scientific knowledge created by them as 'private goods' – a commodity that can be traded or exchanged like other market goods. In public funded organizations (universities and public research institutes), new institutional structures, for example, technology transfer offices, proprietary protection (through various intellectual property instruments) are also trying to create fences in public knowledge. The non-rival, non-excludable character of knowledge is eroded by these activities. The author's policy framework does not factor in these dynamics.

There is a serious attempt to bridge the gap between qualitative and quantitative perspectives but one still finds the author comfortable with the rationalistic, uncritical view of science. The author does not exploit the rich theoretical literature on dynamics and structure of science emerging from sociological and philosophical traditions. The book is sometimes prescriptive!

Overall the book is a very important scholarly work. The book addresses a large community and is not restrictive to a narrow domain of scholars in STS (Science Technology Society) studies. It helps to bridge the gap between the qualitative and quantitative perspectives. It is a must read book for scholars in collaboration studies and those involved in research policy. The narrative style the author uses to glue the different pieces together makes the arguments appealing and entices the readers to agree to many of the arguments she provides.

SUJIT BHATTACHARYA

Centre for Studies in Science Policy,
Jawaharlal Nehru University,
New Delhi 110 067, India;
NISTADS, New Delhi 110 019, India
e-mail: sujit_academic@yahoo.com

Annual Review of Pathology: Mechanisms of Disease, 2009. Abul K. Abbas, Stephen J. Galli and Peter M. Howley (eds). Annual Reviews, Palo Alto, California, USA. Vol. 4. 582 pp.

The Annual Reviews series of books has been in existence since 1932. Beginning with *Annual Review of Biochemistry*, the series now covers a wide range of sciences, including public health, financial economics, genetics, political science and pathology. This edition of *Annual Review of Pathology: Mechanisms of Disease*, as with all other editions, begins with an autobiographical essay; this one by Peter Ward, who is a leading researcher in immunology, in the field of complement and cytokines. All – young and not-so young – researchers would do well to read this essay. It traces his most interesting path from a medical student to professor of pathology and beyond and illustrates the excitement of research. You will learn about the good mentors that he had – and also see how even the experts can get it entirely wrong. Baruj Bennaceraf (who later won the Nobel prize in 1980) tells him at one stage in 1962, 'Young man, there are three areas of research to avoid: endotoxin, fever and complement'!

There are 21 chapters on the pathogenetic aspects of disease. As many as 13 of the chapters are on neoplastic pathology, given that cancer (and cardiovascular disease) is among the biggest killer diseases in the USA. The essays of a general type include those on microRNAs and epigenetic changes in cancer. Most, however, are more focused and include topics such as head and neck cancer, urinary bladder cancer, melanocytic neoplasms, neurodegenerative disease and the sudden infant death syndrome.

Head and neck squamous carcinoma is uncommon in the USA but is the most common cancer seen in Indians. Because of this latter fact (and because I personally have always found the subject fascinating), I shall dwell a bit more on this than on other areas. The term head and neck mucosal cancer includes cancers arising from the oral cavity, pharynx, sinonasal tract and the larynx. More than 90% of head and neck mucosal cancers are squamous carcinomas. Despite their common histology and embryology, it is now obvious that head and neck cancers are not as homogenous as believed previously. There have been many advances, both basic, and epidemiologic in the past decade in this field. For instance, the incidence of oropharyngeal carcinoma is increasing despite the decrease in head and neck cancer in the West. Since the use of tobacco and alcohol is implicated in the causation of oral cancer, and there has been no parallel increase in the consumption of alcohol and tobacco, it suggests that some other agent is responsible for the increase in oropharyngeal carcinoma. HPV (Human Pipilloma Virus), which has been well established as a cause of cervical cancer – for which Harald zur Hausen was awarded the Nobel prize for physiology or medicine in 2008 – is now known to be a cause of oropharyngeal cancer as well. HPV type 16 is the causative agent of approximately 70% of oropharyngeal carcinomas. HPV-associated oropharyngeal carcinomas are strongly associated with sexual practices such as oral sex, which lead to repeated viral exposure.

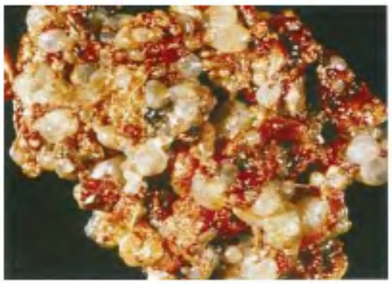
Field cancerization is a well accepted idea in carcinogenesis. According to this theory, put forward by Slaughter in the 1950s, multiple groups of cells independently undergo neoplastic transformation under the influence of carcinogens. However, molecular genetic data now shows that when a primary tumour is compared with a second tumour elsewhere in the same field, both tumours exhibit similar patterns of genetic changes. This suggests that the genetic insult took place in a single cell initially and that at some later stage, cells with these genetic changes migrated to other contiguous areas of the epithelium, accrued other alterations and other growth advantages and finally transformed into aggressive subclones. It appears that during the earliest phase of cancer, some cells express genetic changes without a corresponding morphological change which can be recognized by the histopathologist looking at the tissue biopsy under the microscope. The practical importance of the concept of field cancerization is that it explains why tumours recur locally after they have apparently been excised entirely at surgery.

The authors, both from the Johns Hopkins Medical Institutions, Baltimore, explain how the peculiar anatomy and microanatomy of the tonsils (part of the oropharynx) contribute to the physiology and pathology of the organ. The tonsils have numerous blind cul-de-sac like crypts which increase the surface area of the tonsil by as much as 700%. The tonsils also have an incomplete basal layer of epithelium. Besides, its basement membrane (the layer on which the basal layer stands) is porous and fenestrated. This allows the direct passage of lymphocytes and antigen presenting cells, thus creating the first line of defence. However, the same pores provide easy access to the body when the tonsil is exposed to HPV. The presence of the crypts

also means that small cancers or precancers can remain hidden for long. Finally, the incomplete basement membrane can lead to small cancers having the ability to infiltrate the body and metastasize early on.

