Fluorine minerals like fluospar has been known since the early times as metallurgical flux and was referred to in this connection under the name "fluores" by Basilus Valentinus at the end of the fifteen century and by Agricola in 1529 (cited by Simons 1950). The first biochemical study may be said to have been made by Dominico Morichini in 1803 (cited by Leicester 1949) when he demonstrated the presence of fluoride in the fossil elephant teeth found outside the city of Rome. Together with Gay Lussac, he later showed that fluoride was also present in the teeth of both animals and men. Gay Lussac in 1805 considered that the entrance of fluoride into the body was through nutritive means. A year later Berzelius succeeded in demonstrating the fluoride in urine (cited by Arnold 1957). In 1822, he suspected that water was responsible for the supply of fluoride and demonstrated its presence in some spring water. About the year 1846, George Wilson, carried out investigations on a broader basis and showed that fluoride was widespread in nature especially in spring water, sea water, vegetable ash, blood and milk of animals. Fluoride content of teeth was investigated by Ehrdarht, a German Scientist, in 1874 (cited by Muhler, Hine and Day 1954).

Toxic properties of fluorine compounds were studied for the first time in animal experiments by Rabuteau in 1867. By this time traces of fluoride were found in milk, saliva, hair, bile, egg and brain. The credit of initially describing
dental changes in the form of black spots in teeth, goes to Kuhns (cited by Roholm 1937) who in 1885, reported dental fluorosis, in a family migrated from Durango, in Mexico. Round about 1890 Tappeiner published more detailed records of investigations on acute experimental poisoning. In 1892, Sir James Crichton Brown stressed the importance of supply of fluoride during the development of teeth and consequence of its deficiency in the production of inferior enamel (cited by Cannell 1960).

Hempel in 1897 postulated that fluoride content of teeth influenced its susceptibility to dental caries because of its anti-enzymatic and bactericidal properties. Together with Scheffler in 1899, they reported a difference in the fluoride concentration in carious and non-carious teeth. Eager in 1901 observed that people in certain parts of Italy had a dark discolouring of teeth and considered it to be due to some water borne substance.

In 1912 Bartolucci observed a cattle disease resembling osteomalacia around an Italian superphosphate factory and speculated that it might be due to fluoride content in the waste products of the factory. He introduced the term "fluorosis" for this disease, but his observation did not attract enough attention.

In 1913 McCaughey and Frey found the presence of fluorine mineral in the sample of American soil. The prevalence of mottled enamel in the various parts of United States invited the attention of Black and McKay who published a series of five
About the year 1920-25 the modern work regarding the fluoride intoxication began to appear (Hoholm 1937). Goldemberg (1927) produced experimental goitre by fluoride and studied its biological effect. Cristiani (1930) studied the alteration of thyroid in fluoride intoxication. In 1931 Risi estimated physico-chemical constituents of blood by administration of sodium fluoride.

The toxic effect of fluoride and mottling of teeth was known before but it was only in 1931 that the cause of mottling of teeth was found (Churchill 1931; Smith, Lantz and Smith 1931). In Denmark, Moller and Gudjousson observed for the first time the development of osteosclerosis due to industrial exposure of excessive amount of fluoride in 1932 and focused attention to the disease named "fluorosis".

The amount of fluoride present in various substances is very small and variable. In the absence of a suitable sensitive method for its determination, the results reported up to 1932 cannot be considered to be reliable. In 1933 Willard and Winter reported their method of estimation of fluoride which along with some others has given precision to the results.

In 1933, Hauck et al. (Hauck, Steenbock, Lowe and Halpin 1933; Hauck, Steenbock and Parson 1933) studied the effect of fluoride on growth, calcification and parathyroid in chickens. The effect of fluoride on the metabolism of calcium and phosphorus was the subject of study in the year 1934-35 (Chang, Phillips, Hart and Bonstedt 1934; Greenwood, Hewitt, Nelson 1934;
Lantz and Smith 1934; Schour and Smith 1934 and 1935; Smith and Lantz 1935. Phillips et al. (1934) tried to explain the role of vitamin C in fluoride metabolism.

In 1935, Dean and Elvove planned field surveys of chronic endemic areas and found that 1 ppm of fluoride in water has no public health hazard.

A fresh chapter in the study of fluoride intoxication was opened by Roholm in 1937, when he described fluorosis in detail in cryolite workers in Denmark and also did a lot of experimental work. His review of literature and monograph still remain a monumental work on fluoride intoxication.

In India, fluorosis was first described by Shortt et al. (1937) in the Nellore district of Madras province.

The toxic properties of fluoride were studied by Pierce in 1938. Some important observations in India regarding the endemic and experimental fluorosis were made in 1940 (Day 1940; Pandit, Raghavachari, Rao and Krishnamurthi 1940; Pandit and Rao 1940).

In 1941, Dean, Jay, Arnold and Elvove studied the effect of domestic water fluoride on dental caries and Dean et al. (1942) further investigated the physiological effects by epidemiological method. Ast in 1943 presented a detailed programme for testing what was then called artificial fluoridation and a number of studies on fluoridation were started in the year 1945.

Interest in the biochemical studies in fluorosis grew rapidly after the identification of fluoride as the mottled enamel causative agent. Additional impetus was supplied by
several studies on the control of dental caries by fluoridation of drinking water. The number of research publications on various aspects of fluorine and its compounds increased so much that the Kellering Laboratory at the University of Cincinnati listed more than 5,500 separate references in its classified bibliography (Wilkinson 1955).

From various parts of the world, different types of studies in experimental fluorosis are being carried out and it is not possible to document all these in the present volume. Study of endemic fluorosis has been carried out from time to time and some of the cases from various parts of the world are as follows:

Arabia (Walter 1954); Argentina (Silva, Chapeli & Pedace 1940); Capizzano, Valotta and Maggy 1940; Capizzano, Paterson, Toledo, Maggy, Valotta 1939; Dicio, Quirno, Malenchino 1939; Mascheroni, Munez, Reussi 1939; China (Lyth 1946); Germany (Odenthal, Weineke 1959); India (Singh et al. 1960, 1961, 1962 and 1963); Kasliwal and Solomon 1959; Rao 1955; Murthi, Rao and Venkateswarlu 1953; Khan and Wig 1945; Pandit Raghavachari, Rao and Krishnamurthi 1940; Shortt, McRobert, Barnard, Nayer 1937; Italy (Malbone and Parlato 1957; Garibaldi 1954); Japan (Hamamoto et al. 1954); Morocco (Speder 1936); Persian Gulf (Azar, Nuchco, Bayyuk and Bayyuk 1961); S. Africa (Fichardt, Van Rhyn, Van Selm 1958; Werbeloff, and Sender 1958; Ockerse 1941); Sicily (Frada and Mentesana 1954); Texas (Lisman and McMurry 1943).

In 1956, Singh A. observed a few cases of fluorosis in a
particular region of Bhatinda district in Southern Punjab. This observation led to a very extensive epidemiological, clinical and biochemical investigations of these areas and some of the results have already been published (Singh 1960, Singh, Das, Hayreh, Jolly 1961; Singh and Jolly 1961; Singh, Jolly and Bansal 1961; Singh, Jolly, Devi, Bansal and Singh 1962; Singh, Vazirani, Jolly and Bansal 1962; Singh, Jolly, Bansal and Mathur 1963; Mathur, Singh, Singh and Singh 1962).