SIBTE HASAN ZAIDI

(15 April 1918 – 05 April 2008)

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INDIAN NATIONAL SCIENCE ACADEMY



Sunil K. Dutt

SIBTE HASAN ZAIDI

(1918-2008)

Elected Fellow 1974

BIRTH, PARENTAGE AND FAMILY

SIBTE HASAN ZAIDI was born on April 15, 1918 in the village town of Jarwal, about 50 km away from Lucknow, the capital of Uttar Pradesh. He grew up in Jarwal with his maternal uncle because of the early passing away of his mother, Mrs Zakia Begum. During his schooling he lived with his father, Syed Hasan Zaidi, a revered Barrister-at-Law from the Inner Temple, London, who practiced civil law in Barabanki, about 30 km from Lucknow. Sibte Hasan had two siblings, an older sister, who was the wife of Mr Alim Ali Rizvi from Karachi, Pakistan, and is now deceased (1995), and a younger brother, Ibne Hasan Zaidi, a musician, who died at an early age (ca 1934). Upon the death of his father from the complications of diabetes in ca 1931, Sibte Hasan was taken under the care of his uncle, Mr Sardar Husain, also a Barrister-at-Law from the Inner Temple in London who practiced criminal law. Both Mr Sardar Husain and Sibte Hasan's maternal uncle Jarwal guided his education and career development.

Sibte Hasan married Qamar Ara *née* Shahanshah Husain, a psychologist, in 1948, who was the only daughter of the Shahanshah Husain Khan, the Rajah of Bhatwamau. Her four brothers were Ali Imam Khan (who later became the Rajah, deceased, 1970), Hasan Imam, a state civil servant (deceased, 1974), Husain Imam, a lawyer (deceased, 1985), and Kazim Imam, a writer and philanthropist. Sibte Hasan and Qamar Zaidi remained married for nearly 60 years, before Qamar Zaidi passed away in New York on April 29, 2005. Their only child, Mone Zaidi, was born on April 30, 1960, in Lucknow where he grew up and studied medicine at King George's Medical College. Dr Mone Zaidi married Dr Meenakshi Arora, a physician who had graduated from JN Medical College Aligarh in 1984, and the couple migrated to the United Kingdom. After completing his Ph.D. and clinical training at the Royal Postgraduate Medical School (Hammersmith Hospital) and having held academic faculty appointments at the University of London for 8 years (1987-1995), he moved to the United States of America and is currently Professor of Medicine and Physiology at Mount Sinai School of Medicine in New York. His wife Dr Meenakshi Zaidi is currently Staff Physician at the Veterans Affairs Medical Center in New York. The couple has two children, Neeha Zaidi (born September 14, 1985), a second year medical student at Mount Sinai School of Medicine and Samir Zaidi (born July 1, 1987) currently in his final year at Massachusetts Institute of Technology.

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EDUCATION

School Education

Sibte Hasan obtained his primary and secondary education at Barabanki High School, Barabanki and passed his intermediate from Christian College, Lucknow.

University and Medical Education

After completing the first year of BSc at Lucknow University, Sibte Hasan entered King George's Medical College (KGMC), Lucknow, in 1940, and obtained an MBBS degree in 1945. During his medical school training, he was awarded the Physiology Society Gold Medal for the best dissertation in Physiology (1942) and the Clinical Society Gold Medal for the best dissertation in Medicine (1945). After undergoing his clinical training in Medicine and Pathology, he held an academic appointment in pathology as Lecturer at KGMC, Lucknow.

Postgraduate Education and Training Abroad

In 1950, Sibte Hasan left for United Kingdom to work under Professor Earl J King, famed for the alkaline phosphatase unitage, the King-Armstrong Units, at the Postgraduate Medical School (later named the Royal Postgraduate Medical School and now the Imperial College for Science, Technology and Medicine) and the Hammersmith Hospital, London. During his training at the Hammersmith, he was awarded in addition to Ph.D. (1954), a Diploma in Clinical Pathology from the University of London (1952). His studies showing that the inhalation of coal dust by miners caused serious fibrotic lung disease, which was exacerbated by infection, provided the first comprehensive description of the pathology and pathophysiology of the coal miner's lung. These seminal articles were published in *the British Journal of Experimental Medicine.*

SERVICE CAREER

Central Drug Research Institute, Lucknow (1955-1964)

After completing his education in the UK, Dr Sibte Hasan Zaidi returned to India in 1955 and joined as Assistant Director and Head of Division of Experimental Medicine at Central Drug Research Institute, Lucknow. At this institute, he initiated studies to understand the pathology of peptic ulcer, atherosclerosis and eosinophilia. He and his colleagues demonstrated the presence of a mucous barrier in the prevention of peptic ulcer disease. This fundamental contribution led to the award of Shanti Swarup Bhatnagar Prize in 1963 for the best Research in Medicine in India which he shared with Dr BK Anand. In the area of atherosclerosis, he examined the mechanism of coagulability and thrombosis and also developed rodent models of

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atherosclerotic heart disease and experimental myocardial infarction. Dr Zaidi was promoted as Deputy Director in Central Drug Research Institute in 1963.

