

that Anna would have a lasting role in Hans' life and moved to USA and an insight is offered on how Hans was pre-occupied with taking care of his mother, and the difficulties of elderly immigrants. Chapters in the book are devoted to two women. One of them is on Hilde Levi who Bethe was once engaged to for a short period, but did not marry, which was to also impact his relationship and friendship with Niels Bohr. Levi went on to become a leading biologist in Denmark. The other chapter is devoted to Rose Ewald Bethe, the daughter of Paul Ewald who had been one of Bethe's teachers. Rose was the woman that Hans spent over 60 years with and was the mother of his two children, and according to Schweber the one who provided the moral compass to Hans Bethe's life in terms of his engagement with atomic weapons research and disarmament.

The book, however, essentially stops with the first one-third of Bethe's life, except for the last chapter entitled 'Conclusion', which condenses the second and final thirds of his life into a few succinct pages.

This book indeed provides the reader with much food for thought and contemplation on the difficult times in which Hans was born into and the remarkable achievements that were accomplished by him and many of his peers in that period. In contrast to the chapters entitled 'Maturing', 'Becoming Bethe' and 'Beyond the doctorate: 1928–1933' which are primarily set in Germany, the chapters entitled 'England, 1933–1935', 'Cornell University' and 'The happy thirties' are about exile and then settling into the new permanent home. Cornell University was to be where Bethe would spend the rest of his career and Ithaca, New York, would be where he would spend the rest of his life. After the war, Sommerfeld tried to lure him back with a Professorship in Germany, to which Bethe would politely write a note declining and offering reasons, including that America has been a wonderful home to him and would note that his birth in Germany was perhaps only an accident. Indeed, in his early years in USA, Bethe would write the famous 'Bethe Bible' a series of articles in the *Review of Modern Physics* on the nuclear processes that power the sun. It would be no exaggeration to say that perhaps Bethe was the first human being to have known how the sun shines!

In his grand tour through the life and times of Bethe, the physicist Schweber explains a lot of the physics that went into each of the *tours de force* that Bethe would create. While it is the lore that Bethe was a self-effacing person, a somewhat different picture emerges in this book which points out that he was a supremely self-confident person, fully aware of his prowess and general technical superiority: apparently at a later stage in his life Bethe said that he was still very conceited, but knew how to hide it better! Schweber explains that in Germany in the 1920s academia was rife with intense competition, both for success and for plum academic positions and hence it is no surprise that a person needed many attributes of the type listed earlier in order to succeed. Although Schweber himself says in his introduction quoting Claude Levi-Strauss that biography has always been considered 'weak' history, he has rendered a yeoman service by providing this sensitive yet complex portrait of an 'off-scale' scientist. While the present reviewer feels that true justice cannot be done to this book at the end of a simple reading and what it deserves is repeated and in-depth study, he feels thankful for having had this opportunity.

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Annual Review of Pathology: Mechanisms of Disease, 2012. Abul K. Abbas, Stephen J. Galli and Peter M. Howley (eds). Annual Reviews, 4139 El Camino Way, P.O. Box 10139, Palo Alto, California 94303-0139, USA. Vol. 7. vi + 507 pp. Price not mentioned.

Yet another splendid volume on pathology from the *Annual Reviews* stable! As with all other volumes, this one begins with an autobiographical essay, this time by David Korn, of Stanford Medical School. I do have an interest in history and biography/autobiography, and so may be biased to some extent – but of all the essays in the book, I thought the autobiographical essay was the best. Which is no mean thing, given that there

are 17 other excellent articles on diverse topics. Cancer forms the subject of six of these articles, while neurological disease is the subject of three. General topics such as phagocytosis and the human microbiome are also addressed. The essays range from the diseases known from ancient times, such as tuberculosis to concepts described only in the past decade.

Korn is the pathologist who blew life into the then decrepit department of pathology at Stanford University. Today, Stanford is one of the leading centres in the field and it amazes one to learn that as recently as 1967, it had the 'worst pathology program in the United States' and was 'a pit'. Korn, who was trained at the Massachusetts General Hospital and Harvard Medical School, decided to take up the challenge of transforming the department – and succeeded. It was not roses all the way, however, he explains, as he had to battle tradition, established colleagues and officialdom. It is because of this that I rate the article so highly and strongly recommend it to all – current heads of departments of pathology and indeed, other departments and to potential heads of departments, i.e. all youngsters, to understand the meaning of vision, something many of our present-day academic leaders lack.

NUT midline tract carcinoma (NMC) is an example of a 'new' cancer that is recognized only because of the contributions of molecular biology to medical science. NMC is a highly aggressive, poorly differentiated squamous carcinoma which is characterized by acquired chromosomal rearrangements involving NUT (nuclear protein in testis), usually BRD4-NUT fusion genes. As the name suggests, most of these cancers arise in the midline, particularly the upper aerodigestive tract and the mediastinum. The characteristic cytogenetic abnormality is t(15;19) (q14;p13.1) and a significant number of these tumours is seen in the young, unlike conventional tobacco-related squamous carcinoma, which are seen in adults and have complex karyotypes. Because NMC is almost always diagnosed initially at histopathologic evaluation of the biopsy material, after the tissue has been fixed in formalin and embedded in paraffin wax, the author's (Christopher French, Brigham and Women's Hospital, Boston) group has developed a FISH assay that can detect the NUT locus in archival material; they have even characterized a monoclonal

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antibody for the diagnosis of NMC. A glimmer of hope, albeit a very faint one, is also offered by the author when he elaborates on laboratory data and partial therapeutic success in a single patient by treatment with SAHA, a histone deacetylase inhibitor.

