
The Texas Heart® Institute Award for Undergraduate Writing in the History of Cardiovascular Medicine and Surgery

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Sumit Isharwal (left) and Shubham Gupta
2005 Winners

The joint winners of the 2005 award are Sumit Isharwal and Shubham Gupta, both of whom are students at All India Institute of Medical Sciences (AIIMS) in New Delhi. Mr. Isharwal is from Hissar in the state of Haryana (in the north of India). He completed his secondary education at New Yashoda Public School in Hissar before entering upon the MBBS course of study at AIIMS. He has conducted undergraduate research on metabolic disease—especially diabetes and the metabolic syndrome, and their various determinants in Asian Indians. His outside interests include badminton, table tennis, and swimming. He plans to specialize in a surgical discipline. Shubham Gupta was born in Aligarh in the northern province of Uttar Pradesh. He completed his secondary education at Aligarh Muslim University before joining AIIMS as a medical student. Mr. Gupta's research interests have included BK virus nephropathy in renal allograft recipients and pain mechanisms in rats. His extracurricular interests include quizzing, reading, and watching sports. He too plans to specialize in surgery.

The 2006 competition is open to all undergraduate students enrolled in medical schools in the United States or abroad. For more information on the award, please visit the Undergraduate Award page on the Texas Heart Institute Web site (www.texasheart.org/journal.html) or write the Executive Editor, *Texas Heart Institute Journal*, MC 1-194, P.O. Box 20345, Houston, TX 77225-0345. E-mail on this subject should be addressed to jbagg@heart.thi.tmc.edu.

Rustom Jal Vakil

His Contributions to Cardiology

Sumit Isharwal
Shubham Gupta

Rustom Jal Vakil returned to India in 1938 after earning his medical degree from the University of London and focused on the treatment of heart ailments at a time when cardiology was not a distinct subspecialty in India. In 1949, after years of scrupulous collation and analysis of data, he published a watershed paper on the antihypertensive properties of *Rauwolfia serpentina* and effected a paradigm shift in the management of hypertension. *Rauwolfia* was the world's 1st successful blood-pressure-lowering agent, and its acceptance encouraged research scientists to pursue the development of other hypotensive drugs.

Vakil was a prolific researcher whose contributions to Indian cardiovascular epidemiology—and to the whole of medical literature—were enormous. He was also a fine clinician with a remarkable gift for communication, be it with his patients, students, peers, or the lay public. All of this came together to make him the embodiment of a medically competent India. (**Tex Heart Inst J 2006;33:161-70**)

India, to Western eyes, had always been the land of snake charmers, elephants, and maharajahs: stuck in a time warp, definitely not capable of contributing to the advancement of scientific knowledge, least of all to medical science. There had been a few Indian scientific scholars in the early part of the 20th century—notably the mathematician Ramanujan and the physicists C.V. Raman, Subrahmanyam Chandrasekhar, and S.N. Bose—but most of the scientific research was concentrated in the West. Medical science did not have much contribution from India, which was construed as a place where quackery and nostrums were the rule. Rustom Jal Vakil (Fig. 1), among other Indian innovators of the mid 20th century, changed that. He was the 1st truly international Indian physician. In 1949, Vakil brought out a paper on the role of *Rauwolfia* in treating hypertension, and the world took notice.

Why is Rustom Jal Vakil such an important figure in the history of cardiovascular medicine? Because he scientifically established an efficacious treatment for hypertension when there was none? Because his work on cardiovascular epidemiology added significantly to the growing body of knowledge? Because his writings have contributed more to the medical literature than those of any other Indian contemporary? Or because he helped to shape the spirit of the times in a fledgling nation?

Beginnings

Rustom Jal Vakil was born to Jal and Jerbanoo Vakil on 17 July 1911, in Bombay.¹⁻⁴ An only son, he had his school education at Bharda New High School, Bombay. His father was a busy general medical practitioner. Rustom, however, lost his father while he was still at school. His mother, a lady of wit, determination, and fortitude, largely influenced Rustom's early years. This is exemplified by the following incident.⁴ Before joining the Bharda New High School, Rustom was taken by his mother to meet the principal of an English school that was the preserve of the rich. During the entire interview, which was characterized by bluntness to the point of rudeness, Mrs. Vakil and the young boy were kept standing, while the English principal remained comfortably seated in an armchair. To the principal's brusque verdict, "I am afraid your son is not good enough for our school," Mrs. Vakil rejoined, "I am not sorry my son fails to get admission in your school. He might have picked up the bad manners of the principal who did not even have the courtesy to offer a seat to a lady." This left a profound impression on young Rustom's memory.*

After his early college education in Bombay, Vakil proceeded to England.¹⁻⁴ Having decided to follow in his father's footsteps, he secured admission to the St.

