events in the craton are so complex that it requires a vast volume of data to formulate clear ideas on dyke chronology and crustal evolution

Tertiary period is the time of evolution of the present Indian landscape. Very clear ideas on landform development in Karnataka are fascinatingly presented here, followed by a chapter on laterite. Laterite is a term which originated in India from Malabar. It is extensively developed on the Western and Eastern Ghats. From its humble use as building and decorative stone, it is now being combed for the gold it may contain. The next chapter on black soils is another pet theme of the author. He has analysed its development intricately and provided a decisive account.

The volume concludes with a chapter on morphology and evolution by Prof. Vaidyanadhan. From the early emphasis on mineral wealth which led to intensive studies on the crystallines, geology in the service of man has now moved to societal problems like natural hazard mitigation, land use and conservation, preservation of environment, etc. Consequently, the focus has now shifted to geomorphology, Quaternary geology, engineering geology, environmental geology and seismotectonics. In tune with the times, the last chapter provides a valuable database on land forms for solving geological problems and initiating studies on sustainable development. What is missed here is a mention of the fascinating Talakad sand dunes covering the hoary temples, as pointed out by J. Swami Nath.

The book is a veritable storehouse of the state-of-the-art information analysed incisively and presented in easily readable style by the doyen of Karnataka geology (Padmashri Radhakrishna) and the acknowledged expert on geomorphology (Prof. Vaidyanadhan). The essence of geological knowledge is distilled into the text and adequately backed by appropriate and lovely illustrations. Selected bibliography at the end of the chapters provides good supplementary reading and the exclusion of references in the text has made the narration smooth and absorbing The book is reasonably priced Every student of Karnataka geology should possess this book as a beacon to guide him and every library should have it as a proud possession.

M. RAMAKRISHNAN

Geological Survey of India
27 Jawaharlal Nehru Road
Calcutta 700 016, India

HISTORICAL COMMENTARY AND NOTES

The dilemma of a fame-hunter

Reflections on Yellapragada SubbaRow centenary

S. P. K. Gupta

Doctor Yellapragada SubbaRow, had he been alive in this centenary year of his, might have presented his suit now to Lady Fame, whom he pursued all his life but did not to the end of his time feel himself worthy of For, not only have all his contributions to science and medicine stood the test of half a century, but are also making ever new conquests.

He was a freshman in Harvard Medical School's Biochemistry Department when in 1925 the textbooks carried the description of the Fiske–SubbaRow method for rapid colorimetric estimation of phosphorus in blood and urine. This very sensitive procedure he devised under the guidance of Dr Cyrus Fiske has become a classic in biochemical laboratory and clinical practice. It is taught to all biochemistry students and has helped generations of researchers to advance biochemical studies. It has, moreover, become in recent years a tool for diagnosis of endocrinal and metabolic diseases, including disorders of the thyroid and renal rickets

Yellapragada SubbaRow (1895–1948) 'An eminent medical mind of the century' – *New York Herald-tribune*

The method also helped SubbaRow and his senior collaborator to co-discover phosphocreatine and adenosine triphosphate (ATP), which demolished the claim that glycogen is the fountainhead of energy required for muscular contraction – the claim for which Archibald Hill and Otto Meyerhof were awarded the 1922 Nobel Prize for medicine and physiology. ATP is the key to energy for every sort of biochemical process, including muscular contraction, which gets the world's work done. Because it strengthens cerebral and coronary blood circulation and because of the evidence that adenosine and its nucleotides are present in neuromediators and neuromodulators in the central nervous system, ATP has been used in the management of a wide range of diseases, particularly of the joints and the musculature. This is a bonus SubbaRow himself might not have expected of his research

During his years with Fiske, SubbaRow isolated a series of phosphorus compounds, including nucleotides involved in the synthesis of RNA. This work remained locked up in Harvard notebooks as Fiske underwent a personality change and forbade its publication. The advance of the science of nucleic acids and the advent of biotechnology was delayed because these nucleotides had to be rediscovered by others.

His work on phosphocreatine was adjudged fit for the Harvard Ph D, but it was not until he found time amidst all this Nobel-class research to earn credits for the requisite undergraduate and postgraduate courses that he got the doctorate in June 1930. SubbaRow remained in Fiske's laboratory with a lowly staff position but was allowed independent nutritional research. He, as a vitamin hunter, took beatings from better-endowed competitors outside Harvard. His vain bid to help Fiske get the chairmanship of the Department by sacrificing all credit for the work he did while nominally under him had cost SubbaRow promotion to the faculty. Without a faculty position he could not have the funds and assistants required for the success of his projects on anti-pernicious anaemia and anti-pellagra.

