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BOOK REVIEWS

Retrovirus biology and human disease edited by Robert C. Gallo and Flossie Wong-Stall, Marcel Dekker, Inc, 270, Madison Avenue, New York, NY 10016, 1990, pp 409, $119.50.

A new and fatal pandemic human disease was first described in the December 10, 1981 issue of *New England Journal of Medicine* which has now become the most feared disease. This new disease entity which we now know as AIDS, for acquired immune deficiency syndrome, has created panic all over the world as the very existence of human race is at stake. The social and economic consequences of this dreaded disease of recent times is immense if its spread is not controlled. Public awareness of the transmission of AIDS through sexual contact and blood products has caused unprecedented changes, in western countries, in the patterns of social interactions during the last six years. AIDS has created a challenge of unparalleled proportions for health care workers and scientists since the discovery of the etiological agent called human immune deficiency virus (HIV). Today AIDS represents the single area in biology in which maximum financial resources are invested for intensive examination of various aspects of the biology of HIV.

This book written by Robert C. Gallo, one of the investigators credited with the discovery of HIV as well as the first human retrovirus called HTLV-1, along with his long-time colleague Flossie Wong-Stall is the first of its kind on the biology of human retroviruses. Human retroviruses represent an emerging class of complex pathogens involved in a wide variety of maladies including leukemias and lymphomas, diseases of the central nervous system and immune impairment. Although the book is mainly meant for scientists specialized in retrovirus research, some chapters might be useful to anyone interested in knowing the basic facts about AIDS. The book consists of 15 well-referenced chapters, each one being contributed by eminent scientists in the relevant area. This book is up to date in its concepts and presents much of the recent work done on human retroviruses.

The first chapter contributed by R. C. Gallo himself gives a historical perspective of retroviruses and their relevance in human disease with reference to the four human retroviruses discovered to date: HTLV-1, the etiological agent of acute T-cell leukemia/lymphoma (ATLL); HTLV-II, a virus associated with hairy T-cell leukemia; HIV-1, the etiological agent of AIDS and related disorders and HIV-2, a virus related to HIV-1 but isolated from healthy West Africans. One might wonder why it took almost eight decades to identify a human retrovirus, the HTLV-1, although many animal retroviruses have been discovered and extensively studied from the time the first retrovirus, Rous sarcoma virus, was discovered in 1911. That all the human retroviruses discovered to date are from T-cells most probably reflect our inability to grow large quantities of other types of hematopoietic cells.

The next four chapters are dedicated to animal retroviruses that cause hematopoietic disorders which contributed to the present progress in the study of human retroviruses. These include the bovine leukemia virus (BLV), feline leukemia virus (FeLV) and the lentiviruses that cause slow progressive disorders. Identification of the 'px' regions, consisting of additional open-reading frames that are absent in other retroviruses, and their functions is a significant step towards understanding the mechanism of pathogenesis of these viruses. But for the concepts and techniques developed during the study of these

viruses, the discovery as well as the commendable progress achieved in a short period in understanding the biology of human retroviruses could not have been possible.

The rest of the chapters deal with various aspects of the above-mentioned four human retroviruses. Whereas Chapters 6 and 7 describe the biology of the first human retrovirus, HTLV-I, Chapter 8 deals with that of HTLV-II. Elucidation of the function of *tax* and *rex* proteins encoded by the 'pX' region and the implication of *tax* in the activation of IL-2 receptor-α in certain cells in the early stages of development of ATLL is of significance as these studies accelerated the progress in understanding the biology of HIV.

An account of the epidemiology, geographical distribution, modes of transmission and gene structure and function of the human retroviruses is given in Chapters 9, 10 and 14. Although the genome organisation of the four viruses is similar, the 'pX' region of HIV encodes more functions than that of HTLV-1. Of these, the *nef* protein acts as a negative regulator of viral replication and appears responsible for the cytopathic effect of HIV. These proteins in conjunction with the *env* protein of HIV cause ablation of $CD4^+$ T-cells in contrast to the proliferative disorder caused by HTLV-1.

The discovery of simian immune deficiency virus (SIV) and the observation that it is closely related to HIV-2 resulted in the speculation that HIV might have evolved from SIV. Chapter 12 gives a comparative account of the biology of HIV-1, HIV-2 and SIV. It may be noted that whereas SIV is 80% similar to HIV-2 and 50% to HIV-1, and causes AIDS in monkeys, HIV-2 apparently does not cause AIDS in humans in contrast to HIV-1.