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Fig. 1 Rustom Jal Vakil. Dr. Vakil (left) receives the fellowship certificate of the American College of Cardiology from the American consul in Bombay.

Thomas's Hospital Medical School, London, from which he graduated in 1934. During his medical school career, he won 27 prizes, including the Mead, Seymour, Graves Toller, Wainwright, and Lalkaka medals of the University of London. He passed his MRCP examination in 1936, and this was followed a year later by his MD from the same university.¹⁻⁴

Vakil returned to India in 1938 and started practicing.¹⁻⁴ He served as a consultant to many hospitals and medical colleges in Bombay, including the King Edward Memorial Hospital, Grant Medical College, and Nanavaty Hospital. In his private practice, he confined himself to the treatment of heart ailments and went on to become a popular cardiologist. At that time, cardiology was not a distinct subspecialty in India. Vakil was among the 1st to accord that status to cardiology. Soon, Vakil started a meticulous accretion of clinical data from patients with hypertension who had been treated with the root extracts of *Rauwolfia*, then a promising new agent the indications, efficacy, and safety of which needed to be established. In 1949, after 10 years of research, he published a seminal paper on the management of hypertension that changed the face of medical therapeutics.*

Rauwolfia and Vakil

Rauwolfia serpentina (Indian snakeroot, sarpagandha), a member of the family *Apocynaceae*, is found in the Himalayas, Assam, Java, the Deccan peninsula, and the Malay peninsula.⁵ Mention of the plant is found in old Hindu manuscripts, as well as in the works of Charaka. The root of *Rauwolfia* was popular from

ancient times, both in India and on the Malay peninsula, as an antidote to the stings of insects and bites of poisonous reptiles. It had also been used as an antipyretic, an oxytocic, a sedative, and a palliative for insanity.⁵

In 1891, Dymock detected the presence of an alkaloid and a yellow resin in the root of *R. serpentina*.⁵ In 1931, Siddiqui and Siddiqui found 5 alkaloids that they classified into the ajmaline group of 3 white, crystalline, weaker bases (ajmaline, ajmalinine, and ajmalicine) and the serpentine group of 2 yellow, crystalline, stronger bases (serpentine and serpentinine).^{5,6} On the basis of experiments on frogs, they showed that the ajmaline group acts as a general depressant on the heart, respiration, and central nervous system, while the serpentine group causes paralysis of respiration, depression of nerves, and stimulation of the heart.^{5,6}

In the same year, Sen and Bose⁷ found 2 alkaloids in the root of *R. serpentina*. They were able to demonstrate, in experimental animals, a small drop in blood pressure, depression of the heart muscle, respiratory stimulation, and relaxation of smooth muscles, after the administration of *Rauwolfia* alkaloids. They also demonstrated the therapeutic value of these alkaloids in some cases of insanity.⁷

Chopra and his associates (1933)⁸ observed the hypotensive, sedative, and hypnotic properties of the root of *Rauwolfia* in experimental animals. In 1940, Vakil⁹ made the 1st recorded reference to the therapeutic application of *Rauwolfia* in cases of human hypertension. He observed, "After a trial of this preparation, one finds it useful in a percentage of cases of hypertension only; the indications and suitability of the case for the drug have not as yet been worked out."⁹

In 1940, Hamet observed the sympatholytic activity of the *Rauwolfia* alkaloids, particularly ajmaline and rauwolfine,* and remarked on the hypotensive action of several of the alkaloids.^{5,10}

In 1941 and 1942, Chopra and his associates reported on the pharmacologic and toxic effects of *Rauwolfia* root extracts and of the individual alkaloids.^{11,12} They found the total alkaloid mixture, the alcoholic extracts, and serpentine—particularly the last—to possess hypotensive properties, while ajmaline and serpentinine were found to be hypertensive agents. In 1942, Paranjpe¹³ claimed, without any statistical support, improvement in cases of hypertension with the use of a tincture or alcoholic extract of the root of *Rauwolfia*. Bhatia¹⁴ wrote in 1942, "I have no hesitation in saying that in *Rauwolfia serpentina* we have a drug

*In 1932, Van Italie and Stenhauer, two Dutch chemists, isolated 3 alkaloids similar to the ajmaline, ajmalinine, and serpentinine of Siddiqui and Siddiqui. They named their 1st alkaloid rauwolfine.

*Personal communication with Dr. A.F. Golwalla, July–August 2005.

which is far superior in its effect on high blood pressure to those which we have so far used. . . . the drug is not curative but is undoubtedly the best for the relief of symptoms caused by high blood pressure.” (Now, of course, we understand that in most cases, hypertension can be controlled but not “cured.”)

