HAPPENINGS

A KUHS PUBLICATION ON RECENT ADVANCES

A SAMAGRAM INITIATIVE

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Message from Vice Chancellor

I am happy to note that the Fifth issue of ***'Happenings -A KUHS Publication on Recent Advances'*** *is being brought out. This initiative has caught the fancy of academicians of the affiliated institutions of KUHS in a significant way as evidenced by the responses. The initiative, meant for strengthening the scientific writing skills of the younger generation faculty of each stream of Health Sciences is expected to throw light in to what has happened in the past, and what is in store for us in the future. We have also included some invited articles from the Best Teacher Award winners of KUHS. It is hoped that this will definitely serve as an important outreach educational program of the University, and also that this publication will be well received as the previous issues.*

Prof. [Dr.] Mohanan Kunnummal

Vice Chancellor, KUHS

CONTENTS

Emerging and Re- emerging respiratory viral diseases.

Ms. Saranya V G*

Introduction

- Infectious disease remains as the major cause of human and animal morbidity and mortality leading to significant health care expenditure. Emerging infections that are newly occur in a population (not identified in human earlier) or exist in the past increasing in incidence and geographical changes. Acute respiratory viral diseases cause death of patient and hospitalization in developing countries every year. The emerging viruses that are emerged from wild life or re-emerged one that cause threats to global health. Most of the emerging viruses come from animals and are zoonotic diseases belonging to the families Orthomyxoviridae,Paramyxoviridae, Coronaviridae. Viral pathogens cause out breaks that may be epidemics or pandemics.

- Factors that cause emergence are dormance of pathogen after initial infection and it reappear as more virulent strains, urbanization, globalization, travels international commence, aging, climate changes, changes in the geographic distribution of pathogens, malnutrition, poverty etc.

- Mutation of the viruses produce new antigenic populations and produce high risk chimeric viruses.

Emerging respiratory viruses…

* Influenza virus: It cause both epidemic and pandemics. Most viruses belonging to Orthomyxoviridae, negative sense RNA virus seen as segments. A, B, C, D are the various types of Influenza viruses. These viruses have haemagglutinin (HA) and neuraminidase (NA) protein spikes. These viruses cause flu like illness initially but sometimes it produce pneumonia and other respiratory complications.These viruses are transmitted through inhalation (droplet nuclei, aerosols) and close contact with infected people.

i. H1N1: It belongs to typeA Influenza virus and have antigenic variations antigenic drift (minor change in HA and NA resulting in epidemics) and antigenic shift (significant change in the virus and produce new HA and NA resulting in pandemics.). The most fatal one was 'mother of the pandemic' (1918- Spanish flu where 50million people died).In1977 (H1N1) re- emerged and called it as Russian flu that affect young people and in 2009 (H1N1) reported as new pandemic (cases were reported from Maharashtra).

ii. H2N2: In 1957 new strain isolated from Southeast Asia and spread worldwide. It remain in wild and domestic birds. The emergence of H2N2 humans is significant threat because of absence of humoral immunity and it was the second pandemic of 20th century.

iii. Avian influenza: Humans are susceptible to A subtype of virus- AH5N1,AH7N9,AH7N9.This occur after exposure to infected birds.Sporadic outbreaks were occurred with this virus. Human to human transmission infection is lacking. These are the most dangerous emerging and re-emerging pathogen due to high risk of causing pandemics. Death cases reported with H5N1, H5N6, H7N9, H10N8 infections.H9N2 avian flu reported from India also. Recently (2021) a rare

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strain of avian flu H10N3 virus isolated from China's Eastern province of Jaingsu. But there is no indication to spread easily in humans.

* Hanta virus: It is a negative sense single stranded RNA virus. In 1995 cases reported from USA. Humans get infections by inhalation of aerosolized excreta (saliva, urine, feaces etc) of infected wild animals. The infection shows severe pulmonary edema resulting in respiratory failure and cardiogenic shock.

* Boca virus: It is a member of Parvo virus.also it is a DNA virus. This virus cause respiratory tract infection. Studies shows it act as co-pathogen (in presence of other infections).The prevalence rate is high in asymptomatic patients.

* Corona Virus (CoV): This consist of animal and human virus of atypical morphology. These are the largest positive sense single stranded RNA virus. It consist of alpha and beta viruses. These two cause common cold in last 200 years.But the emergence of SARS (Severe Acute Respiratory Distress syndrome) CoV and MERS (Middle East respiratory Distress Syndrome) CoV cause serious disease (severe respiratory diseases, pneumonia etc) outbreaks.

i. SARS CoV: This virus emerged from ancestral bat viruses.In 2002 it cause first known major pandemic with community acquired atypical pneumonia in Gaungdong, Province, China.The WHO issued worldwide warning on March 2013 about this infection.But the cases were sustained in China and few cases reported from North America, South America, Europe etc. The existing exotic reservoir of SARS CoV in China was a time bomb possibility of emergence of SARS (happened in 2019-20).

ii. MERS CoV: This is a zoonotic viral infection that cause respiratory tract infection.This was first reported from Saudi Arabia in 2012.this infection affects 26 countries.This cause acute respiratory distress syndrome, multisystem failure and mortality.Due to mutation newly emerged one become new genotypes and cause outbreaks. No vaccines and treatment prophylaxis remain unavailable till date.

iii. RSV: Respiratory Syncitial Virus cause acute lower respiratory tract infection (ALRTI) in young children.There is approximately 34 million episodes of ALRTI in children <5years.The exact mechanism of RSV infection need to studied in depth.

iv. SARS CoV2: In December 2019 novel corona virus isolated from patients with acute respiratory illness from Wuhan, China. It is a sixth public health emergency of international concern. By the end of March 2020 WHO declared it as Covid 19.And in March 2020 WHO declared Covid19 as pandemic. This viral infection affects more than 17.6 crore and3.74 lakhs death of the people globally. It have alpha, beta, delta variants. Delta variant is more severe one compared to others.The first wave of the pandemic over and second wave is going on and waiting for the third wave !.. These virus are more prone to antigenic variation and mutation. But vaccines are available.

Conclusion:

The emerging and re-emerging respiratory viral infections are big threat to humans globally. There is a need for strengthen disease surveillance and focus on the epidemiology and disease burden. These emerging strains are more potent one, so we have to learn something from the persistant Covid19 pandemic and get ready for next challenge because we don't know when and where the next pandemic will emerge.

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Biomarkers in COVID-19: An Overview.

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Introduction

* The ongoing pandemic COVID-19 is not a localized respiratory infection but a multisystem disease caused by a diffuse systemic process involving a complex interplay of the immunological, inflammatory and coagulative cascades.

* Diagnosis of COVID-19 is confirmed by direct detection of SARS-CoV-2 nucleic acids in respiratory tract specimens with a polymerase chain reaction (PCR) and continues to pose several diagnostic and therapeutic challenges.

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Potential role of biomarkers in COVID-19

* A biomarker is defined as a "characteristic that can be objectively measured and evaluated as an indicator of normal biological and pathological processes, or pharmacological responses to a therapeutic intervention" .

* Biomarkers in COVID- 19 can be useful in the areas such as early suspicion of disease, confirmation and classification of disease severity, framing hospital admission criteria, identification of high risk cohort, framing ICU admission criteria , rationalizing therapies, assessing response to therapies, predicting outcome and framing criteria for discharge from the ICU and/ or the hospital.

SL No	Organ/System	Biomarkers
1	Hematological	❖ Hemoglobin: anemia and altered iron homeostasis ❖ Lymphocytes: Normal or slightly reduced ❖ Neutrophils-Increased ❖ Eosinophils and Eosinophil-derived neurotoxin (EDN-1) -Reduced ❖ Monocytes and Basophils - Reduced ❖ Platelets -Both thrombocytopenia and thrombocytosis
2	Inflammation	❖ Cytokines/IL, CRP and Procalcitonin-Increased ❖ Ferritin : equivocal results are observed
3	Coagulation	❖ Elevated D-dimer fibrinogen ❖ Normal or mildly prolonged Prothrombin time (PT) & Activated partial thromboplastin time (aPTT) ❖ Platelets -Both thrombocytopenia and thrombocytosis
4	Cardiac	❖ Increased LDH, Creatine-kinase (CK), CK-MB, Myoglobin, Troponin-I, α-HBDH, AST, and NT-proBNP
6	Electrolytes	❖ Hyponatremia ❖ Hypokalemia ❖ Hypocalcemia

General recommendations based on the category of patients

* Asymptomatic/mild category (without underlying comorbidity):
    * No investigations are needed.
* Mild category with associated comorbidity or patients in the moderate category:
    - Complete blood cell count (CBC), C - reactive protein (CRP), serum creatinine, and Liver Function Tests (LFT) are desirable at admission.
    - If any of these markers are abnormal, further investigations mentioned for patients in the severe category may be considered.
    - If symptoms persist in the second week, CBC and CRP must be repeated to see the trends to decide monitoring and further investigations.
* Severe category: In addition to the markers mentioned above
    * PT, APTT, INR, serum ferritin, D-dimer and cardiac biomarkers (NT-pro-BNP and troponin I) are advisable.
* Critical category: In addition to the markers mentioned in the above categories
    * Serum IL-6 levels and serial lactate levels.
* To monitor hospitalized patients on therapy
    * CBC and CRP should be repeated 48 to 72 h after admission or earlier.

Conclusion

While choosing biomarkers for COVID-19, consider the followings

* Biomarker panels rather than single biomarkers may provide more reliable information.
* Consider the availability and cost issues of each biomarker.
* National or regional guidelines which tailor the information available to suit the local population are essential.

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Endocrine disrupting chemicals: Health impacts on humans.

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Relevance

There are emerging evidences for the negative human health impacts of Endocrine Disrupting Chemicals (EDCs). An updated knowledgebase on EDCs in 2020 (DEDuCT 2.0) contains 792 potential EDCs with 2218 research evidences. Of these many of the potential EDCs are still being used as pesticides, food additives, food storage materials industrial solvents, cosmetics and household products. Several of these EDCs are also manufactured in high quantities across the world. The growing evidence of exposures and adverse health impacts supports urgent action to reduce exposure to EDCs.

- Endocrine Disrupting Chemical (EDC) is an exogenous chemical or mixture of chemicals that can interfere with endocrine systems. They represent a broad class of molecules such as organochlorine pesticides and industrial chemicals, plasticizers, phytoestrogens, pharmaceutical agents and several other chemicals that are present in the environment or widely used.

- Exposure to EDCs in humans mainly occurs by ingestion and slightly by inhalation and dermal uptake. Most EDCs are lipophilic and accumulate in the fatty tissues, thus they persist in the body for a very long time.

- The potential health impacts of EDCs are greater when exposure occurs during early stages of development such as pregnancy, childhood and adolescence. Because the developing stage is highly influenced by hormones the foetus and child are very sensitive to any change of their hormonal environment. Also the shaping of the homeostatic mechanisms takes place in the early period of life.

- Early life exposure to EDCs can alter the susceptibility to diseases in later stages of life. The markedly increasing non-communicable diseases (NCDs) in the last few decades might be due to EDC exposure. The four major NCDs are cancers, cardiovascular diseases, chronic respiratory diseases and diabetes mellitus. Several studies documented the link of EDC exposure with diabetes, obesity and metabolic syndrome, which are the underlying factors for development of NCDs.

- Several studies shows an association between exposure to EDCs and male and/or female reproductive system disorders, such as infertility, endometriosis, polycystic ovarian syndrome, breast cancer, testicular cancer and reduced semen quality.

- Evidences are increasing that exposure of EDCs are associated with diabetes development. The increasing prevalence of diabetes is correlated with global industrialization and production of pesticides, plastics, synthetic fertilizers and food additives that release EDCs into the food chain and environment.

- EDCs also greatly effect on puberty, a period of rapid physiological changes like growth spurt, maturation of the gonads and the brain. Several studies have shown that estrogen like EDCs(eg: DDT, dioxin, polychlorinated biphenyls , bisphenol A, polybrominated biphenyls, phthalate esters, and endosulfan) interfere with sexual development during puberty.

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- Experimental evidence also suggests that prenatal exposure to EDCs can predispose exposed individual to increased fat mass and obesity because obesity is largely programmed during the early stages of life including intrauterine period.

- There is emerging evidences for the thyroid disrupting effects of environmental chemicals. Some studies show the potential carcinogenic effects of EDCs on thyroid gland.

- Estrogenic endocrine disruptors also influence the development of complex human brain diseases such as Alzheimer's Disease (AD), Parkinson's Disease, Huntington's Disease, Amyotrophic Lateral Sclerosis, Autism Spectrum Disorder, and Brain Neoplasms.

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Taming the Thyroid.

*Mr. Subin Chungath**

The thyroid gland is an endocrine gland positioned in the neck. This gland is a butterfly-shaped organ composed of two lobes connected by a narrow isthmus.

Functions of the Thyroid gland -Thyroid hormones increase the basal metabolic rate and influence almost all body tissues. Appetite and gut motility are influenced by Thyroid hormone. They increase the absorption in the gut. They stimulate the breakdown of fats and increase the number of free fatty acids. Thyroid hormones are important for normal development. They increase the growth rate of young people.

Effect of the Thyroid gland on the Cardiovascular system - The thyroid hormone increases the rate and strength of the heartbeat. They increase the activity of mitochondria, combined with these factors increases the blood flow and body temperatures.

There are commonly two types of thyroid dysfunctions, they are **hyper** and **hypo** Thyroidism

Hypothyroidism - An underactive thyroid. This can be easily treated with hormone replacement (thyroxine) with fewer side effects.

Symptoms of an underactive thyroid (hypothyroidism)

- Tiredness.
- Being sensitive to cold.
- Weight gain.
- Constipation.
- Depression.
- Slow movements and thoughts.
- Muscle aches and weakness.
- Muscle cramps.

