Remineralisation is the natural repair process for caries lesions. Remineralisation with fluorides results in incorporation of minerals into new crystal surfaces which make them more resistant to acid attacks. It requires no growth factors or soft-tissue biological processes. It had simple inorganic chemistry.¹

**Prerequisites for Natural Remineralisation:**
1. Calcium and Phosphate in saliva
2. Blood rich in minerals, trace elements and vitamins
3. Dentinal fluid
4. Salivary pH
5. Salivary flow
6. Proper mastication
7. Salivary proteins²

**Balance between Protective and Pathological Factors:**
- Whether a lesion will progress, stay same or reverse is determined by the balance between protective factors and pathological factors (Figure 1). If the pathological factors are dominating over the protective factors, it results in dental caries.
- If the protective factors are dominating then it will result in caries arrest.

**Figure 1: The caries balance**
Pathological factors:
- Cariogenic bacteria.
- Salivary dysfunction.
- Frequency of ingestion of fermentable carbohydrates.

Protective factors:
- These include components in saliva such as calcium, phosphate, fluoride.
- Protective proteins that form the pellicle, maintains the supersaturation of minerals in saliva and plaque.
- Saliva contains natural antibacterial substances as protective factors or these can be supplied extrinsically from chlorhexidine, salivary fluoride, fluoride from external sources and chewing gum that stimulate salivary function.

Remineralisation: what are we trying to achieve?
Remineralisation might simply be described as the delivery of calcium and phosphate, from outside the tooth, into the enamel lesion, effecting deposition of mineral onto the demineralised enamel within and it becomes more resistant to subsequent acidic challenges than the original mineral. Analysis of the available clinical (Bjarnason and Finnbogason, 1991) and mechanistic data suggests that topically applied fluoride is more effective at preventing the establishment of early lesions (3).

Various remineralising agents are discussed as follows.

1. FLOURIDE:
It is considered as gold standard to prevent dental caries. It can be supplied in various forms such as topical and systemic fluorides.

Flouride delivery and application:

<table>
<thead>
<tr>
<th>Systemic</th>
<th>Through water supplies or dietary supplementation or food</th>
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<tr>
<td>Topical</td>
<td>Through dentifrices, rinses, or gels</td>
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<tr>
<td>Topical</td>
<td>Dental products applied in dental offices</td>
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MECHANISM OF ACTION
Fluoride reduces decay via three modes:
1. During tooth development: fluoride gets incorporated and form fluorohydroxyapatite, which is more resistant to the acid attacks of the decay process.
2. Topical benefit of Fluoride: It combines the tooth surface make it more resistant to dental decay. It reduces the acid production by interfering in bacterial metabolism.
3. Inhibition of glycolysis in bacteria

DELIVERY METHODS AND BENEFITS
1. Systemic Water Fluoridation
2. Supplements
3. Salt and Milk
4. Topical

Home topical Applications:

Dentifrices:
Various dentifrices such as sodium fluoride (NaF), stannous fluoride (SnF), or sodium monofluorophosphate (MFP) are available, which provides 1000-1500 ppm of fluoride. These should be used by adults and children over 2 years of age.

Mouth rinses:
Sodium-based mouth rinses are 0.02% (NaF), 0.044% (APF) or 0.05% (NaF), which is the most common. The time of rinsing is one minute.

Professional Topical Application:
These are more beneficial for moderate to high caries risk individuals. But not to be used in low risk patients according to ADA council of scientific affairs.

Varnishes:
These contain NaF5% with 22,600 ppm or difluorosilane with 1,000 ppm. It has advantage of ease of application, taste acceptance, ability to set on contact with moisture, and the small amount required for use. It is indicated in individuals with moderate to high risk, patients with xerostomia and other dietary factors.

Gels and Foams:
In-office modalities of gels are 1.23% APF (the most widely used) and 2% NaF formulations. The APF gel is available in 12,300-12,500 ppm of fluoride concentration with a pH of 3.5. It is contraindicated in composite or porcelain restorations because it causes dissolution of filler particles.
- Altenburger MJ et al. in 2009 studied the in situ fluoride retention and remineralisation of incipient carious lesions with different concentrations of fluoride and concluded that remineralisation is more pronounced after application of a higher concentration (1%) of fluoride-containing fluid compared with the 0.5% fluoride-containing fluid.  

**Reasons to seek alternatives to fluorides:**
1. Fluoride is less effective on pit and fissure caries as compared to smooth surface caries.
2. A high fluoride concentration may result in fluorosis.

**Non-fluoride remineralising agents:**

2. **Bioactive materials for enamel mineralisation:**
   A bioactive material stimulates a beneficial response from the body, particularly bonding to host bone tissue and to the formation of a calcium phosphate layer on a material surface.
   - **Bioglass:**
     Hench and Anderson discovered the bioglass in 1969. It is a calcium sodium phosphosilicate material. It was developed as an implant material to regenerate bone, but now used in oral care products (NovaMin®, NovaMin Technology Inc.).
     **Composition and mechanism of action:** It contains 45 wt% SiO2, 24.5 wt% Na2O and Ca, O and 6-wt% P2O5. It is activated with saliva or water and on coming in contact it releases sodium, phosphorous and calcium ions into the saliva which are available for remineralization of the tooth surface and form hydroxycarbonate apatite (HCA).