Around the same time, Gupta, Deb, and Kahali,¹⁵ in reporting the application of Rauwolfia in mental disorders, remarked on its distinct sedative effects and observed that in 1 case of epilepsy, there was marked hypotension and bradycardia that necessitated withdrawal of the drug.

In 1944, Bhatia and Kapur¹⁶ reported, after the administration in animals of the 2 alkaloids isoajmaline and neoajmaline,* stimulation followed by depression of the central nervous system, and lowering of blood pressure in intact, spinal (these animals had their medullary centers destroyed), and decerebrate animals, with or without experimentally-induced hypertension. In the same year, Gupta, Kahali, and Dutt¹⁷ found that the crude resin isolated by Dymock in 1891 also possessed the sedative and hypnotic properties of the serpentina root.

Already in India, Rauwolfia root tablets were highly popular, and by the time of Vakil’s paper in 1949, around 90% of Indian doctors used it as a routine hypotensive agent; around 50 million tablets had been sold by a single manufacturing firm alone.¹⁸ However, the clinical efficacy of Rauwolfia in treating hypertension had not been scientifically demonstrated outside of India, and, until 1949—in spite of many remarkable clinical and pharmacological contributions on the subject in India—enthusiasm for Rauwolfia had remained strictly localized. The international community was, if not oblivious, indifferent to Rauwolfia.

Interestingly, at that time, the West did not have any effective blood-pressure-lowering agent for the treatment of hypertension.¹⁹ Indeed, many physicians continued to think of hypertension as a benign condition, not in need of therapy. Until 1949 and 1950—when Rauwolfia and the methonium group of anti-hypertensive agents, respectively, were first introduced to the Western world—hypertension management was merely supportive, comprising restriction of salt (and proteins and calories), psychotherapy (or reassurance), sedatives, regulation of mode of life, and symptomatic therapy when complications arose. Although patients benefited subjectively, there was little or no objective improvement, no reversal of complications, and no decrease in the mortality rate.¹⁹

* In 1939, Siddiqui isolated 2 alkaloids from the Dehradun variety of *R. serpentina* and found them to be different from any of the previously isolated alkaloids. They named them isoajmaline and neoajmaline.

Vakil, in 1949, published in the *British Heart Journal* the 1st clinical report on *R. serpentina* therapy to appear outside of India,¹⁸ which fired the imagination of the international research community. In this paper, Vakil summarized 10 years of his experience with Rauwolfia. After an extensive trial of various hypotensive remedies in thousands of cases of hypertension, Vakil found Rauwolfia to be the most consistently successful agent. In addition, Vakil sent a questionnaire to 50 physicians from all over India, and 46 of those voted for Rauwolfia as the best hypotensive agent in their experience.¹⁸

In order to form an unbiased and scientifically sound opinion on Rauwolfia’s value as a hypotensive agent, Vakil performed more critical analyses on the subject.¹⁸ Fifty patients were selected from a large number of patients with essential hypertension, who reported regularly at the clinic for treatment and who showed their willingness to cooperate. Only patients with systolic blood pressures over 160 mmHg and diastolic pressures over 95 mmHg were included in the series. Cases of nephritic or renal hypertension, secondary hypertension, and malignant hypertension were excluded. In each case, after an initial examination and blood pressure measurement, the patient was kept on a sedative capsule for 2 weeks; the blood pressure was recorded again and accepted as the “pre-treatment” level. In Vakil’s opinion, the preparatory period of sedation exerted a stabilizing influence on the blood pressure.¹⁸

Rauwolfia preparations in the form of commercially available tablets (serpina) were administered for a 4-week period, during which the blood pressure was checked and recorded once weekly. After 4 weeks of treatment, all medication was stopped for 4 weeks: during this period of no treatment, the blood pressure was recorded twice, at biweekly intervals. A 2nd course of serpina tablets was then started and continued for 2 weeks; at the end of this course, the blood pressure was recorded for the last time.¹⁸

Within a week of the start of serpina therapy, 77% of the hypertensive patients showed an average reduction of 13 mmHg (ranging from 2–38 mmHg) in systolic pressure, and 73% of patients showed an average drop of 6 mmHg (2–18 mmHg) in diastolic pressure.¹⁸ After 4 weeks of the serpina therapy, 85% of the hypertensive patients showed an average drop of 21 mmHg (ranging from 2–54 mmHg) in systolic pressure, and 81% of patients showed an average drop of 11 mmHg (ranging from 4–34 mmHg) in diastolic pressure. After 2 weeks of discontinuance of the drug, residual hypotensive action of Rauwolfia was still apparent in 91% of patients and after 4 weeks, in 74%. Blood pressure after the 2nd course of treatment was very generally similar to that after the 1st course. No serious or permanent adverse effects were

observed, even in the presence of cardiac or renal disease. The most common disturbance was excessive drowsiness or sleep.¹⁸

