A REVIEW OF THE LITERATURE
(Ingestion, Absorption and Excretion of Fluoride)

Fluorine is a trace element of human body. It is not considered to be essential element of the diet (Evans and Phillips 1939), because complete withdrawal of it produces no fatal or disabling symptoms. Fluoride in small amounts has been found beneficial for dental health, but in slightly greater amounts it causes fluorosis. This dual behaviour of fluoride has assumed great importance, due to its use as an anti-carcinogenic agent.

Certain aspects of fluoride metabolism notably fluorine toxicology, fluorosis of bones and dental dystrophy are relatively well-known; on the contrary, we still have little information about the absorption of fluoride, its distribution in the body (apart from bones and teeth) and its elimination (Held 1957). The main difficulty in the consideration of the subject is the wide variation of absorption, storage and excretion of fluorides due to many factors.

All fluorine compounds, for example, fluoroacetate, fluorobenzene, etc. in which whole of the molecule is toxic, are not considered here. The review is only in respect of fluoride ions, for it is only in this form that fluorine is recommended to combat caries; it is in this form also that fluorine occurs in water and minerals and it is in this form that men and animals take it, resulting in fluorosis.
INGESTION

Food, water and air may be the different sources of fluorides ingestion.

Ingestion from food

No food has been found free of fluoride (Harrow and Mazur 1954). The fluoride ingestion will, therefore, be a natural phenomenon. Different authors have different views regarding the amount ingested. Armstrong and Knowlton (1942), Machle, Scott and Largent (1942), McClure (1949a) and Fellenberg (1948) believed that in regions considered to be poor in fluoride, this intake varied from 0.25 to 0.5 mg per day. On the other hand some authors considered that the above figures are too low, and that the range was much higher i.e. 0.3 to 1.5 mg daily (Lang 1952). Sharp (1960) gave the following amounts in some foods:

<table>
<thead>
<tr>
<th>Food</th>
<th>Fluoride (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chicken</td>
<td>1.4</td>
</tr>
<tr>
<td>Liver</td>
<td>1.5</td>
</tr>
<tr>
<td>Lamb</td>
<td>1.2</td>
</tr>
<tr>
<td>Canned fish</td>
<td>4.0</td>
</tr>
<tr>
<td>Honey</td>
<td>1.0</td>
</tr>
<tr>
<td>Beer</td>
<td>1.0</td>
</tr>
</tbody>
</table>

According to McClure (1949a) the fluoride contents of some vegetables and fruits are as follows:

Average (ppm)

<table>
<thead>
<tr>
<th>Food</th>
<th>Fluoride (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cabbage</td>
<td>0.7 - 15.38</td>
</tr>
<tr>
<td>Carrots</td>
<td>1.0 - 8.4</td>
</tr>
<tr>
<td>Cauliflower</td>
<td>0.45 - 0.83</td>
</tr>
<tr>
<td>Cucumber</td>
<td>0.02(w)</td>
</tr>
<tr>
<td>Lettuce</td>
<td>0.42 - 1.3</td>
</tr>
<tr>
<td>Spinach</td>
<td>1.11 - 7.97</td>
</tr>
<tr>
<td>Tomatoes</td>
<td>0.0 - 2.4</td>
</tr>
<tr>
<td>Turnip</td>
<td>0.56 - 2.6</td>
</tr>
<tr>
<td>Apples</td>
<td>0.35 - 1.32(w)</td>
</tr>
<tr>
<td>Apricots</td>
<td>0.08 - 0.24(w)</td>
</tr>
<tr>
<td>Cherries</td>
<td>0.18 - 0.27(w)</td>
</tr>
<tr>
<td>Currents</td>
<td>0.12(w)</td>
</tr>
<tr>
<td>Oranges</td>
<td>0.07 - 0.34(w)</td>
</tr>
</tbody>
</table>

*W* indicates wet basis determination, all others on dry fat free basis.
It was suggested that water and soil fluorides increase the amount of fluoride in plants. Gisiger (1958) found near an aluminium factory, fluoride levels higher in edible plants than normal. Other experimental evidence was against this finding. Machle, Scott and Treon (1939) found no correlation between the amount of fluoride in plants and water fluoride.

Food boiled in fluoride containing water will further increase its fluoride concentration (Martin 1951). Processing and preparation account for additional change. In a saucepan, for instance, vegetables absorb more fluoride than in pressure cooker (Martin 1951).