The complex immunological spectrum of AIDS and HIV infection of various hematopoietic cells and the possible mechanism of escape by HIV of host immune rejection are described in Chapter 11. Further, the presence of suppressor substances of T, B and NK cell functions in the sera of AIDS patients is implicated in the development of immune deficiency.

Chapters 13 and 15 dwell on the strategies towards developing therapeutic drugs and vaccines based on the biology of HIV. Although 3′ Azido 2′, 3′-dideoxy thymidine (AZT) has been shown to be clinically beneficial in prolonging the survival of patients with advanced AIDS, its cytotoxic side effects necessitate vigorous search for better and less toxic therapy. Curative therapy and prevention of AIDS will not be possible until further basic research on the molecular biology of HIV and the structural chemistry of key viral products is done.

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Covalently modified antigens and antibodies in diagonsis and therapy edited by Gerard A. Quash and John D. Rodwell. Marcel Dekker, Inc, 270, Madison Avenue, New York, NY 10016, 1989, pp 248, $ 119.50

Modern diagnostic and therapeutic procedures are utilising monoclonal and polyclonal antibodies more frequently in the process of disease management and investigation. This new book is an effort to put together the diverse chemical methods used to modify antibodies for later utilisation in tumor therapy, clinical medicine and immunodiagnostics. Since the book actually summarises a symposium held in France in June 1987, it serves to cater only to those readers directly involved with such work. Although the book contains excellent chapters, it appears to have been hastily put together resulting in many printing errors. There are eleven chapters spearheaded by a chapter on 'Immunological

approaches to tumor therapy' written by Karl and Ingegerd Hellstrom. This chapter, although ambitious, serves as a good prelude to the later chapters that have been developed so as to include studies on coupling monoclonal antibodies to toxins and to complement proteins, their use in *ex vivo* bone-marrow purging, tumor detection and efficacy of such procedures in cancer therapy. Separate chapters have been devoted to describe the advantages of utilising carbohydrate residues on antigens or antibody molecules for covalent coupling either to toxins or to solid supports. Finally, the use of coated latex particles for identification and localisation of cell-surface receptors and their potential application for immunodiagnostics is described. Due to its very nature of being a book that deals with the proceedings of a symposium held in 1987, it is not a comprehensive treatise on the topics discussed but will serve excellently as a reference book and as a source for studies carried out until 1987.

In Chapter 1, Karl and Ingegerd Hellstrom describe their work being carried out at the Oncogen Laboratories. After giving a brief background, the article concentrates on the melanoma p97 antigen and its specific monoclonal antibodies as a model system to evaluate different approaches towards tumor localisation, diagnosis and therapy. While describing the therapeutic uses of antitumor antibodies, this chapter stresses the importance of using antibodies that can fix complement so that the ensuing local inflammation stimulates blood supply and thereby ensures better delivery of the antibody to the tumor site. Judicious use of IL-2 is also recommended to increase NK activity. The generation of mouse-human chimaeric antibodies by recombinant DNA technology has been mentioned although it must be noted that its general practicality in the larger context of spontaneous tumors is still unclear. The use of antibody-toxin immunoconjugates and anti-idiotypic antibodies for therapeutic purposes seems to hold great promise. Authors also stress the importance of the need to develop recombinant vaccines that stimulate tumor-specific delayed-type hypersensitivity (DTH) reactions for better efficacy. Chapter 2 deals mainly with the chemistry of coupling reactions used for the covalent conjugation of the ricin toxin to monoclonal antibodies and the application of such immunotoxins in bone marrow transplantation. Immunotoxins prepared by coupling the Ricin A chain in a variety of ways to anti-CD5 monoclonal antibodies such as T101 were evaluated for their cytotoxicity and therapeutic applicability. Authors demonstrate not only the improvement of cytotoxicity in the presence of lysosomotropic amines such as monensin and ammonium chloride but also the role that pH can play in modulating the action of such amines or 'enhancers'. Finally they have attempted to overcome the poor pharmacokinetic properties of the glycosylated ricin toxin by deglycosylating the A chain to block hepatic uptake by kupfer cells. Chapter 3 describes the properties of the mouse monoclonal antibody 791T/36 that was prepared against cells of a human osteogenic sarcoma line. The tissue localisation and the nature of the specific tumor antigen have been characterised. The *in vitro* functional reactivity of methotrexate-791T/36 immunoconjugates was then analysed and their therapeutic efficacy demonstrated in immunodeficient mice. Immunoscintigraphy studies were carried out in patients to analyse the blood survival of ^{131}I-labelled 791T/36-antibody conjugates. Similar such studies were also carried out using Ricin A chain-791T/36 immunoconjugates. Methods to limit hepatic uptake and degradation are finally discussed.

