This article by Roholm appeared 6 years after the Meuse Valley disaster. The time lapse made it impossible for him to report his own personal observations. He was obliged to depend upon examination of the data made available to him. However, during the 6 year interval, he had made an intensive study and had acquired greater knowledge concerning fluoride's effect than any living person. He was able to pull together many loose ends. He presented conclusive evidence that the victims of the Meuse Valley disaster had suffered from acute intoxication by gaseous fluoride compounds which emanated from certain factories in that area. This explanation had previously been advanced by Holland's leading lung specialist Storm van Leeuwen and by two other investigators, H.C. Gramm and G. Fenner. To their record, Roholm added new and, hitherto, neglected facts.
Abstracts

On December 3rd, 4th and 5th, 1930, several thousand cases of acute pulmonary disease and 60 deaths occurred in the densely populated Meuse Valley, east of Liege in Belgium. A Commission of Investigation attributed the disaster to unusual climatic conditions and poisonous products from waste gases of many factories located in the valley. The Commission, however, was unable to pinpoint any one chemical as the cause. They presumed that sulfur dioxide (SO₂) or its oxidation products in the factory smoke were responsible.

The Weather

On December 3rd to 5th, a mist covered the entire country of Belgium particularly a 20 km stretch of the Meuse Valley from Huy which lies midway between Liège and Namur to Seraing just west of Liege. In that area, the Meuse Valley runs southwest to northeast. It is 1 to 2 km wide and 60 to 80 m deep. The barometric pressure was high. Temperatures during the day ranged slightly above the freezing point. At night they reached 10° below zero. There was practically no wind except for a slight easterly breeze with a maximum velocity of 1 to 3 km per hour. The smoke from the factories had settled down on the ground and was mixed with fog.

Fig. 1

Fluorine Intoxication in Meuse Valley

The continuous line borders the area in which the cases occurred.

Epidemiology

Illness began simultaneously throughout the entire area on December 3rd. The mist had persisted for about two days and had reached its maximal density about that time. After December 5th no new cases occurred. By December 6th, when the fog had cleared, several thousand individuals had been afflicted with the disease. Fifty-six of
the 60 fatalities occurred in the eastern half of the valley; only four, west of Engis (Fig. 1). Forty-one deaths took place on the north bank of the river, 19 on the south. Most deaths were concentrated near Engis.

Symptomatology

Dyspnea was the major complaint of the victims. They had either asthma-like attacks and labored expiration or continuous polypnea. They became hoarse, nauseated and vomited. They coughed and expectorated frothy sputum at first. Later the sputum turned viscous and muco-purulent. The fatal cases expired in acute circulatory failure with cardomegaly, tachycardia, pallor in the face and occasionally with cyanosis.

The majority of the affected individuals were elderly people whose lungs or hearts had already been weakened. However, young and perfectly healthy persons likewise became seriously ill. Some of the victims had remained in their homes during the foggy days. Cattle on pasture contracted the same disease with fast and superficial respiration, acute emphysema, cyanosis of mucous membranes which followed, in some, by death. Birds and rats also died.

Autopsy Data

Between December 7th and 11th, 10 cases were autopsied. The bodies were in an unusually good state of preservation. The mucous membranes of the large bronchi, the trachea and larynx were hyperemic. Microscopically, these structures showed areas of epithelial desquamation, vascular dilatation and degenerative phenomena in the form of defective staining of the cells of the superficial layer. There were no hemorrhages but only occasional effusion of leucocytes from the vessels. The alveoli contained numerous particles of soot. They exhibited moderate, localized edema, hemorrhages and desquamation of epithelium. All other organs appeared to be intact. The spectroscopic and chemical analyses of the blood and organs were unrevealing.

On the basis of their findings, The Commission of Investigation suspected that a local irritant which had no remote systemic action after its absorption was the cause of death. The Commission, however, acknowledged "a deplorable lacuna (on fluorine) in the literature". Roholm's classical book "Fluorine Intoxication" was not available in 1930.

