. Though immunotherapy (interferon and interleukin) is almost as old as cytotoxic therapy, its use in recent past has slowed down. Advances and knowledge in the field of molecular oncology has led to the discovery of many new molecules mainly for targeted therapy. These agents are considered not only equal or more effective but possibly less toxic. However, for the past few years the same knowledge has made immuno-oncology and immunotherapy the new buzzword in the field of oncology. Understanding of cell cycles, check-points and programmed cell death protein (PD-1) and its ligand (PD-L1) receptors and monoclonal antibodies against these is the latest in many cancers including melanoma, renal cell carcinoma (RCC), lung cancer, and a number of solid organ and haematological cancers. Cytotoxic T lymphocyte-associated protein 4 (CTLA-4) antibody (ipilimumab), PD-L1 antibody (pembrolizumab), and PD-1 antibody (nivolumab) have been approved by the US Food and Drug Administration (FDA) for treatment in melanoma and non-small cell lung cancer. For all these, the American Society of Clinical Oncology (ASCO) has rightly chosen immunotherapy as the 'clinical cancer advances of the year' in its *Clinical Cancer Advances 2016* report.

The editors of this book have compiled the important recent literature and evidence for immunotherapy in different cancers from antibodies to chimeric antigen receptors (CARs). The prototypes are melanoma and RCC. The book begins with a description of new immunotherapy in these cancers. The three main agents being used are ipilimumab, pembrolizumab and nivolumab. The book highlights how two randomized studies published in the *New England Journal of Medicine (NEJM)* led to the approval of anti-CTLA-4 agent ipilimumab by the FDA in 2011. This was the first study to show the survival advantage of any agent in metastatic melanoma. Since then, it is but natural that this agent needed to be studied for use as a first-line single agent, first-line in combination and also in adjuvant setting. Other agents such as nivolumab and pembrolizumab have also undergone various phases of clinical studies and are showing their usefulness in second-line treatment. How these molecules work has been covered in different parts of the book. In the chapter on melanoma there is only one figure and it would have been better if it was in colour. Similarly, the current and emerging role of immunotherapy in RCC is covered.

It is being increasingly appreciated that the immune system participates in both the development and elimination of tumours. Immuno-editing is the process by which the immune system provides protection to the host from development of a tumour and helps in elimination of tumour cells. This is useful information for an average reader who is not familiar with immunology.

Interestingly, this book explains that radiotherapy, which until now was considered to cause its anticancer effect by DNA damage and cell death, has more to it than that. It is becoming clearer that radiotherapy changes the immune composition of the tumour and upregulation of major histocompatibility complex I (MHC 1) and cancer-testis antigens. Initial studies have shown that radiotherapy changes the cytokine pattern, tumour phenotype and induces immunogenic cell death. Similarly, it has been explained how the interaction between the immune system and chemotherapy and targeted therapy occurs. Contrary to the belief that combination of cytotoxic chemotherapy and immune-therapy may be counter-productive, some studies question the detrimental effect of such an approach.

The chapter on T cell engineering explains how T cells can be manipulated for use as a weapon for cancer cells. T cells are naturally specific against various antigens and possess cytotoxic activity. By way of gene transfer, T cells can be manipulated to express CARs. These so-redirected T cells are composed of three domains: an extracellular antibody-derived antigen recognition domain, a transmembrane domain and a cytoplasmic signal domain. This way it works as a specificity of an antibody with the cytotoxic machinery of a T cell. Compared to monoclonal antibodies, which are usually

rapidly removed from the cancer cell surface by various mechanisms such as capping, shedding or endocytosis, T cells are being tested to overcome these limitations. This is a complex procedure. The accompanying cartoon tries to explain how this is achieved: (i) T cells are collected by leukapheresis; (ii) T cells are activated using antibodies (*ex-vivo* expansion); (iii) T cells are transfected or transduced with a gene construct encoding CAR; and (iv) further expansion of the gene-modified cells. The final formulation after few more steps can be frozen and stored for clinical use. Early clinical studies in B cell haematological malignancies and solid cancers have been completed with mixed results.

