**ALAN F. BERNDT, Ph.D.**

*Professor of Chemistry*
*Assistant Dean, The Graduate School*
*Assistant Director of Research*
*University of Missouri — St. Louis*
*St. Louis, Missouri*

**ROBERT I. STEARNS, Ph.D.**

*Adjunct Associate Professor of Chemistry*
*University of Missouri — St. Louis*
*St. Louis, Missouri*

*Director of Research*
*The Lorvic Corporation*
*St. Louis, Missouri*

Although fraught by controversy, the use of fluoride is now widely accepted as an effective inhibitor of dental decay. This text presents a general analysis of the state of fluoride therapy, written for students possessing only fundamental backgrounds in chemistry and dentistry. Practitioners in the dental field will find interesting the discussion of the history of fluorridation. Chemists will appreciate the practical application of this form of chemotherapy.

# DENTAL FLUORIDE CHEMISTRY

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*By*

ALAN F. BERNDT, Ph.D.

*Professor of Chemistry*
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*Assistant Director of Research*
*University of Missouri—St. Louis*
*St. Louis, Missouri*

*and*

ROBERT I. STEARNS, Ph.D.

*Adjunct Associate Professor of Chemistry*
*University of Missouri—St. Louis*
*St. Louis, Missouri*
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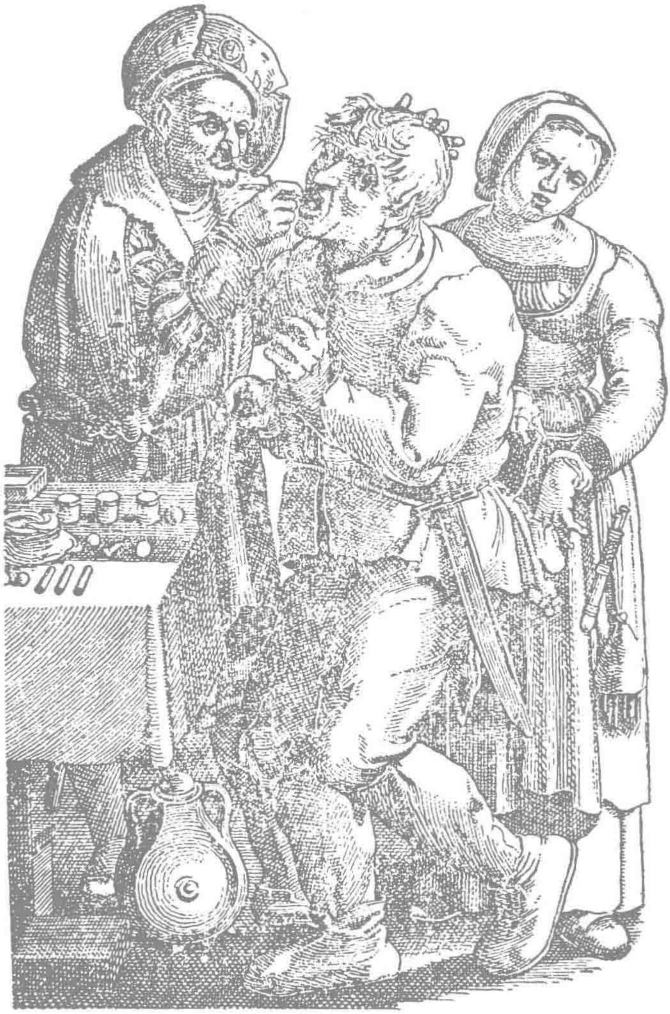

*To our wives, Marion and Sandra,*
*without whose encouragement and understanding*
*this volume could not have been written.*

# PREFACE

ALTHOUGH BESET with a stormy and controversial history, the effectiveness of fluoride as an inhibitor of dental decay is now widely accepted both within the dental profession and by the general public. Fluoridation of community water supplies is commonplace and dentifrices with fluoride added are nationally advertised. The commercial success of these preparations is testimony to the fact that the general population is both aware of and accepts the beneficial effects of fluoride in promoting dental health.

This interest in fluorides has resulted in a large number of research groups, both within the United States and elsewhere in the world, directing their efforts toward a study of the effects of fluoride on human teeth. Millions of dollars are spent annually in support of these programs which are all directed toward the laudable task of seeking improvement in an important area of health.

The results of much scientific research are published in a large variety of scientific journals over a period of many years and are thus separated in both time and space from forming a coherent whole. This, in the extreme, is the story of fluorides. Innumerable investigators have filled many pages in many journals over a period of many decades with the results of studies describing various aspects of the effects of fluoride on dental health. These range from clinical studies on individuals to statistical summaries of data from large population groups to papers concerned with a theoretical understanding of the reactions and processes which occur, both from a biological and a chemical point of view.