Overall, the results were most encouraging. In most patients, Rauwolfia lowered both systolic and diastolic blood pressure. Although its action was temporary in many cases, it could be reproduced successfully by a 2nd course of the drug. No serious reactions to therapy were encountered in any of the patients.¹⁸ Rauwolfia, therefore, satisfied all the criteria of a successful hypotensive agent formulated by Evans and Loughnan,²⁰ who in 1939 had stated that any remedy before it can be established as an acceptable hypotensive agent must satisfy certain standards of efficacy, namely 1) it should be capable both of reducing a blood pressure that is high and of maintaining it at the lowered value; 2) it should be able to exhibit its hypotensive action consistently and in a high proportion of patients; and 3) it should be free of all toxic effects.²⁰

After Vakil's pioneering paper in 1949, there was a flurry of international activity: more than 100 papers on the drug were published around the globe within 5 years.²¹ The paper kick-started an array of research endeavors on the hypotensive, sedative-hypnotic, and antipsychotic properties of Rauwolfia.

In 1952, Muller, Schlittler, and Bein²² isolated reserpine, which accounted for approximately 50% of the activity (psychotropic as well as antihypertensive) of the Rauwolfia root.⁵ Bein (1953)²³ and Muller and associates (1953),²⁴ on the basis of animal experiments, found reserpine to possess marked and long-lasting hypotensive, vasodepressor, and sedative-hypnotic properties.⁵

In 1953, after carrying out clinical trials in more than 100 cases, over periods varying from 1 month to 1 year, Wilkins and Judson²⁵ found *R. serpentina* useful in lowering high blood pressure levels. It was non-habit-forming, free of serious adverse effects, and applicable in most cases of hypertension. According to Wilkins, Rauwolfia was "a distinct addition to the armamentarium against hypertension," possessing both symptom-relieving and hypotensive properties, especially in young labile hypertensives.²⁵

In 1953, Ford and Moyer,²⁶ after treating 25 cases of essential hypertension with combined Rauwolfia and hexamethonium therapy, were able to report adequate reduction of pressure levels in a large number of cases, fewer and milder side effects than with hexamethonium alone, adequate lowering of pressure even with suboptimal doses of hexamethonium, and better stabilization of pressure levels.

In 1954, after a trial of *R. serpentina*, used in conjunction with *Veratrum viride*, in 24 severely hypertensive patients, Joiner and Kauntze²⁷ could not find demonstrable evidence of synergistic action. Bradycardia and lowering of diastolic pressure were observed in some of their patients. In view of the small

sample size and the acknowledged refractoriness of severe hypertension to any form of therapy, the unfavorable results were not surprising.²⁷

As the years mounted, so did the number of studies corroborating the efficacy and safety of Rauwolfia in hypertension: Chakravarty and colleagues (1951),²⁸ Vida (1952),²⁹ Arnold and Bock (1953),³⁰ Sarre (1953),³¹ and Klausgraber (1953),³² among others.

In 1953, Vakil reported a good response to the alkaloid reserpine in 72% of the cases of hypertension, and few side effects.³³ In 1954, he reviewed the indications, contraindications, dosing regimens, efficacy, and adverse effects of Rauwolfia.²¹ He also suggested useful drug combinations for the management of hypertension. In 1955, in another series of 100 cases of essential hypertension, Vakil³⁴ showed that Rauwolfia was a useful antihypertensive remedy, capable of lowering both systolic and diastolic pressures, free of serious ill effects, easy to administer, and applicable to most cases of high blood pressure; he also showed that most cases of mild or moderate hypertension, particularly of the labile type, were amenable to Rauwolfia alone, while more severe forms of hypertension, particularly when associated with fixed levels of pressure, yielded better results with combined therapy.³⁴

Vakil, in 1955, reviewed the entire subject of Rauwolfia therapy in hypertension, including the history of the plant, its various species and types, nomenclature, geographic distribution, chemistry, pharmacologic actions, and the clinical studies of its effects.⁵

Thus, the hypotensive effects of the Rauwolfia root or its constituent individual alkaloids were firmly established by the mid-1950s. The results were uniformly good in mild and moderate cases of hypertension and devoid of any serious ill effects.

