Pevintive sheet #11

**Fluoride toxicity**

Fluoride is very important to us as dentists due to its role in caries prevention, but as many other materials it comes with its toxicity so it is very important to know about fluoride toxicity weather it is acute or chronic and know how to handle it properly.

**Slides #3-7**

In the past, they used NaF in pesticides and because it is a white powder it was easily mistaken for milk or salt,.. and caused a mass poisoning cases and large number of deaths due to fluoride toxicity. Nowadays, we don’t use NaF in pesticides anymore so these big numbers of poisonings do not occur any more.

So fluoride; in certain doses; can be very toxic material.

In these days, the sources of fluoride are vitamins, dietary supplements and dental products (most important form for toxicity is the fluoride tablets because they contain high concentration of fluoride)

Almost 20,000 reports of possible (not actual) over-ingestion each year in the US

**Slide #9**

**Fluoride metabolism**

Absorption of fluoride is by ‘Passive Diffusion’, it doesn’t need a pump, and it only depends on concentration difference and pH (just like the absorption in the enamel, when pH decreases; absorption increases)

 80-90% of ingested F typically absorbed in GI tract, the rest is deposited through feces.

**Slide #10**

Absorption half-time is 30 minutes and after 3-6 hrs it goes back to pre-ingestion levels ; so the toxicity due to over-dose will happen in about 30-60 mins after ingestion. That’s why if you had a call from a parent complaining that her child is having nausea and vomiting the day after fluoride application you don’t suspect fluoride toxicity because it will be already cleared from the plasma

The presence of cations such as Ca and Al reduce the absorption of F, how?

By interaction btw those cations and F that forms insoluble compounds that are hard to be absorbed by the stomach 🡪reduced absorption

**Slide #11**

F in plasma is not bound by proteins, it is free

Diffusion from plasma to other tissues and body fluids is dependent on the pH gradient across the membrane crossed, so the concentration of fluoride will differ from one tissue to another depending on its pH

**Slide #12**

CSF: cerebrospinal fluid

We are concentrating on the fluoride in the milk because we have to keep in mind that if we want to give a lactating woman fluoride supplement, 50% of it will transmit to the baby through milk.

Why we said ductal saliva rather than ‘saliva’?

Because if we want to measure F concentration that is originally excreted through salivary glands, the most accurate measurement will be from the duct because it will be ‘pure’ saliva that contains only the fluoride that came from plasma without the effect of other fluoride sources like topical fluoride,…

**Slide #13**

You can see a chart that shows the absorption of fluoride

It goes to the plasma, after one hour it reaches its peak concentration 🡪 and from there it goes to urine, sweat and soft tissues, also notice that a large portion goes to calcified tissue 🡪distributed through body fluids, like the oral fluids 🡪 enamel (that’s how you can get topical fluoride effect on the enamel if you ingested it systematically)

**Slide #14**

50:50 distribution shifts in favour of retention in calcified tissue in young children, why?

Because growth is happening in young children, so blood supply will be high in the hard tissues 🡪 the surface area of interaction of plasma with the hard tissue will be bigger🡪 more fluoride retention

**Slide #15**

**Fluoride Toxicity is either:**

1. Acute : large amount in small period of time
2. Chronic: small amounts for a longer time

**Slide #16**

**Acute toxicity**

* Inducing efflux of potassium (cation) from RBCs in order to balance the negative charges of F (anion) that are increasing in plasma

**Slide #17**

In low dose 🡪 the signs and symptoms will be due to the production of HF (hydrofluoric acid) which is highly corrosive

They will develop in 30-60 mins

MFP (one of fluoride compounds) might be less of an irritant than NaF because it is bound unlike NaF which is free … still a theory

**Slide #18**

In high dose 🡪 the signs and symptoms will be due to hypocalcemia and hyperkalemia in addition to the production of HF

**Slide #19**

Those signs and symptoms develop if the dose was higher 🡪 shock will happen

**Slide #21**

Probable Toxic Dose (PTD); which is 5mg/kg for F; is only for acute toxicity because a much lower dose can cause chronic toxicity like fluorosis if ingested for long period of time.

**Slide #23**

*There will be calculation Qs in the exam*

* To calculate the total ingested fluoride; first you have to convert it to the unit “mg/mL”

If given in ppm 🡪 divide by 1000

If given in % 🡪 multiply by 10

* Then you have to find F content by multiplying by compound molecular weight conversion ratio

If it was NaF 🡪 multiply by 0.5

If it was SnF 🡪 multiply by 0.25

If it was NaMFP 🡪 multiply by 0.125

If it was APF 🡪 you don’t multiply bcuz the concentration listed is actual concentration of F

* Then you multiply by the amount of solution 🡪 the total amount of fluoride ingested in “mg F”
* If you want calculate the dose ingested per kg to know if it is toxic or not 🡪 divide by the weight in “mg/kg”

**Slide #25**

**Management :**

We calculate the amount of fluoride that has been ingested by the patient ,but the doctor doesn’t agree with this because ( ممكن تكون الحسبة غلط او الاهل لم يعطو معلومات صحيحة )

SO YOU TREAT EACH CASE AS A SEPARATE CASE

* The aims are to:
* Reduce the amount of F available for absorption in the GI tract.