**Studies:**
- Sai Sathya Narayana et al. in 2014
  Remineralisation efficiency of bioactive glass on artificially induced carious lesion – in vitro and concluded that bioactive glass is an effective remineralising agent.
- NovaMin®: It is the trade name for a calcium sodium phosphosilicate bioactive glass, which is originally developed for the treatment of hypersensitivity by the physical occlusion of dentinal tubules.  

3. **Calcium silicate:**
   Studies have demonstrated that calcium silicate materials, such as calcium silicate glass, wollastonite (-CaSiO3), pseudowollastonite (-CaSiO3), Ca2SiO4 and Ca3SiO5, can induce the rapid formation of HAP in Simulated Body Fluid (SBF) and chemically integrate into the structure of living bone tissue after implantation.
   - **Dong et al.** studied the dentine tubule occluding ability of Ca3SiO5, the application of Ca3SiO5 onto the surface of a dentine specimen block the dentine tubules by penetrating into it. The deposited Ca3SiO5 particles were shown to transform into HAP after 1 week incubation in artificial saliva and formed a dense surface layer on the dentine with a thickness of about 3 microns. The tooth enamel remineralisation efficacy of calcium silicate materials has also been studied.
   - **Eunice Kuhn in 2014** studied the role of Glass ionomer Cement on the Remineralisation of Infected Dentin and concluded that the dentin exhibited a better organization, fewer bacteria, and signs of remineralisation after 60-days and later after 10 to 15 months, which indicates the remineralisation of carious dentin.

4. **Casein phosphopeptide amorphous calcium phosphate (CPP-ACP):**
   CPP contains the active sequence –Ser(P)-Ser(P)-Ser(P)-GluGlu- . It stabilizes calcium and phosphate ions in metastable solution as nanoclusters (Cochrane et al., 2008).
   **Mechanism of action:** The CPP-ACP technology increases the concentration of calcium and phosphate ions in plaque, which promotes the remineralisation of enamel subsurface lesions. These results demonstrating CPP-ACP bound to Streptococcus mutans and model plaque produced a reservoir of bioavailable calcium.
Reynolds in 2008 carried out a randomized controlled mouthrinse trial 2.0% CPP-ACP along with fluoride increases fluoride ion content in plaque to 33.0 ± 17.6 nmol F/mg, while NaF attains it to 14.4 ± 6.7 nmol F/mg only.

- Chunhua Zhou et al. in 2014 evaluated the remineralisation effects of casein phosphopeptide amorphous calcium phosphate early enamel lesions of primary teeth and concluded that CPP-ACP is more advantageous than NaF for remineralisation.

- Nikita Aggrawal in 2014 evaluated the remineralisation potential of casein phosphopeptide amorphous calcium phosphate (CPP-ACP) paste, 1.23% acidulated phosphate fluoride (APF) gel and iron supplement on dental erosion by soft drinks in human primary and permanent enamel using atomic force microscopy (AFM) and concluded that the application of CPP-ACP paste is effective on preventing dental erosion from soft drinks.

5. Xylitol:
Xylitol is obtained from birch tree. It consists of five carbon structure. It has demonstrated effectiveness for preventing dental caries. It also causes increase in oral pH, which causes the remineralisation of tooth and prevents dental caries.

- Remineralisation of Caries Lesions During a Two-Year Xylitol Feeding Trial and in a One-Year Chewing Gum Study: It concluded that xylitol diet was associated with the reversal of the caries process. Similar observations were also made in a simultaneously conducted one-year chewing gum study.

6. Tricalcium phosphate (TCP):
Sara Tavassoli-Hojjati 2014 investigated the mechanical properties (flexural strength, micro-shear bond strength) and remineralising potential of fissure sealants by adding various concentrations of β-tricalcium phosphate nanoparticles and concluded that the addition of 1-5 wt.% TCP nanoparticles to the fissure sealants significantly increased the remineralisation potential without affecting the mechanical properties.

7. Dicalcium phosphate dihydrate (DCPD):
DCPD abrasive is unique for fluoride stability. It is suggested that DCPD slurries were more effective than silica in preventing plaque pH drop when compared to silica. Toothpaste containing monofluorophosphate (MFP) and DCPD was significantly more effective and superior than MFP/silica toothpaste. The MFP/DCPD produces more active calcium and a higher degree of saturation with respect to enamel for an extended period of time.

8. Calcium phosphate nano-composites:
It has remineralising property as it releases calcium and phosphate ions.

- M.D. Weir in 2012 studied the remineralisation of Demineralised Enamel via calcium Phosphate nanocomposite and concluded that a novel NACP nanocomposite was effective in remineralising enamel lesions in vitro. Its enamel remineralisation was 4-fold that of a fluoride-releasing composite control.