Other factors influencing oral fluoride intake are certain food habits such as drinking large amount of tea or taking certain drugs habitually with a relative high fluoride content, for example, certain bone meal preparations etc. (Waldbott 1961). He further reported of a patient suspected of fluorosis who consumed 15 to 20 cups of tea daily. Based on Cholak's figure of 0.122 mg fluoride in one cup of tea, this amounted to 1.82 to 2.44 mg of fluoride from this source alone.

Opinion expressed regarding fluoride ingestion through milk are not only variable but contradictory. Milk was considered by some to be a good source of fluoride, when the maternal ingestion was high (Murray 1936; Roholm 1937; Schuck 1938). Held (1952), on the other hand, noted that enrichment of mother's diet with fluoride did not necessarily involve a parallel increase in fluoride in the milk.
Ingestion from water

Water is considered to be the most important source of fluoride ingestion, due to its better absorption (Lawrenz and Mitchell 1941). The effect of fluoride intake will depend upon the water ingested, its fluoride contents, and the period of ingestion.

The effects of temperature on the water consumption by children was studied by Galagan and Vermillion (1957) and Galagan, Vermillion, Nevitt, Stadt and Dart (1957). In tropical countries, the consumption of water is greater than sub-tropical countries, and so will be ingested fluoride.

Muhler and Weddle (1955), Hoffman, Schuck, Furata (1942), Lawrenz, Mitchell and Ruth (1939) and Schuck (1939) found that fluoride is more toxic in aqueous solution than in dried state. Endemic fluorosis is mostly caused by excess of fluoride in drinking water (Churchill, 1931).

Water borne fluoride (approximately 1.0 ppm) in moderate climate effect a marked reduction in dental caries (Knutson 1957; Sognnaes 1954). The optimum concentration of fluoride in drinking water which will provide a balance between the power to resist caries and the tendency to cause mottling was found to vary from 1.0 to 1.2 ppm (Kleiner and Orten 1958). The presence of other substances in water also affect the toxicity.

Mostly the inorganic fluorides are present in water; their amounts and nature vary according to the source of supply. Sodium fluoride, sodium silicofluoride, hydrofluosilicic acid and ammonium silicofluoride are generally used in
fluoridation of drinking water as anti-caries measure (Maier 1957). In the United States no less than 335 localities, in 25 different States, have been found to contain more than 1 ppm fluoride in water (Leicester 1949).

In India, Shortt, Pandit and Raghavachari (1937) found fluoride in ground water in northern parts of Nellore district. The occurrence of fluorides in various localities from Visakhapatnam in the north to Tirunelveli in the south and from Chingleput in the east to Combator in the west, was investigated by Raghavachari and Venkataramanan (1940) and they found fluoride in excess of 3 ppm in various localities. In Punjab a belt having high fluoride contents in soil and water has been found in Bhatinda and Sangrur districts (Singh et al. 1961).

Air

Due to its presence in air, especially near certain factories, the fluoride may be inhaled from air. In the air of Spokane (Washington), for example, fluoride contents were found to be 1.6 ppb (parts per billion) as compared with that of Logan, Utah of 0.02 ppb and that of New York City of 2.0 ppb (Hald 1957). Shaw et al. (1951) reported up to 42 ppb at distance of 3.5 to 7 miles from an "Industrial area" north of Spokane, and 351 ppb within one mile. Largent (1949) found that fluoride level in air ranged from 0.01 to 4.3 ppm expressed as hydrogen fluoride.

The amount of fluoride in air depends upon humidity, velocity of wind, pressure, topography, temperature and distance from contaminating area (Waldbott 1961).
Information concerning the rate of fluoride absorption was obtained through metabolism data (Weddle and Muhler, 1955, 1957; Stookey and Muhler 1962), by using isotopically labelled fluoride (Wallace-Durbin 1954; Bell, Merriman and Greenwood 1961; Perkinson, Whitney, Monroe, Lotz and Comar 1955) and surgical isolation of intestinal segment in intact animals (Foster, Rush 1961; Wagner, 1962, Stookey, Crane and Muhler 1962). The portion of fluoride that can be absorbed from digestive tract was found to vary between 37% and 97% of the total amount fed, depending upon the nature of ingested fluoride (Machle and Largent 1943).

The rapidity with which the various fluorides are absorbed is variable. According to Likins and Zipkin (1954), sodium fluoride, sodium fluosilicate and sodium fluorophosphate are absorbed more or less at the same rate whereas potassium phosphofluoride passes through the wall of the digestive tract more rapidly.

