

**CARIES MANAGEMENT:
FLUORIDE – MECHANISM OF
ACTION, KINETICS, AND
METABOLISM**

E. Angeles Martínez-Mier, DDS, MSD, PhD
Orofacial Biology II 2013



*Oral Health Research Institute
Indiana University School of Dentistry*

OBJECTIVES

Fluoride mechanism of action, kinetics, metabolism and toxicity

○ Objectives:

- Describe the pre and post eruptive effects of fluoride on dental tissues
- Describe the mechanisms and processes by which the presence of fluoride alters caries formation and progression
- Discuss the implications of the use of fluoride in prenatal vitamin supplements, pediatric fluoride supplements, and infant formulas



FLUORIDE - BACKGROUND

- Naturally occurring element, 13th most common, electronegative
- Found naturally in water sources in small but traceable amounts, and in certain foods such as meat, fish, eggs, bones and tea.

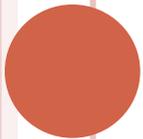
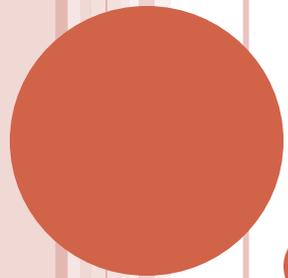


FLUORIDE - BACKGROUND

○ History

- First observations
 - Eager and McKay - Colorado Springs
- Black
- Early studies in the 1930s - Dean and collaborators
 - Initial water fluoridation 1945
- Four classic studies have been conducted comparing pairs of cities (fluoridated vs. non-fluoridated):
1940s, 1971, 1982, and 1992





KINETICS

SOURCES OF FLUORIDE

Systemic

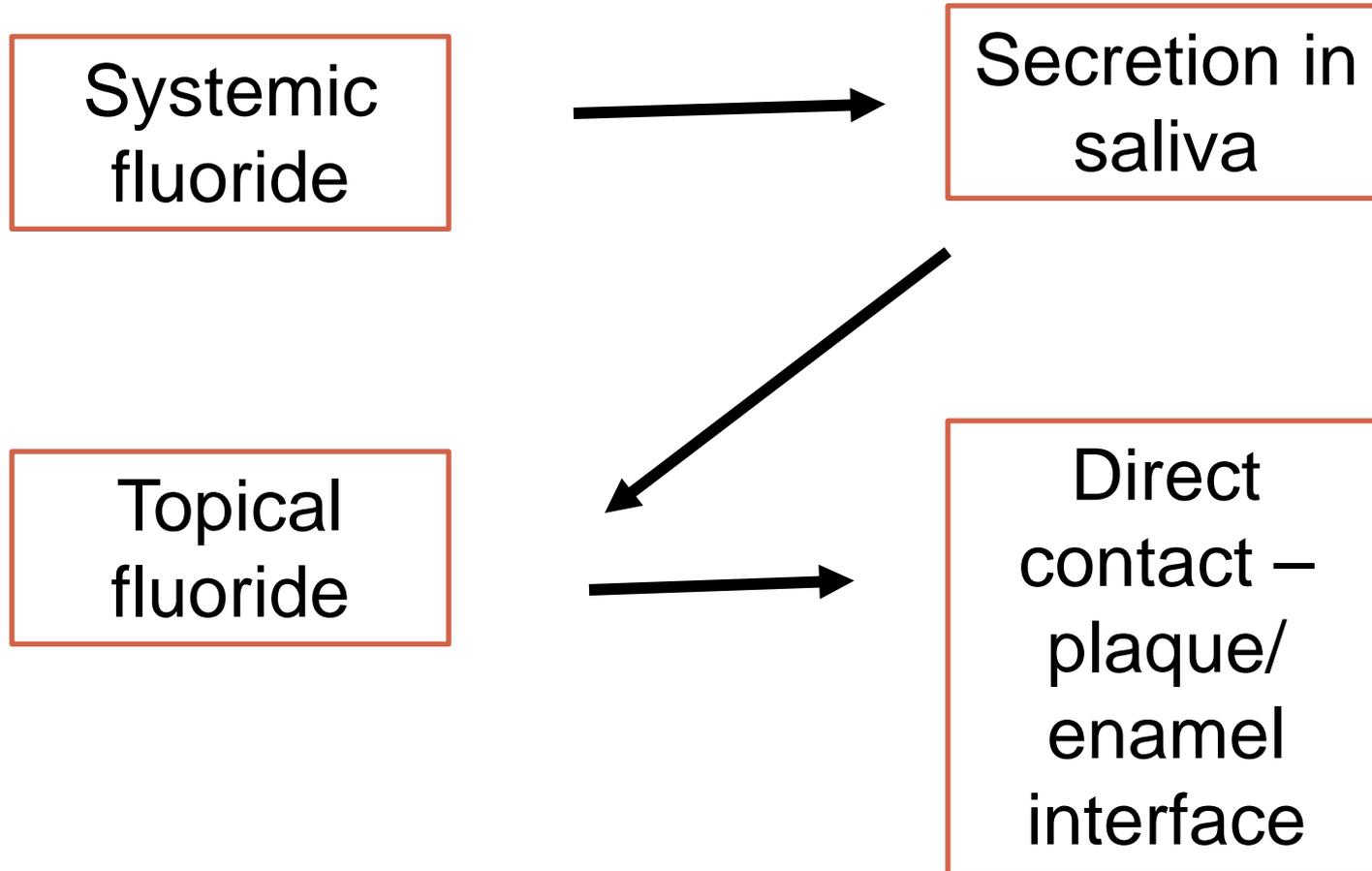
- **Planned**
 - water for drinking and cooking
 - fluoride supplements
 - fluoridated milk and salt (in other countries)
- **Incidental**
 - dentifrice ingestion
 - fluoride rinse ingestion
 - environmental pollution
 - Teflon coatings on pans
 - food/soil/pesticides
 - prescription drugs (Prozac, Lipitor, Ciprofloxacin)
 - smoking

