ANTICARIES AGENTS

Dental caries is a pathologic process of microbial etiology that results in localized destruction of tooth tissues.

The process of tooth destruction involves dissolution of the mineral phase, consisting primarily of hydroxyapatite crystals by organic acids produced by bacterial fermentation.

DENTAL CARIES

Is a multifactorial disease including:
- The host (particularly the saliva and teeth) – susceptible host
- The microflora
- Substrate, the diet
CARIES PREVENTION
• Is based on attempts to:
  – Increase the resistance of the host (fluoride therapy, occlusal sealants, immunization)
  – Lower the number of cariogenic microorganisms in contact with tooth (plaque control and antiplaque agents)
  – Modify the substrate by selecting noncariogenic foods
  – Reduce the time that the microflora is provided with substrate by limiting the frequency of intake of fermentable substrate

MECHANISM OF FLUORIDE ACTION
• Reduction in solubility of calcium hydroxyapatite
• Balance of rates of demineralization (dissolution of enamel) and remineralization (deposition of enamel)
• Antimicrobial effects of F in terms of affecting metabolism and as a killing agent

FLUORIDATION
Hydroxyapatite + fluor• fluorapatite

\[ \text{Hydroxyapatite} + \ \text{fluor} \rightarrow \text{Fluorapatite} \]

\[ [\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2] + \text{F}^- \rightarrow [\text{Ca}_{10}(\text{PO}_4)_6(\text{F})_2] \]
FLUORIDE THERAPY

• Systemic fluoride
• Topical fluoride

RANGE OF THERAPEUTIC FLUORIDE CONCENTRATIONS IN TOPICAL AGENTS USED TO PREVENT CARIES

<table>
<thead>
<tr>
<th>Method</th>
<th>Fluoride concentration (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dentifrices, adult</td>
<td>1000-1500</td>
</tr>
<tr>
<td>Dentifrices, children</td>
<td>250-500</td>
</tr>
<tr>
<td>Mouth rinse, daily</td>
<td>230</td>
</tr>
<tr>
<td>Self-applied gels or rinses, prescription</td>
<td>5000</td>
</tr>
</tbody>
</table>

Concentration in %

– % - 1 part in 100 parts
– ppm – 1 part in 1 mln parts
  • 0.1-0.15% it is ???????
  • How much is it ppm?
  • 5000 ppm
  • How much is it %?
FLUORIDE TOXICOLOGY

- 5-10g of sodium fluoride is a certain fatal dosage for an adult, and lesser amounts are lethal to children

PATIENTS WITH SEVERE FLUORIDE POISONING

- Nausea, vomiting, diarrhea
- Progressive hypotension
- Pronounced hypocalcemia and hypomagnesemia and acidosis
- Cardiac irregularities, including ventricular tachycardia

THE TREATMENT IS BASED ON EARLY INITIATION OF THE FOLLOWING PROCEDURES:

- Steps to prevent further systemic absorption of fluoride (e.g., administration of emetics to induce vomiting, gastric lavage with fluid containing Ca)
- Cardiopulmonary monitoring and preparation for endotracheal intubation and direct-current cardioversion
THE TREATMENT IS BASED ON EARLY INITIATION OF THE FOLLOWING PROCEDURES:

• Prompt and frequent blood analyses, especially for plasma Ca, Mg, K and pH
• Intravenous infusion of salt solutions as needed to correct acid-base imbalances and restore plasma electrolytes to the normal range
• Alkaline diuresis to enhance fluoride excretion
• Appropriate treatment of severe cardiac arrhythmias

CHRONIC TOXICITY – DENTAL FLUOROSIS

• Is hypomineralization of enamel
• Fluorosis may range in severity from a few white flecks to extensive brown staining and pitting

CARIES PREVENTION

• Is based on attempts to:
  – Increase the resistance of the host (fluoride therapy, occlusal sealants, immunization)
  – Lower the number of cariogenic microorganisms in contact with tooth (plaque control and antiplaque agents)
  – Modify the substrate by selecting noncariogenic foods
  – Reduce the time that the microflora is provided with substrate by limiting the frequency of intake of fermentable substrate
ANTIPLAQUE AGENTS

