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BOOK REVIEWS

The enchanted ring : The untold story of penicillin by John C. Sheehan. The MIT Press, Cambridge, Massachusetts 02142, USA, 1982, pp. xvi + 224, $ 15 (Asia $ 17.25).

Despite the large number of monographs, review articles and popular literature available on penicillins and β-lactum antibiotics, many facets of the development of the wonder drug are not known to the lay scientists. The readers of literature on penicillin generally consider penicillin as a triumph of British science as the great names associated with the isolation and structure elucidation of penicillin were British stalwarts such as Alexander Fleming, Florey, Chain, Abraham Heatley and even Sir Robert Robinson. It was English crystallographer Dorothy Hodgkin who elucidated the correct structure. It is also generally accepted that the superior microbial techniques, the dynamic and innovative methodology of the American fermentation industry which made the drug available to millions at the end of the Second World War.

In 1957, when John Sheehan reported the first acceptable total synthesis of penicillin he created a great sensation. The *Enchanted Ring* tells the story of Sheehan's involvement in the process. It is a story of indomitable faith and courage as well as superhuman perseverence which finally led to the success.

The most amazing event in the history of penicillin is the confusion regarding its exact composition and structure. No other compound of a molecular weight of about 300 has baffled so many brilliant chemists. Even after the structure of penicillin was unequivocally established, Sir Robert Robinson held on to his earlier notion that the basic skeleton of penicillin was composed of thiazolidine and oxazolone for many subsequent years. The presence of sulphur in the molecule was completely ignored by so many top chemists even in the early forties !

Professor Sheehan's book to the casual reader would appear as oneman's story of the penicillin molecule. However, it is definitely not an egocentric version. The author gives due credit to all the significant contributions not only from his own students but also to all scientists outside his laboratory both inside and outside the continental United States. He gives the first historically coherent picture of penicillin development.

His personal achievement is no doubt outstanding succeeding in a task in which thirty-nine major laboratories and institutions of the world and more than a thousand first-rate chemists participated many with more funds and resources than Sheehan could

muster. He also describes his failures, pursuit of false trails and moments of triumph with equanimity.

The *Enchanted Ring*, however, is not a book on chemistry of penicillin. It is much more than that. The reader is led step by step into a bizarre world of warring pharmaceutical houses and the intricacies of Amercian and international patent laws. The legal battle on the patents for 6–amino-penicillinic acid and semi-synthetic penicillins was waged for about twenty years. One gets an insight into the ruthless tactics the pharmaceutical companies may bring into operation to squash the individual entrepreneur in smaller laboratories. In the last chapters the author could not help feeling bitter about the interminable litigation he had to face to establish the MIT patents on penicillin.

The book is written as personal memoire. Nevertheless, it sustains the interest of the lay reader till the last page. It is also interspersed of subtle humour and wisdom. Professor Sheehan endears himself to the reader by his incurable optimism in the face of formidable odds. The *Enchanted Ring* also reveals the greatness of the intellect that engineered the synthesis of an ' inaccessible ' molecule.

The impressive American contribution to the chemistry of the miracle drug has never been chronicled before in the historical perspective. From this point of view, Professor Sheehan has done a great service to Amercian Chemistry.

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Genetic alchemy : The social history of the recombinant DNA controversy by Sheldon Kivinsky. The M.I.T. Press, Cambridge, Massachusetts, 02142, USA, 1982, pp. xiii+445. $ 28.70 (Asia Price).

This book is an interesting and lucid account of the background and the history of the recombinant DNA controversy in the U.S.A. starting with the Gordon Conference on Nucleic Acids in New Hampton during 11–15 June 1973, when the first announcement of the new technology was made, through the release of NIH guidelines for recombinant DNA research on 23 June 1976, to the meeting of the NIH recombinant DNA advisory committee on 10 September 1981, where the committee voted to make the guidelines into a voluntary code of practice.

The announcement of the discovery of the technique of gene splicing in genetic engineering was made at a time when the USA was in the throes of student demonstrations against the Vietnam war. Quite a number of faculty members in the universities were also involved in this movement, and they viewed with suspicion any discovery which

might be utilized for furthering the war, and they considered recombinant technology one such discovery. In 1974, Paul Berg, a prominent scientist working on tumour viruses in Stanford published a letter in *Science* in which he called for a voluntary moratorium on certain kinds of recombinant DNA experiments and asked the Director of the National Institutes of Health in the USA to develop guidelines for such research. There followed in February 1975 an international conference on Recombinant DNA Molecules, held at Asilomar in California, under the aegis of the National Academy of Sciences. The attempt by the scientists attending that conference to quantify the conjuctured hazards would have been difficult enough if it had been carried out over a prolonged period of time, with ample opportunity for consultation and discussion. In fact, the formulation of the first draftlines occurred over a period of four-and-a-half days.