Topical

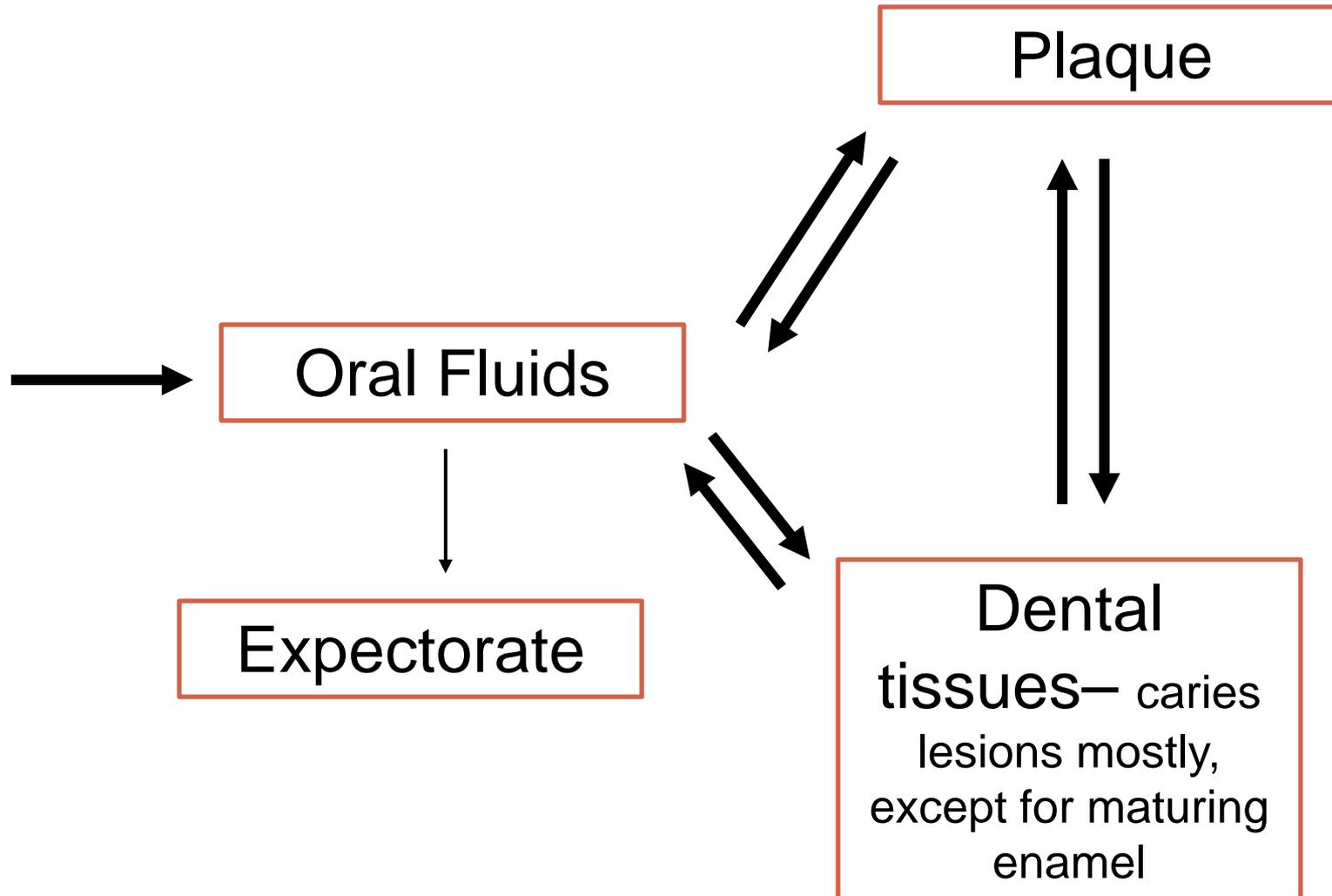
- **Planned**
 - Professionally applied gels and varnishes
 - Dentifrice
 - Home use rinses & gels
- **Incidental**
 - Alginate impression materials



How does fluoride reach the oral cavity?