This volume is not a critique or summary of everything that has been published in the past. Rather, it focuses on a very narrow part of the whole problem of dental health. It deals with the effect of fluoride on teeth and represents the state-of-the-art as we perceive it. The plethora of papers in the dental literature dealing with the effect of fluorides on teeth can lead to the misconception that the answer to dental health problems lies in fluorides alone. That this is not true can be seen from the realization that diet, heredity, and dental hygiene are all well-recognized as major contributors to dental health. However, of all these factors, fluoride in the environment is the one which is most easily controlled, on a mass scale, and is therefore most important from a public health point of view.

Perhaps because of our chemical background and training, we have taken a different approach to the study of the problem of how fluorides interact with teeth. Our philosophy is based on an examination of normal teeth to find out what conditions exist in the healthy (noncarious) tooth. Deviations from these conditions could lead to a situation which results in cavity formation. The orthodox approach differs in that it does not concern itself with a study of normal, healthy teeth but instead looks at the carious process. Chemical reactions are studied which could lead to the dissolution of tooth material and the initiation and propagation of a cavity.

Ours is a macroscopic, as opposed to a microscopic, approach. The enormity of the problem of studying teeth can be appreciated when it is realized that on a microscopic scale, the structure of teeth is extremely complicated. The study of teeth and their interaction with fluorides might thus be akin to the study of a forest with its myriad species of flora and fauna. The microscopic approach would study every plant and animal to learn the properties of each, and then proceed to study the interactions of these with one another. Alternately, one could take the macroscopic approach, and examine the properties of the forest as a whole, from a distance so that the individual details tend to blur into each other. Both approaches are legitimate; both give much vital information, and they complement each other as far as a total understanding of the overall picture is concerned.

The body of this book assumes no knowledge of chemistry above that which would normally be obtained in an introductory college course, or a good high school course. No knowledge of dentistry is required. To maintain the readability of the material arguments which are mathematical in nature are relegated to appendices. No loss of understanding will result from their omission.

The results and importance of the arguments presented in the appendices are discussed in the appropriate places in the text.

We have undertaken to write this volume in order to place, under a single cover, a history of fluoridation as well as a coherent theory as to why fluorides are an effective agent for the promotion of dental health. It should find a place on the bookshelves of chemists who are interested in fields of chemistry other than their own specialties and in the offices of dental practitioners who are interested in the reasons behind the techniques they practice.

We are deeply indebted to Ms. Linda Chickos and Ms. Cathy Brown Disper for their painstaking attention to the details of typing several drafts of this manuscript.

ALAN F. BERNDT
ROBERT I. STEARNS
St. Louis, Missouri

# INTRODUCTION

DENTAL CARIES (tooth decay) is the most common disease of mankind. Although cavities cannot be cured in the sense of regenerating lost tooth material, they can be treated by well-known techniques of filling and capping. In view of the widespread occurrence of cavities and the fact that millions of people do not receive adequate dental care, it is of the utmost importance to complement treatment by finding effective ways of preventing or reducing tooth decay which can reach the general population.

Mottling (discoloration) of tooth enamel is a common affliction in certain geographic areas. Investigations of mottling have demonstrated that this discoloration is caused by excessively large amounts of naturally occurring fluoride ion in the community water supply. The degree of mottling depends on the concentration of fluoride ion in the water supply, being most pronounced where the fluoride concentration is highest.

As a sidelight to these investigations it was observed that people with mottled teeth had statistically less tooth decay than individuals living in communities with little or no fluoride in the water supply. Voluminous and repetitive clinical studies have shown that the fluoride ion is also the agent responsible for the reduction in the incidence of cavities.

The fluoridation of public water supplies has long been recognized as both an effective and perfectly safe way of reducing tooth decay in the general population. Fluoride in drinking water is particularly desirable since it is a passive method which can reach millions of persons who do not brush their teeth regularly or do not see dentists. However, the effectiveness of fluoride is only one facet of the whole problem of the prevention of dental disease. Good dental hygiene, diet and heredity are also recognized factors.

Of two similar population groups, one consuming fluoridated water and the other consuming water with little or no fluoride, the former will experience up to 65 percent less tooth disease as measured by the statistical incidence of decayed, missing and filled teeth. Data from communities in which fluoride has been artifically added to the water supply are now available which give essentially identical results as for communities with naturally occurring fluoride. This is to be expected because the nature of the fluoride ion is independent of the method by which it is introduced into the water supply. However, while the element fluorine may be present in other chemical forms not every fluorine-containing compound is a source of fluoride ion. The evidence indicates that it is the fluoride ion alone which is effective.