Acute Fluorine Intoxication

With respect to its chemistry, Roholm emphasizes that fluorine is a very active element. Its compounds tend to form complexes. Biologically, its inorganic compounds are most active. They exhibit a
local corrosive action on skin and mucous membranes which Roholm attributes to the undissociated hydrofluoric acid molecule. Their specific toxic effect on protoplasm is only partly understood. F compounds might precipitate calcium, act on enzymatic processes and combine with albumin.

Up to 1935, Roholm had reviewed 112 cases of acute pemphig intoxication with NaF, Na2SiF6, HF or H2SiF6. Sixty of these cases had been fatal. In some instances, as little as 0.2 to 0.7 grams of sodium fluosilicate was fatal to adults. He considered the rate of absorption a significant factor in the outcome of acute intoxication.

Roholm distinguishes between two kinds of symptoms, namely local and systemic ones. Among the local manifestations he listed the effect on the gastro-intestinal tract: vomiting (often bloody), abdominal pains and diarrhea. Among the symptoms due to absorption he included alternate painful muscular spasm and paresthesias, weakness, thirst, excessive salivation and perspiration. The face may be pale or cyanotic. Death occurs within a few hours with increasing dyspnea and failing heart action. The autopsy findings are sparse. The gastro-intestinal tract shows corrosive changes. Occasionally degenerative phenomena occur in the parenchymatous organs, especially in liver and kidneys.

According to Roholm, man is more sensitive to fluoride than other mammals. The most toxic inorganic F compounds are hydrogen fluoride (HF) and silicon tetrafluoride (SiF4) and their aqueous solutions. All are readily absorbed into the blood stream from the mucous membranes.

Roholm quotes the two fatal cases of acute poisoning described in 1887 by Cameron in superphosphate workers. They had spent a brief period in the dens where crude phosphate was stored after it had been treated with sulfuric acid. After a few hours of labored respiration, vomiting and cyanosis, death had ensued. Autopsies revealed edema and hyperemia of the lungs. Large quantities of colloidal silicic acid (SiO2) and fluoride were found in the bronchi, probably due to decomposition of silicon tetrafluoride. Roholm referred to similar cases among German beryllium workers who had evidence of bronchiolitis, dyspnea and cyanosis. In a paper by Frostad on a Norwegian aluminum factory, where gaseous fluoride compounds emanated from open melting baths the symptoms simulated those of bronchial asthma. The general health of the workers was gravely affected.

Hydrogen fluoride causes sneezing, lachrymation and cough. Death occurs with restlessness and increasing dyspnea. General convulsions occur in rapidly progressive intoxication, but not in the protracted type. The effect of silicon tetrafluoride is similar. In human experiments, exposure to 0.026 mg/l of HF is unpleasant but tolerable for several minutes. In animals, prolonged respiration of about 0.01 mg/l
Abstracts

causes emaciation, anemia and organ degeneration in addition to the pulmonary changes.

**Chronic Fluorine Intoxication**

Roholm reviews the well-known characteristics of chronic fluorosis. He states that dental fluorosis occurs when drinking water contains 1 ppm or more. He describes the skeletal changes with diffuse osteosclerosis and calcification of ligaments which he had studied in cryolite workers. He also mentions a systemic disease resembling osteomalacia in cattle. He attributes osteosclerosis "in all probability" to prolonged intake of small doses of fluoride, osteomalacia to relatively large doses.

Among general symptoms of fluorosis he includes loss of weight, low food intake, anemia, certain skin and eye symptoms, photophobia, and conjunctival secretion. The disease terminates in animals with cachexia and signs of manifest or latent tetany.

In skeletal fluorosis the fluorine content of ash of bones and teeth increases from 10 to 20 times of what is considered normal. For the rat, Roholm sets up the following approximate daily threshold concentrations:

- Incipient dental changes ............... 1 mg/kg/day
- Incipient osseous changes, nephritis ... 5 "
- Incipient effect on general condition 10 - 15 "
- Severe effect on general condition,
  - organ degeneration ............... 20 - 25 "
- Death after a few weeks ............... 50 - 100 "

In man, dental changes begin to develop on a daily ingestion of about 0.1 mg/kg. Roholm believes, therefore, that man is much more sensitive to fluoride than the rat when fluoride compounds are administered over an extended period.