Kinetics of Fluoride in the Oral Fluids



KINETICS OF FLUORIDE IN THE ORAL FLUIDS

- Clearance more rapid from lingual than buccal
- More rapid beneath tongue
- Slowest upper labial vestibule



FACTORS AFFECTING FLUORIDE KINETICS

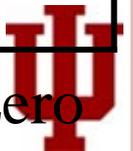
- **Application Phase vs. Retention Phase**
- **Sites of fluoride retention**
 - Tooth surface, plaque, saliva, oral soft tissues
- **Oral clearance forces**
 - Salivary flow, eating and drinking
- **Fluoride Concentration**
 - High vs. Low
- **Method of fluoride delivery**
 - Brushing, rinsing, trays, applicators
- **Timing of fluoride application**
 - **Daytime vs. Nighttime**

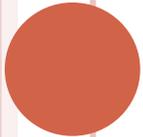
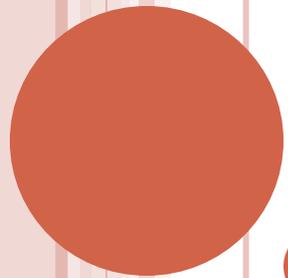


KINETICS OF FLUORIDE IN THE ORAL FLUIDS

< 2hr	2-24 hr	>24 hr
Beverages	Gels	Topical solutions
Dentifrices	Mouth rinses	Varnishes
Tablets		Restorative materials
Chewing gum		Slow-release devices

Slide by Dr. D. Zero





MECHANISM OF ACTION

FLUORIDE: MECHANISMS OF ACTION

○ Post-eruptive

- Topical effect on remineralization
- Antimicrobial effect

○ Pre-eruptive

- Some minor reduction in enamel solubility
 - Burt and Ekstrand, 1999



FLUORIDE: MECHANISMS OF ACTION

- **CDC's guidelines:**

“...fluoride's predominant effect is posteruptive and topical and that the effect depends on fluoride being in the right amount in the right place at the right time.”

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MMWRTM
MORBIDITY AND MORTALITY
WEEKLY REPORT

*Recommendations
and
Reports*

Examination

**Recommendations for Using Fluoride
to Prevent and Control Dental Caries
in the United States**

EVIDENCE OF POSTERUPTIVE EFFECT

- Exposure to fluoride prevented the development of fewer caries, even in older children and adults
 - Kingston/Newburgh study 1946
 - Japanese camps 1945



EVIDENCE OF POSTERUPTIVE EFFECT

- Animal experiments
 - Fluoride administered through gastric intubations in rats produced smaller reductions in caries
- Use of supplements at early age
 - No decrease in caries if discontinued by age two



FLUORIDE: MECHANISMS OF ACTION

Most of the caries preventive effect of fluoride does not occur through the conversion of hydroxyapatite to fluoridated hydroxyapatite while teeth are forming

In an optimally fluoridated area, only about 10% of hydroxyapatite is converted into fluoridated hydroxyapatite



FLUORIDE:

MECHANISMS OF ACTION - EVIDENCE

There is little difference in whole enamel fluoride concentration between those exposed and not exposed to fluoride at an early age

Fejerskov, 1996



FLUORIDE: MECHANISMS OF ACTION

The amount of fluoride in surface enamel is not directly related to caries susceptibility

A clear cut inverse relationship between caries experience and the fluoride content of surface enamel cannot be demonstrated