Concurrently with the use of Rauwolfia in hypertension, its other therapeutic uses came to be appreciated. In 1954, reserpine was introduced as an antipsychotic agent. The 1st paper on the use of *R. serpentina* to treat neuropsychiatric conditions was published in 1954 by Nathan Kline.³⁵ Kline's publication was followed, within 6 months, by the reports of Delay, Deniker, Tardieu, and Lemperiere³⁶ in France. Noce, Williams, and Rapaport³⁷ in the United States also contributed significantly to these advancements. After a short-lived popularity from 1954 to 1957, the use of reserpine and other Rauwolfia alkaloids in psychoses rapidly declined. Nevertheless, well over 30 years later, Christison, Kirch, and Wyatt,^{38, 39} on the basis of meta-analysis of 8 double-blind, placebo-controlled clinical studies, still suggest the use of reserpine as one of the alternative treatments in refractory schizophrenia.

After being initially applauded and then abandoned, reserpine has come full circle. We now largely understand the mechanism of action, the expected effects,

and the indications of reserpine. It blocks the uptake of biogenic amines (dopamine, norepinephrine, and serotonin) into the transmitter vesicles, and the storage there. The uptake pump is probably Mg^{2+} and ATP dependent. This occurs throughout the body, including the central nervous system, where reserpine depletes catecholamines in neurons. This action is largely irreversible. Depletion of peripheral stores of catecholamines accounts for much of the beneficial antihypertensive effect of reserpine. Depletion of central amine stores is responsible for the side effects, including sedation, depression, and parkinsonism. Reserpine is now accepted as a safe drug, having a place in the treatment of mild-to-moderate hypertension. The dopamine-depleting effects of reserpine, responsible for symptoms of parkinsonism, can be therapeutically applied in cases of Huntington's disease.⁴⁰

Vakil's efforts were widely recognized for their brilliance and demiurgic effects. The introduction of Rauwolfia to Western medicine was described by the then U.S. Surgeon General as "trail-blazing and an epoch-making discovery."⁴¹ In 1957, Rustom Jal Vakil received the prestigious Albert Lasker award for clinical medical research for "his brilliant and systematic studies on Rauwolfia in hypertension." Vakil shared the award with Kline, Noce, Laborit, Deniker, and Lehmann, who were honored for their studies on reserpine and chlorpromazine. Shope was also honored, for his contributions to understanding infectious diseases. At the time of the announcement of the award, Vakil was referred to as the "Father of Indian Cardiology" and "Father of Rauwolfia."

In their *Autobiography of Science*, published in 1960, Moulton and Schiffers had this to say about Vakil:⁴

New and more successful lines of treatment for both heart diseases and mental or emotional ailments quickly arose from the introduction of . . . *Rauwolfia serpentina* into Western medicine. Much of the credit for this goes to an Indian physician, Rustom Jal Vakil, of . . . the King Edward VII Memorial Hospital, Bombay, India.

The importance of Vakil's works on Rauwolfia is manifold. Vakil's efforts were invaluable to the Indian research environment. In Vakil, India had its 1st internationally successful clinical researcher, who, by adhering to the principles of research methodology, ensured the production and acceptance of scientifically tenable papers. This went a long way toward improving the quality of research in the subcontinent.

As pointed out previously, there was no effective hypotensive agent in use in the West before 1949. Undoubtedly, Vakil is to be credited with introducing Rauwolfia to the Western world, thereby giving it the 1st effective antihypertensive drug and enabling the

elucidation of other therapeutic uses of Rauwolfia, such as the treatment of schizophrenia.

More importantly, Rauwolfia opened the floodgates to more spirited research than ever before on other possible hypotensive agents.² In 1950, the methonium group of drugs was introduced. It was during the succeeding years that inferences from epidemiologic cohorts began to stream in, and the critical role played by the (even asymptomatic) elevation of the blood pressure in mortality trends was understood. For years, therefore, Rauwolfia derivatives played an important part in antihypertensive therapy, before being supplanted by other agents. Although reserpine is now virtually never used as a 1st-line antihypertensive agent, Vakil's contributions to the management of hypertension are without parallel. Commending Vakil's efforts in a letter to the *National Medical Journal of India* in 1988, D.M. Krikler, of the Royal Postgraduate Medical School, London, wrote of Vakil's 1949 article:²

It is difficult to think of a paper that has had a greater impact on the management of hypertension than Vakil's contribution some forty years ago. . . . It presented a new departure in the medical management of cardiovascular disease. [After Vakil's paper, when] it was seen that there was a substance available that could restore high levels of blood pressure to normal, it seemed feasible to develop many other agents including vasodilators, diuretics and beta blockers. It is highly likely that without the stimulus provided by Vakil's article, later workers would not have been motivated to explore these other possibilities which have proved so fruitful.