The scientists present were concerned primarily with three biological disciplines : microbial genetics, the biology of eukaryotic organisms and animal virology. Collectively they had to agree on the conjectured hazards associated not only with their work but also with the work of others. They were encouraged to embrace the ' worst case ' hypothesis for almost every situation and to design conditions under which such postulated hazards could be contained. As well as providing a basis upon which the Director of NIH later developed the widely-copied ' NIH guidelines ', the conference initiated work on the design of systems of biological containment.

The moratorium and the subsequent guidelines seem to have been widely observed by scientists in many countries, who were convinced either that the experiments were potentially hazardous or that observance of the guidelines was the most responsible action.

In the years following the Asilomar Conference, however, it became increasingly clear to many scientists that there had been very little time at that meeting for serious analysis of the various ' worst case ' hypotheses which formed the basis of the guidelines. Some scientists, particularly microbiologists used to dealing with infectious agents, were convinced that the postulated hazards had been grossly exaggerated.

The participants in the Asilomar Conference had thought of the possible following ' disastrous ' consequences of carrying out recombinat DNA research with the bacterium *Escherichia coli* (*E. coli*) :

(*a*) the random insertion of a small number of foreign genes into *E. coli* may convert it into a pathogen ;

(*b*) cloning viral genomes into *E. coli* may create new pathogens which could disseminate pathogenic viruses through the population by a novel transmission route and perhaps by a route that avoided the normal defence mechanisms :

(*c*) work either with tumour viruses or with monkey or human DNA might create a strain of *E. coli* which possessed both the ability to spread through the population and to initiate cancers in the individuals so infected ; and

(*d*) strains of *E. coli* which produced eukaryotic proteins may produce immune disease.

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Several experiments have now been carried out to examine the first three hypotheses. Detailed reports on much of this work is available in reports of two scientific conferences: the Falmouth Conference in the USA in 1977 and the conference sponsored by the Committee on Genetic Experimentation (COGENE) in Kent, England, in 1979.

The Falmouth Conference concluded that *E. coli* strain K12 used in recombinant DNA technology cannot be converted into a pathogen by laboratory manipulations with DNA inserts. Even the insertion of known plasmids and chromosomal segments coding for virulence factors from other bacteria did not result in the production of a pathogenic strain.

A special case of a conjectured hazard was the inclusion of the genome of a tumour virus in the recombinant DNA introduced into *E. coli* . It had been suggested that such a combination by introducing the viral genome in a novel manner that could bypass host defences, might be more dangerous than infection with the virus itself. Experiments designed to examine this possibility have been carried out with polyoma virus, which produces an inapparent infection with antibody production in mice. When mice were fed *E. coli* containing recombinant DNA (one molecule of viral per DNA molecule of vector), no antibody was detected indicating that the viral DNA as a recombinant was non-infectious.

So far as the last objection (*d*) is concerned, it is not feasible to do experiments to test this hypothesis. However, six eminent immunologists when approached by NIH concluded that the probability of recombinant DNA experimentation leading to autoimmune disease was remote. On the other hand, they pointed out that humans are regularly exposed to all manner of mammalian proteins (milk, meat) which cross-react extensively with their human counterparts, and that the production of autoreactive antibodies is not synonymous with autoimmune disease.

So far as the escape of *E. coli* containing recombinant DNA is concerned, all evidence supports the view that good microbiological practice, like the prohibition of mouth pipetting and proper sterilization procedure would prevent *E. coli* generating a public health hazard. It was against this background that in 1981 the NIH Recombinant DNA Committee voted to make the NIH guidelines into a voluntary code of practice.

The book, in addition to presenting the history of the recombinant DNA controversy, also deals with the commercial prospects of the technology. It is an eminently readable account which should be available in every library.

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Modern concepts in biochemistry (Third Edition) by Robert Bohinski. Allyn and Bacon, 42, Colebrooke Row, London Nl 8AF, 1979, Pp. 600, £ 10.95.