**Fluoride as an Air Pollutant**

Roholm mentions special forms of fluoride poisoning which have a bearing on the Meuse Valley disaster. In a factory employing raw material containing F, HF is likely to be emitted. If silicates or quartz are present in raw materials employed in a factory, silicon tetrafluoride emanates from the chimneys. Humidity produces partial hydrolysis of silicon tetrafluoride to hydrogen fluoride and fluosilicic acid, two extremely active compounds, especially when in atomized form. They produce mists like sulfuric acid and hydrochloric acid, but are much more toxic. The heavy mists disperse slowly. They tend to corrode vegetation when the air is stagnant.

**FLUORIDE**
Abstracts

Roholm refers to damage by fluoride to vegetation described in Europe during the last decade of the 19th century, near superphosphate, copper and brick works, aluminum and chemical factories and iron foundries. Investigators of the industrial smoke problem have paid little attention to fluoride. They have been mostly concerned with the frequent occurrence of SO2 and SO3.

Whenever vegetation near a factory is affected by fluoric gases, herbivorous animals grazing there contract fluorosis, an osteomalacia-like disease. They develop emaciation and cachexia, stiff, laborious gait, muscular restlessness and spasms, thickened nodes on the extremities and ribs, frequent spontaneous fractures. The same disease has been recognized near volcanic eruptions. The gaseous fluorine compounds, ejected from volcanoes, dissolve in tiny drops of water which condense around the ash particles. Local irritation of respiratory mucous membranes has been described from this source, but no deaths have been observed.

Analysis of the Disaster

Roholm gave three reasons for considering fluoride the principal cause of the Meuse Valley disaster:

1. Clinical and autopsy findings showed that death of the afflicted persons was due to a systemic disease, not to a local effect on their respiratory organs.

2. Fluoride was present in the air at toxic levels.

3. The fatal cases occurred in the vicinity of fluoride-emitting factories. No fatalities occurred near factories emitting substances other than fluoride.

1. Systemic Effects

The mucous membranes of the respiratory organs exhibited relatively little damage. Lachrymation was rare, especially near Engis where most deaths occurred. Cough which occurred subsequent to the appearance of dyspnea was much less frequent and disabling. The autopsies showed relatively little irritation in the bronchi and lungs. After the fog had lifted, no more deaths occurred. Had there been local damage to the respiratory mucous membranes the pulmonary disease would have persisted and would have caused additional deaths. The survivors recovered rapidly. Some climbed the hills and improved immediately once they were above the fog. Such prompt recovery would not have been the case had there been significant local damage to respiratory mucous membranes. The fatal cases included individuals with perfectly healthy lungs.
Roholm concludes, therefore, that the poison had a strong systemic effect after it was absorbed. When exposure to the toxic agent ceased, its effect promptly subsided. Acute cardiac failure and rapid death pointed to a severe general effect and to prompt absorption of the toxic agent.*

2. Fluoride in the Air

Of 27 factories in the area, at least 15 employed raw materials containing fluoride compounds in their manufacturing process and emitted SiF₄ and HF. There were:

4 very large iron works with blast-furnaces and steel-works,
3 large metal works,
4 glass works and ceramic factories,
3 zinc works,
1 superphosphate factory.

Steel and metal works employ CaF₂ (fluorspar) in the smelting process. Silicon tetrafluoride escapes according to the formula:

\[ 3\text{SiO}_2 + 2\text{CaF}_2 = \text{SiF}_4 + 2\text{CaSiO}_3 \]

Glass and pottery manufacturers employ fluorspar and cryolite. They are added to raw material to facilitate melting and produce certain properties in the finished product.

Zinc ore frequently contains fluorspar.

In superphosphate manufacturing, the raw material is phosphorite which contains 3 to 5 percent fluorine. The latter is liberated as HF and SiF₄, when treated with sulfuric acid.