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Hypothyroidism and treatment

1. Medication
2. Exercise and self-awareness
3. Nutrition
4. Relaxation
5. Yoga

Exercises for an Underactive Thyroid - hypothyroidism frequently experience muscle and joint pain. Low-impact activities that minimize stress on joints such as the knee, hip, or back may be easier to do as opposed to more strenuous activities. Some options include yoga, Pilates, walking, swimming, and biking. If you have an underactive thyroid, a condition called hypothyroidism; exercise is probably the last thing on your mind. After all, symptoms like fatigue, swelling, and joint and muscle pain do not make you want to get up and go. But experts and a recent review of literature say that physical activity can help you feel better.

What Type of Workout Should I Do? Most recent evidence-based studies say

If your condition is well controlled, you should be able to do the same physical activity as someone without a thyroid disorder, says John C. Morris, MD, professor of medicine and endocrinology at the Mayo Clinic College of Medicine. But if you're starting an exercise plan or if you're still dealing with symptoms, low-impact aerobic exercise and strengthening moves are best. "Low-impact exercise doesn't apply as much pressure. "That's key since hypothyroidism can cause pain and swelling in your muscles and joints."

Best low impact activities

Walking: One of the easy workouts to do. All you need is a pair of comfortable shoes and a heart-monitoring watch smartwatch. It gets

your heart pumping and burns about 280 calories an hour.

Aqua aerobics: If you have swelling in your ankles or feet, some exercises may be painful. Water aerobics is a good option. The water holds you up and lowers the impact on your joints. Many Physical principles of water will make the person do the exercises in a less stressful environment.

Yoga: This can stretch and strengthen your muscles. It also helps you focus on breathing. One study found that people with hypothyroidism had better lung strength after practising yoga breathing for six months.

Tai chi: Described as "moving meditation," this slow-motion form of martial arts is a proven stressbuster. Research shows it can help improve strength, balance, and mood.

Strength training: Whether you lift weights or use your body weight, building muscle helps you burn more calories -- even when you are sitting still. And that can help you shed extra pounds. Strong muscles also help ease pressure on your joints.

There are many ways workouts can help:

Boost your mood. "An underactive thyroid can cause feelings of depression and anxiety," Lopez says. Exercise lowers stress and helps your body make more endorphins will lift your mood and zaps those sad and anxious feelings.

Help you lose weight. A slow metabolism can cause weight gain and make it hard to shed pounds. Exercise burns calories and builds muscle, which can help you slim down. Increase your energy. Low-intensity aerobic exercise can help. People who rode an exercise bike for 20 minutes, three times a week, had more energy and less fatigue.

How Can You Get Started? "Take a consent"
Before you start any workout routine, see your doctor and took a consent. ACSM clearly explains about the special population and taking the consent before any exercises.

Some of the common protocol for weight reduction and cardiac endurance.

ACSM Guidelines for Cardiovascular Fitness

Frequency	**3-5 times per week**
Intensity	**55-90% MHR 40%/50%-85% VO2max**
Time	**20-60 minutes**
Type	**Any Activity that is rhythmical and utilises large muscle groups.**

F.I.T.T. PRINCIPLE

	Cardiovascular Endurance	Muscular Endurance	Muscular Strength	Flexibility
Frequency	Exercise 3-5 times per week	Exercises 2-4 times per week	Weight train 2-4 times per week.	Daily stretching.
Intensity	Train at 60-80% of target heart rate.	Add or maintain weight and repetitions.	60-75% of max 3 sets of 8-12 repetitions.	Stretch muscles and hold beyond its normal length.
Time	20-60 minutes per session.	About 30-60 minutes.	About 30-60 minutes.	Hold each stretch 10-15 seconds.
Type	Any aerobic activity keeping the heart rate within the target zone.	Resistance training yoga, Pilates, light weights.	Anaerobic activities such as weight lifting and sit ups.	Stretches that allow the body to move through the full range of motion.

Aerobic	Resistance	Flexibility
• 150 min/week of moderate-intensity activity, or	• Muscle strengthening activities at moderate intensity >2 days/week for each muscle group	• Stretch major muscle groups and tendons on days other activities are performed
• 75 min/week of vigorous-intensity activity, or		
• Equivalent combination		

Abbreviation: ACSM, American College of Sports Medicine.
[a]The guidelines were adapted from the US Department of Health and Human Services (US DHHS) Physical Activity Guidelines for Americans.[177] In general

Many of the evidence-based literature explains reducing the body weight can improve thyroid function vice versa too.
Obesity and hypothyroidism are two common clinical conditions that have linked closely. The link has become more relevant in the context of an unprecedented rise in the prevalence of obesity worldwide. Obesity is considered secondary to thyroid dysfunction. Novel view indicates that changes in thyroid-stimulating hormone (TSH) could well be secondary to obesity.

Thyroid disfunction and body weight
Body composition and thyroid hormones appear to be closely related. Thyroid hormones regulate basal metabolism, thermogenesis and play a pivotal role in lipid and glucose metabolism, food intake and fat oxidation. Thyroid dysfunction is associated with changes in body weight and composition, body temperature and total and resting energy expenditure (REE) independent of physical activity.

How can one lose weight fast with hypothyroidism? Use these six strategies to jump-start weight loss with hypothyroidism.

1. Cut Out Simple Carbs and Sugars.
2. Eat More Anti-Inflammatory Foods.
3. Stick to Small, Frequent Meals.
4. Keep a Food Diary.
5. Move Your Body.
6. Proper medication without fail.

Hyperthyroidism - An overactive thyroid condition. Hyperthyroidism is a potentially fatal health condition if left undiagnosed and untreated.

Hyperthyroidism Signs and Symptoms

- Nervousness, anxiety, or crankiness
- Mood swings
- Fatigue or weakness
- Sensitivity to heat
- A swollen thyroid (called a goitre). You might see swelling at the base of your neck.
- Losing weight suddenly, without trying
- Fast or uneven heartbeat or palpitations (pounding in your heart)
- Having more bowel movements
- Shaking in your hands and fingers (tremor)
- Sleep problems
- Thinning skin
- Fine, brittle hair
- Changes in your menstrual cycle

The symptoms will vary from person to person. If you're an adult; you're more likely to have subtle symptoms like a faster heart rate or being more sensitive to warm temperatures. Or you could feel more tired after everyday activities. When you first get hyperthyroidism, you may feel energetic because your metabolism is speeding up. But over time, this increase in your metabolism can break your body down and cause you to feel tired. Usually, hyperthyroidism develops slowly. If you are young; when you get it, the symptoms might come on suddenly.

Hyperthyroidism Causes

- **Graves' disease.** This immune system disorder is the most common cause of hyperthyroidism. It's more likely to affect women under the age of 40.

- **Thyroid nodules.** These lumps of tissue in your thyroid can become overactive, creating too much thyroid hormone.

Thyroiditis. An infection or an immune system problem can cause your thyroid to swell and leak hormones. It is often followed by hypothyroidism, in which your thyroid doesn't make enough hormones.

Blunted heart rate response
Hyperthyroidism can be treated with beta-blocker medications which can blunt the heart rate response. Therefore, heart rate may not be an accurate indicator of the exercise intensity and rating of perceived exertion may be enough alternative.

Hyperthyroidism and Exercises
For people with significant hyperthyroidism (commonly caused by the autoimmune

disorder called Graves' disease), exercise can overheat the body. Excessive workouts can cause a patient to go into heart failure if their thyroid hormones are not under control hence proper control of your hyperthyroidism is a must or else it can also lead to dangerous health hazards. Exercises in patients with a hyperthyroid are like double edge sword so, extreme caution should be taken Before any exercises proper consent from endocrinologist is a must. If the conditions are stable, they can do workouts.

Conclusion

Proper diagnosis and routine blood check-ups are inevitable in both hypo and hyper Thyroidism.

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Biological Remedy to Combat Plastic Pollution.

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Relevance

Plastics have extremely transformed our society in a myriad of ways. The light weight and flexibility of plastics has made them ideal material for a large number of applications, including packaging of goods and food materials, medical devices, buildings, transportation, etc. Usage of plastics has become mandatory in all hospitals, especially in eye hospitals where large number of surgeries and other related treatments require the use of plastics. The wide use of these plastics had led to a great amount of plastic pollution in our environment. Once used, these packing materials are discarded in landfills as principal pollutant and remains in our environment as a great threat. Plastics are considered as the most important environmental problem since they are non-biodegradable under natural environmental circumstances1. Though there are various methods for plastic degradation, the eco-friendly and most acceptable method is the use of microbial species.

The following are some of the aspects involved in the plastic biodegradation:

Plastic biodegradation refers to a process of changing the characteristic properties such as tensile strength, colour, chemical structure, shape and the molecular weight of plastic polymers through microbial degradation. This can be done by either enzymatic or non-enzymatic hydrolysis of microorganisms especially bacteria and fungi.

- There are many microbial species of bacterial and fungal origin that have a mechanism in degrading complicated hydrocarbons into simpler biomolecules. They are in particular Gram-positive and Gram-negative as well as a few species of fungal origin like Aspergillus.

- Around 15 bacteria were isolated on soil analysis of which only three of the bacteria were screened (Staphylococcus sp (P1A)., Pseudomonas sp. (P1B), and Bacillus sp. (P1C)) that showed positive results for the degradation of polythene plastics. Out of the above three bacterial species Bacillus sp showed the maximum percentage of degradation2.

- Other species of bacteria and fungi that are less effective in biodegradation system are Streptococcus, Staphylococcus, Micrococcus (Gram-negative), Moraxella, Pseudomonas (Gram-positive), Aspergillus glaucus and Aspergillus niger. In addition, Bacillus megaterium, Ralstonia eutropha, Azotobacter, Halomonas sp are also involved in the breakdown method.

- Biodegradation of plastic is governed by means of different factors that includes the characteristics of polymer, microorganism and the nature of pre-treatment of plastics. Utilization of molecular techniques to detect specific groups of microorganisms involved in the degradation process will allow a better understanding of the organization of the microbial community involved in the attack of materials.

- The mechanism behind the microbial biodegradation includes the release of extracellular enzymes to degrade the plastics which in turn leads to the breakdown of polymer into monomers and oligomers followed by the metabolism of microbial cells.

- The degradation under aerobic condition

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results in the production of carbon dioxide and water. Anaerobic metabolism leads to the production of carbon dioxide, water and methane as the end products3.

- Though there are several works done on plastic degradation, the efficient plastic-degrading microbes at the molecular level is still not characterized.

- The study of the synergism between these microorganisms will give an insight for future efforts towards the biodegradation of plastic materials.

- Greater understanding of the molecular mechanisms of biodegradation can be analyzed from the genes and gene products(enzymes) that hydrolyse the high molecular weight plastic polymers.

- In future the research should be focused in the field of genomics and proteomics, which could speed up the degradation. The genetic engineering approaches to create recombinant microbial strains and/or enzymes could be adopted as the preferred strategy to enhance biodegradation of the most dreaded plastic wastes.

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Advances in Dry Eye Diseases Management.

*Mrs.Nithya S R**

Relevance

Dry eye is the commonest cause of ocular discomfort globally. The symptoms increase with age and most often affects females than males. The burden of pathology interrupts with visual functions, quality of life and professional productivity. As per recent literature (DEWS in 2017), the revised Dry Eye Diseases (DED) definition is "A multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance and tear film instability, with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface"1. The core mechanism of dry eye is caused by disturbance in lacrimal function unit which results in tear hyperosmolarity of tear film and instability. Hyperosmolarity is the cause of ocular inflammation and other complimentary events in dry eye. The symptoms of dry eye involve ocular discomfort, increased blink rate and compensatory reflex lacrimal secretion. Eventually the progression of inflammation leads to secretory dysfunction and reduced corneal sensitivity resulting in greater tear film instability and dryness.

Following are the various treatment modalities of DED.2

- The treatment plans of DED depends on severity of condition, which are determined by subjective scales of symptoms in conjunction with clinical evaluation such as corneal and conjunctival staining, examination of eyelid and meibography, tear film break up time, Schirmer test, measure of tear osmolarity and MMP 9 testing.

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- The treatment for moderate to severe DED is aimed at managing the inflammatory reaction, evaporative defect and secretory deficiency of tear film.

- The traditional treatment of DED includes **artificial tear** supplements for all severity grades of dry eye. A large number of preparations are available. Depending upon the severity, a low viscous preparation to high viscous gel is prescribed. A recent therapeutic approach is an autologous serum eye drop made from patient's own serum that contains epitheliotropic growth factors and anti-inflammatory substances. The use of autologous serum eye drop remains as an experimental approach.

- **Warm compression and lid hygiene** with baby shampoo is the basic treatment for meibomian gland dysfunction. The temperature applied on the lid surface facilitates the melting and release of lipid from the gland.

- Inflammation of glands and ocular surfaces of moderate to severe dry is been treated with topical **corticosteroids** for a short period of 2-4weeks. Topical **cyclosporine-A 0.05%**, is an FDA approved medication for DED, which has been in the next line of treatment for the past 15 years as a long term therapeutic agent. It acts by reducing the IL-2 mediated T-cell activation, thus reducing the inflammation and increases the production of tears via local release of parasympathetic neurotransmitters. Tacrolimus 0.03% is also found to be as effective as cyclosporine-A with a comparatively better tolerance.

Following are the recent advances in the treatment of DED3.

- In July 2016, Lifitegrast 5% became the second FDA approved topical

medication for DED. The clinical trial suggests that it has rapid effect and long term safety with low adverse effects.

- **Omega-3 fatty acid** has an anti-inflammatory action by blocking proinflammatory eicosanoids. Systemic therapy with Linoleic acid and gamma-linolenic acid along with tear substitutes, are able to reduce ocular surface inflammation and improve symptoms of DED. Recently Omega-3 fatty acid has become available as eye drop to treat DED.

- Blood derived proteins such as **Eye-Platelet Rich Plasma (E-PRP)** and **Plasma Rich in Growth Factor (PRGF)** are newer products with higher concentration of growth factors and contains no leukocytes. These beneficial factors facilitate the cell growth and reduce inflammation of ocular surface in DED. However, blood products are under FDA approval.

- **Intense Pulse Light (IPL)** has been recently used to treat evaporative dry eye caused by Meibomian Gland Dysfunction (MGD). The technique uses a polychromatic light with a wavelength of 500–1200 nm to melt the meibum by creating heat.

- **Vector thermal pulsation (LipiFlow)** is a device used to treat MGD by application of heat over the gland while providing pulsatile external pressure.