Clinical studies have led to the widespread fluoridation of water supplies, the incorporation of fluorides in toothpaste formulations and the use of topical fluoride treatments by dentists. We will further discuss the role that the fluoride ion plays in preventive dentistry. The basic laws of physics and chemistry must apply to teeth, and it is the application of these laws and the consequences derivable from them that are of interest.

Any discussion of the interactions between fluoride and teeth must be preceded by a look at the structure of normal teeth. A cross-sectional view of a typical tooth would show four distinct regions: enamel, dentin, pulp and cementum. Most tooth decay is generally believed to start at or near the surface of the tooth, in the enamel, and it is the structure of enamel to which attention is here drawn.

A typical analysis of enamel shows about 97 percent by weight of an inorganic component, 1 percent of organic material and 2 percent water. These components are intimately mixed to form a near homogeneous structure. The inorganic component of tooth enamel, as well as bones in the body, is mainly the crystalline compound hydroxyapatite, $Ca_5(PO_4)_3OH$, containing small amounts of carbonate, magnesium, fluoride and other substances.

The crystal structure of hydroxyapatite shows a loose network of calcium, phosphate and hydroxide ions held together by electrostatic forces. This type of ionic crystal readily admits substitution of other ions. Many crystalline minerals in which this substitution is observed are found in nature and have been prepared synthetically. When fluoride reacts with teeth the fluoride ion readily substitutes for the hydroxide ion. If the substitution were complete the compound fluorapatite, $Ca_5(PO_4)_3F$, would be formed. In general the substitution is not complete and what is formed is a pseudo-binary solid solution termed fluor-hydroxy-apatite whose formula may be written as $Ca_5(PO_4)_3F_x(OH)_{1-x}$.

The fluoride ion is ubiquitous. It is present to at least a slight extent in all water supplies, in food, in body fluids and tissues, and in teeth and bones. As a result, teeth are never completely fluoride free. Although enamel has a complex composition, it may be approximated as the solid solution fluor-hydroxyapatite, which rather than hydroxyapatite may be considered to be the stable phase in a biological system. The amount of fluoride contained in a tooth, as the solid solution fluor-hydroxyapatite, depends on the history of fluoride exposure.

The concentration of fluoride at the surface of the tooth can be measured *in vivo*. From studies of this type it has been found that the fluoride content of the enamel surface correlates directly with the fluoride concentration in the drinking water supply. The higher the fluoride concentration in the drinking water the higher the fluoride concentration in the teeth. This correlation suggests that a steady state condition has been reached. If a steady state did not exist teeth would be constantly gaining fluoride and the teeth of older adults would exhibit markedly higher concentrations of fluoride than the teeth of younger adults, contrary to observation. Since a steady state is attained, removal of a person from a fluoridated water supply will result in the lowering of his enamel surface fluoride concentration with concomitant loss of protection against tooth decay.

Clinical studies have shown statistically that the incidence of decayed, missing or filled teeth decreases with increased fluoride content of the water supply. It has also been shown that the fluoride concentration of the enamel surface increases with the increase of fluoride in the drinking water. Therefore, higher *stable* enamel surface fluoride concentrations correlate with greater resistance to tooth decay. On cursory examination it would seem that transformation of the enamel surface to pure fluorapatite would result in maximum protection against tooth decay.

Solutions containing fluoride ion react readily with hydroxyapatite, *in vitro*. If the fluoride concentration of the solution is low, fluorapatite is the main product formed, whereas if the fluoride concentration is high, calcium fluoride is the predominant product. The fluoride concentration of the enamel surface of human teeth may be increased above the steady state value by topical application of a fluoride solution directly to the teeth, by a dentist. Immediately after such a treatment the enamel surface fluoride concentration corresponds essentially to that of pure fluorapatite. Unfortunately, fluorapatite, *in vivo,* is unstable and decomposes to calcium fluoride and other products which do not adhere to the tooth surface. Within a few weeks of the topical treatment the enamel surface fluoride concentration is reduced from its initial high value to little more than the stable value. The utility of topical treatments lies in their ability to produce the stable concentration in newly erupted teeth within a short time and to restore the stable concentration to teeth from which fluoride has been removed.

Since greater stable fluoride concentration at the surface of enamel correlates with increased protection against tooth decay it seems attractive to increase this concentration. This can be done by adjusting the fluoride content of the water supply. Efforts to develop means of topical fluoride treatments which would maintain a concentration in excess of the stable value are in essence attempts to violate the laws of thermodynamics.