In the area where most deaths occurred, window panes and electric bulbs had lost their gloss more quickly than normally. On the north bank of the river, damage to vegetation was widespread and cattle had contracted a serious bone disease (fluorosis) which had led to numerous law suits.

Roholm calculated that at least 30 milligrams of HF per m³ was present in the stagnant air in the valley. This is considered the minimum lethal concentration for guinea-pigs. In humans 26 mg/m³ is unpleasant but considered tolerable for several minutes.

*Editor's Note: When HF comes in contact with skin and mucous membranes, it penetrates their upper layers in an undissociated state without damaging them. Its corrosive action begins below the surface when free F is liberated. In the pulmonary alveoli, F is promptly absorbed into the blood stream.
On inhaling air with 30 mg/m$^3$ HF, an adult individual will absorb about 0.12 g F during 8 hours. This is the minimum lethal dose in spontaneous peroral intoxication. Thus, there is indication that the F concentration in the Meuse Valley during the four days may have exceeded the lethal dose for man.

3. Distribution of Fatal Cases

The toxic agent emanated from two widely separated areas, from the wide entrance to the valley where the large metal works were located and from Engis with its zinc and superphosphate works.

There were no deaths in a strip of several kilometers between the two regions. The light easterly winds concentrated the poison south-east of both these regions, principally along the north bank of the river at the north wall of the Valley. The immense masses of soot and dust emanating from the works served to promote condensation. Fluorine compounds must have been present in dissolved form in microscopic particles of water, which rendered them very active and easily absorbable.

Other Explanations

Roholm ruled out chemicals other than F which could be considered as the toxic agent:

1. Mist and fog alone, without chemical contamination, could not cause death. It could induce chills and upper respiratory infections but not rapid lethal intoxication as in the disaster. Furthermore, endemic illness did not occur elsewhere in Belgium where heavy fog had blanketed the country.

2. Lack of oxygen due to air deficient in oxygen from rock caves cannot be held responsible for the deaths. The mode of intoxication did not resemble that of acute lack of oxygen. Because of the high atmospheric pressure no lack of oxygen in the air could have occurred.

3. Carbon monoxide intoxication is unlikely: Its symptoms differ from those observed in the area. Blood examinations for CO were negative. Other causes such as carbon dioxide, hydrogen sulfide, arsine, dust of zinc oxide, iron oxide, lime, metal and soot were excluded by The Commission of Investigation as well as by Roholm.

Sulfur Dioxide

There was undoubtedly considerable sulfur dioxide in the air. Its level was estimated by The Commission at 25 mg/m$^3$/day or at 100 mg/m$^3$ during the four foggy days.
The maximum tolerable concentration of SO₂ is considered to be about 35 mg/m³. A wide latitude in tolerance is characteristic of exposure to SO₂. For instance, some have observed symptoms of intoxication from 4 to 8 mg/m³ sulfuric acid whereas others regard 40, and indeed 80 to 120 mg/m³, harmless.

The toxic action of SO₂ differs considerably from that of F compounds. Due to its acid character, SO₂ produces irritation in tissue and tends to form necroses. It has no specific systemic toxic effect like fluoride. SO₂ irritates especially the mucous membranes of the eyes and throat which leads to hemorrhages, inflammation in the upper air passages as well as pulmonary edema. These conditions persist for some time. Although SO₂ and SO₃ occur in industry much more frequently than F compounds, so far very few cases of SO₂ and SO₃ poisoning have been reported. Sulfur compounds have a characteristic sharp odor and an acid taste which furnishes a warning to exposed persons. Fluoride compounds, on the other hand, are usually odorless and tasteless. Hydrogen fluoride is a weak acid. Silicon tetrafluoride does not produce a characteristic smell in low concentrations. Survivors of the Meuse Valley disaster had not detected any particular smell or taste in the mist.

Summary

Roholm concludes that the Meuse Valley disaster which caused illness in several thousand persons and death in 60, was due to acute fluoride intoxication. Of 27 factories in the area, 15 either used F containing raw products or added F compounds to the raw materials. They emitted SiF₄ and HF. Climatic and topographic conditions played an important role.