- **Meibomian gland probing** was first introduced in 2010. Meibomian gland orifice was probed using a stainless steel rod of 2mm diameter. Probing resulted in the improvement of symptoms and signs with no adverse effects. The effectiveness of procedure depends on the skill and experience of the clinician.

- **Intranasal tear neurostimulation (TrueTear**) is an FDA approved device used to electrically stimulate the nerve endings present in the nasal mucosa and thereby increasing natural tear production via nasolacrimal reflex pathway of lacrimal unit.

- **Amniotic membrane** has been used to treat DED by considering its epithelial healing and anti-inflammatory property. Currently there are two commercially available varieties, **ProKera** and **AmbioDisck.** Amniotic Membrane Extract Eye Drop (AMEED) is under clinical trial for use in patients with graft-host dry eye and post Photo Refractive Keratectomy (PRK) dry eye.

- **Lacritin** is an ocular glycoprotein secreted by lacrimal gland. Topical administration of Lacritin has a potential effect on treating aqueous deficiency dry eye.

- **Punctal plugs** are small collagen or silicon plugs that temporarily occlude the punctum, so as to reduce the drainage in aqueous deficiency dry eye.

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Prose device for ocular surface disorder.

*Mrs.Sona Komalam**

Relevance

According to World Health Organization's global data on visual impairment in the year 2021, about 2.2 billion are visually impaired and almost half of it is preventable. About 4.2 million visual impairment or blindness is due to unaddressed corneal opacities. Corneal disorders are one of the major predisposing factors of visual impairment in India. Visual impairment in corneal disorders results from irregular corneal contour and loss of corneal transparency. Contact lenses are the primary mode of correcting irregular astigmatism which results from corneal ectasia. With the increasing severity of the disorder, lessening the usage of the lens due to lens intolerability results in the inability to correct irregular astigmatism. Functional vision in patients with ocular surface disorders is compromised due to the inability to open the eyes due to pain, photophobia, and dryness. Those conditions can be treated with the usage of bandage contact lenses, lubricating eye drops, oral and systemic medications. The scleral contact lenses are of great importance in the management of severe dry eye diseases and irregular corneal disorder. Specialized contact lenses have proven to be a potential & cost-effective treatment for a wide variety of conditions like Ocular surface disease and corneal ectasia.

- Prosthetic replacement of the ocular surface echo system (PROSE) treatment is a nonsurgical option offered to patients who suffer from serious corneal conditions, ocular surface diseases and are approved by US Food and Drug Administration is also a leader in the scleral lens field.

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- PROSE devices are removable transparent device which are made of gas permeable material that allows oxygen to reach the ocular surface.
- By immersing the corneal surface in a pool of tears, the scleral lenses reduce the symptoms, mask the corneal irregularities and thereby improve the functional vision.
- The PROSE device can be customized to each individual eye to deliver treatment effectively.
- The fitting process allows for the use of machine lathed rigid gas permeable Flurosilicone acrylate polymer of varying oxygen permeability that rests on the bulbar conjunctiva, thus allowing positional stability on the eye.
- During each time of application of lenses, they are filled with preservative-free saline and are removed during bedtime.
- Diameter ranging from 17.5mm to 23.0mm and vault to accommodate for non-apical contact are independent of the base curve.
- For subjective correction, residual spherical, cylindrical refractive error and asphericity can be incorporated in the front surface of the device.
- Front surface eccentricity can improve both high and low contrast visual acuity in PROSE treatment patients.
- During the last step of manufacturing of Prosthetic device are plasma-treated, that makes them more wettable so that vision and comfort are improved

MAIN GOALS

1. Improve visual function in patients with irregular astigmatism
2. Improve Ocular comfort for patients with dryness, photophobia, pain
3. Gives Ocular surface support in patients with the integrity of the ocular surface is compromised.

INDICATIONS

1. As a refractive treatment in irregular corneas
2. To prevent ocular surface breakdown promotes healing in cases like :

- Keratoconjunctivitis sicca
- Steven –Johnson syndrome
- Sjogren's syndrome
- Rheumatoid arthritis
- Corneal neuropathy
- Exposure keratopathy

In Corneal ectasia, studies have demonstrated success in fitting and improving vision with PROSE devices. The lens can also remove many of the surgically associated complications with Keratoplasties and the postoperative period.

Quality of life assessment is important in the field Ophthalmology and Optometry as visual impairment can profoundly affect the quality of life. There are studies based on the quality of life with PROSE lenses and showed PROSE treatment is effective and improved vision-related quality of life of patients suffering from ocular surface disorders.

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EXERCISE MEDICINE FOR DIABETES MELLITUS.

*Prof J Andrews Milton**

Relevance

Diabetes is one of the major public health problem and the fastest growing health challenges of the 21st century, with the number of adults living with diabetes having more than tripled over the past 20 years. Non-communicable diseases including Diabetes now make up 7 of the world's top 10 causes of death, according to WHO's 2019 Global Health Estimates.

Types of Diabetes:

Type 1 Diabetes Mellitus (Insulin Dependent) is characterized by autoimmune destruction of insulin-producing beta cells in the islets of the pancreas, the loss of function of the beta cells leads to an absolute insulin deficiency. T1DM is most commonly seen in children and adolescents though it can develop at any age.

Type 2 Diabetes Mellitus (Non-Insulin Dependent Diabetes Mellitus (NIDDM), the body fat, liver, and muscle cells do not respond correctly to insulin, known as insulin resistance. As a result, blood sugar does not get transported into these cells to be stored for energy and builds up in the bloodstream; this is known as hyperglycemia.

Gestational Diabetes Mellitus (GDM) can occur anytime during pregnancy. Generally, affects pregnant women during the second and third trimesters. Women with GDM and their offspring have an increased risk of developing type 2 diabetes mellitus in the future

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Benefits of physical exercise in Diabetes Mellitus:

- Aerobic training increases mitochondrial density, insulin sensitivity, oxidative enzymes, compliance and reactivity of blood vessels, lung function, immune function, and cardiac output
- Resistance training improves the muscle mass, body composition, strength, physical function, mental health, bone mineral density, insulin sensitivity, blood pressure, lipid profiles, and cardiovascular health
- Flexibility exercises increases the overall body flexibility
- Balance exercises prevents the risk of fall in elderly

Exercise Prescription for Diabetes Mellitus:

Frequency of exercise:

- Aerobic, Resistance, flexibility & Balance exercise: 3 sessions per week on alternate days

Intensity of exercise:

- Aerobic exercise: moderate intensity (40%–60% of maximal aerobic capacity (VO2max)) /vigorous intensity (>60% of VO2max)
- Resistance exercise: moderate intensity (>50% of 1-repetition maximum(RM), i.e.1-RM – maximum amount of weight one can lift in a single repetition for a given exercise)
- Flexibility exercises: Stretch to the point of tightness

- Balance exercises: stable surface progress to unstable surface; Bilateral stance progress to unilateral stance

Duration of exercise:

- Aerobic exercise: 20 to 60 mins per day continuously or intermittently in bouts of at least 10 minutes accumulated to total 150 mins per week
- Resistance exercise: 3 sets of 8–10 repetitions
- Flexibility exercise: Hold the stretching for 30 seconds.; 2-4 repetitions each exercise
- Balance exercise: 2-4 repetitions each exercise

Mode of exercise:

- Aerobic exercise: Brisk walking, swimming, dancing, cycling etc.
- Resistance exercise: should involve the major muscle groups (legs, hips, chest, back, abdomen, shoulders, and arms). Multigym, dumbbell, Resistance band etc.
- Flexibility exercise: Stretching, yoga etc.
- Balance exercise: Single leg standing, Tai-chi, balance equipment etc.

Special Precautions:

- Ketosis: vigorous activity should be avoided in the presence of ketosis
- Hypoglycaemia: carbohydrate should be ingested if pre-exercise glucose levels are <5.6 mmol/l
- Retinopathy: vigorous exercise may trigger the risk of haemorrhage or retinal detachment
- Peripheral neuropathy: Non-weight-bearing exercises are recommended
- Autonomic neuropathy: Autonomic neuropathy can increase the risk of exercise-induced injury or adverse events through decreased cardiac responsiveness to exercise, postural hypotension, impaired thermoregulation, impaired night vision due to impaired papillary reaction, and hypoglycaemia
- Albuminuria and nephropathy: Physical activity can acutely increase urinary protein excretion.
- Exercise strategies should be based on comorbidities, contraindications and personal goals

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Impact of aerobic training on body weight and body composition of young women.

*Shri. Premkumar.K**

Introduction

COVID-19 pandemic has spread to almost all countries of the world. Social and physical distancing measures, lockdowns of businesses, schools and overall social life, have also disrupted many regular aspects of life, including sport and physical activity which changed human life in physical and mental health. People all over the world may be experiencing an increasing number of mental health issues. The global outbreak of COVID-19 has resulted in closure of gyms, stadiums, pools, dance and fitness studios, physiotherapy centers, parks and playgrounds. Many individuals are therefore not able to actively participate in their regular individual or group sporting or physical activities outside of their homes. Under such conditions, many tend to be less physically active, have longer screen time, irregular sleep patterns as well as worse diets, resulting in weight gain and loss of physical fitness. Low-income families are especially vulnerable to negative effects of stay at home rules as they tend to have substandard accommodations and more confined spaces, making it difficult to engage in physical exercise. Covid has given a huge lift to online learning both in metros and non-metros which caused physiological and structural changes due to lack activities. Gained a few extra kilograms due to sedentary life there has been a lot of stress in this period it can lead to an increase or progression in the risk of hypertension, obesity, muscle weakness, postural defects, and lean body mass. This study aimed to compare improve functional capacity by aerobic training on body weight and composition of young female populations.

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Aerobic Exercises

Exercise is an important component in physical therapy programs and in maintaining a healthy lifestyle. The conditioning effects gained from an exercise program enable an individual to perform daily activities at a higher functioning level. Physical therapists use a wide range of exercise modes to improve cardio respiratory endurance. An aerobic exercise improves cardio respiratory endurance and fitness. The WHO recommends 150 minutes of moderate intensity or 75 minutes of vigorous-intensity physical activity per week. The ensuing demand for a continuous supply of oxygen creates the aerobic training effect, physiological changes that enhance the ability of the lungs, heart, and blood vessels to transport oxygen throughout the body. Aerobic activities include walking, jogging, bicycling, dancing and swimming etc. Aerobic fitness may be defined as the ability to deliver oxygen to the muscles and to utilize it to generate energy to support muscle activity during exercise. Aerobic fitness therefore depends upon the pulmonary, cardiovascular, and hematological components of oxygen delivery and the oxidative mechanisms of exercising muscles. The benefits of such periodic exercise are proven very helpful, especially in times of anxiety, crisis and fear. There are concerns therefore that, in the context of the pandemic, lack of access to regular sporting or exercise routines may result in challenges to the immune system, physical health, including by leading to the commencement of or exacerbating existing diseases that have their roots in a sedentary lifestyle. Lack of access to exercise and physical activity can also have mental health impacts, which can compound stress or anxiety that many will experience in the face of isolation from normal social life. Aerobic dance is popular during the last few years of the 20th century, primarily young women.

Individuals who are participating in the exercise to music program realize certain movements in the same rhythm and tempo, activating different muscle groups at the same time. Aerobic dance exercises have typically been developed as an aerobic exercise to reduce body compositions as well as improve physical fitness and performance Dance is a popular activity of people of all ages and is both a physical activity and a performing art that provides participants with an opportunity for aesthetic expression through movement. People dance for a variety of reasons. Dance is used to communicate ideas and feelings and is considered a creative art. The dance is an integral part of educational experience as a form of recreation and it provides opportunities for enjoyment, self-expression, and relaxation. Dance can also be used as a form of therapy providing opportunities for individuals to express their thoughts and feelings. It provides means to cope with various stresses placed on individuals. Dance is increasingly used as a means to develop fitness. There are many forms of dance that are enjoyed by individuals including ballet, ballroom, folk, and clog, modern, square and top. Past two decades' aerobic dance provides participants with an opportunity to develop fitness and experience the fun and enjoyment of working out of music.

The types of aerobic exercises and aerobic dances effects are significant for physiological changes and adaptations, which dependent on the ability of the organism to change and training stimulus threshold. In cardiovascular system, the HR is influenced by the parasympathetic nervous system at rest and the sympathetic nervous system by the release of non-epinephrine during exercise. The cardiac output increases because of increase in myocardial contractility, with a resultant increase in the myocardial contractility, with a resultant increase in the blood flow through the working muscles it will result increase in heart rate. During rest the PNS and during exercise this relationship is reversed, causing the heart to heart faster. Heart rate increases linearly with vo2 consumption and exercise intensity in both trained and untrained individual. The average resting heart rate of a sedentary person 68-72 beats per minute in trained athletes is usually a result of an increase in CO as a result of training. The heart is more efficient with each beat and therefore can pump less often maximal heart rate may be as high as 200 beats per minute during exercise. In general, heart rate decreases after the age of 30 years. Respiratory changes occur rapidly, even before the imitation of exercise. Gas exchange (O2, CO2) are increase across the alveolar capillary membrane by the first or second breath. Minute ventilation increase as respiratory frequency and tidal volume increases. O2 consumption of the study increases during exercise. Exercise utilizing larger muscles and greater intensities will increase O2 consumption. The capacity to use O2 is related primarily to the ability of heart and the ability of body tissues to utilize it. Significant increases in O2 consumption are associated with increased exercise intensity because of the tissues are utilizing more O2 during movement. An increase of O2 delivered to the tissues, CO2 returned to the lungs, and the volume of air breathed per minute, (minute ventilation) provide the body 3 with them right concentrations of gases for exercise. Aerobic exercise training results an increased maximal CO and maximal O2 uptake, slower resting heart rate, increased capillary density and increased O2 utilization. The distribution of blood in the body varies from rest to exercise. At rest approximately 20 percentage of blood flows to the muscles. With the remaining 80 percent supplying visceral organs, (kidneys, liver, spleen, etc). During exercise more blood is diverted away from the visceral organs to supply the working muscles. This distribution of blood flow during exercise is a result of vasoconstriction of the arterioles supplying the visceral organs and a vasodilatation of the vessels supplying the active muscles9. The rapid increase in energy requirement during exercise require equally rapid circulatory adjustments to meet the increase need for O2 and nutrients to remove the end product of metabolism such as CO2

and lactic acid and to dissipate excess heat. The shift in the body metabolism occurs through a coordinated activity of all the system of the body. Stimulation of small myelinated and unmyelinated fibers in skeletal muscle involves a sympathetic nervous system response

Materials and methods- 30 subjects selected with inclusion criteria age group between 18 to 22 years' Aerobic exercises protocols performed twelve weeks measured Body weight and BMI. The differences between mean scores were calculated using't' test for paired samples.

cardiovascular diseases, hypertension, diabetes etc.