Fejerskov, 1996

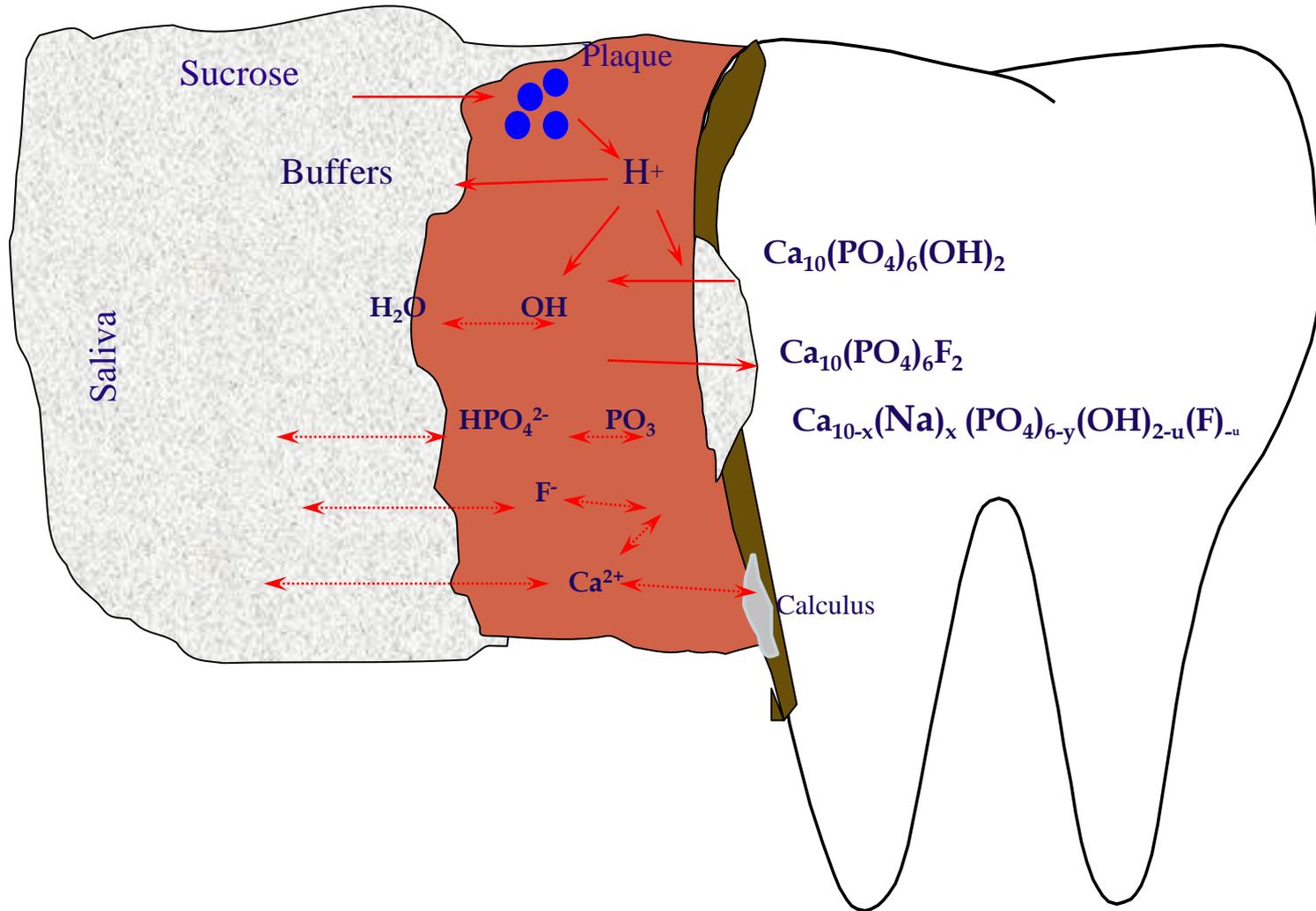


Slide by Dr. Karen Yoder

FLUORIDE: MECHANISMS OF ACTION

- Caries reduction is predominantly affected by fluoride being present during active caries development in the plaque-enamel interface





FLUORIDE: POSTERUPTIVE EFFECTS

Fluoride will render crystals in the lesion less susceptible to acid attack by:

- At very low concentrations (>1 ppm), initiating phase transformations (dicalcium phosphate into fluoroapatite)
- Depending on the calcium and phosphorous concentrations in the remineralizing solutions, help deposit minerals, preferentially in the subsurface lesion (subsurface zone and base)

Fejerskov, Ikstrand, Burt, 1996



Slide by Dr. D. T. Zero

FLUORIDE: POSTERUPTIVE EFFECTS

Fluoride in the oral fluids:

Fluoride may be ionized in saliva, ionized in plaque (fluid plaque), bound in plaque, bound as calcium fluoride, bound to enamel, or bound to soft tissue. Fluoride is distributed to the dental plaque by diffusion.



FLUORIDE: POSTERUPTIVE EFFECTS

Fluoride in dental plaque :

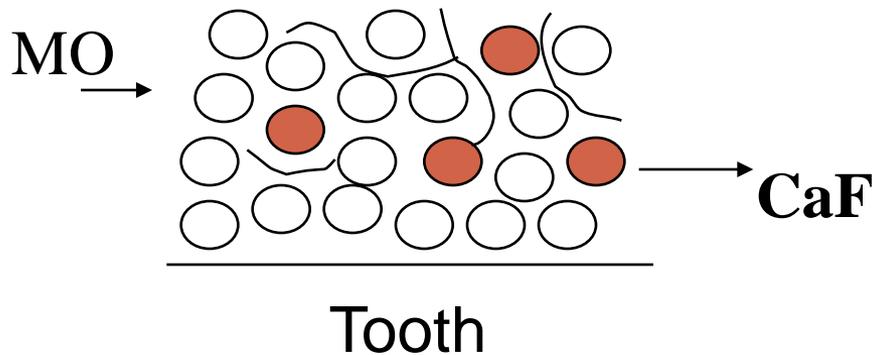
Much of fluoride in plaque exists in complexes in dynamic equilibrium with the fluoride in the fluid phase of the plaque. There are large labile fluoride reservoirs in plaque. Large amounts of fluorides deposits, such as CaF_2 or cellular bound fluoride form in plaque