The solubility of a salt affects the absorption of fluoride. Lawrenz and Mitchell (1941) found that compounds such as sodium fluoride and sodium fluosilicate were more readily absorbed than calcium fluoride.

Absorption also depends upon the physical state of the substance. Largent and Heyroth (1949) found that when ingested in the form of aqueous solution, absorption varying from 93 to 97 per cent of the total amount took place. The solid salts, when ingested, the absorption varied from 62 to 77%.

Fluoride in milk is less absorbed than in water (Muhler and Weddle 1955).

The presence of certain ions for example Ca^{++}, Al^{+++},
PO₄, Mg. etc. in food affect the absorption of fluoride (Weddle and Muhler 1957; Lawrenz and Mitchell 1941).

When ingested with organic matter less fluoride was assimilated in the system (Lawrenz and Mitchell 1941).

**Storage**

After its absorption, fluoride is disposed of within a few hours by excretion in urine, sweat, faeces, nails etc. or deposited in teeth, skeleton or other organs. The storage depends upon many factors such as dosage, regularity, pH, vitamin C, fat, climatic conditions, age and nature of administered salts.

**Dosage**: The amount excreted or deposited bears a constant relation to intake (Cannell 1960). Smith, Gardner and Hodge (1952) consider that storage took place at every level. Ham and Smith (1954) found that considerable retention took place at intakes as low as 0.4–0.79 mg daily. Largent (1952) found that a daily intake of 1.36 mg of fluoride for 315 days resulted in storage of 226 mg (53 percent). The amount excreted in sweat was not included in this study. Lawrenz, Mitchell and Ruth (1939) found that in growing rats 30–40% of ingested fluoride may be retained when the fluoride concentration was 10 ppm. 13 ppm of fluoride in the diet as cryolite or CaF₂ was retained to the extent of 50% to 60% by young growing rats (Lawrenz, Mitchell and Ruth 1939).

**Regularity**: According to Lawrenz, Mitchell and Ruth (1940) continuous intake results in the greater retention than interrupted feeding. Held (1957) was of the opinion that small doses, when regularly absorbed result in lower retention but
in case of higher doses inadequate elimination may cause the excess of fluoride to be deposited in inorganic tissue. Miller and Phillips (1956); Clock, Lowater and Murray (1941) observed that retention of fluoride in the skeleton followed a predictable and characteristic pattern and further observed that the rate of deposition decreased as the period of fluoridation was extended. McCann and Bullock (1957) proved this observation by the vitro studies.

**pH** Muhler and Day (1955) studied the storage of fluoride, when ingested at different pH and found that it was independent of pH.

**Vitamin C**: Vitamin C raised the deposition of fluoride in the skeleton and soft tissues (Buttner and Muhler 1957; and Muhler 1958). Venkateswarlu and Narayanarao (1957) found no effect of vitamin C on retention of fluoride. Phillips and Chang (1934) Phillips and Stare (1934), Phillips (1933), Hauck (1934), Pandit and Rao (1940) found beneficial effect of vitamin C.

**Fat**: Fat seems to affect the storage of fluoride. With increase in the amount of fat content, a larger deposition of fluoride in the bones became apparent, as also did a restriction in growth (Miller and Phillips 1955). An increase in the fat content of diet from 5 to 20 per cent was sufficient to lead to an increased retention of fluoride (Buttner and Muhler 1958). Cotton seed oil increased the toxicity of fluoride. This oil produced also an increased deposition of fluoride in the bones and heart, but not in the kidney, at daily doses of 2 mg.
fluoride (Buttner and Muhler 1957). Buttner and Muhler (1958) found no difference in retention in total carcass due to type or amount of fat. Bixler and Muhler (1960) found that type of fatty material affects the fluoride storage.

**Climatic conditions.** Climatic conditions affect the uptake and retention of fluoride (Gordonoff and Minder 1960). Arnold (1943) pointed out that climate should influence water intake and, therefore, total fluoride ingestion. Galagan (1953) confirmed this view by a more detailed study.