1. Agents acting against the microflora per se
2. Agents interfering with bacterial attachment by attacking plaque matrix components or altering the tooth surface
3. Mechanical removal of plaque

PROPERTIES OF AN IDEAL ANTIPLAQUE AGENT

- Safety (nontoxic, nonallergenic, nonirritating)
- Efficacy
- Specificity (affects only the pathogenic flora)
- Substantivity (binds to and slowly releases from the tooth surface)
- No induced drug resistance
- Acceptable taste
- Low cost

MICROORGANISMS ISOLATED FROM PULPAL/PERIAPICAL INFECTIONS

- Anaerobic
  - Peptostreptococcus micros, Actinomyces
  - Bifidobacterium, Eubacterium, Clostridia, Propionibacterium
  - Bacteroides, Fusobacteria, Porphyromonas, Prevotella
- Treponemes
  - Treponema denticola, T. macrodentium, T. oralis
- Aerobic
  - Staphylococci, Lactobacillus, Corynebacterium, Eikenella corrodens
ANTIMICROBIAL AGENTS TESTED FOR PLAQUE PREVENTION OR REDUCTION

• Fluorides
• Oxygenating agents
• Bis-biguanides
• Phenolic compounds
• Quaternary ammonium compounds

OXYGENATING AGENTS
HYDROGEN PEROXIDE

• Mouthrinses with hydrogen peroxide reduces plaque formation and gingivitis and arrest ulcerative gingivitis.
• 0,5-1,5% hydrogen peroxide
• 3% hydrogen peroxide mouthrinse – oral ulceration
• 3% - wound cleaning
• 30% - tooth bleaching

BIS-BIGUANIDES
CHLORHEXIDINE

• The efficacy of chlorhexidine mouth rinse as an antiplaque/antigingivitis agent is dose dependent in the range of 0,03% to 0,2%.
• Has fungicidal activity and bactericidal activity (gram positive and gram-negative)
## SIDE EFFECTS OF CHLORHEXIDINE

- Yellow-brown stains on the teeth, anterior restorations and the dorsum of the tongue
- Tends to promote supragingival calculus formation
- Disturbed taste sensation

## CLINICAL INDICATIONS FOR CHLORHEXIDINE

### Short term applications
- Healing phase in periodontal surgery
- Healing phase in oral surgery
- Presurgical use to reduce bacteremia
- Therapy for aphthous ulcerations
- Therapy for denture stomatitis
- Therapy for acute necrotizing ulcerative gingivitis

### Intermittent short-term application (3- to 4-month cycle)
- Repeated denture stomatitis
- Adjunct to periodontal maintenance care
- High caries activity
- Dental implants
CLINICAL INDICATIONS FOR CHLORHEXIDINE

• Long-term application
  – Medicaly compromised patient
  – Agranulocytosis, leukemia, hemophilia, thrombocytopenia, kidney disease, allergies
  – bone marrow transplant, AIDS

• Triclosan
• Thymol 1%
• Eugenol 0,5-1%
• Menthol 0,5-1,5%

• Triclosan
  – Inhibit growth of Gram negative bacteria
  – Toothpaste 0,2-0,3%
  – Mouth rinse 0,03-0,045%
QUATERNARY AMMONIUM COMPOUNDS
CETYLPYRIDINUM CHLORIDE
• 0.05-0.1%
• Side effects: oral ulceration, unpleasant taste

Sanguinaria canadiensis)

ANTIFUNGAL AGENTS
NYSTATIN

- Polyene antibiotic
- Binding to ergosterol of fungal membrane
- Active against: *Candida, Histoplasma, Cryptococcus, Blastomyces*
- Is not absorbed from the skin, mucous membranes, GIS
NYSTATIN

- Is used to treat candidal infections of the mucosa, skin, intestinal tract and vagina
  - Is used prophylactically in immunocompromised patients
  - For the treatment of oral candidiasis, 2-3 ml of suspension containing 100,000 units/ml of nystatin are placed in each side of the mouth, swished, and held for at least 5 minutes before swallowing. This regimen is repeated every 6 hours for at least 10 days.