Aerobic exercise programme is beneficial in reducing body weight and body mass index (BMI). It is very important to perform aerobic exercise at specific intensity to obtain the proper effect and benefit. While prescribing exercise programme it is crucial to monitor appropriate exercise intensity during the whole programme.

Exercise intensity should be kept in proper training heart zone. 50-60% of MHR (maximum heart rate) is effective to reduce body fat and this zone is called as healthy heart zone or fat burning zone. Exercise intensity of 60-70% of MHR is required to

Variables		mean	SD	T test	p-Value
Body weight (in kg)	Body weight before training	77.09	4.81	7.05	0.00
	Body weight after training	71.2	3.4		
BMI (kg/m2)	BMI before exercise	29.7	1.9	6.6	0.00
	BMI after exercise	27.1	0.6		

DISCUSSION

Aerobic exercises training was significant in both body weight and Body Mass Index (BMI) was significantly reduced (p=0.00) from 77.09 kg to 71.20 kg in experimental group at the end of 8 weeks aerobic training programme was effective in terms of reducing body weight and BMI in experimental group.

Body mass index (BMI) was 27.16±0.73 kg/m2 and 29.7±1.37 kg/m2 in experimental group and control group respectively after 8 weeks of aerobic exercise training programme.

Sedentary life style is one of the predisposing factors of overweight and obesity which lead to several diseases like

and lactic acid and to dissipate excess heat. recommend aerobics and aerobic exercise for 60 to 90 minutes in 5 to 7 days a week due to the increase in VO2 max and HDL levels.

CONCLUSION

Aerobic exercise programme is effective in reducing body weight and body mass index in sedentary overweight and obese individuals. It is concluded that aerobics with appropriate intensity should be recommended to overweight and obese people to reduce body fat.

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Post Covid 19 Mucormycosis

*Ms. Saranya V G**

Introduction

Covid 19 (SARS CoV 2) cause mild to life threatening pneumonia and acute respiratory distress syndrome. Recently Mucormycosis (black fungus disease) is reported from patients who were recovered from Covid 19 disease. Mucormycosis is a fungal infection that mainly affects person who are on medication for other health problems that reduces their ability to fight with environmental pathogens.

- **Mucormycosis** affects patients who are recovered from Covid 19 disease because of the use of steroids, monoclonal antibodies for therapy, mechanical ventilation, ICU stay, diabetes mellitus, chronic obstructive pulmonary disease etc. Covid 19 patients have lower CD4+ and CD8+ T cells and decreased phagocytic activity of WBCs. This virus damages the air way tissue and blood vessels that enable the patients more susceptible to secondary and bacterial infections.

- Studies shown that Mucormycosis may occur in the earlier stage of covid19 infection or after the treatment of infection.

- **Mucormycosis** (previously called Zygomycosis) is a serious but rare fungal infection caused by a group of molds called Mucormycetes and it belongs to order Mucorales (Mucrales include Rhizopus, Mucor, Rhizomucor, Absisia, Cunninghamella, Syncephalastrum species). These are present in the environment mainly in soil in association with decaying organic matter.

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- **Mode of transmission:** Inhalation, percutaneous inoculation of spores of Mucormycetes.

- **Predisposing factors:** uncontrolled diabetes, immunosuppressive drugs, prolonged ICU stay, post transplantation, malignancy etc.

- **Pathogenesis**: Spores inhaled and reaches the lungs and these are ingested by alveolar macrophages and it cannot be removed by these cells. These spores have predilection for elastic lamina of large and small arteries cause thrombosis, ischemia and tissue necrosis.

- **Clinical signs and symptoms:** It depend upon the sites involved by the fungus. It includes rhinocerebral, pulmonary, cutaneous, gastrointestinal, isolated renal, disseminated Mucormycosis. Rhinocerebral and pulmonary Mucormycosis is common in Covid19 patients.

i. Rhinocerebral Mucormycosis: Facial pain, head ache, lethargy, advanced case loss of vision. Physical examination shows brownish blood stained nasal discharge on the affected side, black eshcar on the palate. Orbital Mucormycosis presents chemosis, periorbital cellulitis, ophthalmoplegia, abrupt visual loss,orbital pain and facial hypoesthesia.

ii. Pulmonary Mucormycosis: symptoms include chest pain, dyspnea, hemoptysis, infiltration of lung.

iii. Cutaneous Mucormycosis: painful lesions, nodular ecchymotic areas.Necrotizing fasciitis has high mortality rate.

iv. Gastrointestinal Mucormycosis: abdominal pain, diarrhea, hematemesis and melena

v. Isolated renal Mucormycosis: pain, fever, pyuria, haematuria.

vi. Disseminated Mucormycosis: pneumonia, stroke, subarachnoid hemorrhage, brain abscess, cellulitis or gangrene.

- **Diagnosis:** Direct KOH mount, lacto phenol cotton blue mount, Fungal culture and sensitivity (MALDI- TOF if available), Nasal swab/ endoscopy, RT-PCR for Covid 19 positive patients.

- **Treatment:** Amphotericin B, Posaconazole, Isavuconazole, surgical removal of the infected tissue.

- **Do's:** Control hyperglycemia, monitor blood glucose level post Covid 19 discharge, use steroids in correct dose, time and duration, use clean sterile water for humidifiers during oxygen therapy, timely checking of eyes, nose and mouth for any suspicious lesions.

Conclusion:

Early detection and timely management will reduce the risk factors of Mucormycosis in Covid 19 patients. The extensive use of corticosteroids, monoclonal antibodies and broad spectrum antibiotics in Covid 19 patients leads to secondary fungal infections because of their altered immune status. So the treatment agents should be monitored to provide a therapeutic effect at the lowest dose and shortest duration in order to reduce the hardship of fatal Mucormycosis.

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ESKAPE pathogens and its antibiotic resistance....

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Relevance

Nosocomial infections are caused by a variety of microorganisms, which includes bacteria, fungi, viruses, parasites, and other agents. **ESKAPE** pathogens include **E**nterococcus faecium, **S**taphylococcus aureus, **K**lebsiella pnuemonia, **A**cienetobacter baumanii, **P**seudomonas aeruginosa and **E**nterobacter species. These are responsible for the majority of nosocomial (hospital acquired) infections and they effectively **"ESCAPE"** the biocidal effects of antibacterial drugs. Most of them are multidrug resistant strains, which is one of the greatest challenges in treatment. By understanding the resistance mechanisms of these bacteria that enable the development of newer antimicrobial agents or other alternative weapons to fight with these public health challenges.

- Antimicrobial resistance genes may be carried through bacterial chromosome, plasmid, or transposons. Mechanisms of drug resistance occurs by inactivation/alteration, modification of drug binding sites/targets, changes in cell permeability resulting in reduced intracellular drug accumulation, and biofilm formation.

Antibiotic Resistance in ESKAPE Pathogens

- **Enterococcus faecium:** They are Gram positive facultative anaerobes, which are often found in pairs or chains and are normal gut flora of human and animals. There is an increase in Ampicillin- and Vancomycin-resistant Enterococcal infections in healthcare facilities recent years. The incidence of Vancomycin-resistant Enterococcus (VRE), which is mainly associated with E.faecium. There are six genotypes of VRE (Van-A– E and Van-G), and van-A being the most crucial one with highest levels of resistance to all glycopeptide antibiotic. The treatment of significant infection depends upon second-line antibiotic therapies (e.g., Tigecycline and Daptomycin), which are often associated with increased cost, diminished efficacy, and a greater risk of toxicity

- **Staphylococcus aureus:** They are Gram positive facultative anaerobes and are normal flora of skin. The excessive use of antibiotic Penicillin led to the emergence of -lactamase-producing Staphylococcus and make it resistant to Penicillin. MRSA is a top priority for public health systems worldwide.The first-line antibiotics used for treatment of MRSA infections are Vancomycinand Teicoplanin. Vancomycin-intermediate and ancomycin-resistant S.aureus (VISAandVRSA,resp.) become more common now a days. VRSA isolates contain both the van-A and mec-A resistance gene of VRE and MRSA, which result in multiple drug resistance, including Methicillin and Vancomycin. BORSA is characterized by intermediate resistance to penicillinase-resistant Penicillins, with Oxacillin MICs being between 1 and 8µg/ml.

- **Klebsiella pneumoniae:** It is a nonfastidious Gram negative bacillus, which is encapsulated. K. pneumoniae strains have acquired variety of lactamase enzymes, which can destroy the chemical structure of -lactam antibiotics such as Penicillins, Cephalosporins, and Carbapenems. Carbapenamase resistant K. pneumoniae (CRKP), with resistance encoded by blaKPC, is a significant challenge for physicians. K.pneumoniae superenzyme, NDM-1 which is encoded by blaNDM- 1

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, has increased the proportion of resistance to Carbapenems. Recent reports suggest that AMR hypervirulent K. pneumoniae (hvKP) strains are also emerging

- **Acinetobacter baumannii:** It is a nonfermentative Gram-negative coccobacillus and causes infections at a various body sites, including the respiratory and urinary tracts. The emergence of carbapenemase producing A.baumannii strains have Imipenem metallo -lactamases, encoded by blaIMP, and Oxacillinase serine lactamases, encoded by bla . These strains show resistance to both Colistin and Imipenem drugs.The combination of resistance genes makes them escape from the action of most traditional antibiotic compounds

- **Pseudomonas aeruginosa:** It is a Gram negative, rod-shaped, facultative anaerobe that is part of the normal gut flora. It develops resistance during therapy in carbapenem-resistant (Imipenem) strains. Imipenem resistance in P. aeruginosa is due to the combination of chromosomal AmpC production and porin change. P. aeruginosa also produces ESBLs and can carry other antibiotic resistance enzymes such as K. pneumoniae carbapenemases (KPC), and Imipenem metallo-lactamases which is carried by the same plasmid. The continuous increase of multi drug resistant isolates results complications for antimicrobial therapy; but Colistin is still effective.

- **Enterobacter spp:** They are Gram-negative rods that are sometimes encapsulated. Enterobacter strains contain ESBLs and carbapenemases, including OXA, metallo--lactamase-1, and KPC. The stable derepression of the AmpC -lactamases expressed at high levels by mutation in this bacterial group. These multi drug resistant strains are resistant to almost all antimicrobial drugs, except Tigecycline and Colistin. Moreover, pandrug-resistant E. aerogenes has also emerged, shows resistance to the last-resort antibiotic colistin.

- Due to the resistance by these pathogens novel therapeutic strategies are developed. Newer glycopeptide like Dalbavanacin, Fluoroquinolones-Delafloxacin, aminoglycoside-Plazomicin, Omadacyclin for Tetracyclin resistant strains, Beta lactamase inhibitors- Ceftazidime Avibactum, Clavulanic acid, efflux pump inhibitors, nano formulations, phage therapy etc

- **Conclusion:** Antimicrobial resistance in these pathogens is a major threat to public health systems worldwide and looks likely to increase in the near future as resistance profiles change. This results in the lack of potential therapeutic agents in the treatment that causes real concerns but should trigger research and development of new antibiotics or new approaches to control the infections they cause. These newer weapons provide hope for prevention and treatment of infectious diseases caused by these ESKAPE microorganisms.

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Blood Banking and Transfusion Medicine

*ReenuSujaKuriakose**

Relevance – Blood transfusion can be a lifesaving intervention and blood transfusion services form vital and integral part of any modern health care system. The safety and effectiveness of transfusion depends on two main factors; the supply of blood and blood products that are safe, accessible at reasonable cost and adequate to meet the community needs and secondly the appropriate clinical use of blood and blood products. Inappropriate use cause serious complications and endanger life.

Blood bank generally refers to a division of a hospital where blood products are stored and proper testing is performed to reduce the risk of transfusion related issues. The term'blood bank'was coined by Bernard Fantus in 1937 and the blood collection program was initiated in 1940 in US.

Transfusion medicine deals with the transfusion of blood and blood components. Blood collection, processing, testing, separation and storage of various blood components, typing the blood for transfusion and testing for infectious diseases are performed in blood bank.Every units of blood is broken down into many components, including red blood cells, plasma, cryoprecipitate and platelets which may be transfused to several patients according to their specific needs.

The present trend avoid use of absolute hemoglobin or hematocrit values to assess the need for blood transfusion and employ physiological parameters including use of venous oximetry (to monitor oxygen level), cardiac outputs and arterial oxygen saturation (to calculate oxygen carrying capacity), patients ability to maintain appropriate arterial pressure with hemo-dilution and exact assessment of coagulation profile to ensure judicious use of blood components. Transfusion is only just one element of patient management. Careful assessment of clinical and laboratory indication is absolutely necessary to decide on transfusion of blood or blood products.

Standard tests performed once after blood is donated are ABO group typing, Rh typing and cross–matching.Screening for any unexpected red cell antibodies or irregular antibodiesagainst antigens such as Rh,MNs,Duffy and Kiddand screening for ongoing or previous infections such as hepatitis B and C viruses, human immunodeficiency viruses (HIV), syphilis, the most important agents causing transfusion transmitted infections (TTIs) are conducted. Other tests to screen human T-lymphotropic viruses (HTLV) I and II, West Nile virus, Chagas diseases, Human cytomegalovirus, malaria are also performed to avoid transfusion associated infections and complications.