**Age.** Age seems to affect the fluoride storage. The rate of deposition was found to decrease as the period of fluoridation was extended (Miller and Phillips 1956; Clock, Lowater, and Murray 1941). Miller and Phillips (1956) found more marked effects in young than older animals. Savchuck and Armstrong (1951); Zipkin and McClure (1952); Suttie and Phillips (1959); Jackson, Tisdall, Drake and Wightman (1950); also found decreasing rate of retention with increasing age of the animals. But with the increase of age the concentration of fluoride in skeletal and perhaps in dental tissue increases. Smith, Gardner and Hodge (1953) found that fluoride concentration in bone increased in a linear fashion with increase of age. Jackson and Weidmann (1958), Suttie and Phillips (1959), also demonstrated increase of fluoride with age.

According to Wagner, Stookey and Muhler (1958), the rate of retention decreased particularly after skeletal maturity was reached.
Nature of administered salt: All fluorides do not give rise to identical retention by the skeleton. Muhler and Weddle (1955) found that tin fluoride and sodium monofluorophosphate were retained to a lesser extent than sodium chlorofluoride or sodium fluoride.

Amount of fluoride in various organs
The absorbed fluoride is stored in different tissues:

Storage in skeleton - Most of the absorbed fluorides are deposited in bones or teeth. Lawrenz, Mitchell, and Ruth (1939) found that about 96% of fluoride retained in the body of rats was present in the skeleton. In experiments on rabbits, Gardner, Scharff, Smith, and Hodge (1957) established that half of the ingested fluoride was retained and that of this half probably 76.5 percent was locked up in the skeleton.

It is difficult to find the critical value of bone fluoride beyond which skeletal fluorosis may be expected to occur and it is not precisely known due to clinical difficulty in diagnosis unless it had progressed to an advanced state (Algate et al., 1949). Wolff and Kerr (1938) suggested this value to be 200-300 mg per 100 g.

In bone under normal conditions, the fluoride content was estimated at 10-30 mg/100 g. (range 0.66%-0.21%) by Roholm (1937), but in certain circumstances it may reach 100 mg/100 g. (Harvey 1952). According to Heyroth (1942) the normal amount of fluoride in human skeleton was 1-6 gms, but two cryolite workers ingesting high amounts of fluoride, contained 90 gms and 50 gms respectively. Roholm (1937) reported 0.65% and 0.72%
of fluoride (6,500 to 7,200 ppm fluoride) in costal cartilage of two cryolite workers, normal costal cartilage according to him contained 0.03 to 1.14% fluoride (300 to 1,400 ppm). There seems to be a level of fluoride intake which may be tolerated by the skeletal tissue safely. Peirce (1938) suggested that skeletal tissues may perhaps increase 8 to 10 times without abnormal symptoms in bone. Heyroth (1942) found the amount of fluoride ten times in ash contents of the bone of a dog given sodium fluoride as compared with control.

Various researchers demonstrated differences in the rate of fluoride incorporation of bones. Volker, Sognnaes and Bibby (1941) found differences in $^{18}F$ uptake by various types of bones, such as shaft and mandibular bones. Durbin (1954); Perkinson, Whitney, Monroe, Lotz and Comar (1955); Weidman and Weatherell (1959) also found different rate of deposition in different types of the bone. The form in which the fluoride is deposited in the bone has been studied by many workers. Neuman, Neuman, Main, O'Leary and Smith (1950) found that fluoride replaced OH or HCO$_3^-$ ions in the bone apatite and gave rise to fluorapatite. McCann (1955) also came to the conclusion that fluoride was incorporated in the bone in the form of fluorapatite. Some other workers think that OH group in apatite was replaced and not HCO$_3^-$. Gordonoff and Minder (1960) were of the opinion that it would be a gross over-simplification to designate the crystalline portion of bone as apatite and consequently the fluoride may not be in the form of fluorapatite.

It would not seem that fluorapatite has any biological drawbacks (Neuman et al., 1950). When incorporated in the bone
lattice fluoride is effectively immobilised. Its removal under normal conditions is at extremely slow rate over a number of years.

Rachitic bone is said to contain less fluoride than non-rachitic bone (Zipkin, Likins, and McClure 1953).

Storage in teeth: That fluoride is stored in teeth has been known for a long time. Developing teeth contain similar amounts of fluoride as bone—10 mg/100 g (McClure 1948)—but the amount is not comparable after calcification and eruption. Shaw, Gupta, and Meyer (1956) found high fluoride contents in the teeth on greater fluoride ingestion. The highest quantity of fluoride was found in mottled teeth (Smith 1956). McClure (1939) could not detect more fluoride in non-caries teeth than carious from the same individual. Armstrong and Brekhus (1938a, 1938b) demonstrated the higher amounts of fluoride in mottled enamel and lower amounts in carious teeth. Ockerse (1943) obtained similar results. The values of Bowes and Murray (1936) which indicated the same content of fluoride in enamel and dentine did not entirely agree with the above observations. According to McClure and Likins (1950) enamel took less fluoride than dentine.

