

Endomyocardial Fibrosis. M. S. Valiathan, K. Somers and C. C. Kartha eds. Oxford University Press, YMCA Building, New Delhi 110 001, India. 1993. 302 pp. Price: Rs 500.

In December 1991 a group of scientists belonging to clinical, epidemiological and related disciplines from different parts of the world assembled, appropriately, in Trivandrum, Kerala State, India, to discuss the enigma of Endomyocardial Fibrosis (EMF). It was here that nearly three decades ago Gopi, a local physician, drew attention to the endemicity of EMF in the State, it is now here that EMF is the chief research mission of the recently-established Sree Chitra Tirunal Institute for Medical Sciences and Technology under the leadership of its Director, M. S. Valiathan. This book incorporates the presentations and discussions that took place at this unique conference. The conference was opened by Jack Davies, the discoverer of the syndrome of EMF (also sometimes called Davies' disease) in the halcyon days of the Makerere University and the Mulago Hospital way back in 1948. Some of the actors in the early drama of EMF in Uganda were in attendance such as Gerry Shaper and Krishna Somers. The result is an outstanding publication, carefully edited and easily readable which brings one up-to-date with the totality of existing knowledge on this form of endemic restrictive type of tropical cardiomyopathy.

The book is organized in six parts, ranging from geographic spread, to etiology, pathology, clinical presentation, treatment and experimental studies. The overall picture that emerges is of an incapacitating and fatal disease with worldwide distribution, a fascinating model of pathology, whose acute (early) stages of the disease are not clear but whose established chronic stage is well characterized clinically, haemodynamically, angio-cardiographically and through non-invasive 2D echocardiography and Doppler. As a result there is today an expanded vision of the clinical picture and diagnosis of EMF, the ventricular involvement including the systolic and diastolic dysfunctions, the progression of changes and the correction of observed abnormalities following surgery. Surgery, in the form of endocardial decortication and atrio-ventricular valve replacement, is the

treatment of choice for patients with severe heart failure and irreversible disease; some improvement in the quality of life is recorded among the survivors of this rather drastic surgery, especially in the experiences from Brazil and Ivory Coast but the Indian experience is somewhat less enthusiastic, what with factors such as the low socio-economic status of most subjects and the difficulties in ensuring compliance of anticoagulant therapy following surgery in Indian patients.

The crux of EMF is its etiology. The equatorial distribution of the disease with its geoclimatic implications, its predilection to affect the young and the poor, conjure up a vision of a geochemical basis for the disease or of an infectious process with infectious agents, parasites and vectors, and eosinophils in play, and with transmission enhanced by poor living conditions and increased man vector contact. Ideas about etiology had ranged widely from time to time from nutritional deficiency, serotonin excess, Vitamin E deficiency, obstruction of cardiac lymphatics, a variation on the theme of rheumatic heart disease, hypersensitivity to malaria, a role for *Toxoplasma gondii* but none of these stands on a firm footing. The trouble is that descriptions of the pathology of the end stage of the disease are unexciting and not very illuminating, possibly representing a stereotypic response to diverse initiating events; there is, however, no clue as to what these initiating events might be.

Two other outcomes of the conference are worthy of note. One is the experience of almost everyone at the symposium that EMF is different from Loeffler's endocarditis and the eosinophil is not a major determinant of tropical EMF. The other outcome is the series of epidemiological and experimental studies presented at the conference by scientists from the Sree Chitra Tirunal Institute that propounded the hypothesis that a geochemical basis of EMF in the form of a deficiency of magnesium and excess of cerium constituted the initial injury in EMF. The disease is considered essentially as interstitial in origin with such myocyte changes seen being regarded as secondary events. There are no extra cardiac lesions to provide any more

clues. The rare earth-trace metal hypothesis of EMF is a dominant image emerging out of the symposium.

Despite much progress the present status of the etiology of EMF is best summed up in the words of Charles Sezi of Uganda: 'The etiology continues to linger in darkness, treatment is unsatisfactory and prevention completely unknown'. The undersigned reviewer is reminded of a statement by the renowned epidemiologist Geoffrey Rose: 'Etiology confronts two distinct issues: the determinants of individual cases and the determinants of incidence rates. The corresponding strategies in control are the high risk approach which seeks to protect susceptible individuals, and the population approach which seeks to control the causes of incidence. The two approaches are not usually in competition but the prior concern should always be to discover and control the causes of incidence'.