Apheresis (meaning removal or withdrawal in Greek) involves the passing the blood of a person through apheresis machine (or cell separator) that separates out one particular constituent and the remaining components are returned to the circulation. Basic principle employed in the machine involves physical separation methods such as differential centrifugation based on the different specific gravity of the blood components and cellular size, membrane filtration and adsorption of proteins or cells from whole blood or from separated plasma.

Therapeutic apheresis procedure selectively removes abnormal cells or substances associated with causative agent of certain diseases in blood using apheresis technology wherein the patient may benefit

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from both removal of the blood component and the fluid given as replacement. Different types of therapeutic apheresis includes therapeutic plasma exchange, red blood cell exchange and cellular depletion.

Erythrocytapheresis,RBC (or Red blood cell)depletion and RBC exchange transfusion involves apheresis techniques that lower circulating RBCmass or exchange the patient RBC with donor RBC. RBC exchange compared to simple RBC transfusion have the advantage of lowering iron accumulation hazard and offers treatment of sickle cell disease in patients with risk of complications such as stroke. RBC depletion is indicated in cases of ABO-incompatible allogenic bone marrow transplantation when donor RBC needs to be removed from the patient's circulation. Reduction in greatly elevated number of RBC by erythrocytapheresis reduces blood viscosity, red cell volume and iron overload.

Therapeutic plasma exchange helps in removal of large volumes of patient plasma and replacement of plasma with appropriate fluids. Diseases mediators such as alloantibodies, autoimmune antibodies, antigen-antibody complexes, high cholesterol levels, metabolic wastes, plasma bound toxins, poisons, drugs circulating in the plasma can be removed relieving the symptoms. Plasma derived (natural) colloids prepared from donated blood or plasma include fresh frozen plasma, liquid plasma, freeze dried plasma and albumin etc.

Platelet depletion or thrombocytapheresishelps to lower elevated platelet count in patients with myeloproliferative neoplasmas or to prevent recurrent or progressive thrombotic or hemorrhagic events. White blood cell depletion or leukapheresis reduces the circulating blast count in acute leukemia's patients. Photopheresisis used in the treatment of cutaneous T-cell lymphoma and chronic graft-versus-host disease. Donated blood with T lymphocyte can cause transfusion reactions and graft - versus - host problems with repeated exposure to foreign cells. Irradiation of blood cells disable such T-lymphocyte present in donated blood.

The thriving information and communication technology holds future for online ordering of collection, real time and remote delivery ofblood and its products for transfusion purpose via virtual blood bank using computer controlled, electronically linked information management system. Virtual blood banks would further ensure the right person receives right amount of blood at the right time, bring accountability to patient accuracy, blood component identification, system security, personel traceability and minimize transfusion risks via a paperless system.

Recent advance in blood banking

Advances over the last decade in blood banking are categorized into phase : In phase I- infrastructure development The National & State Blood Transfusion Counsil'S (SBTC) were registered as societies in 1996 Phase II- Introduction of new programmes like Accreditation of Blood Banks, External Quality Assessment Scheme (EQAS) for HIV testing, organizing workshops for clinicians.

1. Recent advance in Grouping & Crossmatching- I.D.Micro-typing system (Gel Technology) -Glass microbeads technology -Erythrocytes Magnetized technology (Automated or Semi-automated instrumentation)
   -The ORTHO AUTOVUE INNOVA System is an automated imunohematology testing system used for blood typing, antibody screening and compatibility testing using ORTHOBIOVUE System cassettes. The ORTHO AUTOVUE INNOVA System is a computer software driven, fully automated system which provides automated liquid pipetting, cassette handling, incubation, centrifugation, reaction grading and interpretation.

2. TTD Testing • Compulsory testing for: HIV, HBsAg, HCV, VDRL & malaria

3. Nucleic acid technique (NAT)This is a molecular technique for screening donated blood to reduce the risk of transfusion-transmitted infections in the recipients, thus providing an additional layer of blood safety

4. Thromboelastography (TEG), Rotational thromboelastometry (ROTEM), and SONOCLOT are various point of care testing devices widely used globally for the controlled release of blood products

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2017 Classification of periodontal disease: A pathway to personalised periodontics.

*Dr Ambili.R**

Relevance: T2017 classification for periodontal disease can be considered as a major happening in the last decade in Periodontology which may last for many more years in the future.

- Numerous classifications were proposed for periodontal disease in the last century. The disease associated terminologies and their diagnostic criteria underwent many changes.

- Periodontitis was categorized into adult and early onset based on age and rate of progression according to classification proposed by American academy of periodontology in 1989 and European workshop in 1993.Early onset was subdivided into prepubertal and juvenile, both having localized and generalized forms.

- American academy of periodontology ,1999 classification was a major revision in the existing system where it was renamed into chronic and aggressive, eliminating the age dependent terminologies to avoid confusion.

- In addition, many disease categories like gingival diseases, abscess, endodontic periodontal lesions and mucogingival deformities and conditions were introduced.

* 1999 classification was followed world-wide for almost 2 decades. But during this time many controversies and confusions developed about this classification

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* In 2017 American academy of periodontology and European federation of periodontology jointly came with a new system of classification, which was described in detail in 23 articles in Journal of periodontology as well as in Journal of clinical periodontology.

- The conspicuous modification in this classification was elimination of terminologies like chronic and aggressive and they were unified into a single category named **"periodontitis",** thus avoiding unnecessary confusions.

- Previously there were many diagnostic dilemmas in periodontitis and the disease was often over-diagnosed or misinterpreted. A new case definition was introduced to bring clarity in this aspect which made the diagnostic process easy and precise.

- Moreover, a multidimensional staging and grading system was introduced for periodontitis. Staging is based on severity and complexity of disease management and grading gives an idea regarding rate of progression of disease.

- In current era of personalised periodontics, staging and grading offer an opportunity to identify of individual patients who require greater effort to prevent or control their chronic disease and who respond well to conventional treatment.

- Periodontists were very obsessed with the term aggressive periodontitis over the past 2 decades. The proponents of the 2017 classification do not deny the existence of such a disease category, but they suggest that data from larger, more diverse, better defined, and controlled populations are required to confirm and to define it better.

- Diabetes and smoking are included as risk modifiers in the grading process, again helping to customise the diagnosis, prognosis, and treatment plan. The future possibilities of including emerging risk factors like osteoporosis and rheumatoid arthritis are also discussed.

- Periodontal health is a newly added category and clear cut criteria are provided to define health in intact periodontium as well as reduced periodontium in periodontitis and non-periodontitis patients.

- The workshop presents a new dimension to gingival disease as a variant to health rather than a true disease and a reduction in taxonomy of gingival diseases is a remarkable feature in this classification.

- Gingival recession classification has been revised including the hidden recession along with visible recession. Periodontal phenotype, supracrestal tissue attachment and traumatic occlusal forces are some of the new terms introduced in this classification.

- Implant dentistry is a rapidly expanding field in periodontics and 2017 classification has provided space for separate categorization of peri implant health, diseases, and conditions.

- 2017 classification identifies the drawbacks of current diagnostic methods. The future of biomarker research as a non-invasive tool for periodontal diagnosis and risk assessment are also envisioned in this classification.

- 2017 classification involved the tireless efforts of a group of dedicated professionals and without doubt it be considered as one of the most promising development in the field of periodontology in the last decade which duly considered the available research evidence and revolutionized many existing concepts.

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'Sticky bone' and concentrated growth factor membranes for guided bone regeneration.

*Dr Annie Kitty George**

Clinical relevance: An atrophied alveolar ridge necessitates guided bone regeneration (GBR) prior to implant placement. Stability of the bone graft and space maintenance in the early healing period is critical for successful GBR. Since particulate bone graft is not stable, it has to be contained by barrier membranes- stabilized by bone tacks or encased within titanium meshes. These procedures are time consuming and technique sensitive. Also, premature exposure of the barrier can lead to infection and failure. As 'sticky bone' is stable and solid it can be used alone or in combination with concentrated growth factor (CGF) membranes in GBR.

Background and biologic rationale: Autologous platelet and fibrin concentrates are being extensively used alone or in combination with bone grafts and barrier membranes in reconstructive periodontics and implant surgeries. These healing biomaterials harness the beneficial effects of the growth factor rich platelets, fibrin matrix and in some cases their cell contents. (mainly leucocytes).
Platelets on activation and degranulation, release growth and chemotactic factors such as transforming growth factors ß-1 (TGFß-1), platelet-derived growth factor (PDGF), epithelial growth factor (EGF), insulin growth factor-I (IFG-I) and vascular endothelial growth factors (VEGF). In addition to its structural and mechanical entrapment characteristics, fibrin mesh facilitates cellular migration and angiogenesis

Evolution: The use of blood concentrates for wound healing began with the use of fibrin glues or sealants. Platelet concentrates have evolved continuously from the first-generation platelet concentrates- platelet rich plasma (PRP) and platelet rich growth factors (PRGF) to the second-generation concentrates such as platelet rich fibrin (PRF) and concentrated growth factors (CGF) and further into the newer titanium prepared PRF(T-PRF), advanced PRF (A-PRF) and injectable PRF (i-PRF).

'Sticky bone' utilizing autologous fibrin glue (AFG) was first described by Sohn in 2010.It is based on the novel concept of a growth factor enriched bone graft matrix. Sticky bone is a solidified, cohesive and pliable bone graft aggregate which can be condensed into bone defects, extraction sockets and alveolar ridge deficiencies.

Preparation:10 mL of patient's intravenous blood is collected from the antecubital vein into non-silica-coated tubes. The collected blood is centrifuged at 2700 rpm for 2 min to separate blood into two distinct layers- The lower red blood cell layer, and an upper layer of straw-coloured AFG. AFG is collected using a syringe and admixed with bone graft particles. After 5-10 minutes of polymerization, yellow coloured 'sticky bone' is obtained. 'Sticky bone' is a mouldable polymerized mass rich in platelets, leukocytes, and mesenchymal cells

Advantages: Sticky bone, with its more organized structure can be precisely adapted into osseous defects and packed on deficient alveolar ridges. The encasement of particulate bone within the dense fibrin matrix prevents movement of the graft. The volume of augmented biomaterial remains unchanged during the early healing period, minimizing the use of autogenous block bone and non-resorbable barriers.

The fibrin mesh holds platelets, growth factors and leukocytes enhancing regeneration. Unlike the first-generation platelet concentrates, biochemical additives are not needed in the preparation of sticky

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bone. The dense and strong fibrin matrix may minimize epithelial ingrowth into the sticky bone.

Concentrated Growth Factor (CGF): To prepare CGF, 10 ml of patient's venous blood is collected in glass coated test tubes and centrifugation is carried out in a specific centrifuge. (Medifuge MF200, Silfradent srl, Forlì, Italy) Centrifugation is done with the following alternated and controlled programme specifics: An initial 30 seconds acceleration, 2 minutes at 2,700 rpm, 4 minutes at 2,400 rpm, 4 minutes at 2,700 rpm, 3 minutes at 3,000 rpm followed by 36 seconds deceleration and then stopped. At the end of centrifugation, glass coated tube will show three different layers of which the middle layer is the fibrin buffy coat. It is a dense, large polymerised fibrin matrix encasing platelet aggregates and concentrated growth factors.

The CGF can be taken in a test tube, it can then be placed in a metal storage box with a perforated rack and pressed with a metal cover to form CGF membranes. On pressing the CGF mass, an exudate seeps through the perforated rack and can be collected in the bottom of the metal box.

Addition of this growth factor and autologous thrombin containing exudate to the yellow-coloured 'sticky bone' accelerates auto-polymerization of the AFG and particulate bone cocktail, reduces polymerization time to one minute, and turns it into a rich red colour.

Application: Since first described by Sohn, 'sticky bone' alone or in combination with CGF membranes have been effectively used in alveolar ridge and sinus augmentation procedures.

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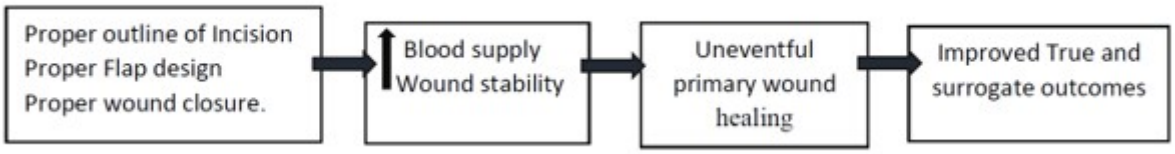
Recent advances in Periodontal Flaps - Incision free flaps

*Dr K Harikumar**

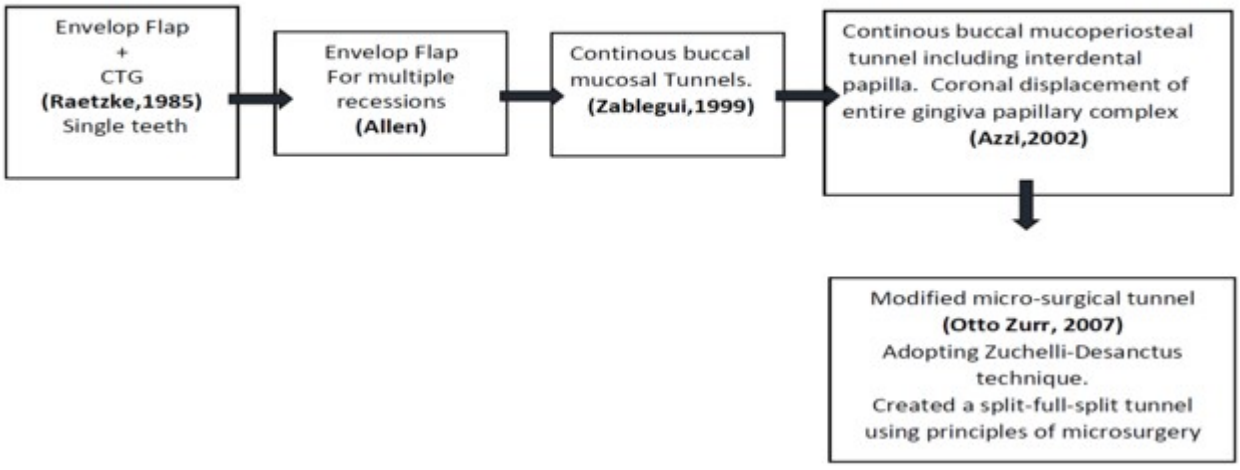
Relevance:

Periodontal surgery, over years has evolved in such a way, that the clinical therapeutic outcomes are improved in terms of tangible benefits. Apart from conventional pocket therapy, periodontal flaps are widely used in reconstruction of hard and soft tissues around natural tooth, implants and edentulous sites. As augmentation surgical procedures are increasingly shaping the treatment spectrum of dentistry, it is the need of the hour to incorporate relevant technical innovations in soft tissue management (Flap management).

