Annual Review of Medicine, 2017. C. Thomas Caskey, Mary E. Klotman and Peter Scardino (eds). Annual Reviews, 4139 El Camino Way, P.O. Box 10139, Palo Alto, California 94303-0139, USA. Vol. 68. vii + 487 pages. Price: US$ 107.

This volume of *Annual Review of Medicine* as in the previous years contains enlightening updates on several medical problems of current interest. There are 33 reviews in this expertly composed compendium.

Viral diseases are the theme of five reviews. Lo and colleagues provide the public health concepts obtained from the epidemiology of the West Africa epidemic of Ebola virus disease which affected a total of nearly 30,000 people. The epidemic was an important pointer to global relationships and common susceptibility to infectious diseases. Nearly 50% of Ebola survivors across three countries have persistent symptoms which provide a means to further understand reasons for viral persistence in these survivors. Ebola's natural reservoir is not yet identified. Inadequate surveillance and response capacity have been identified as salient factors in the spread of the epidemic.

Keshwara *et al.* survey the progress in the efforts to develop Ebola virus vaccine. DNA, Δ VP 30 whole virus, virus-like particles, nanoparticle vaccines and other agents have been evaluated in clinical studies. A safe and efficacious vaccine has not yet emerged. Be that as it may, there is hope that the advances made until now would help limit the severity and duration of the outbreaks.

Interferon-free direct-acting anti-viral (DAA) is a great revolutionary progress in the treatment of hepatitis C virus (HCV) infection. The eradication rates are more than 95% for the HCV-infected, including those with co-infection and end-stage renal and liver diseases. Naggie and Muir discuss the various anti-viral combinations with DAA, their mechanisms of action and treatment regimens for chronic HCV infection. There are issues of DAA failures and of resistance to be overcome in select patient groups. The high cost of DAAs is also a worry in low- and middle-income countries. Another concern is that the potential benefit of DAA therapies in children, pregnant women and nursing mothers is presently unclear.

An exciting strategy on the horizon to treat chronic viral diseases is the use of CRISPR/Cas for gene editing and viral elimination. This is expected to evolve into popular use to target pathogenic DNA viruses. The potential viral targets are those of hepatitis B virus, herpes simplex viruses and human immunodeficiency virus type-1. Kennedy and Cullen delineate the likely benefits and challenges of the gene editing approach.

Middle East respiratory syndrome (MERS) caused by MERS-corona virus is endemic in camels in the Arabian Peninsula and Africa. The virus can infect humans and mutants pose the threat of human-to-human transmission. MERS cases have been identified in 27 countries since 2012. There are no specific drugs or vaccines for MERS. Fehr *et al.* scrutinize pathogenesis, clinical and pathological features, current efforts on establishing diagnostic criteria and for identification of measures to control transmission of MERS.

The first article in the volume is on the clinical benefits and cost-effectiveness of cardiac implantable electronic devices (CIEDs) used for the treatment of patients with a variety of cardiac rhythm disorders. These devices consist of both different types of pacemakers and defibrillators. During the last three decades, these devices have been critically evaluated for their cost-effectiveness, effect on patient survival, quality of life and public health impact. Yet, several critical issues that affect assessment of value of CIEDs have not been entirely addressed. These include variability in the degree of benefit in individual patients and whether the clinicians follow any guideline criteria in the selection of patients for CIED, device replacement strategies, management or deactivation of implantable cardioverter defibrillators (ICD) at the end of life and device reuse. Further evidence is needed to personalize the device-implantation decision and predict risk–benefit and survival in patients. Ongoing innovations in the electronics, materials and engineering of CIEDs are expected to improve clinical outcomes and delay the need for device replacement. An example of the efforts in this direction is the intra-cardiac leadless pacemaker that has undergone two clinical trials, and is observed to be safe and efficacious.

There are three more reviews related to cardiovascular diseases. One of them surveys the status of technological advancements in transcatheter aortic valve replacement (TAVR) and the future of this therapy in the treatment of aortic valve disease. Advances in the field include assessment of the role of TAVR in patients with intermediate and low risks for surgical aortic valve replacement and development of newer devices which have small profile, repositionability and reduced paravalvular leak.