The evidence that the presence of fluor-hydroxyapatite at the enamel surface retards tooth decay is overwhelming. What is not clear is how the desired effect is accomplished. The classical theory of tooth decay holds that cavity formation is the direct result of the action of acidogenic (acid-forming) bacteria on a suitable substrate. Acid is produced which attacks tooth enamel at the location of the cavity. The decay process is a dissolution of enamel by the action of acid and the decay preventive action of fluoride is due to a reduction of the acid solubility of enamel. While some investigators feel that this effect is important, it does not explain why tooth decay occurs as localized phenomena, initiated slightly below the surface, rather than as general dissolution of enamel, nor does it explain the beneficial effects of fluoride since the difference in solubility between fluor-hydroxyapatite and hydroxyapatite is too small to account for the observed effects.

A recent theory of tooth decay proposes that cavities could be formed by a mechanism analogous to that of the electrochemical corrosion of metals. When exposed to salt concentration gradients such as those which exist between the saliva external to the tooth and the fluids in the interior of the tooth, enamel produces an electrical ionic membrane potential. Exposure of small portions of enamel to acidic solutions degrades these ionic membranes and locally eliminates the normal membrane potential. A self-perpetuating flow of electric current is initiated which causes a cavity to form and propagate. The cause of the cavity is the source of the localized acidity but the mechanism of formation of the cavity is the hypothesized electrochemical mechanism. The beneficial effects of fluoride result from an increase in electrical resistivity and ionic membrane potential of the enamel. Although no definitive statement of the mechanism of cavity formation can be made it is most probably a very complex combination of many of the proposed theories.

Up to this point we have been concerned with the concentration of fluoride at the enamel surface, but what about the concentration as one goes into the tooth? Studies on extracted teeth have shown that, although the concentration of fluoride at the surface may be relatively high, the concentration falls off rapidly with depth. Several theories have been proposed to explain this distribution.

Fluoride ion diffuses rather slowly into enamel. Although fluoride may be introduced at the surface by a variety of methods, the fluoride ion can find its way into the interior only through a diffusion process. If the kinetics of diffusion were sufficiently slow the observed depth distribution could be explained. If diffusion at constant temperature were the dominant factor we would predict that the fluoride distribution with depth would become constant within a few years and the teeth of older adults would show a more uniform distribution of fluoride. Experimental evidence indicates this not to be the case. Slow diffusion kinetics must play at most only a minor role in determining the observed distribution of fluoride with depth.

Another explanation of this distribution, based on solubility considerations, proposes that the fluoride gradient is the direct result of the existence of a pH gradient within the fluids which permeate the enamel. The aqueous solubility of fluor-hydroxy-apatite decreases with increased fluoride content and at constant composition increases as the acidity of the water increases (pH decreases). *In vivo,* normal teeth are stable which means that there is no difference in solubility as a function of depth within the tooth. The necessary constant solubility is accomplished by the fluoride concentration adjusting itself with depth. This theory says that the fluoride concentration gradient is a consequence of a pH gradient but gives no mechanism for the generation and maintenance of such a pH gradient.

A third explanation can be based on a temperature gradient. The interior of a tooth, the pulp, contains blood vessels and must be at normal body temperature. The long term average temperature at the surface of the tooth should be somewhat lower than this value because these surfaces are cooled by evaporation of saliva and are in contact with air which, on the average, is cooler than the body.

In a tooth there are two processes which can occur simultaneously: flow of heat due to the temperature gradient and diffusion of fluoride (accompanied by an equal but opposite flow of hydroxide). If flows of both energy and matter can occur, a steady state results when a constant temperature gradient is maintained and the concentration gradient allowed to adjust itself so that the flow of mass, but not of energy, becomes zero. This says that the fluoride concentration gradient is a direct consequence of the existence of a temperature gradient in the tooth. We feel that the observed distribution of fluoride with depth is most easily and simply explained in terms of the existence of a temperature gradient within the tooth and that the other effects are relatively unimportant.

Basically, all commercial toothpastes and powders contain a mildly abrasive compound as an agent to clean and polish the teeth. To this abrasive are added detergents, flavors and sweeteners and sometimes other ingredients such as a bacteriocidal agent are included. Several brands have added fluoride in the form of sodium fluoride, stannous fluoride or sodium monofluorophosphate (MFP). Sodium fluoride in a dentrifrice acts in essentially the same way as does a topical application of fluoride except that the reaction is greatly subdued since the concentration of added sodium fluoride is low.

The first toothpaste recognized by the Council on Dental Therapeutics of the American Dental Association as "an effective decay-preventive dentifrice" contained stannous fluoride. Stannous fluoride reacts with enamel, *in vitro,* at room temperature to produce several possible compounds all of which are crystallographically unrelated to apatite. The decay inhibiting effect of stannous fluoride may result from the formation of an adhering layer of one of these compounds or may result from the formation of some fluor-hydroxyapatite.

A toothpaste containing sodium monofluorophosphate is also recognized by the Council on Dental Therapeutics. Here too, the reaction responsible for cavity inhibition is not known, although a number of possible explanations have been postulated.

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