- Three critical factors influencing the outcome of periodontal surgery are patient related, site related and technique related. Of these, the technique related factors are related to soft tissue handling. Proper handling of soft tissues during the procedure facilitates uneventful primary wound healing.
- Uneventful primary wound healing depends on blood supply, wound stability and prevention of infection. All these are in turn dependent on proper handling of flaps during the procedure like planning of incision, design of flap and wound closure.
- Marginal structures of a flap, marginal gingiva and the anatomical papilla or surgically created papilla are the most vulnerable for untoward outcomes if handled carelessly. Incisions on these structures always compromise the vascular content in the flap.
- It is in this context role of incision free flaps/tunnel flaps where incisions on papilla are avoided, become significant. This flap design, commonly used in periodontics since 2014, avoids any kind of incisions on tissue surface, thereby maintains blood supply in the flap and reduces the risk of post-operative scar thus improving esthetic outcomes.



EVOLUTION OF TUNNELING FLAP PROCEDURES



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Tunnel flaps are indicated in Shallow multiple recessions, Soft tissue augmentation around teeth/implants, Pontic site development, Implant second stage surgery and Socket preservation.

- The advantages of tunnel flaps are that it improves tangible outcomes, gives better esthetic results due to absence of scars and can be used for treatment of multiple recession sites.

- But tunnel flaps cannot be used for recessions greater than 3mm due to limited coronal displacement. Other drawbacks are that procedure is technique sensitive, require special instruments & training and also increases post-operative patient morbidity

- Further, incorporation of microsurgical principles in clinical practice resulted in more predictable and widespread application of incision free flaps

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Intraoral Scanners- A Recent Digital Boom in Orthodontics

*Dr Ravisankar V**

Relevance

Over the last decade, diagnosis and treatment planning in orthodontics is seeing a growing popularity in the availability of virtual technology with a move towards 'digital patient'. This three dimensional technology has the potential to replace hard copy records with electronic records like digital models for treatment planning, appliance construction and simulated treatment outcomes. This concept becomes even more significant to prevent cross-contamination. This article deals with the currently available intraoral scanners, its advantages and disadvantages. Clinician should be aware of the available devices as it will become increasingly common place in the orthodontic profession over the next decade [1].

What are Intraoral Scanners?

- They are devices for capturing direct optical impression in dentistry and orthodontics by projecting a light source [laser or more recently, structured light] onto the dental arches [2].

- The images captured by imaging sensors are processed by the scanning software, which generates point clouds

- These point clouds are then triangulated to form a 3D surface model [mesh], which are virtual alternatives of traditional plaster models [2].

Digital Scanning for Orthodontic Application [1]

1. Treatment planning
2. Indirect bonding tray fabrication
3. Palatal and lingual custom appliance design and fabrication
4. Clear aligner technology
5. Orthognathic surgery simulation and wafer construction
6. Scoring of surgical outcomes in patients with cleft lip and palate abnormalities.

Advantages [2]

1. Less patient discomfort- no unpleasant experience of impression taking
2. Accuracy- comparable to traditional impression.
3. Time efficiency- no need to pour casts and send physically to the labs.
4. Simplified procedure for clinician
5. No more plaster casts
6. Better communication with dental technician and patient

Disadvantages [2]

1. Learning curve
2. Purchase and managing costs- range from Rs 100000 to 200000

Available Intraoral Scanners in the market [1,3]

1. The TRIOS Intraoral Scanner marketed by 3Shape
2. The Lythos Intraoral Scanner marketed by Ormco
3. The True Definition Scanner marketed by 3M ESPE
4. iTero Intraoral Scanner marketed by Align Technology Inc.
5. PlanScan marketed by Planmeca

The Future

- The ability to improve patient care, efficiencyand effectiveness in orthodontics will continue to drive the development of new technologies.
- Cone Beam Computed Technology, clinical photographs and radiographs can be merged to facilitate advanced treatment planning and simulated outcomes for the patient.

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- In orthodontics, it is anticipated that the construction of complex removable appliances by hand will continue until technology can integrate both robotic wire bending and 3D printing for acrylic components.

Conclusion

Technology is shaping the future of healthcare provision, not least in orthodontics. Clinician should be aware of the available devices and the possible advantages they may offer patients.

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Nanotechnology: A New Frontier in Dentistry:

*Dr Tarun Nanu**

Since its inception by Nobel Prize Winning Physicist Richard Feynman, in 1959, Nanotechnology has been rapidly applied to various aspects of dentistry, and enabled us to harvest its potential in terms of great health benefits.

The basic idea of nanotechnology is to use “nano” sized particles which are about 1-100nm in size in order to create functional structures, that help us to control, monitor, repair and improve human biological systems.

Nanotechnology can have one of 5 main different approaches, namely:

1. Top-Down Approach: Where Conventional Particles are msde smaller by grinding or milling, these solid state materials can be used to create devices known as NEMS (nanoelectromechanical systems) which can be used in cancer diagnosis
2. Bottom-Up approach: Here smaller components are built up into more complex assemblies at an atomic or molecular level. These are employed in repairing of cells and tissues, protein synthesis etc.
3. Functional Approach: Components which are produced for a specific use
4. Biomimetic Approach: Components using biomolecules as their basic structures.
5. Speculative Approach: It deals with envisioning the use of nanomaterials for future applications in dentistry

Current use of nanotechnology has a wide reach all across the various streams of dentistry.

In the field of Operative Dentistry, it has spawned newer materials such as nanocomposites, Glass ionomer cements having nanoionomers,bonding agents with silica nanofiller technology,light cured agents containing nanosized fillers are being used as a final coating to enable better gloss and wear resistance to restorations.

In the field of Preventive Dentistry, ultrafine polishing of the human tooth leads to nanoscale roughness, from which cariogenic bacteria can be removed easily and in turn cause less staining of the teeth when exposed to the oral environment.

In the field of Prosthodontics, the advent of nanozirconia ceramic for dental crowns and dentures show excellent corrosion resistance, translucency and fracture toughness. Alterations of surface properties of implants using nanoscale topography or coatings provide better osseointegration of implants.

In the field of Periodontics, bone defects can be treated with nanobone graft materials which have better osteoconductivity, high porosity, and could absorb natural proteins that can be degraded by osteoclasts. The various Hydroxy Apatite nanoparticles used in repairing the osseous defects are:Nano Bone, Ostim HA,VITOSS HA+TCP, and NanOss HA.

Oral surgical procedures are being done using nanoneedles and nanotweezers at a cellular level, and nanosized stainless steel crystals are being used to perform incisions precisely at the cellular level.

Nanosterilizing solutions are being developed, which have desired benefits on use, such as being hypoallergenic, broad spectrum, non corrosive, non staining and compatible with various impression materials, in addition to being environmentally friendly.

Hydroxyapatite nanorods are enabling us to synthesize enamel to mimic the tooth structure, and nanorobots are being used to reduced dentinal hypersensitivity.

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Dentrifobots used in dentrifices are used to destroy harmful bacteria, while allowing the growth of 500 species of harmless microflora to remain and maintain homeostasis.

Fluoroscent Quantum dot proteins that attach themselves to antibodies via target cells and on stimulation to UV light can destroy the target cells have been developed.

Stem cells tracking can be done in vivo by using labelling techniques, such as fluorescent dyes,magnetic nanoparticles,supermagnetic iron oxide etc. to evaluate their therapeutic efficacy,survival,migration and regenerative impact.

Local Nanoanesthesia containing a colloidal suspension of nanorobots have been used to induce anesthesia, and after the procedure is over,nanocomputers can be employed and the nanorobots may be ordered to withdraw and re-establish the normal sensations of the tooth.

Nanoparticles such as NEMS and gold nanoparticles can be used as biomarkers in the diagnosis of oral cancer.

Inspite of the various benefits nanotechnology has to offer us, it also has it's own share of drawbacks such as:

1. Precise positioning and manufacture of nanoscale parts can be cumbersome
2. Cost effective manufacture of nanoparticles
3. Social issues of public acceptance, ethics, human safety etc.
4. Synchronization of numerous independent nanorobots.

Conclusion: Although there are many exciting applications for nanodentistry in the future, with it's perceived benefits being manifold, it is not currently possible to manufacture the same due to various biological, engineering and social challenges. And though it currently finds applications in many fields in dentistry and provides faster and better results than conventional methods, it's entire potential still remains untapped across many fields in dentistry.

Relevance: The use of nanotechnology in the fields of dentistry and medicine have enabled us to produce far better results than conventional techniques and materials, owing to the fact that these nanoparticles can be engineered to do specific tasks, For Eg. They can be made to target certain cells, such as cancerous cells, at the same time leave healthy tissue untouched and being nano sized, they can be applied anywhere and cause less trauma to healthy tissue and also have the ability to heal injured tissue at a microscopic level, which in turn leads to less scarring in case of surgical procedures, which in turn leads to better prognosis to the treatment procedures that are being currently done in the fields of medicine and dentistry.

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Flipped-Classroom Approach in Health Science Education

*Dr. Anoopkumar N, Ms.Shalu Varghese**

In flipped classrooms or inverted classrooms, students review lecture materials before class as homework. The materials reviewed prior to class can take the form of recorded lectures, curated videos, reading assignments, video broadcasts — any material that the instructor assigns as relevant to the topic at hand. In-class time is dedicated to discussions, interactive exercises, and independent work that would have previously been completed at home — all under the guidance of the teacher, who is present and available to respond to any questions that may arise.

Definition

"pedagogical approach in which direct instruction moves from the group learning space to the individual learning space, and the resulting group space is transformed into a dynamic, interactive learning environment where the educator guides students as they apply concepts and engage creatively in the subject matter" (The Flipped Learning Network, 2014).

Four pillars of F-L-I-P

- **F- Flexible Environment:** Educators often physically rearrange their learning spaces to accommodate a lesson or unit, to support either group work or independent study. They create flexible spaces in which students choose when and where they learn.

- **L- Learning Culture:** Flipped Learning model deliberately shifts instruction from traditional teacher-centered approach to a learner-centered approach.

- **I-Intentional content:** Educators continually think about how they can use the Flipped Learning model to help students develop conceptual understanding, as well as procedural fluency. They determine what they need to teach and what materials students should explore on their own.

- **P- Professional Educator:** Professional Educators take on less visibly prominent roles in a flipped classroom, they remain the essential ingredient that enables Flipped Learning to occur

Phases of Flipped Classroom

1. **Plan:** Figure out which lesson in particular you want to flip. Outline the key learning outcomes and a lesson plan.

2. **Record:** Instead of teaching this lesson in-person, make a video. A screencast works. Make sure it contains all the key elements you'd mention in the classroom.

3. **Share:** Send the video to your students. Make it engaging and clear. Explain that the video's content will be fully discussed in class.

4. **Change:** Now that your students have viewed your lesson, they're prepared to actually go more in-depth than ever before.

5. **Group:** An effective way to discuss the topic is to separate into groups where students are given a task to perform.

6. **Regroup:** Get the class back together to share the individual group's work with everyone. Ask questions, dive deeper than ever before.

After the six steps, Review, Revise, and Repeat!

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Advantages

- Flipping speaks the language of today's students.
- Flipping helps busy students, struggling students and students of all abilities to excel.
- Flipping allows students to pause and rewind their teacher.
- Flipping increases student-teacher interaction.
- Flipping allows teachers to know their students better
- Flipping changes classroom management and make the class transparent.

Recent Research on Flipped Classroom Learning

A most recent systematic review examined 46 articles on the effectiveness of flipped classrooms in medical education and found that students reported increased enjoyment, decreased boredom, and greater task value in flipped classroom. There is improvement in student's knowledge and skills with the flipped classroom than the traditional lecturing.

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ARTIFICIAL INTELLIGENCE IN DENTAL AND MAXILLOFACIAL RADIOLOGY

*Dr. Sonia Susan Philip**

RELEVANCE

Artificial intelligence is a breakthrough in the in the field of technology which is rapidly progressing and has captivated the minds of researchers across the globe. Ever since its inception, radiology has witnessed some of the exceptional achievements. Hence, this situation demands every dentist to get acquainted with this technology as the future of dentistry is abutting the implementation of its applications.

Artificial intelligence (AI)

- The term AI was coined by John MaCarthy in 1956 at Massachusetts Institute of Technology. AI is a branch of computer science dedicated to the development of computer algorithms to accomplish tasks traditionally associated with human intelligence such as, the ability to learn and solve problems. It is the ability of machines to mimic the cognitive functions of humans (i.e., the ability of a computer program to function like the human brain). It includes machine learning and deep learning.

Clinical applications

Broadly three areas can be distinguished:

1. Detection- for identification of an abnormality within an image that may be unnoticed by the naked human eye.

2. Automated segmentation- which provides information on the functional performance of tissues, boundaries, and the extent of the disease, with the goal of reducing the radiologist's workflow by reducing the need to carry out segmentation manually.

3. Disease classification- in which, an abnormality within an image is classified into a category (e.g., high or low risk, or a good or bad prognosis)

Applications in dental and maxillofacial radiology

- **Orthodontics:** Computational algorithms used in AI serve as excellent tool that precisely locate cephalometric landmarks even in scenarios where overlapping images are not visible to human eye. They also assist in determining the necessity of tooth extraction, monitoring tooth movements and staging tooth development.

- **Endodontics:** AI software have been found to be accurate in establishing working length by determining exact location of apical foramen and detect vertical root fractures on cone beam computed tomography (CBCT) images. They also accurately diagnose the periapical pathologies by delineating their boundaries and extensions. Though various AI models have shown high degree of accuracy in detecting dental caries, it is still not clear if this model could detect secondary caries or caries on overlapping teeth.