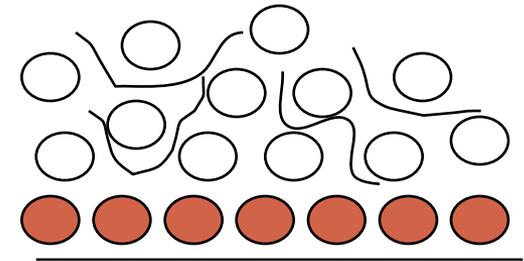
FLUORIDE: POSTERUPTIVE EFFECTS

Fluoride in plaque :

- Calcium F may be distributed randomly through heavy undisturbed plaque



- May adhere to the tooth surface during brushing and later be covered by plaque holding it closer to the tooth-plaque interphase



Slide by Dr M. Fontata

FLUORIDE: POSTERUPTIVE EFFECTS

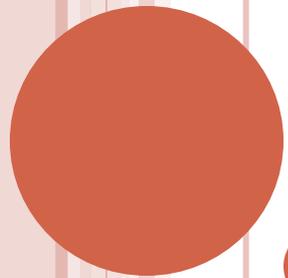
Fluoride in plaque will:

- Accumulate and be released when the pH level decreases at the plaque-enamel interphase - Not necessarily when it is applied
- Accelerate crystal growth of fluoridated hydroxyapatite, when present at low concentrations during an acid attack
- Dynamic not static process!!