In Chapter 4, authors discuss the problems encountered in the application of monoclonal antibodies to combat tumors. A variety of strategies utilised for drug-antibody conjugation and the problems of increasing the access of drugs into tumor tissues are dealt with. Authors use three *in vivo* and *in vitro* models to evaluate anti Ly2.1 or anti-transferrin-receptor immunoconjugates coupled to various analogs of adriamycin and anthracycline, folic acid antagonists, alkylating agents like chlorambucil and melphalan as well as toxins. β-Adrenergic agents and tumor necrosis factor were used in studies designed to increase permeability of blood vessels and blood flow to the tumor. The entire chapter is eloquently summarised at the end. In Chapter 5, authors demonstrate that site-specific coupling of a tripeptide chelator to oligosaccharide sites on the antibody offers great advantages. This could serve as an alternative approach to direct coupling of antibody tyrosines, lysines or acidic amino acids. The

effects of coupling reactions on the antibody reactivity of a panel of monoclonal antibodies are analysed. Imaging of such conjugates as well as their blood distribution studies were conducted in tumor-xenograft models. The inclusion of a photograph demonstrating localisation of labelled antibodies to a tumor site *in vivo* is a plus point. In addition, the authors delineate the points to be considered before selecting appropriate labels for the purpose of antibody radiolabelling and radiotherapy. In Chapter 6, Reiter and Fishelson use the bifunctional reagent N-succinimidyl-3-(2-pyridylthio) propionate to prepare heteroconjugates composed of human C3b complement and a murine monoclonal antibody against the transferrin receptor. After demonstrating good binding of the coupled antibody to the receptor on K562 cells by Scatchard analyses, authors study the efficiency of K562 lysis by the complement-antibody immunoconjugate and its capacity to activate the alternate complement pathway.

In Chapter 7, Combaret *et al* describe the various immunological and chemical methods used for marrow purging during autologous bone-marrow transplantation. A comprehensive table that summarises the various methods presently used has been included. The more recent methods of immunomagnetic depletion and use of immunotoxins provide additional information for the reader. Experimental models that examine the efficiency of the purging process are described. These include recent models that utilise bone marrow samples mixed with exogenously added malignant cell lines. The importance of clonogenic efficiency of the malignant cells contaminating the bone marrow cells being purged is discussed. In Chapter 8, authors examine the advantages of site-specific coupling of antigens or antibodies to solid supports relative to simple protein adsorption in the routine use of diagnostic tests such as agglutination, ELISA and RIA. They describe methods for the site-specific covalent coupling of antigens or antibodies. These methods are more likely to preserve the native configuration of epitopes in a protein when it is attached to solid supports such as latex spheres, polystyrene microtiter plates, nylon and cellulose acetate strips. A latex agglutination test to measure viral neuraminidase has been developed as an alternative to the method recommended by WHO. Authors also describe the advantages of their methods in determining the titers of specific antibody present in circulating serum immunocomplexes obtained from patients infected with cytomegalovirus. In Chapter 9, Tseng, Freytag and Craig delineate the procedures for the preparation of covalently linked antibody-enzyme conjugates. The enzymes used, *i.e.*, β-galactosidase and horse radish peroxidase were prepolymerised prior to coupling with antibody in order to amplify the signals obtained finally. The antigen-binding properties of such enzyme-immunoconjugates and their advantages in sandwich as well as normal ELISA are reported.