Indian Institute of Biochemistry and Experimental Medicine, Kolkata (now known as Indian Institute of Chemical Biology) (1964 -1965)

Dr Zaidi joined this institute as Director and initiated his research on his basic love of industrial toxins. He demonstrated the mechanism of pulmonary fibrosis following exposure to a wide range of toxins, including asbestos, silica, wood dust and bagasse. He elegantly showed that the presence of tuberculosis initiated massive incurable pulmonary fibrosis in coal and asbestos workers.

At this time, Dr Zaidi also advocated the importance of Industrial Toxicology to elucidate the impact of industrial toxins on health of people working in industries. Recognizing the importance of industrial toxicology in India, the Council of Scientific and Industrial Research (CSIR) established Industrial Toxicology Research Centre (ITRC) in Lucknow, now known as Indian Institute of Toxicology Research.

Industrial Toxicology Research Centre (1965 -1978)

Dr Sibte Hasan Zaidi took over as the Founder Director of this new institute on 4th November, 1965. This institute was initially housed at the Central Drug Research Institute (CDRI) campus. In addition to his own research, he supervised the construction of this Institute on the land given by CDRI adjacent to its campus. The foundation stone of this institute was laid by the then President of India Sri VV Giri in 1965 and it was dedicated to the nation in 1973 by the then President of India Sri Fakhrudin Ali Ahmad. Housed at its new campus, ITRC became functional in early 1973. Dr Zaidi not only developed state-of-the-art facilities and infrastructure, but also made outstanding scientific contributions and created a dedicated cadre of research scientists at ITRC. His own research centered on every aspect of lung diseases due to toxins. He elucidated the cellular mechanism through which asbestos, silica and other dust as well as a host of other industrial toxins affected human health. His research was supported by the Public Health Service of United States of America through its PL 480 scheme. In 1965 his monograph "Experimental Pneumoconiosis" published by John Hopkins Press was regarded as a definitive treatise of its time in the field. Dr Zaidi superannuated in 1978.

a) Involvement in Policy Making

After retiring as Director of ITRC, Dr Zaidi continued his research at his ITRC laboratories up to 1981, funded by his PL480 grant. He became increasingly involved in policy making in the area of industrial toxins, not only within the country, but also outside India. He served on both international and national bodies.

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In India, Dr Zaidi was inducted to serve as Honorary Advisor to the Ministry of Railways, a position that he retained between 1978 and 1989. His editorial on the "Bhopal and after", published in the *American Journal of Industrial Medicine* is a classic, which highlighted gaps in policy that could lead to spillage of chemicals of such a magnitude, even in the 1980's. He subsequently chaired the Environmental Research Committee of the Ministry of Environment, Government of India between 1990 and 1993.

Internationally, Dr Zaidi served as Senior Consultant to the United Nations Development Program (UNDP), World Health Organization (WHO), and the International Labour Organization (ILO). Most notably, he was Advisor to the Occupational Health Committee of the WHO, Member of the Scientific Advisory Committee of the UN International Registry on Potentially Toxic Chemicals in Geneva (1977-1979), Senior Consultant to the United Nation Environmental Program (1982). He also established international courses on preventive toxicology under the United Nations in Switzerland, USSR, Czechoslovakia and Germany to promote the cause of industrial medicine (1982). He was Senior Lecturer on Particulate and Fibrous Industrial Toxicants in the Industrial Training Course on Preventive Toxicology in Moscow in 1983.

b) Association with Academic Bodies (including Fellowships/ Honours/ Awards)

International

1. The William P Yant Memorial Award given by the American Industrial Hygiene Association, USA (1977), for life-time contributions to industrial toxicology in the world;
2. Venezuelan Award of Honor Sociodad Venezolana De Medicina Del Trabajo, Caracass, Venezuela (1978).

