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## IMPLICATION OF GLUTATHIONE IN ENDEMIC FLUOROSIS

by

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**SUMMARY:** In a new approach to an understanding of the genesis of nonskeletal and skeletal fluorosis, glutathione content in blood was investigated. Thirty cases of fluorosis and forty controls (20 from fluorotic and 20 from nonfluorotic areas) were studied. In fluorotic subjects, blood glutathione concentration was significantly elevated. Urinary hydroxyproline and serum alkaline phosphatase data were also correlated. It appears that the persistent stress of the F<sup>-</sup> ion demands a protective redox maintainer and that glutathione fulfills that need.

**KEY WORDS:** Alkaline phosphatase; Blood; Fluorosis; Glutathione

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### Introduction

Endemic fluorosis has been reported from all parts of the world. In the Punjab, where it has posed a challenge to the sociologist, the medical researcher, and the politician, the endemic fluorosis belt has been demarcated. Since the 1960s, the Department of Medicine at the Medical College Patiala (1) has been the center for research on the problem.

Drinking water is the main source of excess fluoride ingestion in this area. The highly electronegative fluoride ion is biologically very reactive and plays an ubiquitous role in living systems. Fluorosis is a multiple organ pathology (2), and blood glutathione (GSH)\* has been selected to study the intracellular facet of fluorosis. Clinical, radiological and biochemical data have been used for statistical evaluation.

### Materials and Results

The study comprises 30 cases of fluorosis and 40 normal healthy controls, 20 from the nonfluorotic area (group A) and 20 from the endemic belt (group B). All other routine and relevant special investigations were carried out. Blood glutathione was estimated by the Beutler et al. method (3). The duration of the study was 14 months. The teeth of patients were fluorosed in varying degrees. There was no evidence of dental fluorotic changes or skeletal fluorosis in control groups.

The blood GSH levels were  $57.8 \pm 10.6$  mg% in fluorotics, normal values of Group A =  $40.1 \pm 5.9$  mg% and of Group B =  $42.2 \pm 6.3$  mg%. The elevation is statistically significant with  $p=0.01$ . The mean serum alkaline phosphatase levels were  $12.7 \pm 3.0$  K.A. units compared to control values of  $9.5 \pm 3.0$  and  $9.5 \pm 2.6$  K.A. units of A and B controls respectively. Urinary hydroxyproline data indicated increased collagen turnover with mean levels of  $39.2 \pm 10.7$  mg/day and controls at  $24.9 \pm 10.0$  mg/day (Table 1).

Table 1  
Effect of  $F^-$  on Glutathione, Serum Alkaline Phosphatase and Urinary Hydroxyproline Levels

Patient Group	GSH Level (mg%)	Serum Alkaline Phosphatase (K.A. units)	Urinary Hydroxyproline (mg/day)
Control Group A nonfluorotic	$40.1 \pm 5.9^*$	$9.5 \pm 3.0$	$24.9 \pm 10.0$
Control Group B fluorotic	$42.2 \pm 6.3^*$	$9.5 \pm 2.6$	
Fluorotic patients	$57.8 \pm 10.6$	$12.7 \pm 3.0$	$39.2 \pm 10.7$

\*Significantly different at  $p=0.01$

\* GSH is the standard abbreviation for glutathione, a tripeptide:  $\gamma$ -L-glutamyl-L-cysteinylglycine.

Both of these parameters were significantly elevated in the fluorosis cases ( $p = 0.01$ ). The GSH had positive correlation ( $r = +0.24$ ) with alkaline phosphatase, while  $r = +0.029$  with urinary hydroxyproline levels. Both these correlations were insignificant.

Associated with neurological symptoms, in 17 patients the GSH levels were  $57.7 \pm 10.6$  mg% vs. the other 13 fluorotics at  $58.3 \pm 11.8$  mg% which indicates that the lesion is anatomical and not at a molecular level.

The hypothesis evolved is that, in the fluorotic area controls, GSH levels were not elevated, as there probably existed hemostatic control(4). Since GSH is an intracellular thiol, small increments of  $F^-$  are effectively combated. However the fluoride, after it has entered the bone and saturated it, goes to the tissues where GSH helps to maintain membrane structure and molecular function in the presence of this reactive and toxic ion. At a critical level, it spills over and is seen in the circulation. Had the nonskeletal tissues not had the GSH umbrella, fluorosis would have been a much more severe disease, manifested earlier in life. In these respects, fluorosis is still a molecular enigma.

#### Conclusion

Blood glutathione was significantly elevated in fluorotic subjects and positively correlated to increases in serum alkaline phosphatase and urinary hydroxyproline. Glutathione is concluded to have a protective effect and helps maintain membrane structure and molecular function in the presence of the reactive fluoride ion.

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