1 'Genetics and Environment Geoffrey Rose revisited' by Kay-Tee Khaw, *Lancet*, 1994, 343, April 2, 838-839

V. RAMALINGASWAMI

*Department of Pathology
All India Institute of Medical Sciences
Ansari Nagar
New Delhi 110 029, India*

Proceedings (Mathematical Sciences). K. G. Ramanathan Memorial Issue. Indian Academy of Sciences, P.B. No. 8005, Sadashivanagar P.O., Bangalore 560 080, India 1994. 304 pp.

Professor K. G. Ramanathan was a colourful personality, who played a major role in the development of Mathematics in post-independence India. He was one of the people responsible for the evolution of the Mathematics School at Tata Institute of Fundamental Research from the fledgeling that it was in 1950 (when he joined that institution) into an international centre of excellence in mathematics. Ramanathan was a Fellow of the Indian Academy of Sciences and the Academy has brought out a special issue of its *Proceedings (Mathematical Sciences)* dedicated to

his memory. It is indeed a fine tribute to the man and his mathematics*.

Ramanathan's primary interests were in Number Theory. He is well-known for his contributions to the analytic and arithmetic theory of hermitian quadratic forms over involutorial division algebras, work that was the result of the direct influence of his teacher C. L. Siegel, one of 20th century's greatest mathematical intellects. A fourth of the articles that appear in this special issue are related to the general theory of automorphic forms, a subject that has been profoundly influenced by Siegel's work and closely connected to much of Ramanathan's own. Ramanathan succeeded in building an excellent group in this area at TIFR and this memorial tribute contains a contribution from the leading member of the group, S. Raghavan (jointly with J. Sengupta). Andrianov, a distinguished Russian mathematician from St Petersburg, provides in his paper a new approach to a famous result of Siegel. Don Zagier (who divides his time between Maryland in the USA and Bonn in Germany), a leading expert in the theory, explores anew the relationship between modular forms and special differential equations, taking up a 19th century theme that has been almost forgotten. Sato, a famous Japanese mathematician extends the theory he developed in collaboration with his compatriot, the late Shintani (in a famous work published in 1974). Yet another illustrious name in the list of contributors in this area is the Japanese, Igusa, a personal friend of Ramanathan's. M. Ram Murty a leading Canadian number theorist from McGill University has contributed (in collaboration with A. Hashim) a paper dealing with Fourier coefficients of certain modular forms introduced by Zagier.

There are among the contributions almost as many papers in what is usually classified as analytic number theory, as there are in the theory of automorphic forms (this separation is somewhat artificial but there is a difference in flavour). Ramachandra, an internationally known expert in this kind of number theory and the leader in the field in India, was a student of

Ramanathan. His paper written in collaboration with R. Balasubramanian, himself a student of Ramachandra's and a number theorist of high repute, is on the zeros of a class of Dirichlet series. The paper is 15th in a series devoted to the subject, pursued (obviously!) with great tenacity by the two authors. Another of Ramachandra's students, T. N. Shorey, a well-known number theorist on the TIFR faculty, has contributed an article in collaboration with N. Saradha; the problem dealt with has (like many others in the area) a simple formulation, a formulation that can be understood with merely a High School background in mathematics. Bambah is a famous name in Indian mathematics, a close friend of Ramanathan's he had a major role in building a very good department at Panjab University. This volume has an article by him written in collaboration with A. C. Woods of Ohio State University, a contribution to the 'geometry of numbers'. Heath-Brown of Oxford and Huxley of Wales College, both Number Theorists of the first rank, have made very interesting contributions, the latter in collaboration with his colleague N. Watt. Heath-Brown gives new estimates for the number of lattice points on a nonsingular hypersurface given by a homogeneous integral polynomial. The Huxley-Watt paper deals with estimates for the number of ideals in a quadratic number field of norm less than a given integer.