- **Oral and maxillofacial surgery:** Image guided surgery has revolutionized the field of oral surgery in the recent years. In future, these systems also have tremendous applications in orthognathic surgery due to the remarkable power of image recognition for various dentofacial anomalies.

- **Periodontics:** AI tools assist periodontist in early detection of alveolar bone loss, bone density changes and areas of furcation involvement with a higher degree of accuracy. They also predict the early risk of osteoporosis by evaluating bone

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architecture and bone mineral density. In future, they may also benefit implant dentistry by enabling early detection of peri-implantitis with appropriate interventions.

- **Oral oncology:** A higher degree of accuracy has been observed with AI systems in assessing cervical lymph node metastasis in head and neck cancers in CT and MRI images. In near future, deep learning survival predictions may guide the clinicians in choosing the best treatment option for these patients, thereby preventing unnecessary treatment interventions.

- **Forensic odontology:** From the limited studies on AI in forensics, it has been suggested that these computational neural networks can serve as a reliable tool for age and gender determination, but rather further research should be done to establish their accuracy.

- **To classify/ segment maxillofacial cyst and tumors:** Though different AI working models are in progress, it still remains a challenge to develop a fully automated model that can identify cysts and/or tumors.

- AI also has various applications in dental biometrics and in detecting sinus pathologies, temperomanibular joint disorders, Sjogren's syndrome, and headache.

Advantages

- Accuracy in diagnosis with standardization of procedures that can help in preventing the errors due to cognitive bias.

* Tremendously reduce radiologists' workload and allow radiologists to improve their relevance and value.

- AI integration helps in reaching larger population with accuracy; enhancing patient care.

Will AI replace radiologist?

Despite those above advantages, the dilemma is whether this technology will replace radiologists in the future. Intelligent systems have reduced radiologists' workload, but cannot replace human intelligence. Though AI assists in many ways, the final call has to be made by the radiologists as this field is in its nascent stage, with ongoing active research.

Limitations

- Requires a very huge and sound data base of knowledge, if not may result in inappropriate answers when presented with images outside of their knowledge set.

- May not adapt with new imaging software or new machine immediately.

- Not all the algorithms used are apt for clinical application. More trials to recommend the apt analytic programs for different scenarios.

Future recommendations

Radiologists should educate themselves about computational software in order to implement these new developments in a safe and appropriate way. Radiology programs should begin to integrate health informatics, computer science and statistics courses in their curriculum. It is time to set aside fears and begin to develop internal AI practices. While, in no ways AI can replace radiologist, it is of prime importance to be aware of the possibilities to integrate this technology in the future for a gratifying and successful practice.

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A NOVEL PUBLIC HEALTH PROBLEM: INFODEMICS

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Relevance

Throughout history, man has tried to control diseases. But new problems have always emerged to hinder mankind's progress towards its health goal - "health for all". At this moment of time, the inability to control health-related misinformation is one such novel problem. Amid the COVID-19 pandemic as health workers all around the world fought to control the disease but the disease was not the only problem they faced, misinformation had caused more problems and brought the world to its knees. It deeply disturbed the lives of millions of people around the world. This crisis has been called "infodemics" by WHO. "We're not just battling the virus," The WHO Director-General Tedros Adhanom Ghebreyesus said as he addressed the world "We're also battling the trolls and conspiracy theorists that push misinformation and undermine the outbreak response."

- **An infodemic** is an overabundance of information, both online and offline. It includes deliberate attempts to spread wrong information to destabilize the public health response and advance alternative agendas of groups or individuals. Eysenbach G defined an infodemic as "an excessive amount of unfiltered information concerning a problem such that the solution is made more difficult."

- **WHO defined the "infodemiology" as the science of managing infodemics.** Eysenbach G defined it as **"science of distribution and determinants of information in an electronic medium, specifically the Internet, or in a population, with the ultimate aim to inform public health and public policy."**

To understand further Infodemics and Infodemiology and few terms have to be defined

- **Information** can be defined as messages that are accurate to the best of our current knowledge. If not accurate, messages become problematic. Such problematic Information is categorized into **misinformation, disinformation, and mal-information.**

- **Misinformation** is incorrect information created without the intention of causing harm (e.g. asking people to wear face shield without realizing how ineffective it could be).

- **Disinformation** is incorrect information and intentionally created to hurt an individual, a group, or a country (e.g. alcohol prevents COVID-19 with an intention to raise profit.)

- **Mal-information** is correct information (based on reality), but used to cause harm to an individual, a group, or a country (e.g. justifying the high rate of confirmed cases by claiming that it is because of increasing the rate of testing.)

- Weaponized information: It is a message or content piece that is designed to affect the recipient's perception about something or someone in a way that is not warranted to cause harm. It has been called the 5th era in biological warfare. It causes mortality and morbidity by undermine socio-political- economical systems through ''weaponizing'' or ''virtually escalating'' health problems.

How to manage Infodemics?

- **Infodemic management:**

Is defined as "Systematic use of evidence-based analysis and interventions to manage the infodemic,

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mitigating harmful effects of health misinformation and on health behaviours during acute health events."

Challenges are for infodemic management is

- **Manage** the creation and dissemination of trusted information to ensure that the information is not excessive,overwhelming or confusing.

- **To counter misinformation.** All scientific research is to be organized and assessed for evidence to make correct endorsements and policies for the health of individuals and populations. Meanwhile, mis- and disinformation needs to be identified to counteract them.

FRAMEWORK OF INFODEMIC MANAGEMENT

1. **IDENTIFYING MISINFORMATION AND EVIDENCE**

- Evidence-based management and control and dissemination of accurate information.

- The use of Infodemiology data for surveillance purposes has been called "infoveillance".

- **Also there is a need for social listening**, or examining social media and forum posts, can reveal trends in public attitudes and behaviors about various health care topics

2.TRANSLATING KNOWLEDGE & SCIENCE

- Rapid delivery of decisive messages and communication in clear language

- All good information should be presented in ways that are accessible to all

3. **AMPLIFYING ACTION**

- Expanding and adding to the best and evidence based information

- The ultimate aim should to build trust and spreading the right information

4. **QUANTIFYING IMPACT**

- Analyzing data that can help measure classify and describe the infodemic, and track trends and the impact of messages and interventions.

5. **Coordination & Governance**

- Evidence generation and synthesis activities should be internationally coordinated to avoid duplication.
- Ensure slow down and streamline the flow of information of all kinds

6. **Build e-health literacy**

The most downstream approach in the management of Infodemics would be **building e-health** literacy it is "the ability to seek, find, understand, and appraise health information from electronic sources and apply the knowledge gained to addressing or solving a health problem."

7. **e-Health Marketing**

it is a public health promotion approach that applies traditional marketing principles and theories alongside science-based strategies to protect and promote the health of diverse populations.

- **The 3e of e-health marketing –** the message should be (1) Easy to understand, (2) Entertaining (3) Exciting

INFODEMIC MANGER: A PERSON WHO MANAGES INFODEMICS

Infodemic manger should be able to:

- **Address harmful effects** of infodemics and health misinformation

- **Reduce burden** of infodemic
- **Develop and maintain** trust in health workers & institutions
- **Reduce susceptibility** towards misinformation
- **Reduce confusion**, risk-taking and harmful attitudes and behaviors.
- **Report misinformation**

COMPACTING INFODEMICS AT AN INDIVIDUAL LEVEL

o Health workers should ensure that every individual should have the ability to critically think about the information they see and hear

- Personal experience is not scientific evidence.
- Fact checks -Always double-check the information
- "Slow down before you Share-Health information "
- Conform its trustworthiness
- Always keep yourself updated.
- Beware of fraudulent websites
- Appearances can be deceptive. It is possible to impersonate official accounts.
- Report misinformation.

Conclusions

Just like vaccination the best method is to reduce misinformation is immunization against the infodemics. This immunization should be with the help of good information and as it is the health care workers who should impart the good information to the public. Inoculating a certain degree of good information to the community can make them less susceptible to fake news or disinformation. It is believed that to have 'herd" immunity against misinformation at least 30% of public should be imparted with good information."

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HAPPENINGS IN PROSTHODONTICS

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Prosthodontics is a specialty of Dentistry with sub divisions like, removable complete/ partial denture, fixed partial denture, implant prosthodontics and maxillofacial prosthodontics. All these branches are growing and developing at an exponential manner technically and material-wise taking this specialty to an utmost height.

- **Advancements in Implantology**

a) Surgical techniques for ridge preservation in anterior esthetic zone

i) Socket shield technique

This technique involves intentional retention of a section of the remnant root at the time of immediate implant placement there by preserving the buccal or proximal bone from resorption.

ii) Osseodensification

It is a method of bone compaction by the application of controlled-deformation by rolling and sliding contact along the inner surface of the osteotomy with the rotating lands of the densifying bur.

iii) Ridge splitting and horizontal ridge expansion

Ridge splitting is done to widen the alveolar ridge, by splitting atrophic crests into two parts causing a longitudinal greenstick fracture for implant placement between them. Ridge expansion is a procedure that expands the ridge in a stepwise technique using screws of gradually increasing width.

b) **Changing concepts in dental implantology**

i) ALL ON FOUR technique

It is an advanced implantology technique that consists of placing a prosthesis on four osseointegrated dental implants for each of the two arches. 4 implants are placed two in parallel at the center and two more perpendicular (inclined up to 45º) at the ends. Thus a fixed dental prosthesis with 4 implants is achieved. Grafts are not necessary since the implants placed at an angle at the ends allow to save those posterior sectors where bone is normally lacking.

ii) Zygomatic implants

With extremely resorbed maxilla, fixed prosthesis can be provided with four zygomatic implants, without any graft.

iii) Pterygoid implants

The pterygoid implants are placed in the region of the first or second maxillary molars, follows diagonal direction posteriorly towards the pyramidal process. The implant get anchor in the pterygoid fossa of the sphenoid bone. The angulation of implants range from 45°-50° towards the maxillary plane.

iv) Trefoil concept

Trefoil is a dental implant surgical protocol for the lower (mandibular) arch. The process includes analog guided surgery in a precise location, placing 3 implants using a pre-fabricated titanium bar wrapped in acrylic and teeth can be placed within 1 week of dental implant surgery.

c) Recent advancements in maxillary sinus lift technique

i) Hydrodynamic ultrasonic approach

The hydraulic sinus lift technique allows the hydraulic detachment of the maxillary sinus mucosa through injection of liquid and, at the same time filling of the space with the graft material.

ii) minimally invasive antral membrane balloon elevation (MIAM)

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Minimally invasive technique for the maxillary sinus lift using a balloon catheter: the Balloon Lift- Control system. By this approach bone graft material can be placed through a small, round, supracrestal approach, avoiding the need to raise a wide flap.

d) The 3D dental scans

The 3D dental scans differ from traditional CT because their cone shape, allows for the incorporation of the entire field of vision and has replaced conventional dental X-rays, providing far more detail for improved patient care. CBCT scans help in the treatment planning of oral implants; enable measurement of the distance between the alveolar crest and mandibular canal to avoid impingement of inferior alveolar nerve, avoid perforation of the mandibular posterior lingual undercut, and assess the density and quality of bone; in maxilla distance between alveolar crest and maxillary sinus can be clearly assessed which can help in sinus augmentation/maxillary implant placement.

e)Implant materials

i) Biomimetic coating

In this system nanoparticles are coated over dental implants based on the principle of bio mineralization. It may enhance adsorption of proteins, adhesion and differentiation of cells and also may favor tissue integration.

ii) Tooth regeneration using stem cells

Experimental studies with tooth scaffolds supplied with growth factors are going on. Expected outcome is to regrow lost tooth with the supporting growth factors in the scaffolds so that these metal inserts can be avoided.

iii) Nano sensor incorporated Dental implants for detecting myocardial infarction

Dental implants are incorporated with RFID (Radiofrequency identification chip) which will detect special cardiac biomarkers in saliva. A wrist band is also utilized for providing alarm signal in case of a close heart attack.

- **Maxillofacial prosthodontics (MFP)**

Current researchers focus on fabrication of maxillofacial prostheses in a more efficient way through computer aided design and computer aided manufacturing (CAD/CAM) and computer supported rapid prototyping techniques (RP).

Digitization (Visualization) capture very clear topographic data of the patients through intra oral camera. Distortions/over compressions caused by the conventional impression techniques are eliminated as these data are collected without touching the tissues.

Designing converts the virtually formed designs into physical models by converting data to a print- format file and a stereo lithography file. The created digital models are transferred to CAD/CAM and form successful prototypes for intraoral/extraoral maxillofacial prostheses with good contours and tissue adaptation.

RP techniques have been utilized effectively in facial prosthesis fabrication over the past decade. Through this technique, practitioners can easily manage the formation of inner details of complex structured substances and undercut areas.