• NIH, 2002

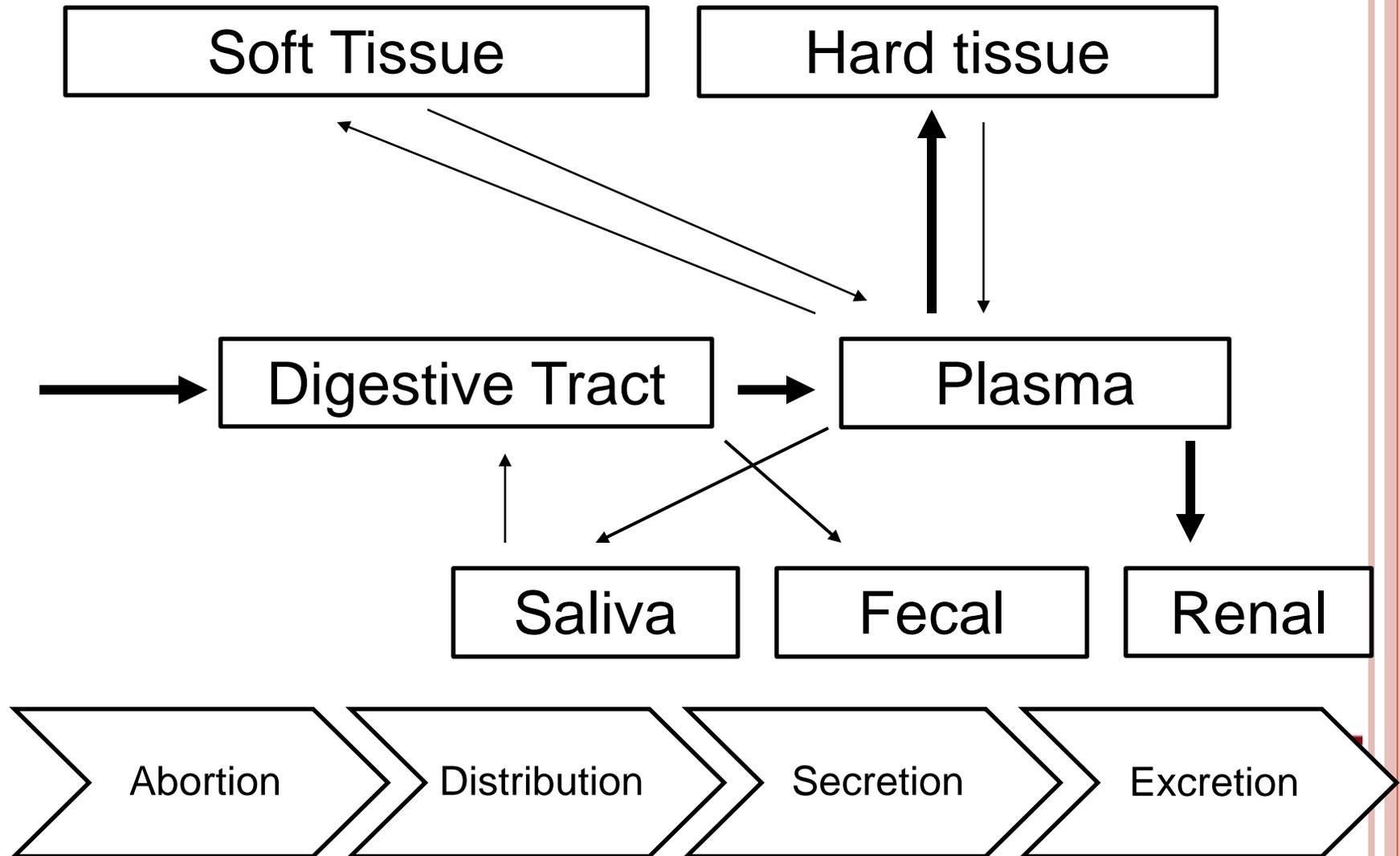


Slide by Dr. M. Fontana



METABOLISM

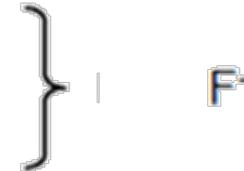
ABSORPTION, DISTRIBUTION, AND ELIMINATION OF FLUORIDE FROM THE BODY



SOLUBILITY OF FLUORIDE

Soluble fluoride compounds: NaF, HF, Na₂PO₃F

Less soluble compounds: CaF₂, MgF₂, AlF₃



$$\text{pH} = \text{pK}_a + \log \frac{[\text{A}^-]}{[\text{HA}]} \quad \text{or} \quad \text{pH} - \text{pK}_a = \log \frac{[\text{A}^-]}{[\text{HA}]}$$

Diffusibility of HF explains physiological behavior of fluoride

Low pH (<3.5) e.g., stomach:

More as undissociated form HF

At pH 2.45

$$\log \frac{[\text{F}^-]}{[\text{HF}]} = -1 ; \frac{[\text{F}^-]}{[\text{HF}]} = \frac{1}{10}$$

pH > 3.45 e.g., blood, saliva,

tissue fluid: ionized form F⁻ dominates

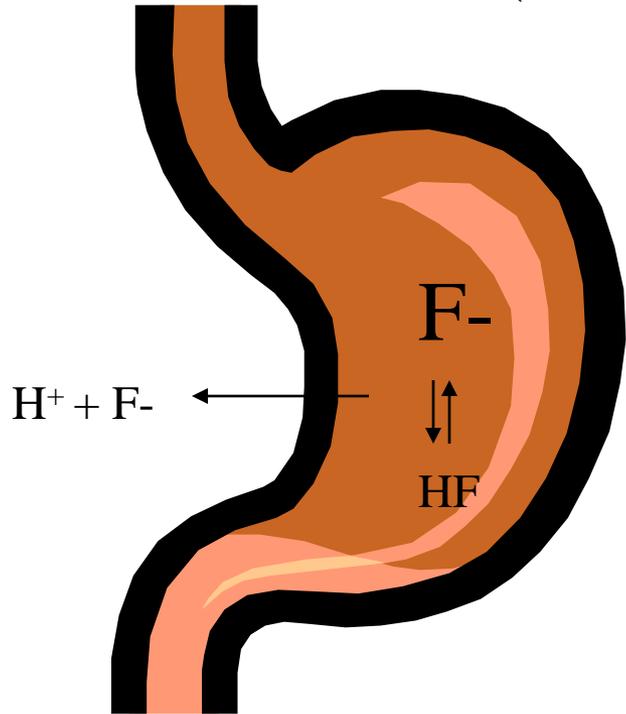
At pH 6.45

$$\log \frac{[\text{F}^-]}{[\text{HF}]} = 3 ; \frac{[\text{F}^-]}{[\text{HF}]} = \frac{1000}{1}$$

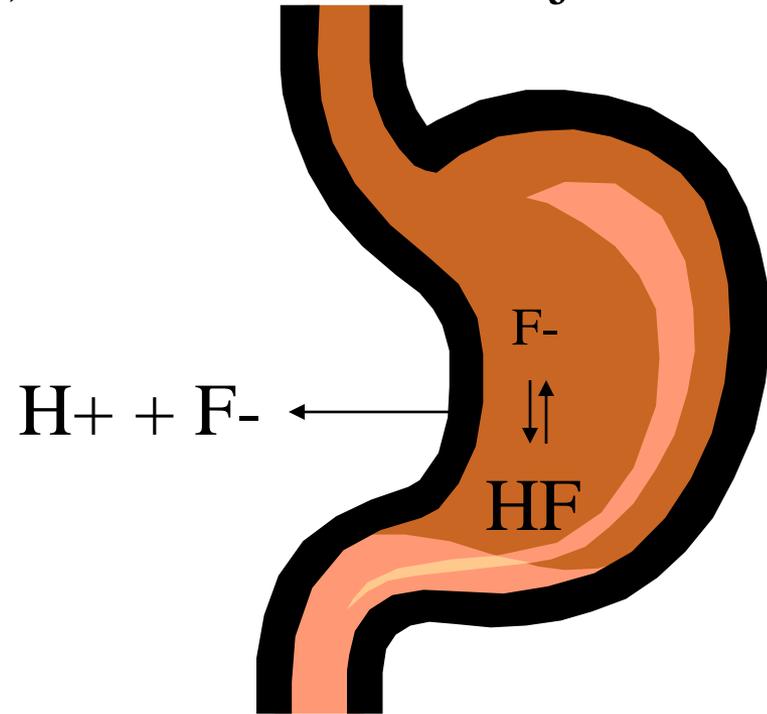


FLUORIDE METABOLISM

Alkaline contents (milk, cheese)