. Admit to hospital to remove F from body fluids and

. support vital signs

**Slide # 26**

1. Reduce the amount of F available in the GI tract.

How ?

Induce vomiting by using something called (Ipecac syrup)

* ), providing no risk of aspiration.
* RISK OF ASPIRATION IN PATIENT WHO HAS GAG REFLEX
1. Reduce bioavailability of F ( GIVE 1% calcium chloride or calcium gluconate).
2. If not available, give as much milk as can be ingested.

Because milk contain calcium so it reduce the bioavailibilty of floride

If we have symptom’s of hypocalcemia or hypercalemia we admittion the patient to the hospital

What they do in hospital ??

1-They clear the floride from GI tract by using a stomach wash or using lime water !! (have calcium )

2-The second thing they do iv fluid replacement :

* Calcium gluconate to maintain blood calcium levels.
* Sodium bicarbonate to maintain urine flow rate(so more calcium execrete ) and elevate urinary pH.
	+ - 3-monitoring and supportive therapies until the vital signs and serum chemistry are within normal ranges.

**Slide # 28**

**How to prevent floride toxicity**

We give them advices

Precautions at home:

* F mouthrinses and tablets should be in child-proof containers.
* Parents should keep these products out of reach of young children
* Parents should supervise their children when brushing or rinsing.

(mouth rinse usually for patient 7 year or more )

* Pea-sized ( > 3 years -3-6 years )or smear-sized(<3 years ) amounts of toothpaste need to be used in young children

**Slide #29**

**Precautions in clinic:**

We follow the guide line and instruction for every product that we use )

* Use the recommended dose and procedure for every topical product (gel, foam, varnish).
* Avoid gel in young children or those who are at risk to swallow (favour varnish).
* Don’t combine methods of application at once.
* Keep containers of topical F out of the reach of patients.

(لا تترك ال FLORIDE VARNISH

مفتوح في العيادة و تروح تجيب غراض من برا العيادة )

* Never leave the patient unattended during F application.

**SLIDE # 31**

**Chronic fluoride toxicity:**

* Induced by a low dose of F for a long time (can be much lower that PTD).

( PTD = 5 ml /kg )

* Most fluoride absorbed into hard tissues, leading to:
* Dental fluorosis
* Skeletal fluorosis

**Slide #32**

**Dental Fluorosis :**

* Occurs as a result of excess F ingestion during tooth formation.
* Impacted by the amount and duration of F ingestion.
* Enamel might have white opaque appearance due to hypomineralized subsurface. (not surface )
* Pitting and loss of enamel surface might occur in more severe cases , leading to secondary staining.( brown discoloration )

**Slide #33**

Floride is impact in enamel matrix by two mechanism

1. Impacts on enamel matrix mineralization:
* Interacts with nucleating sites in the enamel matrix disrupting crystal growth in all stages of enamel formation.
* Fluoroapatite binds more tightly to enamel proteins than hydroxyapatite , leading to decreased matrix proteinase activity and increased retention of amelogenin proteins in maturation stage.

2-Impact on ameloblast function:

* Enamel development can be divided into 4 major stages:
* Pre-secretory.
* Secretory.
* Transitional.
* Maturation stages.

**Slide #35**

**Mechanism of dental fluorosis:**

* **Pre-secretory. Chronic exposure to F:**
* Does not affect tooth morphogenesis.
* The size and form of the teeth is not changed**.**
* **Secretory. Chronic exposure to F:**
* Disrupts the vesicular transport in ameloblasts.
* Increases intracellular degradation of protein matrix.
* Might lead to reduced thickness of enamel

**Slide #36**

* **Transitional stage. Chronic exposure to F:**
* Induces ameloblasts to detach occasionally from the surface and form subameloblastic cysts.
* Gives rise to shallower occlusal pits.
* Leads to formation of accentuated perikymata (grooves).( groove in enamel we can see it when we dry the tooth , )

**Slide #37**

* **Maturation stage. Chronic exposure to F: most dangerous**
* Causes abnormal modulation cycles and reduces their number in a dose-dependent manner.
* Delays final mineralization of the enamel matrix, contributing to subsurface hypomineralization**.**

**Slide #38;**

**Factors influencing fluorosis:**

* Amount and duration of F ingestion.
* Timing of fluoride exposure in relation to tooth development.

If we apply fluoride after this stage there is no fluorosis

* **Metabolic factors:**
* Rate of skeletal growth.
* Periods of bone remodelling.