The results of several randomized clinical trials of neprilysin (NEP) inhibitors in patients with hypertension or heart failure are delineated by Owens *et al.* Discovery that a combination of a NEP inhibitor and an angiotensin receptor blocker can reduce hospitalization and mortality in patients with systolic heart failure is anticipated to change the paradigm in the treatment of heart failure. NEP, a cell membrane-bound zinc metalloprotease enzyme, abundant in the kidney, catalyses the breakdown of many endogenous peptides, including natriuretic peptides whose levels rise in heart failure. Inhibition of NEP is considered to increase levels of natriuretic peptide promoting sodium excretion and diuresis. The authors also discuss unanswered questions on criteria for selection of patients for the combination therapy and non-cardiovascular adverse effects.

Milewicz *et al.* present evidences which indicate that gradual increase in haemodynamic load on a structurally defective aorta is the dominant cause of thoracic aortic aneurysms. It seems that aberrant aortic smooth muscle cells result in dysfunctional mechanosensing. The authors review the studies in genetically engineered mouse models. These studies aim at delineating the molecular pathways through which defects in genes encoding components of smooth muscle contractile function as well as those encoding components of aortic elastin contractile unit induce aortic disease. They also present the results of various prospective clinical trials using losartan in patients with Marfan syndrome.

The causes of most neurodegenerative diseases are unknown and hence targets for drug designing remain elusive. Common neurodegenerative diseases such as Parkinson's disease and Lewy body dementia have been linked to some hydrolases that are mutated in lysosomal storage diseases. Defects in endolysosomal–autophagy pathway are also associated with neurodegenerative diseases. McDonald and Krainc analyse why lysosomal enzymes and transporters as well as current new therapies for lysosomal storage diseases could be

appealing targets for therapy of neurodegeneration. Many other treatment targets may be identified in the future when genes related to mechanisms of neurodegeneration are discovered.

Graham *et al.* (Karolinska Institute, Sweden) summarize the current understanding on the molecular pathophysiology and potential drug targets of Alzheimer's disease. Emerging drug targets are neuroinflammation and metabolic pathways such as insulin signalling. Modulation of amyloid-β production, increasing its degradation and/or clearance, inhibiting protein aggregation, neurofibrillary tangles and Tau aggregates are other potential targets. These are the basis of more than 50 advanced-phase clinical trials for prevention and treatment of Alzheimer's disease. The challenges to overcome the high failure rates of drugs in clinical trials are the insidious onset, long prodromal phase and varying rates of progression of the disease among individuals. There is also lack of a quantitative biomarker for early diagnosis and for assessment of diseases progression.

Failure of development of myelin in the central nervous system (CNS) and loss of myelin as can occur in multiple sclerosis and after trauma to the CNS have significant effects on neural functions. Myelin is a trophic factor to arrest axon degeneration. Hence, discovery of ways to promote CNS remyelination is of clinical relevance. Bothwell focuses on the intracellular signalling pathways and receptor systems which regulate myelination. He also delineates the drug trials that target mechanisms which assist remyelination. The drugs include (i) an inhibitor of the function of the membrane protein LINGO1; (ii) a recombinant human monoclonal IgM antibody rHIgM22 which binds a component of oligodendrocytes and promotes remyelination; (iii) clemastine, an H1 histamine receptor antagonist, and M1/M3 muscarinic receptor reverse antagonist; (iv) olesoxime, a cholesterol-like component which promotes oligodendrocyte progenitor cell differentiation; (v) quetiapine and domperidone which target G-protein coupled receptors; (vi) GSK 239512, a histamine H3 receptor antagonist, and (vii) Vaccinex (VX15), an anti SEMA4D monoclonal antibody which targets inflammatory mechanisms causing demyelination in multiple sclerosis.

An advancing frontier in genomic medicine is the use of non-invasive prenatal DNA tests. Screening tests using circulating DNA fragments in the plasma of pregnant women have provided new avenues for personalized medicine for the foetus. The clinical and social impacts as well as the new biological insights from non-invasive prenatal testing are summarized by Hui and Bianchi. They also provide a model to incorporate non-invasive prenatal testing with other prevailing screening methods.

Recent developments in the advancing field of tissue engineering are the subject of another review. Flat, tubular and hollow organ structures have been developed and successfully implanted in humans. However, challenges continue in the fabrication of solid organs such as liver and heart. Appropriate sources of cells and suitable scaffolds for extracellular matrix are yet to be identified. Production time and cost have to be improved and a market for engineered parts is to be established.

A strong programme has been established in USA for developing and licensing biosimilars and interchangeable biological products. Four biosimilars have been licensed and many new ones are expected to be in the market in the coming decade. Christl *et al.* describe the regulatory framework for these products and provide a survey of FDA's stepwise approach to assess biosimilars. They also discuss the unaddressed questions and the barriers to the growth of the biosimilar market.