National

1. Shanti Swaroop Bhatnagar Prize (1963);
2. Sir Ardeshirlal Dalal Memorial Gold Medal (1975);
3. Padma Shri (1983)

Memberships

1. Member of Pathological Society of Great Britain and Ireland;
2. Member of Indian Association of Pathologists.

Fellowships

1. Founder Member, then Fellow of the Royal College of Pathologists, London;
2. Fellow of The National Academy of Sciences, India;

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3. Fellow of the Indian National Science Academy;
4. President of the Asian Society of Environmental Industrial Toxicology (1975)

c) Organization and Participation in International Symposia

i) Organized First International Symposium on Industrial Toxicology at Lucknow (1975);

ii) Co-Rapporteur in the International Symposium on the Control of Air Pollution in the Working Environment jointly organized by ILO and ASF (Stockholm, 1977);

iii) Co-Rapporteur in the Fifth International Conference on the Etiopathogenesis of Pneumoniconiosis organized by the ILO (Caracass, Venezuela, 1978);

iv) Vice-Chairman of the International Workshop on the Program for the Training Courses on Preventive Toxicology (Moscow, USSR, 1982);

v) Chairman, Scientific Session in the Sixth International Pneumoconiosis Conference (Bochum, FDR, 1983)

d) Member of Scientific Advisory Committees

i) Member of The Executive Committees of Aligarh Muslim University, India and nominated Member of the Court and Selection Committees of the Banaras Hindu University (nominated by the President of India);

ii) Member of Scientific Advisory Committee of The National Institute of Occupational Health, Haffkine Institute, Bombay;

iii) Member of Expert Committee on Occupational Health of The Indian Council of Medical Research, Government of India;

iv) Member of Governing Body of the Council of Scientific and Industrial Research, Government of India;

v) Member of the Governing Body of The Indian Standards Institute, Government of India.

e) Academic Professorships and Editorial Activities

i) Chandrashekhar Azad University, Kanpur (1974-1981);

ii) Visiting Professor, University of Dusseldorf, Germany (several occasions);

iii) Visiting Professor, Department of Community Medicine, Mount Sinai School of Medicine (1997);

iv) Editorial Board, American Journal of Industrial Medicine.

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f) Establishment of Institutions

Professor Zaidi promoted the need of the facilities for studying the problems of Industrial Toxicology in the developing world. He was instrumental in establishing the following institutes:

i) Industrial Toxicology Research Center under the auspices of the Council of Scientific and Industrial Research, India (1965).

ii) Laboratory of Environmental, Occupational Safety and Health in the Ministry of Railways, India (1981)

iii) Unit of Environmental Toxicology under the Ministry of Labour in Colombo, Sri Lanka, under the aegis of the United Nations (1979).

iv) Laboratory of Industrial Toxicology and Occupational Health, Rangoon, Burma (1982).

RESEARCH CONTRIBUTIONS

Fibrogenic Activity of Silica

The silica – solubility theory of silicosis which has received widest attention in recent years was the direct result of a critical study by Dr Zaidi. His studies have shown that the different specimens of quartz of identical composition, but of markedly different solubility, may have the same fibrogenic effect in the lungs of animals. Different forms of free silica of identical composition have very similar solubility, and given in amounts to ensure similar surface areas, had markedly different fibrosis-producing capabilities. The same mineral prepared in different ways with similar particle size distribution, surface areas and identical composition had appreciably different solubility, and yet produced similar degrees of fibrosis at the same rate in animals. He also studied the fibrogenic action of free silica which occurs in different forms i.e. fused silica, quartz, cristobalite and tridymite of high purity and almost identical silica content, size distribution and silica solubility in the liver of mice. Tridymite was the most rapid in producing acellular collagenous silicotic nodules; cristobalite was next; quartz third and fused silica, the least fibrogenic. The optimum fibrogenic size of flint particles in the livers of mice was between 0.2 and 2μ in diameter, when administered by intravenous injection. Dr Zaidi has further shown the importance of particle size in the pathogenesis of silicosis. The optimum size of flint particles to yield maximum fibrosis in the lungs of rats was found to be between 1μ and 2μ diameter, when given to rats by intratracheal injection. These experiments showed that, inspite of the same chemical nature of various forms of free silica, their fibrogenic action was different.