The book on the whole is an excellent treatise on modern biochemistry. It is distinct from most other textbooks of general biochemistry in that it includes comprehensive accounts of very recent findings in biochemistry such as the opioid peptides, the molecular basis of memory and the concepts of overlapping genes and also introduces the reader to the frontier area of genetic engineering. In comparison with other standard text books, the descriptions in this book run into a slightly greater detail, but the matter is so well organised as to make systematic and easy reading. A unique feature of the book is that it is replete with excellent illustrations which include a large number of figures, space-filling models and photographs. At the end of several chapters are provided a large number of useful exercises. Some of the highlights of the book are listed below as examples.

Chapter II : A clear description of the basic principles of common experimental techniques such as electron microscopy, electrophoresis, radio immunoassay, etc., along with illustrations.

Chapter IV : Detailed description of the isolation and separation of aminoacids, photograph of an aminoacid analyser; chart depicting the net charge on each aminoacid as a function of pH; reactions of aminoacids such as the reaction of lysosine with tetranitromethane and phosphomolybdotungstic acid; opioid peptides; memory peptides and the molecular basis of memory.

Chapter V : Theory of membrane filtration; space-filling models for the interaction of the ligands at the active site of enzymes.

Chapter VII : Detailed description of the methods of sequencing DNA.

Chapter VIII : Overlapping of codons and the reading of codons in different frames; Restriction of enzymes and genetic engineering.

Appendices : Applied aspects of biochemistry in medicine.

Although the book lays sufficient emphasis on modern biochemistry, it is obvious that it lacks in a historical perspective. A brief sketch of the pioneering work in the fields such as nutrition research would enable the reader appreciate better the enormous progress made in the field. The book is clearly deficient in a proper treatment of endocrine biochemistry. It would also be desirable to include a chapter on the molecular basis of evolution.

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The inorganic chemistry of biological processes (Second Edition) by M. N. Hughes. John Wiley and Sons, 1981, pp. ix + 325, £9·90.

Inorganic chemistry forms overlap regions with several disciplines like organic chemistry, biological chemistry and physics. In recent years, exciting and significant developments have been taking place in these interfacial areas. This book presents an introductory account of such developments at an undergraduate level in the area of inorganic biochemistry. Though the discipline of inorganic chemistry has been applied in some detail to biological systems, the importance of this has been recognised after the conference in 1969. The first edition of this book was brought out in 1972. At that point of time, the contents of the book appealed more to inorganic chemists who want to stray away, but the biochemists were at a disadvantage in following the first few chapters. Later on, as significant advances have been made especially with the appearance of new treatises, series editions and an international journal on this subject, increasing attention was given to understand the role and functions of inorganics in biological systems. Viewed from this point, an introductory account is a welcome relief especially for those who would like to introduce this area into their curricula.

In the new edition, the author has added two new chapters over the earlier edition bringing the total chapters to eleven. The first few chapters are conventional topics to illustrate the study of an element in biological systems and a review of transition metal chemistry. The new chapters on storage and transport of iron and the role of non-metals in biology are well written and are very useful. There are a few notable omissions in the book. The functional role of metal ions in photosynthesis and the reactions of photoexcited transition metal complexes do not find a place. Though this reviewer reckons that the present book is only introductory in nature and not expected to cover all developments in a manner comprehensive enough for the reader, an intelligent reader or a teacher would however be benefitted by the inclusion of these topics. However the reader has been richly rewarded by exhaustive references and bibliography appended to each chapter.

The book is lucidly written and is suitable for pedagogic purposes at the undergraduate level in chemical and biological sciences. However, the high price will keep this out of the reach of many students.

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Jenner's smallpox vaccine by Derrick Baxby. Heinemann Educational Books, 22, Bedford Square, London WCIB 3HH, 1981, pp. xiv + 214, £8.50.

The book is timely just when the world and its peoples have won freedom from smallpox, thus giving credit to Edward Jenner for his demonstration that man can be protected from one viral disease by infecting with a related virus.

The book runs into 196 pages in 13 chapters. Derrick Baxby has dealt the events surrounding the introduction and development of smallpox vaccines and has interpreted the events in the light of various theories for the origin of vaccinia. In the first chapter, the author outlines the contents and the purpose of the book. He then deals with the impact of smallpox on the world, its historical account and clinical aspects. The smallpox prevention before Jenner and his biographical information are given. Two chapters deal with Jenner's Inquiry (into the causes and effects of the variolae vacciniae) and reactions to the Inquiry. The author then analyses the origins of various vaccines introduced by Jenner and his contemporaries and the behavoiur of smallpox, cowpox and vaccinia viruses. In the last three chapters, Baxby gives a detailed account of attenuation of smallpox and the development of vaccination.

This expensive book is detailed well to a professional interested in the field and proves to be a useful addition to the reference library.

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