An *et al.* review the chemistry of antimalarial drugs and their mechanisms of action, and discuss how they influence several pathways of innate immunity. These antimalarials could thus be of value as immune modulators in the management of auto immune diseases such as systemic lupus erythematosus, rheumatoid arthritis and monogenic interferonopathies.

Lee-Kirsh examines the genetic defects, inheritance pattern and protein function abnormalities associated with the widening spectrum of genetically determined diseases of the innate immune system classified as type-1 interferonopathies. The diverse phenotypes are characterized by systemic auto-inflammation and different degrees of autoimmunity or immunodeficiency. Research on cellular and molecular functions of the genes causing the disease has led to the discovery of the cytosolic nucleic acid sensors which act as defence against viruses, and nucleic acid metabolizing enzymes which contribute to the synthesis of immunostimulatory nucleic acids or present innate immune responses. The new knowledge on the mechanisms that prevent inapt type-1 interferon activation is expected to spur discovery of targets for specific therapies for type-1 interferonopathies or autoimmune diseases.

Mavragani presents the important factors in the pathogenesis of Sjogren syndrome and difficulties in unravelling the distinct pathways linked to different clinical phenotypes of the disease. He also discusses the promising therapeutic targets, which include cathepsin S, CD40, B7 function-related molecules, CD20 and CD22 blockers, PI3Kδ and lymphotoxin β receptor repressors. The safety, efficacy and dosage of these molecules as well as reliable markers of response to these agents remain to be identified.

Diagnostic challenges, the revised Sapporo classification criteria, the role of hydroxychloroquine, rituximab, eculizumab, sirolimus and defibrotide in the treatment of patients with catastrophic anti phospholipid syndrome (CAPS) and who are refractory to commonly used treatments are reviewed by Unlu and Erkan.

Management of women with systemic lupus erythematosus (SLE) during their preganacy is the core of Sammaritano's article. She lists out the risk factors for adverse pregnancy outcome, and foetal and neonatal outcomes. Strategies for monitoring patients and medications that can be used are deliberated. Her message is 'With careful planning, most women with SLE can anticipate a successful pregnancy'.

Kim and Krueger provide the contemporary thinking on immune mechanisms in the pathogenesis of psoriasis vulgaris and current immunotherapy of the disease. The present strategy specifically targets the interleukin-23/type-17 T-cell axis. It is expected that this approach would usher in new therapies for other immune mediated diseases.

New personalized approaches and advances in technologies for the treatment of obstructive sleep apnea (OSA) comprise the theme of the article by Lima and Pack. Hypoglossal nerve stimulation during inspiration is an emerging treatment option, though currently expensive. The issues related to OSA identified for research in future include biomarkers to assess efficacy of therapies for the disorder, elucidating the gene variants and

identifying associated risks and determining whether treatment of OSA affects progression of neurodegeneration and alters outcomes of cancer in patients with the disorder.

Multiple factors determine disease progression and outcome in patients with nonalcoholic steatohepatitis (NASH). The role of hepatocyte metabolic stress, cellular adaptive mechanisms and hepatic inflammation in the pathogenesis of NASH are delineated by Suzuki and Diehl.

Ten reviews relate to various types of malignancies. One of them addresses why the rates of bilateral mastectomy for breast cancer on one side is increasing in the USA. This tendency is prominent among educated and younger women, and those who have access to the highest quality hospital care through insurance. The authors recommend new communication strategies to guarantee that patients understand the risk, benefits and outcomes of bilateral breast removal, and thus assist them in taking apt decisions.

Krymskaya and McCormack discuss the genetic basis of lymphangioleiomyomatosis, and how the genetic studies of this rare monogenic disease and tuberous sclerosis have contributed to the delineation of the vital role of mTOR signalling in the regulation of cell metabolism, cellular growth, cell death, evasion of immune detection and activation of invasion. The new knowledge has surprisingly aided to gain insights into the pathogenesis of common cancers.

Other articles on cancers focus on (i) screening, surveillance and management of oesophageal adenocarcinomas; (2) controversies in the treatment of breast ductal carcinoma *in situ*; (3) concepts of treatment of rectal carcinoma; (4) benefits of liver resection in the optimal management of colorectal liver metastases; (5) advances in the understanding of the biology of non-small cell lung cancer (NSCLC) and their contribution to development of targeted and personalized therapy for advance NSCLC; (6) challenges of chimeric antigen receptor (CAR) T-cell therapy for solid tumours and approaches to overcome immunosuppressive barriers within the tumours; (7) advances in next-generation sequencing technology and problems encountered in the utilization of the technologies in clinical oncology, and (8) limitations in the application of precision medicine concepts in myelodysplastic syndromes and leukaemias, despite advances in genomics.