In Chapter 10, Fan *et al* alter the stability and physical properties of magnetic tape chromium dioxide particles in order to utilise them for rapid magnetic separation of reaction components during immunoassays. After coating with amino-silane the chromium dioxide particles were coupled to the antibody or protein using gluteraldehyde. Such coupled particles were used in digoxin and follitropin enzyme immunoassays to demonstrate their wide range of applicability. The ease with which magnetic separations can be done will probably determine the increasing frequency with which such methods will be used in the future. Chapter 11 by Robert *et al*, although describing studies in the field of mycological ecology, includes novel experiments that may well hold a very promising future and application, not only in biology but also in other interdisciplinary fields. Clear electron micrographic studies delineate the use of fibrinogen-coated latex particles for identifying and localising the fibrinogen receptor on the mycelial surface of *Candida albicans*. It is not clear, however, if these methods are applicable in cases where the identity of the protein and its receptor are unknown such as in many virus-host interactions.

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Opportunistic infections in patients with the acquired immunodeficiency syndrome edited by Gifford Leoung and John Mills, Marcel Dekker, Inc., 270, Madison Avenue, New York, NY 10016, 1989, pp 476, $107.50.

The editors of this little book with the arresting title are at the Department of Medicine, University of California, San Francisco. This is the key to explaining its contents. Acquired Immunodeficiency Syndrome (AIDS) has become an enormous health problem, especially in the western countries, and in its wake, infectious diseases, which had almost disappeared there after the advent of antibiotics and antiviral vaccines, have staged a comeback. This is because on infection by human immunodeficiency virus (HIV), the general immunity of the patients against these diseases breaks down, and these individuals become prone to bacterial diseases like pneumonia and tuberculosis, viral diseases like herpes, fungal infections like candidiasis and protozoal infections like toxoplasmosis. This book focuses on the unique problems of managing such opportunistic infectious in HIV-infected patients. Though the main intention of the book is to provide a practical approach to patient management, basic science and pathophysiologic issues have been discussed where relevant.

The book is divided into four parts. The first, a general introduction, reviews the epidemiology, virology and immunology of HIV infection, with special reference to opportunistic infections. In part II a systematic approach to the evaluation of HIV-infected patients who present with clinical syndromes like fever, cough or diarrhoea is provided. Part III discusses the major infections, grouped by etiologic agent, known to occur in HIV-infected patients. Finally, there is a part on the optimal usage of laboratory services.

The book will be immensely useful not only to students of medicine but also to microbiologists who will find it very interesting and informative.

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Adverse reactions to drug formulation agents edited by Murray Weiner and I. Leonard Bernstein. Marcel Dekker, Inc., 270, Madison Avenue, New York, NY 10016, 1989, pp 480, $150.

Many 'inactive' ingredients are used in pharmaceutical preparations. The ostensible purpose of these agents known as 'excipients' is to give bulk or coating to a capsule or tablet, to colour, to extend shelf life, to mask unpleasant taste or to render the active principles soluble in drug formulations. Of these, colours used such as tartrazine, the yellow colour, are known to produce adverse effects particularly among those who do not tolerate aspirin. Other side reactions due to excipients have also been documented in literature. The presence of such agents in 'generic' products can be harmful.

In the handbook under review the authors have assembled a great deal of information found scattered in medical literature. The book is divided into four parts. The first part gives a critical overview of the state of art of adverse reactions of excipients. Direct toxicity, immunotoxicity, hypersensitivity and allergy, intolerance and idiosyncrasy are the main adverse side effects encountered. An exceedingly useful account of the mechanism of allergic and immunopathogenic reactions is given as background chapters. In view of the rapid progress made in recent years in immunological investigations, the chapter on diagnostic procedures will be welcomed widely.

The adverse health effects associated with excipients have been dealth with for oral, topical and parenteral preparations, suppositories, flavouring agents and preservatives. The side reactions associated with materials used in the construction of plastic and rubber appliances (valves, defibrillators), needles and sutures, dialyzers, adhesive tape, vaginal and intrauterine devices and contact lens have also been reviewed. The appendix contains an 84-page table of inactive ingredients currently marketed in USA as drug products.

This handbook is issued as Vol. 14 of a popular Series on Clinical Pharmacology. The price would unfortunately put this book out of the purchasing reach of many Indian scientists. Nevertheless, this is an excellent handbook and is strongly recommended for libraries of R & D institutions, Food & Drug Administration of the Ministry of Health and libraries of all manufacturing houses of processed and formulated drugs and foods.