SubbaRow left his frustrating position in Harvard when Lederle Laboratories built the facilities he asked for and allowed him to gather the team he desired to secure the company a competitive edge in vitamins and antibiotics. The academics then, as now, looked down upon drug company work and he himself frowned upon what the firms put on the labels of their merchandise. But as though one possessed, he used his company's men and money to isolate the anti-pernicious anaemia factor (later identified as Vitamin B_{12}) from liver. Others who began the race with him got tired and fell by the side; he himself was blinded to his own success ironically by perceptions and prejudices acquired during the long chase. He thought the pure pink vitamin solution to be a liver fraction contaminated by the poisonous Reinecke salt. What saved SubbaRow was his conversion to the mistaken belief that pernicious anaemia, the target of Vitamin B_{12} hunters, and tropical sprue, his own antagonist, were analogous. He led the group which isolated folic acid, the cure for tropical sprue, from liver, but it was an expensive curiosity. So he looked for alternative sources and got it isolated from a microbial fermentation broth also. He did not know it but it actually was a folic acid analogue. Luckily this too cost too high and he worked out its synthesis with his team of young Ph Ds fresh out of graduate colleges.

Folic acid has, in the last fifty years, proved itself as a specific against megaloblastic anaemias other than pernicious anaemia, and as an adjunct to treatment with vitamin B_{12} in pernicious anaemia cases. Its isolation from a microbial source inspired the isolators of the vitamin B_{12} too from similar sources. It has also received much attention from bioscientists because it participates in the synthesis of amino acids like methionine and serine, purines, pyrimidines and in the exchange of choline.

Folic acid was Lederle's first own vitamin but SubbaRow and his researchers secured the company patent position on several vitamins by finding alternative routes to their synthesis. Nor were vitamins the only preoccupation of SubbaRow's research laboratory. His chemists and biologists, along with their clinical collaborators all over the United States, were engaged in battles against a whole range of ailments. SubbaRow orchestrated the brilliant new ideas of the young scientists in their creative years and induced new creativity among veterans by assigning tasks they had no previous experience in. As an MD he motivated Ph Ds with his dedication to the alleviation of human ailments, and as a Ph D he got MDs to help him fashion chemicals to match the microbes. A man of all sciences, he was a chemist among chemists, a parasitologist among parasitologists and a clinician among clinicians. He went from laboratory to laboratory, paced up and down with doctors and project leaders, discussing problems on which they were stuck and telling them, 'You should do this and this and this,' and the project would go forward.

After the May 1946 presentation of folic acid, the medical world received with enthusiasm from SubbaRow's laboratory an antifilarial, several promising anticancer drugs and an outstanding antibiotic.

The last was the result of his search for a panacea – a cure for all fevers. Rene Dubos's gramicidin and tyrothricin were the first antibiotics to be produced commercially, and this was achieved in SubbaRow's laboratory in 1941. When in July that year H. W. Florey and N. G. Heatley came to the United States to arrange commercial production of Alexander Fleming's penicillin, they found SubbaRow producing penicillin that was 'somewhat more potent' than that reported by anyone else. His apparent success and his company's suspicion of Roosevelt's creeping socialism kept his laboratory outside of the cartel that won war contracts for penicillin. His company wanted him to obtain a licence for streptomycin but Selman Waksman had worked on grants that obliged him to assign patents to Merck. So SubbaRow set up his own antibiotic programme, hiring a botanist to screen moulds from all over the world, a bacteriologist team to test the microbial secretions in experimental animals, a pharmacological group to check toxicity, and fermentation technologists to cook broths in which to grow mould A-377, which secreted what was deadly like cobra to a broad spectrum of disease germs and yet mild like a kitten to their animal hosts. With the golden antibiotic Aureomycin born of the labours of botanist Benjamin Duggar, bacteriologist Doris McKenzie, pharmacologist Ben King Harned, fermentologist Joseph Niedercorn and isolation chemist George Krupka, SubbaRow went to the top clinicians of the day and was cold-shouldered. But the distinguished Harlem surgeon Louis Tomkins Wright was impressed by SubbaRow's data on viricidal A-377 and got dramatic cures of viral VD. Now the famous Harvard and Johns Hopkins clinicians vied with each other to get physician's samples. The antibiotic helped control a Californian epidemic of rickettsial infections, cured bacillary and influenzal conjunctivitis, combated urinary tract infections resistant to sulphas and penicillin, and cured brucellosis. Large-scale clinical trials in Boston hospitals proved its broad spectrum of activity against diseases caused by gram-positive as well as gram-negative bacteria, rickettsiae, large viruses, some spirochetes and pathogenic amoebae. Aureomycin is chemically chlorotetracycline and a whole group of 'tetracyclines' were subsequently derived from other moulds and by manipulating the 'tetracycline' molecule One could tailor the tetracycline to a specific ailment and to attack a microbe that had

become resistant to one of the derivatives.