Contributions to Cardiovascular Epidemiology

From a researcher's perspective, India is both a dream-come-true and a nightmare. With its huge population base and inexpensive labor, India affords a gold mine of clinical data. However, poor infrastructure, the inaccessibility of villages (whose inhabitants actually constitute the majority of India's population), extreme variations in the socio-cultural practices across the country, lack of effective reporting on health events, apathy of the official health bureaucracy, and a dearth of motivated researchers, among other factors, have ensured that India's potential as an epidemiologic contributor remained unrealized for a very long time. Not surprisingly, erroneous conclusions about the disease dynamics in the subcontinent have been derived for many years. For instance, rheumatic heart disease was considered to be rare in India on the basis of Rogers's studies (see below); now, however, we know that rheumatic heart disease is rampant in India. Lately, even the body mass index thresholds used to define

obesity have been challenged as being inaccurate when applied to the Asian populace.⁴¹

Vakil practiced at a time when these obstacles were even more pronounced. Despite these problems, he studied the patterns of cardiovascular disease in India and helped define the general outlines of cardiovascular epidemiology there. As he started his practice, he began to conscientiously and systematically codify data from his patients. In 1962, he statistically analyzed the clinical material of 15,063 cardiac patients, observed from 1946 to 1955.⁴² In this analysis, 8,238 cases were taken from Dr. Vakil's private practice, which was mainly cardiology, and 6,825 cases were taken from the King Edward Memorial Hospital of Bombay. Most of the patients taken from private practice were from high and moderate income groups, while the K.E.M. Hospital patients were from a lower income group. Thus, the clinical material considered in the study was drawn from the upper, middle, and lower classes of society and represented a fair cross-section of the population of Bombay.⁴²

Vakil was able to draw several important conclusions from these data.⁴² First, the incidence of heart disease at the hospital was around 7.3%. Age, sex, and race stratification revealed the importance of rheumatic and congenital lesions in the earlier decades of life, and the high incidence of hypertensive, pulmonary, and coronary heart disease in middle-aged and elderly patients. The incidence of heart disease in males was roughly twice that in females. A relatively higher incidence of heart disease (especially ischemic heart disease) than in Hindus was reported in the minority communities of India (Muslims, Christians, and Parsis).⁴²

Hypertension, rheumatic fever, and coronary artery disease were jointly responsible in the majority of organic heart disease patients.⁴² A relatively insignificant role was played by congenital anomalies, syphilis, subacute bacterial endocarditis, chronic lung disease, and miscellaneous disease groups. A higher incidence of coronary disease (by 10.9%) and of hypertensive disease (by 11.4%) was observed in private patients than in hospital patients. The incidence of syphilitic heart disease and pulmonary heart disease was about 4 times higher in hospital patients than in private patients.⁴²

This study⁴² changed the impression perpetuated by Western authors regarding the prevalence of both rheumatic fever and rheumatic carditis. Both were considered "rare in the tropics," on the basis of Rogers's study of 1,600 autopsies in Calcutta.⁴³ Works of Stott,^{44, 45} Kelly,⁴⁶ Raghavan,⁴⁷ Fernando,⁴⁸ Vakil,⁴⁹⁻⁵³ Padmavati,⁵⁴ and Mathur⁵⁵ not only helped to disprove the original contention of Rogers, but also to establish beyond any doubt the high incidence of rheumatic heart disease in the country. A steady decline in the incidence of syphilitic heart disease was reported due to

early diagnosis and better treatment (12.9% in 1948 vs 2.5% in Vakil's 1962 study⁴²).

In 1963, Vakil published his experience with 5,615 cases of ischemic heart disease in the *British Heart Journal*.⁵⁶ Ischemic heart disease accounted for 26.6% of all cardiac ailments. Cardiac disease in Indians tended to peak in the 5th decade of life, a decade earlier than in Western surveys. The incidence of ischemic heart disease was relatively higher in minority communities of India (for example, Muslims, Parsis, Jews, and Christians) than among Hindus. This difference derived primarily from dietetic habits and social customs. While the majority of Hindus were vegetarians, the great majority of non-Hindus were not. These data supported the contention that ischemic heart disease occurred more commonly in non-vegetarians than in vegetarians. Men were more prone to have acute myocardial infarctions than were women (ratio, 3.6:1). A relatively higher incidence of acute myocardial infarction was observed in people whose occupations involved increased levels of stress. Vakil also reported a higher incidence of acute coronary attacks during the summer months, which might have been due to increased humidity and temperature, which could lead to excessive sweating, exhaustion, and increased susceptibility to respiratory infections. Electrocardiographic investigation of 1,360 cases of acute myocardial infarction showed that the most frequent infarct locations were anteroseptal, posterior wall, and anterolateral.⁵⁶

Vakil's epidemiologic studies contributed in a major fashion to the growing body of knowledge on cardiovascular disease during that period. He helped corroborate a number of contentions and associations, at the same time underlining the uniqueness of the subcontinent's populace.