Acidic contents (juice, chile)

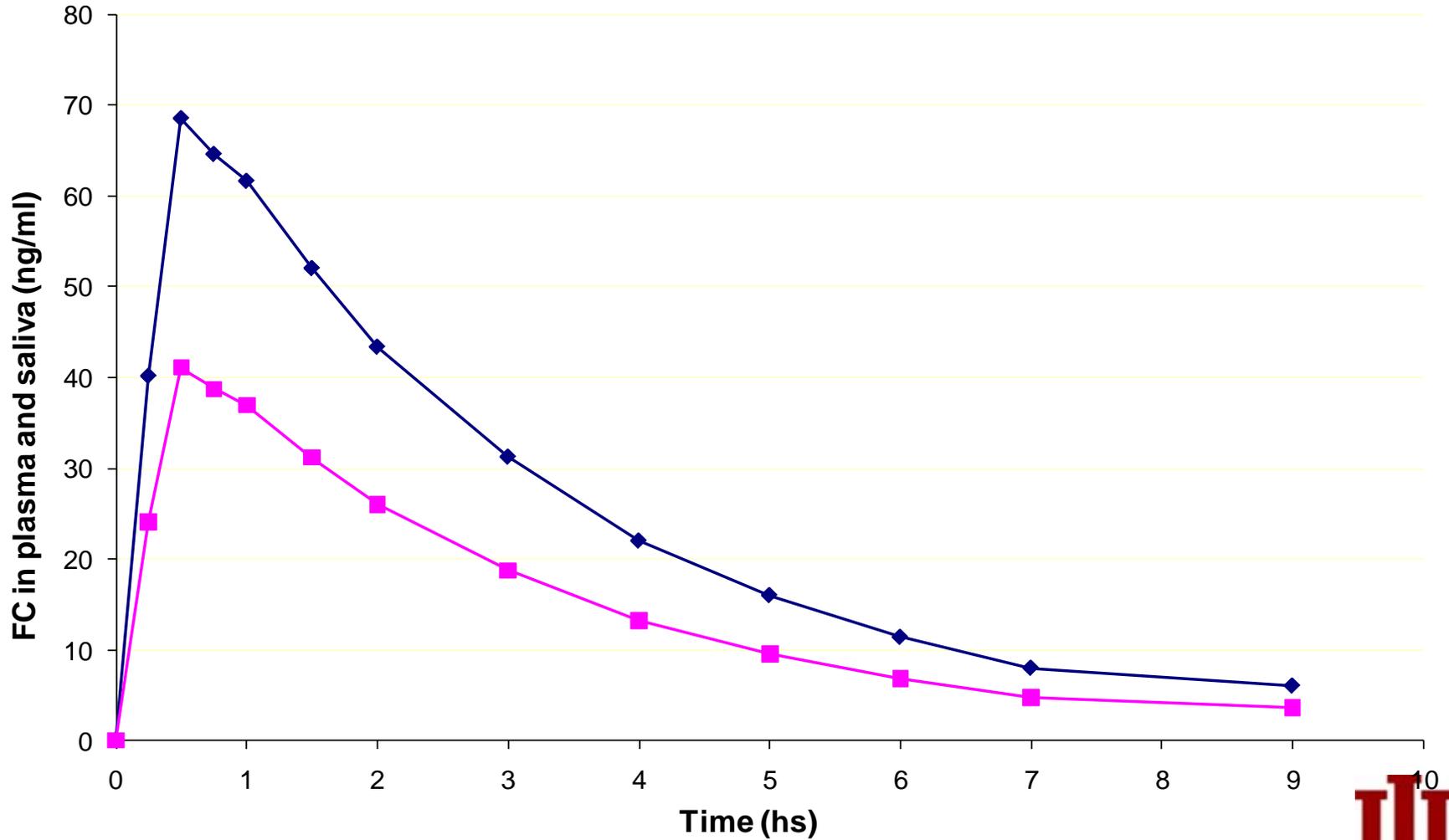


FLUORIDE METABOLISM

- **Plasma fluoride increases at 10 min**
- **Peak levels at 60 min**
- **Basal levels at 11-15 hrs**