In developing the first tetracycline antibiotic, SubbaRow had found the panacea – a single drug to combat many fevers. the management of which could now be done without hospitalization and without the pain of the needle as it can be and is administered orally as capsules.

But the moment of his greatest success found SubbaRow obsessed with the dream of conquering cancer. A series of false leads set him furiously analysing clinical reports of folic acid and its derivatives by cancer specialists Everything pointed to folic acid *antagonists* as the therapeutic agents against acute leukaemia among children. Sydney Farber confirmed this by securing remissions in two kids admitted at Boston's Children's Hospital with the fatal ailment by administering aminopterin. Methotrexate, the less toxic chemical cousin of aminopterin, later got into the general armamentarium of cancer hsopitals. This has been used not only in childhood leukaemia but also in some adult cancers, notably Burkitt's lymphoma. More importantly, this pointed to antimetabolites in the chemotherapy of cancer. Folic acid antagonists presumably inhibit the synthesis of nucleic acid on which depend division and multiplication of leukaemic cells. Since purines are essential for the completion of nucleic acid synthesis, helped initially by folic acid, purine antagonists developed independently by George Hitchings – a Harvard collaborator of SubbaRow – supplement folic acid antagonists in cancer chemotherapy. Together with 5-fluorouracil, which blocks DNA synthesis, these antimetabolites have helped cure more than half of the children treated for acute leukaemia. Hitchings got the 1988 Nobel Prize partly for this contribution. But cancer remains unconquered and colleagues say that this was because SubbaRow died in his sleep on August 8, 1948, while gathering men and material for a cancer research institute his company had agreed to build for him.

Yellapragada SubbaRow's ardent courting of Dame Fame was motivated by the circumstances of the family in which he was born a century ago in Bhimavaram, West Godavari district of Andhra Pradesh, on January 12, 1895.

Grandfather Subba Raju had given up a comfortable village post and ancestral lands so that his children could be ready with education to meet the twentieth century in prestigious government service. But father Jagannadham was forced by illness to seek early retirement on a meagre pension Mother Venkamma was determined to see SubbaRow fulfil the mission set for the family by his grandfather. SubbaRow at school was like an ocean-liner stranded on a shallow river and ran away from home to seek a fortune catering to pilgrims in Varanasi. Overtaken and brought back from halfway and put back in school by his mother, SubbaRow was sent to Madras for a third attempt after he failed to matriculate from the hometown school and then under elder brother's tutelage in Rajahmundry. On Jagannadham's death, Venkamma sold her *mangalasutram* to maintain SubbaRow in Madras. He passed the matriculation examination but as a college student spent more time at the Ramakrishna Mission, deciding that his prime motive in life (*paramartha*) lay in finding from religion 'the knowledge about relation of man to God'. Seeing no way of his mother permitting his entry into the monastic order, the Mission persuaded him to enter the Madras Medical College so that he could serve in its hospitals. He married the grand-daughter of a landlord who lent funds for him to continue medical studies, resisted the temptation to enter the 1921 Non-Co-Operation Movement lest he fail in his revised prime motive – quest of knowledge about the responsibility of man to fellow humans His concession to Gandhiji, khadi surgical gown, offended the English professors and cost him the MBBS degree. Awarded the LM&S certificate, he decided against medical practice. In any case its failure to save him from tropical sprue had exposed the limitations of Western medicine. He would explore Ayurveda, whose simple potions had cured him after the top English physicians had given up hopes for him.

As vice-principal of Madras Ayurvedic College run by his saviour Achanta Lakshmi Pathi, he organized presidency-wide clinical trials by vaids of Ayurvedic drugs for elephantiasis, compiled a volume on properties of vegetable drugs described by Charaka, Drudhbala, Vrudha, Susruta and Vagbhata the Elder and the Younger He wanted to reinterpret the Tridosha Theory from the modern endocrinological point of view besides standardizing Ayurvedic drugs. The facilities and the atmosphere at the Madras institution was not conducive to this The American medical establishments where he wanted then to pursue these objectives were not sympathetic. He nevertheless landed in Boston on October 26, 1923, with a hundred dollars remaining of the loan advanced by his in-laws. Dean Richard Strong loaned the balance of the fee for enrolling at the Harvard School of Tropical Medicine SubbaRow earned his DTM supporting himself with such lowly jobs as hospital orderly. A Malladi Satyalinga Naicker scholarship permitted him to stay on and he enrolled for a biochemistry course at the Harvard Medical School as it was not tenable for medical studies as such. His research in 'pure' science would also find applications in practice of medicine, and step by step he was inexorably caught in the veils of modern medicine, through which he discharged his 'responsibility... to fellow humans'.