Merkel cell carcinoma is an uncommon cancer of the skin that was first reported in 1972. Merkel cell carcinoma falls into a category that histopathologists term 'small blue round cell tumours'; tumours with this histologic appearance look quite similar under the light microscope with the usual stains, but are of varying histogenesis, treatment and prognosis. After little progress in our understanding of this disease for almost three decades, came the discovery in 2008 that it was caused by a virus, the Merkel cell polyomavirus (MCV). That viruses could cause cancers in fowls were described almost exactly a century ago (Peyton Rous, Rous sarcoma virus, 1911) and subsequently, Epstein-Barr virus and Human papilloma-virus have also been implicated in human carcinogenesis. Thus, the discovery that yet another virus was linked to cancer was not greeted with preposterousness. Chang and Moore elaborate on this tumour virus, which is a DNA virus. About 80% of Merkel cell carcinoma are caused by the virus and to my great interest, I learnt that these appear slightly different under

the light microscope from the other 20%: MCV-positive tumour cells have round and relatively regular nuclei and little cytoplasm compared to MCV-negative Merkel cell carcinoma tumour cells which show much more cytoplasm and irregular nuclei. MCV-positive tumours also are associated with better prognosis than MCV-negative tumours.

The ultimate aim behind understanding concepts of disease is only to arrive at a cure and this is exemplified in practically all essays. It is brought out well in the chapter on psoriasis. Psoriasis vulgaris is a chronic inflammatory disease of the skin which also affects the joints. The aetiology is multifactorial and involves genetic, immunologic and environmental factors. Because T helper cells are involved in its pathogenesis, cytokines, secreted by T helper cells, and their receptors are now being targeted. Drugs such as Adalimumab, Infliximab, Etanercept, Alefacept and Ustekinumab are currently used in the treatment of severe, non-responsive psoriasis.

The human microbiome is another relatively new concept. We learn that 90% of the cells in and on the human body belong to bacteria! Thus, a very small part of you is really you! Or put differently, you are really a conglomerate of your own cells and innumerable bugs! (I see interesting parallels here: those who have been following the excitement around the Higgs boson finding would know that ordinary matter forms only 4% of the universe; 84% of the universe is dark matter. Indeed, even in the biological world, from the point of view of DNA, much of it is non-coding or so-called junk DNA!) The Human Microbiome Project was launched in 2007 by the National Institutes of Health, USA. The current concept is that we live in a difficult balance with bugs and that disease is often the result of an imbalance. The human microbiome of the adult is developed by the time a child is one year old. To be sure, the microbiome is different in those living in developed nations compared to those in the developing world because environment, food and social customs affect it. However, bacterial communities at each site are more similar across humans than the communities at other sites within the same person. Majority of the bacteria are within four phyla – Actinobacteria, Firmicutes, Proteobacteria and Bacteroidetes.

The human microbiome is implicated in dental caries and periodontal disease, diabetes mellitus and in obesity. The spectacular Nobel-Prize winning finding by Robin Warren and Barry Marshall that ulcers in the stomach are caused by *Helicobacter pylori* and the subsequent treatment of this condition by antibiotics (and not major surgery, which was the treatment for almost a century) is now tempered by this fact: removal of *Helicobacter* from the stomach has changed the bacterial flora of the gut – and resulted in an increase in oesophageal carcinoma! The human microbiome also probably plays an important role in the development of irritable bowel disease and inflammatory bowel disease. Because bugs are common on the skin and in the vagina and urethra, diseases associated with these body parts are also linked with the microbiome. Indeed, the human microbiome is the subject of the cover story and leader in a recent issue of *The Economist* (18 August 2012).

Cardiac valvular pathology is decidedly an esoteric topic. It was a pleasure – and an eye-opener to learn so much from this essay. It seems only too obvious now that I have read it – though it was not at all obvious to me before – that valvular endothelial cells are considerably different from vascular endothelial cells which are present in the adjacent aorta in response to fluid shear stress. However, the authors are wrong when they state, on page 172, that the carcinoid syndrome is seen in half the patients with carcinoid tumour. The real figure is undoubtedly much less. Humour and romance are, of course, conspicuously lacking in books of this nature. However, I was amused to see two consecutive references in the bibliography of one of the chapters. Reference 64 has Rabkin and Aikawa as the first two authors, while the next reference has Rabkin-Aikawa and Aikawa as the first two authors, indicating that Cupid had struck inbetween! Which chapter is this from? The references (*Circulation*, 2001, **104**, 2525–2532 and *J. Thorac. Cardiovasc. Surg.*, 2004, **128**, 552–561) are from the essay on cardiac valves – matters of the heart after all!

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Clinical images showing the spectrum of psoriasis phenotypes. **a**, Guttate psoriasis. **b**, Lichenified hand psoriasis. Courtesy by St John's Institute of Dermatology.