In summary, this volume has articles on epidemiological features, pathogenesis, diagnostic tests, novel drug targets, untested yet promising treatment options, results of clinical trials of new therapeutic strategies, advancing frontiers of research and forthcoming public health strategies related to several common and rare diseases, some of them less explored. Assuredly, physicians would find them useful to update their clinical management skills, while experimentalists would discover new challenges and exciting ideas for their pursuits in medical science.

C. C. KARTHA

Division of Cardiovascular Diseases and Diabetes Biology,
Rajiv Gandhi Centre for Biotechnology,
Thiruvananthapuram 695 014, India
e-mail: cckartha@gmail.com

Encyclopedic Dictionary of Zoological Terms: Sanskrit–Sanskrit–English. Compiled by B. Thirumalachar. Smt Chokkamma and Dr Thirumalachar Memorial Trust, Basavanagudi, Bengaluru 560 004. 2016. x + 238 pages. Price: Not mentioned.

The work done by Thirumalachar is tremendous and commendable. It will be of much help to students, researchers and the writers who write zoological articles in their mother tongue or in local languages and are proud of using Sanskrit terms for animal/s of their choice. They will be able to search for Sanskrit term/s in this dictionary if they do not know the Sanskrit term or have forgotten it. For researchers, this dictionary is an open field to do research on a zoological Sanskrit terms which may have been changed from time to time. Probable reason for change can also be traced.

Having said that, may I point out certain discrepancies that have occurred in this dictionary? The discrepancies are the following:

1. On page no. 4 under the Sanskrit term अदन्त (toothless), Leech has been placed referring to MMW. Is this placement correct? As far as I know, leeches have three jaws (ref. Parkar and Haswell, 1962, vol. 1). The jaws have serrated border with which they create a small wound or puncture and suck blood from its host. May I suggest to place *Earthworm*, under this term? Earthworms neither have teeth nor have jaws with serrated border.

2. On p. 198 *Shrew* has been placed under Sanskrit term लालन (Lalan) with a question mark. The author himself was not sure, it seems. Answer to that basically, is that saliva of shrew is not poisonous. But if it comes in contact with other infected animal, then, there is possibility of a shrew-saliva becoming poisonous (R.V. Ranade, pers. commun.).

3. On p. 215 under the Sanskrit term शतपाद (giving reference of MMW/Susr.), insect or worm has been placed. I am sorry, I do not agree with this placement. Insect bears six feet (appendages). So, if it is an insect it does not come under the term शतपाद, traditionally a centipede (गोम), Gom. in Marathi can be placed under this term (Ref: *Girväna Laghukosh-Sanskrit-Marathi*) by J. V. Oak Shake, 1837 (i.e. 1995), p. 229. Another example of centipede is, 'Scolopendra'. It is not mentioned in this dictionary. Julus is certainly not a centipede. It is a millipede. Surprisingly it is not placed under Sanskrit term सहस्रपाद p. 229. Surprisingly the millipede Julus has not been placed under that Sanskrit term. Thirumalachar may have forgotten to ask the question, why not Julus be a millipede?

Some other points: (a) I would like to place cattle ticks under the Sanskrit term इन्द्रगोप (ref. मृग नक्षत्रे संजातो, राज निघण्टु, 22, 125) In Marathi, one is called as 'Mrugachakida' (ref. *Girvana Laghu Kosh* by J. V. Oak, Shake 1837 equivalent to 1915 AD). This tick appears over the soil from its hide in Mriga Nakshatra round about June in Maharashtra.

(b) The sketch of ishneumon wasp drawn on page 2 is incorrect (see, Imms 1963, p. 701 for correct sketch).

(c) Under the Sanskrit term, कारस्कराटिका (p. 46) Japyx centipede is given as example. Well, *Japyx* is not centipede. It is an insect (Imms, 1963, p. 264, Leftwich, *Dictionary of Entomology*, 1983, p. 142).

(d) On some pages Bangla terms, चीरिका झिझिंपोका p. 37, झिझिंपोका p. 107, have been mentioned. This means B. Thirumalalchar knew Bangla language. It is remarkable!

PURUSHOTTAM V. JOSHI

11, Gruhakalpa Co-Op Housing Society,
Erandavana,
Pune 411 004, India