

*Short report***Fluoride in cerebrospinal fluid of patients with fluorosis**

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SUMMARY The CSF fluoride level of individuals drinking water with normal fluoride content and of patients with endemic fluorosis were studied. For the purpose of studying the relationship between the dynamic equilibrium of the CSF fluoride and other body fluids, urine and blood fluoride were examined simultaneously. Fluoride was revealed in every CSF sample of the control group and its mean value was lower than that of the blood. The CSF fluoride concentration of patients with fluorosis was slightly higher than that of the control group, although there was no statistically significant difference. The results suggests that fluoride is a normal component of CSF. In severe cases of fluorosis or breakdown of the blood-brain in some diseases of the central nervous system, the CSF fluoride value might be increased.

We have previously reported the fluoride content of body fluids in individuals drinking water containing higher fluoride concentrations (average level more than 10 ppm) and of those whose drinking water contained fluoride less than 1 ppm.¹ The mean value for urinary fluoride concentration of the control group was 0.62 ppm. Sex, age and nationalities made no difference. The normal mean concentrations of fluoride in serum and plasma were 0.198 and 0.194 ppm respectively. The mean concentration of urinary fluoride in the patients with fluorosis was 4.5 ppm and that of their serum was 0.25 ppm, which are higher than those of the control group. The difference is significant ($p < 0.05$). However, there is overlapping in distribution between the two groups and the result lacks clinically diagnostic significance. These findings are similar to those recently reported elsewhere in China.²⁻⁵ We have also examined CSF of patients receiving low fluoride water, undergoing lumbar anaesthesia (routine examinations of CSF were normal). Fluoride was detected in every sample and the mean value was 0.17 ppm (table). So far as we know, there has only been one report of CSF fluoride levels.⁶ However, the patients in that report did not suffer from fluorosis and the fluoride concentrations of their drinking water or foods were not mentioned. Moreover, there was no control group in the study. In order to confirm our previous findings and investigate the dynamic relationship between CSF and other

body fluids, it is necessary to study further the fluoride levels in CSF, blood and urine in patients with fluorosis.

Patients and method

Forty one endemic fluorosis patients, aged 14-65, 19 females and 22 males, from districts where fluoride in drinking water was elevated were admitted. All of their clinical fluorosis features were positive. Spot sample of urine fluoride was measured in all patients and serum fluoride in 39 as well as CSF fluoride in 40 patients were determined at the same time. CSF fluoride concentrations in patients undergoing spinal anaesthesia, which had been reported previously with the same method of determination as in this report, were regarded as the control group.

An iron selective electrode technique was used for the determination of the fluoride concentration. This method was used in our previous work and by others in China.³

Results

Table CSF, blood and urine fluoride (ppm)

	No	Range	\bar{X}	S
CSF of Control Group	32	0.14-0.23	0.17	0.03
CSF	40	0.10-0.36	0.20	0.062
Fluorosis	39	0.10-0.38	0.20	0.065
Urine	41	1.20-2.2	5.87	3.82

Discussion

The findings and the data reported previously showed that blood fluoride can be maintained at a steady level even though the urinary fluoride concentration in fluorosis is higher and ranges more widely. The level of CSF fluoride in fluorosis patients was higher than that of the control group, though there is no significant difference ($t = 0.108$, $p < 0.5$). It is possible that there is a physiological mechanism to maintain dynamic equilibrium of fluorine metabolism in the body and to keep a steady level of fluoride in the blood and CSF. In 36 patients, CSF and blood fluoride concentrations were examined simultaneously. CSF fluoride concentrations were higher than those of blood in 16, lower than blood in 18, and at the same level in two patients. We draw the preliminary conclusion that the fluoride is a normal component of CSF, as it could be detected in every sample whether patient or normal control. In normal individuals, fluoride is in dynamic equilibrium between the blood and CSF, and CSF fluoride concentration is similar to or slightly lower than that in blood. These facts indirectly indicate that the passage of fluorine through the blood-brain barrier is by no means a passive diffusion, but an active transport function which is similar to that of other halogen and ionic substances. The normal CSF/blood ratio is below 1.0.⁷ Only in patients with severe fluoride intoxication or the breakdown of the blood-brain barrier, as with some diseases of the central nervous system, would the fluoride content in CSF be increased.