Other Research Pursuits

Vakil had an eye for observation and a knack for writing. He worked tirelessly throughout his life and had a string of impressive "firsts" in research to his name. The term "intermediate coronary syndrome" was recommended independently in 1951 by Vakil⁵⁷ in India and by Graybiel⁵⁸ in the United States. Vakil⁵⁹ investigated the incidence, clinical features, electrocardiographic manifestations, laboratory findings, and clinical course of the syndrome. He pointed out the fact that this syndrome of prolonged pain in the chest, with recognizable clinical and electrocardiographic characteristics, could develop in any case of coronary atherosclerosis, and predisposed subjects strongly to the development of acute myocardial infarction within 3 months of onset. Because of this, the term "pre-infarction syndrome" was considered a suitable substitute for "intermediate coronary syndrome."⁵⁹ He investigated the role of anticoagulant therapy as a pro-

phylactic measure against myocardial infarction in cases of preinfarction syndrome and suggested the use of the same as a routine measure.^{60,61}

Vakil investigated the lesser known aspects of the natural history of a coronary thrombosis attack (pre-disposing factors, pathogenesis, prodromal phase and precursory manifestation, mode of onset of coronary attacks, various clinical forms of coronary attack, and course of the disease). He suggested the designation “prethrombotic syndrome” as more suitable than “precursor symptoms” or “prodromata.”⁶²

Abnormal cardiac rhythms were of great clinical interest to Vakil. In his opinion,⁶³ “it is very unfortunate that so many general practitioners regard their differentiation and recognition as a highly complex problem to be left to the better judgment of the specialist.” He proposed a systematic method of instruction for history-taking and physical examination which, when followed, rendered the majority of abnormal cardiac rhythms clinically recognizable, even without recourse to instrumental aid.⁶³

Besides the pre-infarction syndrome, Vakil described many other clinical entities, including “transitory pulsation in coronary thrombosis”⁶⁴ and “subacute pulmonary edema.”⁶⁵ Vakil also defined new clinical signs of diagnostic value in ventricular aneurysms.⁶⁶ In 1961, he published a report evaluating cardiac parameters in 100 cases of tropical eosinophilia and concluded that the involvement of the cardiovascular system in tropical eosinophilia was not rare, contrary to the hitherto-held view.⁶⁷

Vakil had to his credit numerous unique case reports, some making the transition from the rare to the fantastic. In 1950, he reported the live burial and subsequent disinterment of a healthy yogi after 62 hours of confinement, 6 of which were spent completely immersed in water—an event witnessed by around 10,000 people near Bombay.⁶⁸ He attempted to give a physiologic explanation for such remarkable feats of endurance, which are by no means rare in India. He published several other reports, mostly of unusual cases he encountered in his cardiology practice. The more notable of these include

- A case of patent ductus arteriosus associated with Corvisart’s disease in 1954.⁶⁹ This was the 2nd such case ever reported. In his report, Vakil stressed the fact that coexistence of a patent ductus arteriosus in a case of Fallot’s tetralogy or Corvisart’s complex should be considered a contraindication to surgical intervention.⁶⁹
- A unique record of the occurrence of as many as 5 cases of *maladie de Roger* in a single Parsi family over 2 generations.⁷⁰
- Probably the 1st case of fusion beat in conjunction with repetitive paroxysmal ventricular tachycardia associated with normal sinus rhythm.⁷¹

- Probably the 1st case of transitory aberration of Wolff-Parkinson-White type after an intravenous injection of a single nontoxic dose of k-strophanthin in an elderly hypertensive patient with left ventricular failure.⁷²
- An unusual case of a 70-year-old Punjabi man with hypertensive and atherosclerotic heart disease, showing 2 to 1 idioventricular block superimposed on complete heart block, a ventricular rate of 14 per minute, and complete atrial arrhythmia with wandering of the cardiac pacemaker.⁷³
- A case of a 60-year-old Parsi man, who evinced a transitory shortening of the P-R interval from 0.16 sec to 0.08 sec, reduction in the width of the P wave, and sinus tachycardia during phases of emotional disturbance.⁷⁴ After evaluation of the various possible mechanisms for such an electrocardiographic anomaly, the theory of sympathetic stimulation resulting in accelerated atrioventricular nodal conduction was put forward as the most likely explanation.

Recognition

Vakil’s efforts were marked by brilliance, dedication, and relevance, and he was feted appropriately. Besides being the 1st Asian to receive the Lasker award, Vakil was the recipient of numerous honors, awards, and medals, both in India and abroad.