Fluoride concentration in plasma and saliva vs time



FLUORIDE SECRETION

○ Secretion

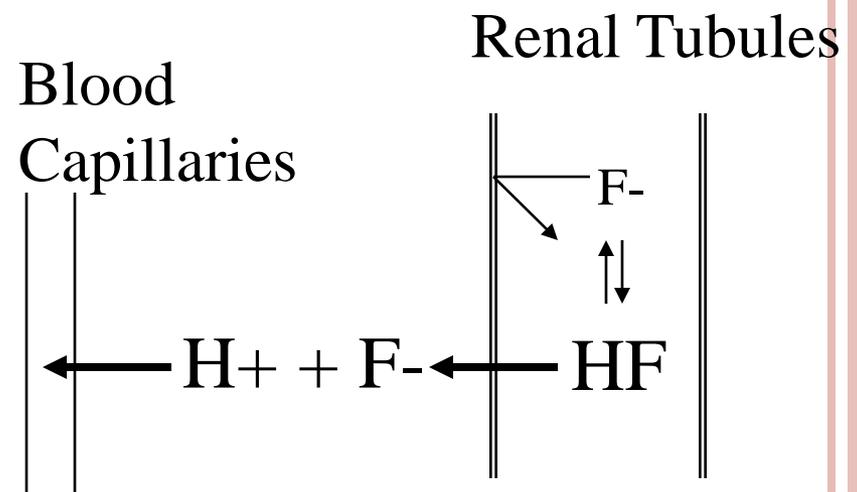
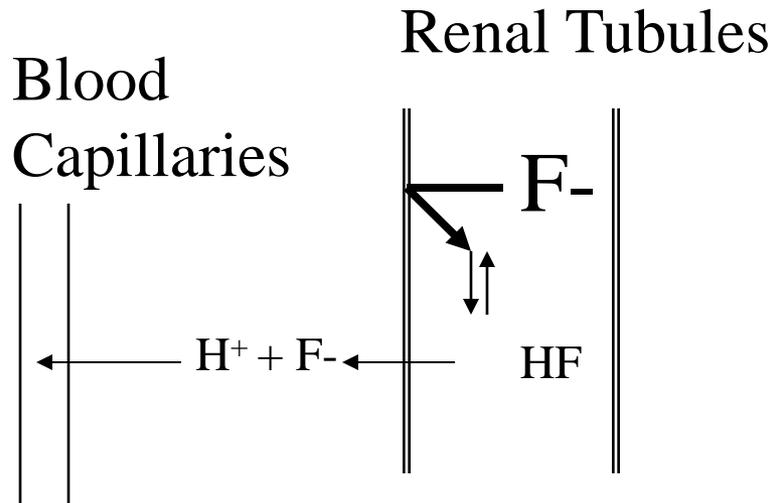
- Salivary levels increase as plasma increases 0.01 ppm- 0.06 ppm
- Milk



FLUORIDE METABOLISM

Alkaline urine (vegetarian diet)

Acidic urine (meat rich diet)



VALUES FOR FRACTIONAL URINARY FLUORIDE EXCRETION AND (FRACTIONAL RETAINED FLUORIDE) FOR YOUNG ADULTS

	Day time	Nighttime	Daily
(FUFE)	0.57	1.27	0.78
(FR)	0.43	- 0.27	0.22



VALUES FOR FRACTIONAL URINARY FLUORIDE EXCRETION AND FRACTIONAL RETAINED FLUORIDE FOR CHILDREN

Study	Age	N	Ingestion (ug/d) (ug/kg)	Daily excretion (ug/d)	FUFE (%)
Brunetti & Newbrun (1983)	3 - 4	10	330 0.022*	280	84.8
Villa y cols. (1999)	3 - 5	48	1.000 0.067		30.7
Ketley & Lennon (1999)	4 - 5	8	1.100 0.065*	330	30
Villa y cols. (2000)	3 - 5	20	1.019 0.064	358	35.5
Ketley & Lennon (2001)	5 - 6	13	750 0.034	260	42.7
		13	2.000 0.091	610	30.5
Zohouri & Rugg-Gunn (2000)	4	78	426 0.028*	339	80.0
Haftenberger y cols. (2001)	3 - 6	11	931 0.053 (0.023-0.086)	476	51.5
Franco y cols.	4 - 5	30	1721 0.102	495	28.8



RECOMMENDED TOTAL DIETARY FLUORIDE INGESTION

Age	Weight (kg/lb)	Adequate intake (ppm)	Tolerable intake (ppm)
0-6 mo	7/16	0.01	0.7
6-12 mo	9/20	0.5	0.9
1-3 yr	13/29	0.7	1.3
4-8 yrs	22/48	1.1	2.2
≥ 9 yrs	40-76/ 88-166	2.0-3.8	10.0



REVIEW OF FLUORIDE BENEFITS AND RISKS

**Review of Fluoride Benefits and Risks
Conducted by the Department of
Health and Human Services**

- **There is no evidence linking fluoride to cancer and other systemic diseases**



EXPERT COMMITTEES AND SYSTEMATIC REVIEWS

- **All are in agreement**
- **Evidence does not support an association between water fluoridation and any adverse health effect or systemic disorder**



QUESTIONS YOUR PATIENTS MAY HAVE ABOUT FLUORIDE

- Is it true there was a lawsuit for a child who developed fluorosis and the parents won?
- Is it true fluoride causes cancer or dementia?
- Is it true fluoride causes arthritis?
- Is it true that fluorosis weakens the teeth?
- Is it true that there is new evidence on the harmful effects of Fluoride on the developing brain?