Fluorine is considered to be an essential element. It is stored chiefly in the osseous system. The study of the biological effects of fluoride has centered chiefly on bones, teeth and enzyme systems. There has been little interest in the accumulation and effects of fluoride in the nervous system. Recently, reports have shown normal brain tissues which contain fluoride and its concentration was higher in the hypothalamus and hippocampus than other regions.^{8,9} Kay *et al* found that anion fluoride could affect calcium conductance by an intracellular action in hippocampal neuron of guinea pigs.¹⁰ Still *et al* reported that the incidence of primary degenerative dementia (Alzheimer's disease) in some districts having 1.0 ppm fluoride level in the drinking water was higher than in districts having a higher level of fluoride in the drinking water. They suggested that fluoride might decrease brain aluminium, which is thought to be related to the development of Alzheimer's disease.¹¹ However, fluoride metabolism in the central nervous system has not yet been thoroughly and systematically studied.

There have been reports of damage to the nervous system caused by endemic fluorosis and longterm

fluoride therapy with dosages of sodium fluoride in some cases as high as 200 mg/day.¹²⁻¹⁵ Interpretation was complicated, however, by changes in the osseous system or its neighbouring structures such as ligament, meninges etc. Whether or not high concentrations of fluoride could directly damage the nervous system (especially the central nervous system) is still not known. We have seen some patients with high body fluoride levels and unclassified nervous lesion of unknown aetiology. After removal from the higher fluoride exposure, fluoride in their body fluid decreased and their symptoms improved.¹⁶ We thought that fluorine might damage the nervous system directly. Therefore, a determination of CSF fluoride level would be helpful for the diagnosis of fluoride intoxication and would provide some information regarding the physiopathological effect of fluoride on the central nervous system.

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Little's disease

Every student is taught about Little's spastic diplegia, but how many know that William John Little (1810-94) was himself afflicted with a congenital equinus deformity of his left foot? He was founder of the Royal Orthopaedic Hospital and Senior Physician to the London Hospital. His several disquisitions¹⁻³ are quite brilliant and repay study in full.

"I have witnessed so many cases of deformity, mental and physical, traceable to causes operative at birth, that I consider the subject worthy of notice³ of the Obstetrical Society." He mentions 200 cases encountered in 20 years of orthopaedic practice. He stressed the "larger proportion of dead, stillborn, apoplectic, or asphyxiated at birth have been rendered so by interruption of the proper placental relation of the foetus to the mother, and non-substitution of pulmonary respiration, than from direct mechanical injury to the brain and spinal cord." The consequences were "internal congestions, capillary extravasations, serous effusions which correspond with . . . asphyxia, suspended animation, apoplexy, torpidity, tetanic spasms, convulsions of newborn children, and the spastic rigidity, paralysis, and idiocy subsequently witnessed."

"The flexors and abductors of the thighs, flexors of the knees, and the gastrocnemii preponderate. . . thighs cannot be completely abducted or extended, the knees cannot be straightened, nor the heels applied to the ground. The elbows are semi-flexed, wrists partially flexed and pronated and fingers incapable of perfect voluntary direction. . . upper extremities sometimes appear unaffected. . . Muscles of speech are commonly involved, . . . articulation is slow and difficult. . . in the majority of cases the intellect suffers—from the slightest impairment up to entire imbecility."

Little relates presentations with convulsions, opisthotonus or laryngismus in the early days and the delay in recognising paralysis until the child starts to walk in milder cases; he describes the deformities of posture, trunk and the impediment in walking. He had sparse necropsy evidence "Case LX showing cicatrised apoplexies on surface and interior surfaces of the brain. . . effusion of blood in both ventricles of brain—a true apoplexy (case XLI—a precipitate labour). But, curiously, he concluded "that the spinal meningitic and myelitic affections may play a considerable part in the phenomena of spastic rigidity." His finale is a brief but optimistic reference to "therapeutic effects producing amelioration surprising to those who have not watched such cases."

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