KETOCONAZOLE

- Synthetic compound, imidazole antifungal
- *Is active against Candida, Histoplasma, Blastomyces, Coccidioides*
- Inhibits an enzyme involved in the synthesis of ergosterol

KETOCONAZOLE

- Side effects:
  - Gastrointestinal disturbances
  - Nausea, anorexia, vomiting
  - Endocrine effects: gynecomastia, decrease libido, impotence and menstrual irregularities
  - Hepatic toxicity
  - Inhibitor for cytochrom P450
FLUCONAZOLE

- Lack of the endocrine side effects of ketoconazole
- Is administered orally or intravenously
- Very well penetrate into CSF
- Is approved for the treatment of systemic candidal infections and is less toxic than amphotericin B

FLUCONAZOLE

- Is active in suppressive therapy and primary treatment of cryptococcal meningitis, which may occur in patients with AIDS

FLUCONAZOLE

- Is drug of choice in the treatment of oropharyngeal, esophageal and vulvovaginal candidiasis in immunocompromised adults
- May be used for primary prophylaxis and for long-term suppressive or chronic maintenance therapy to prevent recurrence and relapse of serious fungal infections in patients considered at high risk for developing such infections (AIDS). These infections include blastomycosis, coccidioidomycosis, cryptococcosis, histoplasmosis and mucocutaneous candidiasis.
OTHER TOPICAL AGENTS

• Miconazole
• Clotrimazole
• Butoconazole
• Terconazole

ANTIVIRAL AGENTS

VIRAL LIFE CYCLES. THE LIFE CYCLE OF VIRUSES MAY BE DIVIDED INTO THE FOLLOWING STAGES:

• Attachment to a host cell
• Penetration. Release of viral genes and possibly enzymes into the host cell
• Replication of viral components using host-cell machinery
• Assembly of viral components into complete viral particles
• Release of viral particles to infect new host cell
EXAMPLES OF PATHOGENIC VIRUSES

• DNA viruses
• RNA viruses

DNA VIRUSES

• Poxviruses  • smallpox
• Herpesviruses  • chickenpox, shingles, cold sores, glandular fever
• Adenoviruses  • sore throat, conjunctivitis
• Papillomaviruses  • warts

RNA VIRUSES

• Orthomyxoviruses  • influenza
• Paramyxoviruses  • measles, mumps
• Rubella virus  • German measles
• Rhabdoviruses  • rabies
• Picornaviruses  • colds, meningitis, poliomyelitis
• Retroviruses  • AIDS, T-cell leukaemia
INHIBITORS OF VIRAL UNCOATING

- Amantadine
- Rimantadine

AMANTADINE, RIMANTADINE

- Antiviral spectrum: Influenza A virus
- Clinical uses: prophylaxis of influenza A infection
- Pharmacokinetics
- SE: nervousness, drowsiness, difficulty in concentration, insomnia, depression, seizures.

NEURAMINIDASE INHIBITORS

- Oseltamivir
- Zanamivir

Get the flu, take Tamiflu
INHIBITORS OF TRANSCRIPTION OF THE VIRAL GENOM
DNA POLYMERASE INHIBITORS
• Acyclovir and valacyclovir
• Foscarnet
• Ganciclovir and valganciclovir
• Famciclovir
• Cidofovir
• Penciclovir

HSV-1, HSV-2 AND VZV
• Acyclovir (5x) and valacyclovir (3x)
• Foscarnet (topical, i.v. intravitral)
  – Acyclovir-resistant herpes simplex
  – Acyclovir-resistant varicella-zoster

ACYCLOVIR
• A.S.: Herpes simplex virus (HSV) and Varicella-zoster virus (VZV) and Epstein-Barr virus
• C.U.: treatment of primary and recurrent herpes genitalis, herpes encephalitis, mucocutaneous herpetic, infections in immunocompromised patients, neonatal herpetic infection, and VZV infection, CMV (cytomegalovirus) prophylaxis
• S.E.: headache, arthralgias, vertigo and nephrotoxicity and encephalopathy
ACYCLOVIR

- Pharmacokinetics: i.v., oral, topical
- 4-5 x per day
- Valacyclovir – 3 x per day