The effectiveness of nivolumab is aptly highlighted in the chapter on lung cancer. This is interesting as in comparison with melanoma and RCC, which are known to be responsive to bio-therapy or immuno-therapy, no such evidence was available for non-small cell lung cancer. Nivolumab has been approved for both squamous and non-squamous, non-small cell lung cancer.

The book is readable and the appearance is good. However, the first chapter itself could have covered immune check-point inhibitors and historical aspects. This would have been useful for a beginner. The book has done justice to its name and possibly its shelf-life is 3–5 years when new knowledge is likely to be available. This is because currently a number of clinical studies are ongoing in a variety of cancers. A glance at *clinicaltrials.gov* using the search criteria of 'immune-therapy in cancer' reveals that >1100 different clinical studies are either ongoing or have been completed. Assuming that a small fraction of these will add new molecules to our therapeutic armamentarium, this book will need revision.

Lastly about the price. The book is priced at 198 Swiss Franc (CHF) which is close to ₹13 800—on the higher side from the Indian perspective.

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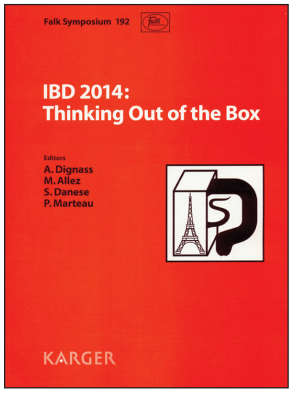
IBD 2014: Thinking out of the box. A. Dignass, M. Allez, S. Danese, P. Marteau (eds). Karger, Basel, 2015. *132 pp, price not mentioned*. ISBN 978–3–318–02806–5.



This book narrates the proceedings of the Falk symposium IBD 2014. It covers different areas of the pathophysiology of inflammatory bowel disease (IBD) and newer avenues for its management. Importantly, it defines the current role of immunosuppressives and biologics in the management of IBD.

The book begins with updates on the natural history of IBD, which seems to be more favourable compared to that based on previous research. The results of 20 years' follow-up in the Inflammatory Bowel Disease in Southern Norway (IBSEN) study are discussed. This suggests that the natural course of the disease in an individual patient can be predicted on the basis of identified prediction matrices. Newer data have been presented, which not only improves our knowledge about the natural course of the disease but could more accurately predict the risk of colorectal cancer (CRC) in patients with IBD.

H. Sokol defines the current role of probiotics and antibiotics in IBD and explores the manipulation of microbiota through probiotics, antibiotics and barrier enhancers that could target early treatment of IBD. Here a discussion on faecal transplantation, which is considered the best probiotic and is currently in the limelight as a potentially promising therapy in IBD, could have been added; maybe even as a separate chapter.

The section on fibrosis in IBD is a good aggregation. This moves from the basics of why and how fibrosis happens to an informative account of the current state of investigation on profibrogenesis. This is followed by the clinical science of management of fibrotic complications. The possible option of endoscopic balloon dilatation as an alternative to surgery in uncomplicated fibrostenotic Crohn disease would actually alter or enhance the clinical practice algorithm. The insight on the future development of effective pharmacotherapy—an area that is largely unexplained, is interesting. The authors attempt to extrapolate data from therapy of pulmonary and liver fibrosis to intestinal fibrosis in IBD. The combination of chapters in this section ensures that both basic scientists and clinicians would gain a broader perspective.

Newer therapeutic approaches that are at a nascent stage such as mesenchymal stromal cell therapy and immune cell therapy have been described with details of current and earlier studies. This can be useful as a ready-reckoner for researchers on these newer targeted therapies, which can change the future treatment of IBD. Different novel molecules that target underlying immunodeficiency in IBD or early intestinal barrier or dysbiosis have been summarized. The role of parasites such as *T. sueis ova*, phosphatidylcholine, barrier stabilizers such as peroxisome proliferator activated receptor (PPAR)–γ agonist and sodium chlorate has been mentioned. Many of these molecules are far from the arena of clinical practice. Yet different pathways that can be useful in treating IBD have been defined, and could stimulate further research. Curcumin, an active ingredient of turmeric, with its anti-inflammatory properties has shown promise in recent placebo-controlled trials. Additionally, direct leucocytes trafficking by different pathways can enhance the therapeutic armamentarium in IBD. Relevant clinical trials are also described in detail.