Storage in epidermal structures: Nails, hairs, feathers, wool, horns, hooves, scales, skin, etc. may also store fluoride and the amount may be proportional to the quantity ingested and period of its duration (Cannell 1960). According to another view the storage in these tissue is doubtful.
Storage in soft tissues: Durbin (1954) found that very little fluoride was deposited in the soft tissues. Settler and Ellerbrook (1939); Herman (1956) determined the fluoride contents of the various tissues and noticed that fluoride was deposited in the muscles and every organ, chiefly thyroid, liver, kidney and heart. Wagner, Stookey and Muhler (1958) found no increase in fluoride contents in heart, liver or kidney even when saturation of skeleton was approached. In soft tissues there is usually no such buffering agent like apatite in bones and teeth, which is believed to neutralize fluoride ions (Waldbott 1961). Damage to the tissue may be natural in case the fluoride content increases.

Blood fluoride level

The amount of fluoride reported in blood show a very considerable variation. According to Smith, Gardner and Hodge (1950) the blood contained 0.01 ppm of fluoride when the drinking water had less than 0.1 ppm of it. Goldenberg and Schraiber (1935) found 0.08 mg/100 ml fluoride in human serum and Goutier found 0.05 mg (cited by Held 1957). Suttie, Phillips, and Faltin (1964) considered that an efficient homeostatic fluoride control existed in man and certain other species of animals.

The fluoride blood level is not appreciably changed on extra dietary ingestion of fluoride (Held 1952 and 1954). Singer and Armstrong (1960) found no relation between the concentration of fluoride in water and that in blood. Smith, Gardner, and Hodge (1950) found that on increasing the water concentration from 0.06-1.36 ppm (twenty three fold) the mean fluoride concentration increased from 0.014-0.40 ppm (three fold).
There may be an initial increase which may be decreased by fixation in inorganic tissue or excretion. Parkinson, Whitney, Monroe, Lotz and Comar (1955); Smith, Gardner and Hodge (1950) found that following the administration soluble fluoride blood level rose rapidly, reached a peak, thereafter declined rapidly and returned to normal level in approximately 24 hours even after large doses.

The exact form in which fluorine occurs in the blood is not known. The fluoride in blood has not led to fixation of blood calcium even on administration of comparatively larger doses (Held 1957).

The blood fluoride concentration in fatal cases of acute sodium fluoride has been found to be 0.35-1.55 mg of fluoride per 100 ml (Gettler and Ellerbrook 1939).

**EXCRETION**

Excretion of fluoride is one of the main defensive mechanism of the body to reduce its fluoride concentration. Skin, gut and urine may be the various routes.

**Excretion in urine.**

Fluorides are excreted mainly in urine (Machle, Scott and Largent 1942; Majumdar and Ray 1946). Machle (1936) showed that the normal individual not exposed to usual amount of fluoride also continuously excrete fluoride (0.5-2.8 mg per litre).

Urinary fluoride excretion is believed to parallel closely fluoride intake in water (McClure, Kinser 1944; Smith,
Gardner and Hodge (1950); Machle and Largent (1943). Urinary excretion of fluoride has now become a generally accepted criterion for the estimation of fluoride ingestion and absorption (Brum, Buckwald and Roholm 1941; Largent and Ferneau 1944; Largent 1947). Smith, Gardner and Hodge (1950) found that twenty-three fold increase of fluoride (0.06 ppm to 1.36 ppm) resulted in nineteen fold increase (0.06 to 1.12 ppm) of urinary fluoride.

Zipkin, Likins, McClure and Steere (1954) noted that the amount of fluoride excreted increased with age. Generally speaking, excretion in case of children receiving 1 mg of fluoride daily, reached a maximum limit by sixth year of absorption (Held 1957).