The fulfilment of his *paramartha* did not, however, mean SubbaRow was a wordly success. Nor did he achieve the fame the pursuit of which was his other motivating force. For he was far too squeamish when it came to sharing credit with collaborators This went back to the time when he compiled his 'Hindu Pharmacology'. The manuscript records that he dictated it and that students M. V. Sastry, B. Subramanyam and Rella Kamayya, respectively, wrote down the three parts. At Harvard Medical School, his guide Cyrus Fiske not only wrote up the phosphorus method but also presented it to the scientific world and published the joint paper with himself as the first author. SubbaRow wrote home why: 'I worked under the supervision of Dr Fiske and it is courtesy in research that both names should go to the method. Moreover, a method bearing the name of one with a big reputation like Dr Fiske's would be entirely genuine rather than one bearing the name of a novice unknown to the scientific world' The arrangement continued even with SubbaRow's seminal work in muscle chemistry. the isolation of phosphocreatine and ATP This was unfortunate not only because it denied SubbaRow credit due to an increasingly independent collaborator but also because it caused loss of

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Dear Milton:

I am glad that you are well and happy in the army. I don't know what you are doing there, but it is all right with me.

An unfortuneate incident has occurred, which though I know you will not care about, it still bothers me a little. You remember that you made a summary of our paper "Ergebnise vitamin forschung" for the CURRENT SCIENCE. I passed it along with the idea that it would never reach India, and thus I neglected to put any names on it. But it did reach India, and they did not send me any proof, and even though I did not put any names on the paper, they published it under my name. I had intended it to be a joint paper, and I had intended to introduce the names when the proofs came to me.

I realize that you probably don't care about this, but now that I have told you about it my conscience is clear.

Very truly yours,

Y. SubbaRow

YS:EM

publication priority. As Fiske underwent a personality change, publication was unduly delayed and then completely blocked. This, of course, ruined Fiske's promotion as departmental chief. Fiske was not helped by SubbaRow declaring, out of a misplaced sense of loyalty, that he had merely been an extra pair of hands for him in unravelling muscle contraction. The sacrifice turned out to be scientifically suicidal. Harvard denied SubbaRow facilities for the success of his vitamins hunt. Although Fiske dissociated himself from the vitamin work and new departmental chief A. Baird Hastings was even less concerned with it, they have been cited as co-authors of SubbaRow's Harvard vitamin work. The sole exception is the paper in *Current Science*, which cites SubbaRow as the sole author. He had only summarized a joint paper with Hastings and medical student Milton Elkin, who did library research. For there appeared no chance of it being published by the German journal for which it had been originally written. The United States was at war with Germany. Mailing the summary with no hope that it will reach India, SubbaRow did not put any names on it. He would introduce the joint authors if and when the proofs came. The proofs never came. But the article did reach Bangalore and the exceptional sole-author paper in his bibliography came into being. How much this troubled SubbaRow is revealed in the letter (see box) he wrote to Elkin, who had, in the meantime, spurned his offer of a war-related job that would have granted him exemption and joined the airforce as a lieutenant.

SubbaRow, now head of several research teams, established his own credit regime. The scientist who made the key contribution would be the first author and also present the paper at a scientific gathering; co-workers would be listed alphabetically and his own name would be the last. And, he thought it a compliment and agreed to him also being listed alphabetically in the announcement on the synthesis of folic acid when his 'boys' argued that his own contribution to the overall team success had been as important as any one of theirs.

When it came to patents, his name appears only on those for phenosulphazole, the chemical that did not live up to its promise to conquer polio. The application for the worthless patent was made after his death. The claim by the executor of his estate is inexplicable. The patent attorneys could usually find no evidence of his contributions in the laboratory records.

Scientists as a class cannot be expected to be any less indifferent to rewards and recognition than others but would do well to remember what SubbaRow once said: 'The victories of science are rarely won single-handed. No one man should get the (entire) credit.'

Scientists in India have been, during this centenary year, assessing the enduring significance of Dr Yellapragada SubbaRow's gifts to humankind, and are eager to win for him the recognition due to him. Participants in the first centenary symposium – held in New Delhi in March – were for a Bharata Ratna to him. The President of India should respond to this proposal when the Padma awards are resumed. SubbaRow insisted on remaining an Indian citizen after winning his right to claim American citizenship. And, although he made his contributions abroad, they all came from his India-born talents, drives and inspirations. Besides, they have improved the well-being of the entire world community, of which India is part and parcel. (June 17, 1994).

A former foreign editor of Press Trust of India, S. P K. Gupta is also a science writer and author of the full-length biography, 'In quest of panacea Successes and Failures of Yellapragada SubbaRow' (New Delhi Evelyn Publishers)