Some head and neck cancers can present as metastatic cancers ('secondaries') with occult or unknown primaries. Because we now know that certain viruses are associated with specific cancers, we can use this knowledge to detect the origin of the occult primary. For instance, a metastatic tumour containing HPV-16 as seen by *in situ* hybridization suggests an oropharyngeal primary whereas the one expressing Epstein–Barr virus is strongly suggestive of a nasopharyngeal primary (given that practically all nasopharyngeal carcinomas are associated with Epstein–Barr virus).

Unlike head and neck squamous carcinoma, colorectal carcinoma is a common neoplasm in the West. Our understanding of colorectal cancer and carcinogenesis in general got a fillip with the adenoma–carcinoma model described by Vogelstein's group in 1988, wherein an adenoma converts to carcinoma after multiple genetic insults. Later, another model was described to explain the colonic cancers in patients with hereditary nonpolyposis cancer. In 1990, Longacre and Fenoglio-Preiser made the fascinating discovery that a subset of a group of common colonic polyps ('hyperplastic polyps') which had been interpreted as absolutely benign and non-neoplastic for many decades, were in reality neoplastic and precancerous. These polyps were termed serrated adenomas and subsequently, the cancers which arose in them were called serrated adenocarcinomas. Serrated adenomas are now known to be of two types – traditional (polypoid) and sessile. Although space constraints do not permit me to elaborate on this more, suffice it to state that we now know that there are five molecular pathways to developing colonic carcinoma: the first two are the adenoma–carcinoma model and the hereditary nonpolyposis models as mentioned above. The others are carcinomas which probably arise from pre-existing sessile serrated adenomas, those arising from traditional serrated adenomas and finally, a group of cancers which arise from a fusion of different pathways.



Histopathology of neoplasms that arise in association with an imbalance of parental chromosomes.

NOD-like receptors (NLR) and their role in immunity and disease are discussed by a group from Ann Arbor. NLR are intracellular, cytoplasmic sensors and are one among thee types of pathogen recognition receptors, the other two types being Toll-like receptors (TLR) and RIG-1-like receptors. There are 22 proteins in the NLR family. NLRs recognize specific bacterial and endogenous molecules and dysregulated NLR signalling is involved in the genesis of many diseases. For instance, mutations of NOD2 are associated with the development of inflammatory bowel diseases such as Crohn's disease, a form of inflammatory bowel disease, which has increasingly been seen in India (unlike the conventional belief over the past few decades that the disease was rare in India). Four possible models have been suggested. In the first two, deranged NOD2 function is associated with either increased invasion of intestinal bacteria due to deficient production of alpha-defensins or reduced clearance of bacteria by intestinal phagocytes, resulting in inappropriate activation of NOD2 independent pathogen recognition receptor-signalling pathways. The third model has NOD2 acting as a brake of commensal bacteria-driven inflammation; deficient NOD2 alleles result in enhanced TLR-induced activation. In the last model, NOD2 mutations lead to inappropriate interleukin-1-beta production, which leads to colitis.

Ovarian carcinoma, a not uncommon disease in the West and in India has a relatively poor prognosis. Cystic epithelial ovarian tumours have been traditionally classified into adenomas, carcinomas and an unusual third type, the borderline tumour, which falls somewhere between the other two types. Research in the past two decades has changed much of our understanding of these unusual neoplasms. For instance, there was a belief that adenomas turned into borderline tumours and then converted into adenocarcinomas. Genetic analysis now demonstrates that there are two pathways for the development of ovarian carcinomas – one for low grade carcinomas and the other for high grade carcinomas. Low grade carcinomas and borderline tumours express KRAS or BRAF mutations in about 50% cases while *p53* mutations are common in high grade carcinomas. *p53* mutations are seen in stage I (early) high grade carcinomas, which suggests that it is an early event in carcinogenesis. Further, recent evidence suggests that the distal fallopian tube may be the origin of some purported cases of high grade ovarian carcinoma! Not only is such data useful in changing our concept of ovarian carcinogenesis, but it may herald a change in therapeutic approaches as well. Specific chemicals which inhibit growth of ovarian tumour cell lines containing specific mutations are now being investigated.

Rheumatoid arthritis (RA) is an inflammatory polyarthritis that can affect many joints, particularly those of the hands and wrist. Although it is believed to be of autoimmune origin, there has been speculation about the triggering autoantigen and the environmental factors. Current research shows that there are autoantibodies to citrullinated protein antigens (called anti-CCP antibodies), which are specific for RA and are probably of pathogenetic significance. Autoantibodies to citrullinated protein antigens are present in about 70% of RA patients and these patients have a more severe disease than those who do lack the antibodies. Studies have shown that blood samples from donors who developed RA at a later date, have contained serum anti-CCP antibodies. The fact that the antibodies were present before the formation of clinical arthritis and are present in the joints when the arthritis develops, suggests that the antibodies may be pathogenic. A genetic cause for RA is obvious based on epidemiologic studies and on the fact that the genetic loci HLA-DRB1, PTPN22 and STAT4 are associated with RA.

Overall, this is an excellent volume. For those involved actively in research – often in specific, niche areas, it would be a very practical way of learning what is happening in other fields. For people like me, who are no longer in the trenches, but wish to know what is happening out there, it is an absolute boon!

SANJAY A. PAI

Columbia Asia Referral Hospital,
Malleswaram,
Bangalore 560 055, India
e-mail: sanjayapai@gmail.com