The amount of fluoride excretion is not affected after the ingestion of weak doses (Schweinsberg and Muhler 1955, 1956). When the doses ingested are relatively higher, elimination commences after sometime, probably after a relatively large amount of fluoride has accumulated in the bones. According to Weddle and Muhler (1955), in rats which ingested a certain amount of fluoride for considerable time and then put on a diet poor in fluoride, there was a relatively accentuated elimination at the outset, after which the excretion was the same as in normal. Largent and Heyroth (1949), Likins, McClure and Steere (1956) and Siddiqui (1955) found fluoride in urine long after administration of fluoride had ceased.

Largent and Heyroth (1949) found that the general increase in the dose of fluoride resulted in its 50% excretion in urine. On prolonging the period of low fluoride intake, excretion was found to be proportionately higher.
Urinary excretion of fluoride is prompt. Hodge and Smith (1954) noted that three hours after the ingestion of small amount of fluoride by man, it appeared in the urine.

The selectivity of the kidney for fluoride is outstanding. It does not enter the halogen pool, but instead is selectively excreted to a much greater extent than chloride or bromide. The fluoride clearance rate was considered to be ten times greater than chloride (Smith and Gardner 1955). Over 99.5 percent of the chloride in the glomerular urine was re-absorbed, whereas only 93 percent of fluoride was reabsorbed (Chen, Smith, Gardner, O'Brien and Hodge 1956; Largent 1954; McClure, Mitchell, Hamilton and Kinser 1945).

Fluoride concentration in the urine may indicate the quantity of fluoride ingested by the individual. Prompt appearance of fluoride following exposure to air-borne fluoride was shown by Collings, Fleming and May (1957), and Irwin (1954). The amount of fluoride excreted may show a wide variation. In some cases as little as 3.6% and in other cases as much as 99.5% of ingested fluoride was recovered in 24 hours (Waldbott 1961). He was of the opinion that the excretion of fluoride under regular living conditions may give erratic results.

Urinary fluoride may be indicative of toxicity. Irwin (1954) found no ill effect when urinary excretion did not exceed 5 ppm. Largent, Bovard and Heyroth (1951) observed greater density of bones when the excretion was 10 mg/litre. Hodge and Smith (1954) considered 8 ppm border line level.
Zipkin, Likins, McClure (1953) found no difference between sodium fluoride and sodium fluosilicate as regards the urinary excretion rate. Weddle and Muhler (1955) found that in rat, sodium fluoride is less easily eliminated than sodium fluosilicate. Renal tubular injury had no effect on fluoride excretion (Smith, Gardner, Hodge 1955).

**Excretion of faeces**

Fluorides are excreted in faeces and may be due to unabsorbed dietary fluoride (Weddle and Muhler 1955). The excretion in stool may originate from the saliva, bile, pancreas or unabsorbed fluoride (Held 1957). According to Gautier and Clausman the stool contained 0.4 mg % fluoride. Machle, Scott and Largent (1942) found it to be 0.6 mg % (0.8 -1.2 mg per day).

**Excretion in sweat**

The fluoride may be excreted in sweat, depending upon temperature and humidity (McClure 1945). Machle and Largent (1943) considered that daily elimination through the perspiration and lungs was 0.3 mg.

Shedding of the skin and the growth of nail involved a small amount of fluoride excretion (Truhaut 1948).

**TRACER STUDIES**

With the advent of tracer techniques, the fluoride metabolism was studied with radioactive fluorine. Volker, Sognnaes and Bibby (1941) detected fluoride in the teeth 45 minutes after an interperitoneal injection of F18. No fluorine
could be detected in the tip of incisors and none was observed in the crowns of the cat's teeth. Ericsson and Ullenberg (1958) noted the distribution of fluoride in rats and mice. 18F was rapidly lost from blood and soft tissue except the kidney, and almost all was concentrated in the calcifying zones of bone, in developing teeth and in collecting tubules of kidneys. Neither thyroid nor liver showed notable uptake. Ericsson and Ullenberg further noted that a small amount which passed placenta in the pregnant mice was found in foetal bones and some of it was concentrated in calcified granules in the placenta. Perkin son, Whitney, Monroe, Lotz and Comar (1955) found rapid absorption of ingested fluoride. Durbin (1954) found particularly high concentration of fluoride in kidneys and bones. Meyers, Hamilton and Beck (1952) noticed the accumulation of fluoride only on the surface of defective teeth.

Tracer studies cannot be profitably applied for the study of fluoride metabolism because fluorine is an element which is taken up rapidly, but slowly eliminated. An accumulation of fluoride occurs and it is impossible or nearly so, to establish its elimination by means of short lived radioactive fluorine, which has a half-life period of 112 min.