Nutrition

**Slide #39**

**Amount and duration of F ingestion:**

* Risk increases with fluoride dose (ingestions of fluoride from multiples sources, including F supplements).
* Longer duration of exposure before maturation stage increases severity of fluorosis.

**Slide #40**

**Timing of exposure: very important ,**

* Exposure during maturation is most important factor.
* Lower risk with F exposure only during the secretory stage (< 15 months of age).(usually for permanent teet )

We concern about permanent anterior teeth , if happen fluorosis on posterior teeth is not much concern (because the concern is mostly esthetic )

If patient take fluoride from (0-15 ) month then stop it ,they have lower risk than patient continuous take of floride .

* Highest risk occurs with exposure during both secretion and maturation stages.

(the most dangerous stage is maturation ,but the most dangerous state that might happened is during all stages .)

**Slide #41**

* Highest risk of fluorosis is when child is ≤ 3 years old.(while central and lateral are still calcifying )
* (Ishi and Suckling, 1986):
* Children who had high F water (7.8 mg/L) and then changed to low F water (0.2 mg/L).
* Change at around 35 – 42 months (tooth in maturation stage): had severe fluorosis of upper central incisor.

Change at 11 to 33 months (secretory stage): had very mild or no fluorosis

**Slide # 42;**

**Metabolic factors:**

* **Rate of skeletal growth:**
* Large surface area and rich blood supply means that F is rapidly absorbed from the plasma by the bones.

(fluoride that present In plasma rather than it goes to enamel,It goes to skeletal bone )

* Removal of F from plasma initially reduces the amount of F available to the developing enamel.
* However, F accumulated in bones forms a large reservoir of F to be released locally to the toothgerms**.**

**Slide #43**

* **Renal activity:**
* Renal insufficiency can result in F retention and result in fluorosis.> increase the risk of fluorosis
* **Nutrition:**
* Ca inhibits F absorption> reduce the risk of fluorosis

**Slide #44**

**Histological appearance:**

* Enamel subsurface porosity.
* Hyper and hypomineralized bands within enamel.
* Increased severity porosity extends to EDJ and enamel surface can break – pitting and secondary discolouration.
* Severity of fluorosis is directly related to amount of F in enamel and subsurface porosity.



**Picture D is the most severe .**

**Slide #45**

**Clinical appearance:**

* Bilateral opaque white areas in the enamel

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**Slide #46**

* With increasing levels of fluoride – enamel becomes striated, mottled and/or pitted.
* Severe cases – opaque areas become stained yellow to dark brown.

**Slide #47**

**The doctor said read the box by your self .**

**Why we concern about classification of the case ?**

**1 –to know what should I do**

1. **Report between the dentist**

**Slide 48:**

Skeletal Fluorosis:

Skeletal fluorosis is an excessive accumulation of [fluoride](http://en.wikipedia.org/wiki/Fluoride) in [bone](http://en.wikipedia.org/wiki/Bone) associated with increased bone [density](http://en.wikipedia.org/wiki/Density) and outgrowths ([exostoses](http://en.wikipedia.org/wiki/Exostoses)).

* Associated with high fluoride intake (8-10 ppm or more in the drinking water) for approximately 10 years or more.

So the dose that require to reach the skeletal fluorosis is high

**Slide 49:**

* Endemic problem India, Pakistan, China (High F in water and hot climates).
* The total quantity of F ingested is the single most important factor.
* The severity of symptoms correlates directly with the level and duration of F exposure**.**

**Slide 50:**

**The mechanism of Skeletal Fluorosis:**

* F stimulates osteoblasts (abnormal).
* F increases the stability of the crystal lattice in bone, but makes bone more brittle.
* Bone changes include osteosclerosis, osteomalacia(they simulate osteoarthritis>misdiagnosis), osteoporosis and exostosis formation.
* Secondary hyperparathyroidism **in a proportion of patients.**

**Slide 51:**

**Signs and Symptoms:**

* Joint pain and stiffness (arthritis-like)
* Osteosclerosis.
* Calcification of ligaments.
* Crippling deformities (spine and major joints)
* Muscle wasting.
* Neurological defects/compression of spinal cord.(vertebrae are getting thicker)
* Clinical symptoms mimic arthritis, could be easily misdiagnosed.

**Slide 52:**

Prevention of skeletal fluorosis:

* Education of population
* Provide safe drinking water

**Slide 53:**

**Other suspected effects of F:**

* Some peoplesay that F cause cancer but No detectable risks of cancer associated with the consumption of optimally F water.
* No indication that organ systems are affected by chronic, low level fluoride exposure**.**
* Fluoride exposure is not associated with birth defects, including Down’s syndrome.
* The beneficial or harmful effect of fluoride on osteoporosis & bone fracture is inconclusive.(dubious!!!)