9. Grape seed extract:
Grape seed extract contains proanthocyanidin (PA), mainly composed of monomeric catechin and epicatechin, gallic acid and polymeric and oligomeric procyanidins. Proanthocyanidins increases collagen synthesis and accelerates the conversion of soluble collagen to insoluble collagen and strengthen the collagen-based tissues by increasing collagen crosslinks. Grape seed extract positively affects the remineralisation process of root caries. Since collagen can serve as a substrate for apatite formation.

- Mahkameh Mirkarimi in 2013 investigated the effect of grape seed
extract (GSE) on artificial enamel caries in primary human teeth and concluded that GSE enhanced the remineralisation process of artificial enamel lesions of primary teeth, and thus, might be considered an effective natural agent in non-invasive dentistry.13

10. Nano hydroxyapatite:
The nanoparticles of 20-nm size act as biomimetic for the building blocks of natural enamel and as anticaries agent. These crystals interact with bacterial adhesins, reduces there bacterial adherence, and decrease biofilm formation.

• J. Shanti swarup et al. in 2012 evaluated the effects of synthetically processed hydroxyapatite particles in remineralisation of the early enamel lesions in comparison with 2% sodium fluoride and concluded that the use of biomimetic nanohydroxyapatite as a remineralising agent holds promise as a new synthetic enamel biocompatible material to repair early carious lesions.14

11. Remin Pro® (VOCO GmbH):
It is composed of hydroxyapatite, xylitol and fluoride. It has applications in management of dentinal hypersensitivity in promoting remineralisation of enamel subsurface lesions. Xylitol has good antimicrobial property and Hydroapatite help in sealing of dentinal tubules.

12. Enamelon:
Enamelon consists of unstabilized calcium and phosphate salts with sodium fluoride. It is a Liquid Calcium(TM) Formula, which delivers fluoride along with soluble calcium and phosphate, the building blocks of enamel. Enamelon toothpaste is beneficial in the reduction of white spot lesions and the repair and remineralisation of tooth enamel compromised by acidic beverages.16

13. Vanish™ XT Extended Contact Varnish:
Vanish XT varnish is a site-specific highly durable coating that can remain on the tooth for six months or longer. The XT reflects “extended varnish”, having a long-term durability with fluoride release.

Liquid component: consists primarily of polyalkenoic acid, HEMA (2-hydroxethylmethacrylate), water and initiators (including camphorquinone) plus calcium glycerophosphate.

Paste: consists of HEMA, BIS-GMA, water, initiators and fluoroaluminosilicate glass (FAS glass).

Physical properties:
Vanish XT is varnish which stays on the tooth surface for 6 months without any effect from the toothbrushing.

18. Ozone therapy:
Ozone disrupt the cell walls of microorganisms within seconds leading to immediate functional cessation. It is a powerful oxidizing agent.

Working Principle of ozone:
• The HealOzone is a device that produces ozone from room air with the aid of an ozone generator.
• Choose an appropriate size of Delivery Cup on the basis of the size of the area to be treated, and place it on the treatment area (Figure 2).

• The HealOzone device is then activated, and an initiation vacuum pump established a seal around the surface, which prevented the leakage of ozone to the oral cavity.
• Ozone treatment is then applied for 40 seconds at a concentration of 2100 ppm at a flow rate of 615 mL/min.
• During the treatment, the ozone is sucked back through the waste filter and reconverted to oxygen.
Advantages of topical ozone therapy:
There is always a chance of development of resistance against antibiotic. The Ozone has ability to directly inactivate bacterial toxins, while antibiotics are not capable of this.

Recently a New technique is invented to remineralise the teeth: Electrically Accelerated and Enhanced Remineralisation (EAER):
The perception of the dental treatment as a Victorian setting where pain is a by-product of the experience frustrates Professor Nigel Pitts (Figure 3), a dentist who invented painless treatment of tooth decay. He created a system along with Dr Chris Longbottom through which the early to medium tooth decay can undergo self healing. This new technique is called Electrically Accelerated and Enhanced Remineralisation (EAER), which uses the current of low frequency.

Figure 3: Professor Nigel Pitts

STAGES
1. First is to devise a method that chemically cleans the inside three-dimensional surface of the lesion and produce a surface that is ready to remineralise.  
2. and Then iontophoresis was used in which the inside of the tooth is turned into the electrode, which drive minerals into the most damaged areas leading to rebuild of the tooth from inside. This process takes 15 minutes. It was done with “healing hand piece” which is the size of a highlighter pen. It can be carried out by a dentist or a hygienist, depending on the local regulations.17

CONCLUSION
Dental caries is an infectious disease that may result in an oral infection. The impact of a high rate of dental caries and its consequences as a public health problem was recognized in the 1940’s. As dental clinicians are primary providers of preventive services, they develop an array of types of preventive plans for patient. Earlier the treatment of caries was surgical but the philosophy of minimal intervention dentistry has now arisen is an attempt to combine all the present knowledge of prevention, remineralization. Various remineralising agents are put forward to strengthen the remineralising process along with newer techniques.

REFERENCES