ACYCLOVIR

- Is used in ointment for the treatment of primary herpes genitalis and, in immunocompromised patients, for the treatment of initial and recurrent mucocutaneous herpetic lesion that are not life threatening
- Is used as topical for symptomatic relief of recurrent herpes labialis in patients with normal immune system

ACYCLOVIR

- Oral acyclovir is used for the prevention of recurrent herpes genitalis and treatment of primary and recurrent herpes genitalis and VZV infections
- Parenteral acyclovir is effective in the treatment of chronic and recurrent mucocutaneous HSV infections in immunocompromised patients, VZV infections and herpes encephalitis
ACYCLOVIR
- 5-10mg/kg of body weight is administered intravenously for a 1-hour period and repeated every 8 hours for 5 to 10 days
- 200 to 400 mg orally is given two to five times per day

ANTIVIRAL THERAPY IN THE ORAL CAVITY
- HSV causes:
  - Oral mucosal lesions
  - Herpetic gingivostomatitis
  - Recurrent intraoral herpes simplex
  - Herpes labialis

CYTOMEGALOVIRUS (CMV)
- Ganciclovir (i.v.) and valganciclovir (p.o.)
- Foscarnet
ANTIRETROVIRAL AGENTS

HIV INFECTION
- NRTIs – nucleoside and nucleotide reverse transcriptase inhibitors
- NNRTIs - nonnucleoside reverse transcriptase inhibitors
- HIV protease inhibitors
- Entry inhibitors (enfuvirtide, maraviroc)
- Integrase inhibitor (raltegravir)

REVERSE TRANSCRIPTASE INHIBITORS
- A.S.: HIV (human immunodeficiency virus)
- M.A.: inhibition of viral DNA synthesis
- C.U.: treatment of HIV infection and AIDS
- Zidovudine
- Didanosine
- Zalcitabine
- Stavudine
PROTEASE INHIBITORS

- A.S.: HIV
- M.A.: Blockade of HIV protease
- C.U.: treatment of HIV infection and AIDS
  - Saquinavir
  - Indinavir
  - Ritonavir

HEPATIC VIRAL INFECTIONS

- Hepatitis viruses: A, B, C, D and E
- Hepatitis B and C are the most common and they cause:
  - Chronic hepatitis
  - Cirrhosis
  - Hepatocellular carcinoma

- Interferon-
- Lamivudine
- Adefovir
- Entecavir
- Telbivudine
- Ribavirin (RSV and hepatitis C)
HERBAL INGREDIENTS IN ORAL HEALTH CARE PRODUCTS

- Aloe vera – mouth rinse, toothpaste – antiinflammatory, antiseptic
- Eucalyptus – mouth rinse, toothpaste – antiseptic
- Green tea – toothpaste – antiviral, cariostatic, antineoplastic, used for gingivitis/periodontitis

HERBAL INGREDIENTS IN ORAL HEALTH CARE PRODUCTS

- Peppermint (Mentha piperita) – mouth rinse, oral gel, dental gum – antibacterial, breath freshener, used for gingivitis/periodontitis
- Thyme (Thymus vulgaris) – mouth rinse – antiseptic, breath freshener

XEROSTOMIA

- Atropine and atropine like drugs
  - Antihistamines
  - Tricyclic antidepressants
MUSCARINIC AGONISTS

- Xerostomia - in patients with Sjögren’s syndrome, those who have had head and neck radiation, and those undergoing treatment involving drugs that produce dry mouth.
  - Pilocapine 5-10mg 3 times daily before each meal
  - Cevimeline (selective M1 and M3 agonist) 30 mg 3 times daily

ATROPINE. IMPLICATIONS FOR DENTISTRY

- Xerostomia

- Decrease the flow of saliva during dental procedures. Small doses given orally or parenterally 30 minutes to 2 hours before the procedure are effective

- Tetracyklin – brown discoloration of teeth and hypoplasia of teeth
- Anti-plaque agents – Chlorheksydyna
- Anticancer drugs –
- Glucocorticoids –inhaled, topical aerosol
- Antibiotics –broad spectrum - disbacteriosis