The triumvirate Andrews, Askey and Berndt have become practically household names in this country. Their efforts at getting some parts of Ramanujan's work better known and better understood by the mathematical community have been stupendous. Ramanathan in his last years was also deeply interested in the Ramanujan Notebooks, an interest that brought him close to these three. It is no surprise that their contributions are related to the Ramanujan Notebooks and add immensely to the value of this volume. That these articles are particularly appropriate, is brought out best in Askey's introduction to his paper (and I quote): 'K. G. Ramanathan was a gentle man, who had a strong sense of duty. Part of his duty was the understanding of Ramanujan and his mathematics and we can all feel pleased that he helped us in understanding some of the mathematics Ramanujan did'

There are two other papers in Number Theory that do not quite fall into any of

the three groups above. One is a paper by a distinguished Dutch mathematician T. A. Springer 'Reduction Theory' the subject matter of Springer's paper was close to Ramanathan's interests too. Springer was also a personal friend of Ramanathan's. Kitaoka, yet another Japanese number theorist of the first rank continues in his contribution his earlier study of finite subgroups of the general linear group over the ring of integers in a number field.

Algebraic geometry is represented in the issue by a paper of M. S. Narasimhan and A. Hirschowitz. Narasimhan is one of the pioneers in the study of moduli of vector bundles on curves and undoubtedly the most versatile among Indian mathematicians. The paper itself is on vector bundles, a subject far removed from Ramanathan's own interests but it was Ramanathan, who drew the attention of Narasimhan and Seshadri to a paper of A. Weil that was to inspire their fundamental work on the moduli problem. C. L. Siegel was a powerful personality and it is not surprising that Ramanathan initially absorbed along with the mathematics of that master some of his aesthetic intolerance but fortunately the attitude did not last and he reacted with enthusiasm for diverse areas of mathematics, among them algebraic geometry, an area Narasimhan and some of Ramanathan's other colleagues have made TIFR famous for. Sridharan, a well-known algebraist and (his erstwhile student) Parimala, who has established for herself an excellent international reputation, have contributed a joint paper on the Clifford invariant of a quadratic form; this brings in Algebra as well into the range of areas covered by the papers in the issue.

R. Ranga Rao at the University of Illinois at Urbana is one of a small group of mathematicians, who worked at Indian Statistical Institute, Calcutta, in the early sixties and established themselves as outstanding mathematicians. He has contributed a paper which belongs to the domain of Harmonic Analysis. K. R. Parthasarathy, also a member of the Calcutta ISI group, is an outstanding expert in probability. His joint paper with a student B. V. Rajarama Bhat as well as an article of K. B. Athreya, another well-known Indian Mathematician (also originally from ISI, Calcutta) are in the area of probability.

M. A. L. Thathachar and his colleagues V. V. Phansalkar and P. S. Sastry of the

*In 1980 Ramanathan's colleagues at TIFR wanted to organize a conference in his honour on the occasion of his 60th birthday. He however would have none of it, a reaction typical of him.

Electrical Engineering Department of the Indian Institute of Science, have contributed a paper in Game Theory. Thathachar was actively involved in the programme of 'Applicable' (Ramanathan preferred this adjective to the more familiar 'Applied') Mathematics initiated by Ramanathan, a collaborative enterprise between TIFR and IISc in Bangalore. This programme which has produced some excellent work was helped greatly by a group of French mathematicians led by J. L. Lions, a major figure in French mathematics. Both he and one of his close associates and a distinguished mathematician P. G. Ciarlet have contributed papers in their fields (Control Theory and Elasticity respectively).

The mathematical spectrum covered by the contributions is truly impressive as also the diverse nationalities of the contributors. Ramanathan was a respected figure in the world of mathematics and the present volume bears ample witness to it. The contributors are internationally well-known personalities in mathematics. The Academy deserves to be congratulated for undertaking the venture and doing justice to the excellent purpose it set out on.

There are other friends, colleagues and admirers of Ramanathan, who would no doubt have liked to pay their homage through this volume, but creative work does not always comply with demands of a time frame.

The Memorial Issue also carries an obituary note on Ramanathan giving some interesting information about him.