These agents are the need of the day as at present there are few options for patients resistant to biologics. These new molecules can be useful in changing the future management of IBD and can target the basic category of IBD.

The section on the best use of biologics is precise and concise for gastroenterologists. Biologics were considered a magic pillar of treatment of IBD in the past decade. Today loss of response to biologics is increasing among such patients. Additionally, with a rising incidence especially in the emerging world, the cost implications are large. In this scenario, the role of biosimilars in treatment of IBD is often unclear to the practising physician. As pointed out, biosimilars are here to stay and can prove their mettle in IBD as in rheumatology. The authors emphasize the need to develop guidelines to optimize the use of these agents and give a

concise review of these promising agents synthesized chemically, which 'look alike but are not the same' as biologics. Similarly, biological therapy needs to be tailored according to the risk profile of individual patients and therapeutic drug monitoring as patients with IBD have varied clearance of biologics. It may be costly to monitor drug levels, but it can be cost-effective as it can reduce overall drug costs by optimizing drug dosage and response.

The chapters on the use of immunosuppressants are well written. The readers are reminded that the long-tested efficacy of immunosuppressants should be explored and is often an effective low-cost option.

The complex pathogenesis of IBD is based on environment factors, genetic make-up, gut microbiota and the immune system. The recognition of a unique concept of an IBD interactome or IBD integrome composed of the exposome, genome, microbiome and immunome which interact with each other is interesting. This is important because numerous bioinformatic tools are now available which would and could herald an era of personalized medicine in IBD.

Surgeons and clinicians will read the book for clinical management and literature on aspects of complicated IBD. The book describes step-wise multidisciplinary management algorithms for abdominal abscess in Crohn disease and refractory proctitis, which are often management dilemmas in clinical practice. There are adequate discussions on whether all patients with refractory ulcerative colitis need procto-colectomy, and on comparisons between two- and three-stage restorative proctolectomy with ileal pouch–anal anastomosis (RP-IPAA for RDUC). The book also describes preoperative management issues such as withdrawal of biologics and review of nutritional status, which again are questions with no clear-cut answers.

The book describes some grey areas of IBD therapy including the pros and cons of anti-tumour necrosis factor or immunosuppressive therapy, possible guidelines on commencing immunosuppressive therapy, drug holiday before re-administration of these agents and careful selection of patients who would benefit from these immunosuppressives.

Thus, the book focuses on the unmet and sometimes unclear needs of IBD management. It enlightens us about the management of IBD in complex situations and potential new therapeutic arenas just round the corner. It also throws light on different pathogenetic mechanisms of IBD, fibrosis, animal models of IBD research and natural history of IBD.

This book is a must-read for IBD investigators. Even the most complex pathogenetic mechanism is well-illustrated in a readable manner. It also serves as a ready-reckoner of upcoming novel therapies in IBD. It tries to provide evidence-based answers to difficult clinical scenarios especially in complicated IBD. This book is also a good read for clinicians, surgeons and therapeutic endoscopists interested in the management of IBD. The discussions on pathogenesis may seem too complex for general IBD practitioners but even the most complex pathogenetic factors have been described in a relatively simple and detailed manner considering the complexity of IBD.

On reading this book, the thought that comes to one's mind is that it focuses on selected areas. However, the reader cannot guess from the title which area of IBD is included. The chapters move from environment to fibrosis to cell-based therapies and then suddenly there is the immunosuppressives and clinical case-based marathon. The book might have done better if only the newer pathological and treatment options (thinking out of the box) were discussed.

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