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Clinical epidemiology of chronic obstructive pulmonary disease (Lung biology in health and disease, Vol. 43) edited by Michael J. Hensley and Nicholas A. Saunders. Marcel Dekker, Inc., 270, Madison Avenue, New York, NY 10016, 1989, pp 408, $132.

Claude Lenfant's Lung biology in health and disease has become an established tradition; one looks forward to each of the additions to this series. Volume 43 on clinical epidemiology of chronic obstructive lung disease is the latest in this series. Epidemiology, the study of distribution and determinants of disease in human populations, is a somewhat neglected sphere insofar as clinicians are concerned. Only recently is the importance of this branch of knowledge being increasingly appreciated. This volume fills the void in the area of the literature on COPD (chronic obstructive pulmonary disease), a very common syndrome causing considerable morbidity and mortality. The volume contains many chapters of interest to clinicians such as those on small airways disease, natural history of chronic airflow limitation and the chapters on smoking. The details on strategies of smoking cassation and the role of the physician are dealt with in an excellent manner. The chapter on the economics of smoking cessation is an eye opener.

The epidemiologic principles underlying the study of COPD are outlined comprehensively. The complex interplay of factors that may confound the longitudinal study of COPD is described in an elegant and lucid manner. The question of the role of airway reactivity in the causation of COPD is dealt with in a competent and very interesting fashion. Many unanswered questions that will need intense research efforts in the future are raised. The chapter on the quality of life of patients with COPD is very revealing. Likewise, clinicians will find the topic of current therapy of COPD informative.

Overall, the volume is bound to be a valuable addition to the reference libraries frequented by internists, pulmonologists and postgraduate students involved in work in the broad area of COPD research.

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Chronopharmacology—Cellular and biochemical interactions edited by Bjorn Lemmer. Marcel Dekker, Inc., 270, Madison Avenue, New York, NY 10016, 1989, pp 744, $180.

Bjorn Lemmeri's effort in bringing out this volume is praiseworthy. It presents an interdisciplinary approach for study of drug utilisation and pharmacological actions in humans and animals, with special reference to 'circadian rhythm', a new concept. This concept, which forms the basis of this series, is well brought out not only in drug utilisation but also its role in causing foetal congenital abnormalities. A deeper understanding of such a concept is very important for gaining insights into effective drug action *in vivo*.

The information and data presented in this volume should prove useful to physicians for adjusting dose-time schedule as per circadian phase. The subject matter is well organised and the contents nicely presented. In the overall, the volume can be regarded as containing three major sections—the first dealing with chronopharmacology (Part I), the second with different classes of drugs (Parts II–VII) and the last the chronotoxicity (Part VIII). The utility of the book is further amplified by generous incorporation of illustrations by way of tables, figures and graphics.

The most thought provoking of the topics is concerned with the circadian rhythm and embryotoxicity. Research into this area might give rise to answers to many congenital abnormalities.

Although the Editor notes that circadian rhythm is genetically determined, it is disappointing to see that there exists no discussion on pharmacogenetics. In terms of the role of genetics in circadian rhythm the reviewer feels that a topic on pharmacogenetics should have been included in the first section.

Similarly, in the presentation of antihistaminics and anti-allergic drugs, Theophyllin is discussed more extensively in asthma than other drugs in this area. The number of subjects chosen for some of the study groups appears to be small to preclude statistically significant results. There were differences in the results among different authors for the same drug (Theophyllin) and even for the same formulations.

On the whole, this volume presents insights into certain mechanisms not explored fully today. Thus it should provide stimulating reading to researchers in life sciences and should also serve as useful reference to physicians to optimise drug dosage and thereby minimise the side effects of the drugs. Life sciences research libraries should find this volume a useful addition.

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From gene to animal edited by David De Pomerai. Cambridge University Press, The Edinburgh Building, Shaftesbury Road, Cambridge CB2 2RU, UK, 1985, pp 293, $25.

Developmental biology is much talked about these days, and with good reason. Progress has been fast on a number of fronts, two in particular. On the one hand, we are beginning to assemble a catalogue of 'morphogens', substances which by being distributed non-uniformly in the embryo in different regions call forth the activities of different subsets of genes. On the other hand, our understanding of the genetic basis of patterning – the characterisation of genes which specify the primary pattern of the body, conceivably in response to a morphogen gradient – is improving practically day by day. These advances, in combination with an elucidation of the mechanisms of gene regulation in higher organisms

will, it is hoped, lead to a solution of the basic problem of development (at least in particular organisms) in the forseeable future.