Role of Silica in Pneumoconiosis: Dr Zaidi's research has shown the role of small amounts of free silica in the pathogenesis of pneumoconiosis. He showed that the

rats dusted with a very low concentration of quartz did not develop fibrosis of the lungs or lymph nodes. A mixture of 98 percent anthracite coal and 2 percent quartz led to the development of dust foci throughout the lungs but without any fibrosis. This research indicated that the quartz content of coalmine dust in the range of 2 percent or below did not appear to produce deleterious effects. His studies on the relationship of pulmonary tuberculosis and coal miners' pneumoconiosis consisted of the combined action of a mixture of tubercle bacilli of an attenuated strain intimately mixed with coalmine dust on the lungs of guinea pigs. The combined lesions, produced by the dust and bacilli, persisted over a prolonged period with the deposition of reticulin fibres within the lesions. The tubercle bacilli alone produced lesions which regressed within a much shorter period and the coalmine dust produced no pulmonary fibrosis. He showed that tubercle bacilli of low virulence when combined with coalmine dust produced pulmonary massive fibrosis in the lungs of guinea pigs. These studies indicated that the inhalation of coal dust may aid in the progression of tuberculosis and consequently pulmonary massive fibrosis.

Nutritional Factors in Silicosis

Dr Zaidi studied the role of ascorbic acid on developing pulmonary silicosis of normal and scorbutic guinea pigs. In normal silicotic guinea pigs an increasing concentration of ascorbic acid in lungs with the advancement of silicosis was observed. The increase of ascorbic acid was directly related to the percentage of collagen. Adrenal ascorbic acid showed an increase with lapse of time, but blood ascorbic acid did not show any alteration. In scorbutic silicotic guinea pigs, collagen fibre formation was retarded but the hydroxylproline and acid mucopolysaccharide levels remained the same as in normal silicotics. The effect of feeding a multideficient diet low protein or a stock diet on the development of pulmonary silicosis was studied in rats over a period of 300 days. The increase in the total dry lung weight and amount of hydroxyproline, measured analytically, were of the same order in silicotic animals fed either diet. In these experiments Dr Zaidi observed that the macrophage response, formation of dust aggregates as well as the development of nodular lesions, dry lung weight and collagen and acid mucopolysaccharide contents revealed no significant difference. These studies clearly revealed that nutrition did not have a major role in the development of silicosis.

Research on Peptic Ulceration

Acute and chronic peptic ulceration was produced experimentally, and their pathogenesis studied. Acute ulceration in rats was produced by the ligation of pylorus or with massive doses of histamine dihydrochloride in guinea pigs which were protected with an anti-histaminic, promethazine hydrochloride. This resulted in gastric ulceration of varying degrees. During the healing process, a marked increase in mucin was noted, which underscored significance of mucin in the healing

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of experimental ulcers. The more the production of mucous, the lower was free acidity and lesion and lesser degree of ulceration. Mucous also protected mucosa from inflammatory reaction. His studies suggested that mucin neutralized the action of acid gastric juice and also adhered to the surface of the mucosa to form a barrier against peptic ulceration. He also showed that prolonged feeding of phenyl butazone gradually destroyed the mucous barrier, so that the ulcers could not heal and thus persisted. The free acid in the absence of mucous was possibly sufficient to have its corrosive action and maintain the chronicity of ulcers. He demonstrated a positive relationship between increased peptic activity and the presence of ulceration. Hyperacidity, however, was not a constant feature in increased degree of ulceration. The compounds sodium, barium and calcium eugenates, when administered in the stomach, liberated eugenol which stimulated mucous secretion to form a mucous barrier against ulceration and the alkali neutralized the free acidity. Calcium eugenate appeared to be more active in the prevention of ulceration than other compounds used. Curcuma Longa also protected gastric disorders probably due to its mucous stimulatory effect. Capsicum (Lal Mirch) in small doses for a short period did not produce any mucosal hemorrhage or ulceration or even depletion of epithelial cells of the gastric mucosa of guinea pigs.

Research on Atherosclerosis and Coronary Heart Disease

Dr Zaidi's studies on experimental atherosclerosis have shown that cholesterol alone and in association with neutral fats led to atheroma formation and the lesions were aggravated by the use of fats containing high content of saturated fatty acids. In the prevention of this condition, vitamins C and B12 were effective but vitamin E increased the lesions. The anticoagulant, Tromexan proved to be less effective in arresting the experimental disease. Oral feeding of butter and intravenous administration of ethanolamine phosphatide increased the tendency of the blood to clot easily. In addition, damage of the arterial wall and acute haemodynamic change induced thrombi in the coronary arteries causing myocardial infarction in both rabbits and rats.

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VED PRAKASH KAMBOJ, FNA
C-1111, Opposite Church
Indira Nagar
Lucknow-226016
*E-mail:*Kambojvp@yahoo.com
Kambojvp@rediffmail.com

PK. SETH, FNA
Biotechnology Park
Sector G, Kursi Road,
Jankipuram
Lucknow-226021 (U.P.)
E-mail: pkseth@hotmail.com

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