M. S. RAGHUNATHAN

*School of Mathematics
Tata Institute of Fundamental Research
Bombay 400 005, India*

Annual Review of Cell Biology 1993. Volume 9. Palade, G. E., Alberts, B. M., Spudich, J. A., eds. Annual Reviews Inc., 4139, El Camino Way, Palo Alto, P.O. Box 10139, California 94303-0897, USA. Price USA \$ 46, elsewhere \$ 51. 659 pp.

Cellular biology is growing at a relentlessly rapid pace. Modern instrumentation techniques and highly sophisticated microscopes have illuminated the inner working of the cell as never before. Major advances have been made in recent years in areas as diverse as intra-

cellular trafficking of molecules, signal transduction pathways, cell-cell interactions, membrane organization and supramolecular assemblies. Moreover, the fields of cellular and molecular biology are now so intertwined that the series *Annual Review of Cell Biology* reflects what is new and exciting in both these areas. This is of special advantage to the researcher, who is thus encouraged to take a holistic view of the cell.

Five reviews are devoted to recent advances in understanding intracellular transport and signal transduction pathways. S. Subramani gives a detailed account of peroxisomal protein import, peroxisome biogenesis and the genetic basis of human peroxisomal disorders. The conservation of peroxisomal targeting signals as well as genes involved in peroxisome import and assembly have revealed a unified mechanism for peroxisome biogenesis. Considerable progress has been made in understanding human peroxisomal disorders by the use of peroxisome-deficient mammalian and yeast cells, and should eventually lead to better diagnosis and possible therapeutic intervention for these debilitating diseases. I. S. Trowbridge and coworkers have discussed recent findings on membrane protein trafficking in the endocytic pathway, the chief route for recycling of plasma membrane-bound receptor proteins. The importance of this pathway is evident when one realizes that an amount of membrane equivalent to the entire cell surface is internalized and recycled every 1-2 h. New insights have been obtained into the nature of signal sequences required for internalization and their ability to form distinct three-dimensional structures. S. Ferro-Novick and P. Novick have documented the different types of GTP-binding proteins involved in vesicular transport along the exocytic pathway wherein proteins are recruited to form vesicles that migrate from the endoplasmic reticulum through the subcompartments of the Golgi complex to the cell surface. Although GTP-binding proteins have been implicated in most steps of the pathway, comprehension of their exact role must await future studies, and hence the title of the review is somewhat misleading.

The heat shock proteins are essential components in diverse biological processes. Their role as molecular 'chaperones' whose function is to ensure that proteins fold and assemble

properly in the cell has been highlighted by C. Georgopoulos and W. J. Welch. Discussion of recent findings such as the role of hsp90 in steroid receptor activation makes this review highly topical. Despite the authors' best efforts, however, the confusion in nomenclature of this large family of proteins persists. A comprehensive review on signal transduction in guard cells (which control the stomatal pores in plants) by S. Assmann is the only article in plant cell biology. The signalling systems that sense hormones, light and CO₂ in the guard cells have been clearly defined and placed in perspective with what is known about signal transduction in animal cells, for the benefit of non-plant biologists. The advent of antibody and recombinant DNA technology has opened up a whole new area of investigation into the macromolecular organization of functional domains within the cell nucleus, which has been ably reviewed by D. Spector. New evidence on the dynamic order of DNA replication, the localization of transcriptionally active domains and distribution of splicing factors, together with a model for the functional organization of the nucleus, strengthen the view that the nucleus is a highly organized system of defined structural and functional activities. Newly emerging concepts on gene regulation in eukaryotes by transcriptional repression have been highlighted with chosen examples in a review by B. M. Herschbach and A. D. Johnson.

Several reviews cover different aspects of the host immune response to foreign antigens via both B and T lymphocytes. The antigen receptor of B lymphocytes plays a critical role in regulating B cell behaviour, in addition to its primary function of antigen presentation. New findings on the signal transduction function of the antigen receptor have been reviewed by A. L. De Franco. Although low concentrations of host proteins called cytokines have been implicated as essential for various immunological responses, current thinking is now focussed on the pathogenic aspects of cytokine action. The injurious and beneficial effects of one cytokine, tumor necrosis factor- α , have been documented in detail by K. J. Tracey and A. Cerami. M. R. Jackson and P. A. Peterson have discussed the impressive progress in the area of assembly and intracellular trans-