The rapid accumulation of new facts that we are now witnessing imposes a heavy burden on the writers of text books. They risk whatever they write becoming out of date very soon, or uninteresting, or both. As it happens, two recent attempts, *From egg to embryo* by J. M. W. Slack and *Genetic analysis of animal development* by A. S. Wilkins, have been conspicuously successful. By this I mean that they provide an orderly account of known facts *and* convey a sense of anticipatory excitement about what remains unknown. On top of this, Davidson's *Gene activity in early development* is now available in a third edition. The book under review here, *From gene to animal* by David De Pomerai, was published in 1985 and so ought to stand assessment in comparison with the ones just named. How does it fare? In my opinion, not too well.

The problem is that De Pomerai takes a long time to come to grips with essential questions, and when he does, he handles them more in the manner of a purveyor of bald data than as an analytical critic. The first three chapters, occupying slightly over a third of the book, deal with the organisation of eukaryotic DNA, the structure of chromatin and transcription; it is only in the fourth chapter that the issues of variable gene activity and mosaic *versus* regulative development are raised. The second half of the book stands out better; it contains a discussion of three 'specific systems' – erythroid cell differentiation, oogenesis and insect development. Of these I am best able to comment on the section dealing with insect development; it struck me, once again, as a somewhat hasty assemblage of facts. In contrast, erythroid differentiation seemed to be well covered, extending as it does to a brief account of the organisation of globin genes (though even here, for reasons which can only be guessed at, there is a curious omission: no mention is made of the stochastic basis of stem cell differentiation). The book as a whole contains far too many conspicuous gaps for it to function as a well-integrated text on animal development. To name just three. *Caenorhabditis elegans* finds no mention worth the name and neither the phenomenon of mesoderm induction in amphibians nor the concept of gradients gets the treatment it requires. Perhaps a strict definition of 'molecular biology' would exclude gradients, but surely not the other two topics. In summary, the best one can say about this book is that it can serve as a partial guide to the literature pertaining to a few specific problems in developmental biology, a poor man's Davidson in short.

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Geomicrobiology (Second edition, revised and expanded) by Henry Lutz Ehrlich. Marcel Dekker, Inc., 270, Madison Avenue, New York, NY 10016, 1990, pp 646, $162.

The effective application of the normal activities of microorganisms like solubilisation, transport and deposition of metals in nature has now developed into an attractive technology meeting many of the needs of mining and mineral industry. Even though *Thiobacillus ferrooxidans*, the most worked out organism, was discovered in the 1940s in acid mine drainage, it was in mid-50s the role of microorganisms in leaching was clearly defined. With more information accumulating on the how and why of microbial activity, 70s saw the gradual development of the technology. Currently, the application of bacterial leaching at industrial level is limited to the extraction of copper, uranium and enhancement of gold recovery.

Very few publications in bioleaching/bioprocessing of minerals/geomicrobiology appear without a reference to Prof. Ehrlich's book on geomicrobiology. Since the publication of the first edition in 1981,

there has been a tremendous increase in the number of people working and consequently the publications in the area. We are sure that those who work in geomicrobiology will welcome this long-awaited revised edition with cheers. The variety of topics covered in the second edition shows that geomicrobiology has come of age and is no more a kid loitering in the backyard of microbiology.

Almost all chapters are thoroughly revised and updated. Literature coverage extends up to 1987; even though not intended to be extensive, it can lead the reader to pertinent references. The stress of the current edition is on examination of specific geomicrobial processes, microorganisms responsible for them and their relevance to geology as in the first edition. The chapters on the geomicrobiology of nitrogen and chromium are additions to the second edition. The second chapter is divided into two – earth as microbial habitat and origin of microbial life on earth. Microbial physiology and biochemistry is given due share in Chapter Six by extensive revision.

The luxuriant illustrations and excellent photographs make the new edition a comfortable reading material. The glossary of the special terms used will be useful to the readers of biological and non-biological background. The present edition will serve as a valuable source book for microbiologists, ecologi ogists, environmental and mining engineers, and metallurgists.

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