Padma Bhushan, a high civilian honor, was conferred on him by the President of India in 1958.¹ He also received the 1st Dr. B.C. Roy Award of the Indian Medical Council for promoting the specialty of cardiology in India, the Shanti Swarup Bhatnagar Award of the Council of Scientific and Industrial Research for outstanding contributions to cardiology, and the 1st Dhanvantari Award for being “the most outstanding medical personality of the year” (1973).¹ Other winners of this award include the renowned cardiac surgeons Denton Cooley and Christiaan Barnard. He was awarded the World Congress of Cardiology Souvenir Award given by the Cardiological Society of India in 1971.²

Vakil was elected fellow of over 20 international and national medical and scientific bodies¹ and was a mesmerizing speaker who blended the impartation of knowledge with an endearing charm. These attributes made him an excellent teacher and a sought-after speaker. He traveled across India to deliver lectures.^{4,*} He was Sir Nilratan Sirkar Lecturer for 1957 and Dr. S.N. Bhansali Lecturer of Calcutta and Prizeman of the Bombay Medical Union in 1960. He delivered the Arustha Memorial Lecture in 1962 in Hyderabad.⁴ He was the Foundation Lecturer for the *Maharashtra Medical Journal*, Poona, in 1965 and the Netaji Bose

*Personal communication with Dr. A.F. Golwalla, July–August 2005.

Orator at Gwalior in 1966. He was chosen as the Vythilingam Orator at Vellore in 1967 and the Edward Pinto Orator at Secunderabad in the same year. Vakil was the Awalanada Das Memorial Lecturer of the Cardiological Society of India in 1970.⁴

Vakil was governor of the Western India Chapter of the American College of Chest Physicians; coordinator of the All India Heart Foundation; president of the Cardiological Society of India; president of the Bombay Medical Union; patron of the Society for the Prevention of Heart Disease, Bombay; and trustee of the Wadia Institute of Cardiology, Poona.^{1,3}

The Person and the Legacy

Dr. Vakil was easily India's most famous doctor and sought-after cardiologist. Yet his mannerisms were completely devoid of arrogance and affectation. He was a simple man who was in love with what he did. Vakil was jovial company, was fond of music and merriment, and told jokes with panache.^{3,*}

A philanthropist, he established by donation the Dr. R.J. Vakil Gold Medal for the All India Heart Foundation, the Mrs. J.N. Vakil Medal and Lectureship in cardiology for the Association of Physicians of India, and the R.J. Vakil Lectureship of the Bombay Medical Union.^{3,4}

Dr. Vakil believed in empowerment through knowledge. In addition to more than 380 contributions (in the form of original articles, reviews, and case reports) to medical literature, he wrote several books on cardiology and other subjects, which were well received by students and peers alike.¹ His *Clinical Diagnosis*, a textbook of symptoms and signs, is an authoritative treatise on the subject.⁷⁵ He was the editor of the 1st *Text-Book of Medicine* published by the Association of Physicians of India.⁷⁶ Lord Rosenheim, president of the Royal College of Physicians of London, lauded his textbook *Diagnosis and Management of Medical Emergencies*.⁷⁷

Prolific writer that he was, Dr. Vakil did not restrict himself to writing for the medical profession. *The Romance of Healing and Other Essays*⁷⁸ was based on his lectures and addresses and on articles that he had contributed to the *Illustrated Weekly of India* and other periodicals. In this book, Vakil discussed a wide variety of medical and allied subjects in a simple and lucid manner, adopting a historic perspective in his presentation. The essay "The Physician in Shakespeare" was an evaluation of Shakespeare's 37 plays in relation to medical references and descriptions.⁷⁹

Our Glorious Heritage, commended by the late President of India, Dr. S. Radhakrishnan, gave a brief history of medicine, with emphasis on India's contribution.⁸⁰

*Personal communication with Dr. A.F. Golwalla, July–August 2005.

Vakil's *Heart in Health and Disease* contained information about the structure, functions, and behavior of the human heart under physiologic and pathologic conditions.⁸¹

Dr. Vakil had longed for a center of excellence devoted to the prevention, early detection and treatment of diseases of the heart. His vision was realized on 28 September 1974, with the establishment of the Institute of Cardiology and Research Centre at the K.E.M. Hospital, an endeavor for which he himself donated 100 thousand rupees.³

Not quite 2 months later, on 20 November 1974, the world was shocked by the news of Vakil's untimely death at the age of 63, from aortic dissection and myocardial infarction.¹⁻⁴ He was survived by his wife, Jeroo. They had no children.* Rustom Jal Vakil passed away at what might be called the acclivity, rather than the acme, of his life—had he lived on, he would have gone much further. Dr. Vakil provided a greatly needed role model in post-independence India, a model who affected the lives of millions through his own efforts and through his inspiration of a new generation of healers.

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