- **Fixed partial denture**

a) Advancements in FPD materials

i) Multilayered zirconia

This system was introduced in 2015, aiming for superior esthetic properties. The system is still showing improvement in gradation of chroma and translucency, imitating the shade gradient of natural teeth: Gradual increase in translucency from incisal area of the crown to the gingival region.

ii) Polymer infiltrated ceramics

This contains 86% ceramic and remaining polymer infiltrate; have both very good elastic modulus similar to resin composite and esthetic quality similar to ceramic.

iii) Calcium aluminate GIC/Ceramir

This cement is a recent hybrid combining the properties of calcium aluminate and GIC. It combines the pH, early strength, and adhesive property of glass ionomer with the long-term strength, better sealing, and biocompatibility of calcium aluminate cement.

iv) Luxatemp materials

Luxatemp fluorescence has superior esthetics with unique handling properties, Luxatemp Ultra by incorporation of nanotechnology, shows very high flexural strength and Luxatemp Solar light- cured material, enables for flexibility in working time.

v) Tuff-temp plus

This is a rubberized resin available in six shades and is either self-curable or light curable. Margin refinement is very easy because the materials gets grinded without distortion or softening.

vi) The Structur

Structur 3 and Structur Premium are the recently developed materials in the Structur family of provisional materials. With the application of nanotechnology, Structur 3 is highly fracture resistat and has high compressive strength of about 500 MPa. This material is highly esthetic with gloss and fluorescence similar to natural teeth. Structur Premium is having high fracture resistance and so ideal for long-term bridges along with excellent gloss, tooth- like fluorescence, and fast setting.

vii) CAD-CAM PMMA provisionals

CAD-CAM polymethyl methacrylate,PEMA provisionals are the recent trends in provisional restorations which can provide meticulous anatomic detailing. These restorations are block-milled out with much reduced porosity compared to traditional materials.

b) Advancements in Techniques

i) Handpieces with speed-sensing intelligence

These handpieces are having inbuilt sensors for detecting the frequency of vibrations of the bur and can adjust the speed accordingly. If higher load is encountered by the bur, signals are sent by the chips to increase air pressure which in turn maintain speed and eliminate stalling. When bur is free of load, automatically speed is reduced. The sensor monitors the speed several times/sec.

ii) Microturbine head

Handpieces with turbine head of <9 mm and height of 10 mm that are lighter and smaller than the conventional ones are introduced which allow greater accessibility and visibility. This can provide better control and maneuverability, thus increase the efficiency of practice and comfort of patient.

iii) Light-emitting handpieces

Handpieces with integrated light sources have been introduced in recent decades, which can directly illuminate the treatment area. This innovation is a breakthrough in dentistry that provides complete shadow-free illumination intraorally.

iv) Laser tooth preparation

Lasers have been successfully tried for both soft and hard tissue preparation in the past few years. Innovations are continuing in this area like Laser application in wide area is made possible by adding scanner systems to the existing dental laser units.

v) Robotic tooth preparation

Shortcomings of manual tooth preparation like insufficient/excessive preparation, iatrogenic soft/hard tissue damage etc. can cause discomfort to both patient and dentist.To overcome these discomforts, a robotic system with ultrashort pulse laser system was invented in China in 2019 for tooth preparation. More in-depth researches are going on in this field so that more patient/dentist friendly Robotic preparation systems are yet to be evolved.

vi) Digital impressions

Highly precise impressions are made now a days within few minutes with the use of optical oral scanners. Instant visualization of preparation from all perspective is possible with the digital scanners.

vii) Shade matching

Digital shade matching eliminates the subjectivity in the analysis and provide an exact color matching for the prosthesis at a reduced chair side time which is comfortable for doctor and patient.

• Complete Denture

Digital dentures

It has been more than a quarter century since the first report about the utilization of CAD/CAM methods for complete denture (CD) fabrication. The clinical steps for digitizing the tissue surface of a denture are still evolving. In digital impression either directly scan the supporting tissues utilizing an intraoral scanner or indirectly scan a stone cast, or even the impression, utilizing a laboratory desktop scanner or an intraoral scanner. CAM part of the new approach for CD production, currently two principal methods exist: one is additive and the other is subtractive.

•Artificial intelligence (AI) in Prosthodontics

AI is a globally growing innovative field, playing great role in bringing drastic improvements in modern medicine including dentistry. It is very much helpful in patient education, treatment planning, documentation etc. In Prosthodontics AI is an auxiliary to clinician in MFP, implantology and FPD in designing and fabrication of prostheses but require intensive research and trainings in this field is required to make it more useful for the specialty.

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ARE WE PREPARED FOR A NEXT PANDEMIC

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ABSTRACT

In 20th century, contrary to the popular belief that most infectious diseases are caused by bacteria, many diseases such as chickenpox, measles, influenza, small pox could not be substantiated with a bacterial origin. Louis Pasteur during his investigation of rabies on dogs made an assumption that diseases could be caused by microbes too small to be seen even under microscope. Shedding light throughout the history, words of Louis Pasteur "Gentleman, it is the microbes that will have the last word" has been proven right time after time. These fatal infectious diseases have claimed very large number of lives in the form of pandemic, epidemic or endemic. These outbreaks are usually a result of pathogenic emergence transmitting via person to person, animal to person, vectors, environment or other media.

KEYWORDS: Outbreak , Pandemic, Preparedness , Public Health.

INTRODUCTION

History marks 541-549 the beginning of first plague pandemic as plague of Justinian which wiped out 15-100 million lives i.e., 20-60 % population of Europe.[1]Yesinia Pestis repeated this attack killing 75-200 million lives in 1346-1353 worldwide known as Black death.[2]Smallpox, Ebola, Influenza virus and many other contagious has the history of paving its way again. These bio catastrophes cause more death than those of all war

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Bio risk management beginning with assessment, identification and initiation of treatment plan by production of vaccines or cure to minimize morbidity and mortality should not be the only sector to pay attention.[4]All of this past experience has made it important for us to have a clear idea about how to manage any kind of disease outbreak. The impact is widespread at various aspects of livelihood of the public. Controversies regarding doctor to patient ratio are a sensitive topic during outbreaks. Proper training to health sector workers is essential to deliver health care at the best.[5]Public awareness is most essential in management to ensure quality of life and overcoming the infectious spread. The mental health and emotional stress is often neglected in terms of measures taken against these situations. A strategic approach in planning precautionary measures should begin at individual level at households. Storage of important medicines becomes a necessity at times of pharmaceutical production and distribution halt. Basic necessities like clean water and farming of organic food for self support should be encouraged. At extreme case scenarios shortage of food and other basic necessity supplies can lead to panic, devastation and havoc to the public life apart from debilitation. With reference to historical outbreaks and studies conducted, precautionary measures and their implementation should be taken in consideration before enforcing actions. A well informed society should be molded ready to fight along with the health faculties in order to minimize the impacts of the next outbreak.[6]

DISCUSSION

Drawing light from the current pandemic situation of Covid-19, the impact of a pandemic has an effect in every aspect of life. Uncontrolled spread increasing the morbidity and mortality rate has direct influence in the individual, community and global levels. The effects has devastating impacts on under developed and developing countries due to the poor management strategies.[7]The havoc caused by the panic between the citizens and only give rise to their withdrawal of participation in work places giving a major shattering of economic growth. With product manufacturing and supply taking an edge off, a significant forshortening of revenue is inevitable.[8] Healthcare system also take a large toll on itself with new challenges popping up rapidly like diagnosis of the unacquainted conditions. Often individuals with other diseases may be neglected with proper support and treatment. With infections on the loose healthcare professionals are overworked despite heeding themselves being at higher risk. This situation demands more number of healthcare workers. Higher personal protection and consistent medical supply should be ensured for smoother functioning of the medical system.[8] Smooth operation of the society is brought to a halt with cancellation of various activities and undue stress engorge within individuals leading to panic and mental outbreak. Daily routines are disrupted with occupational, educational and entertainmtment sectors are forced to shutdown. Rapid spread of infection may demand social distancing and quarantining which can further worsen the mental health of the individuals.[9]

Evidences from history has shown the repeated incidence of the pandemic and mutation of the pathogens. Spark risk and spread risks has additive effects hastening and worsening the pandemic situation. Universally accepted preventive and responsive strategies should be put forward for effective mitigation. Each pathogen has different characteristics and pathogenesis which restrict in coming up with a single management agenda. But effective public awareness and preparedness along with a strong health care system act as a shield in battling against the sparks.[10]The population at risk is never overprepared scaling up the healthcare infrastructure and delivery systems. Reduction of the pathogen transmission require a combined effort from different sectors like water and sanitation. LMICs lacking the efficiency to scale up their healthcare systems are likely to be provided with the some by foreign aid providers. Thus focusing on individual population with proper continency management bring out a positive result in controlling the global pandemic.

A globally acceptable guidelines should be put forward. Initially along with identification and epidemic modeling,isolation and observation of symptomatic patients. Clinical care appropriately at this stage helps in rapidly reducing the risks of spread. Spillage of the infectious disease can be contained only if animal health and environment is also equally prioritized. Determining the severity of the epidemic , public sectors should be alerted and trained for emergency measures. Public awareness and intructions to contain the situation should begin at basic household level. Storage of basic necessities and functioning of

manufacturing sector without interruption should be ensured inorder to eliminate increased demand, panic buying and chaos. When the disease spread is not constrained by intial management, appropriate strategical changes in control and treatment should be introduced along with the intial preventive measures. Protective measures should be made easily available and accessable for the public. Mental health of the community should be kept at bay. When the pandemic situation steps into severe intensity, the upheaval in community is inevitable. Administrative and defense sectors should be deployed in assisting the crisis response. The government should maximize the technical and laboratory support. Production of basic necessities as well as pharmaceutical needs should be thrusted. Global humanitarian system come to the aid in crisis response capacity.

CONCLUSION

Predicting a pandemic beforehand may not be possible. But the course of action to be taken when a pandemic strikes can be laid out in advance to eliminate the chaos and limit the spark period. Lessons through out the history and present suggests ample measures to be taken in case of an infectious break out. Epidemiologists, health care professionals, governments, and citizens should be able to work hand in hand to mitigate any upcoming pandemic. Re emergence and re infection is always around the corner. Though successful control is attained, It leaves traces in the form of returning, ongoing or new consequences.

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EMPTY SELLA SYNDROME MANAGED BY HOMEOPATHY

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- Empty sella syndrome (ESS), is a rare disorder characterized by enlargement or malformation of a structure in the skull known as the sella turcica, resulting from herniation of the subarachnoid space through the diaphragm sella displacing the normal pituitary gland. It may be either partial empty sella or completely empty sella. (1)

- Many people with empty sella syndrome presents as chronic headaches and aren't sure that this is related to empty sella syndrome or due to high blood pressure, which many people with empty sella syndrome also have.

- In rare cases, empty sella syndrome is associated with pressure building up in the skull, which can lead to spinal fluid leaking from the nose, swelling of the optic nerve inside the eye or vision problems.

- Primary ESS is most common in adults and women, and is often associated with obesity and high blood pressure. Secondary ESS is the result of the pituitary gland regressing within the cavity after an injury, surgery, or radiation therapy.

- When the pituitary gland shrinks or becomes flattened it cannot be seen on the MRI scan making it look like an empty sella. Partial empty sella is suggestive that some of the pituitary gland is visible on the MRI scan.

- The most common symptoms are Headaches, High blood pressure, Fatigue, Impotence (in men), Low sex drive, No menstrual periods or irregular ones and Infertility (in women). Severity depends on the extent to which the hypothalamus, hypophysis and optic structure are involved.

- Endocrine abnormalities are GH deficiency is being the commonest, elevation of prolactin (PRL) and reduction of ADH. These patients show a normal PRL rise with TRH stimulation (whereas patients with prolactinomas do not) (2).

- Total empty sella syndrome means more than half of sella is filled with CSF, and pituitary gland is 2 mm thick or less. Treatment include prevention of CSF from leaking out of nose and medication, for headache relief. Secondary empty sella syndrome focuses on treating the underlying condition.

- Patient had recurrent attacks of sudden and excruciating pain in head that radiated to right eye, ear, face and back of head with redness in right eye. Pain get worsened by pressure, lying on rt side and got relief by absolute rest. Moreover had multiple drug allergy also.

- Vital signs were normal. MRI Brain including the whole spine screening had shown as 1) PARTIAL EMPTY SELLA 2) MILD PROMINENCE OF B/L PERIOPTIC CSF SPACE & MECKEL'S CAVE (Idiopathic Intracranial Hypertension?)

- Homoeopathic Medicines has the power of affecting the body in health and disease. There are different causes for pain in head and medicines can be selected based on nature of pain, its duration, radiation and associated other symptoms. But the Similimum can only be selected based on Totality of Symptoms.

- Dr. Hahnemann says in Aphorism 9,

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"Now as in a disease, from which no manifest exiting or maintaining cause has to be removed. We can perceive nothing but morbid symptoms, it must be the symptoms alone by which the disease demands and points to a remedy suited to relieve it- and moreover, the totality of these symptoms, of this outwardly reflected picture of the internal essence of the disease, that is affections of vital force (3).

- In Homoeopathy, if the physician clearly perceives what is to be cured in disease, what is curative in medicines, and if he knows how to adapt according to principles, and to remove the obstacles to cure if persists, then can treat judiciously and rationally.

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SHERLOCK HOLMES OF PATHOLOGY- MOLECULAR DIAGNOSTIC TESTS

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Introduction

Molecular pathology is defined as the testing of nucleic acids for the diagnosis, prognostication and treatment of various diseases. It is also useful in genetic counseling and research of newer diseases. It is often considered a "crossover" discipline because it shares aspects with molecular biology, biochemistry, and genetics. In the current covid 19 pandemic it has become a layman's term because of rt PCR testing for SARS-CoV-2.

However, its use is still in nascent phase in many pathology laboratories

Significance

A key consideration in the use of molecular methods is the personalized diagnosis and targeted therapy which is possible when the diagnosis is based on both the morphologic changes in tissues (traditional pathology) and molecular pathology.

Uses

- Diagnostic tool-infectious agents, tumors, inherited diseases
- Genetic counseling-inherited genetic disease (e.g., cystic fibrosis and hemochromatosis), and in certain tumors.
- Genetic counseling includes predictive testing, carrier testing and prenatal testing.
- Pharmacogenomics-targeted therapy
- Assessing disease prognosis and therapy response
- Detecting minimal residual disease.

Advantages

- Few of the methods available including FISH can be performed on fresh frozen as well as prepared cytological smears and also in paraffin-embedded tissue sections.
- FISH especially is often used in evaluation of HER2/neu oncogene amplification in breast carcinoma and for detection of different translocations in chronic myelogenous leukemia and acute myelogenous leukemia
- Chemiluminescence detections assays allow for rapid diagnosis and prognosis for expeditious and personalized patient management
- A helpful feature especially in metastasis from unknown primary is that Patterns of gene expression in tumors are linked to the primary site of origin. A lung primary tumor, for example, has a different fingerprint than an ovarian or colonic primary. Hence DNA microarrays have been shown to predict the correct primary site with an accuracy rate of 99%

Tests include

Quantitative polymerase chain reaction and real-time PCR
DNA microarray
In situ hybridization
Fluorescent in situ hybridization
In situ RNA sequencing
DNA sequencing
RT-PCR
Spectral karyotype imaging

The next step

- Making the tests more accessible and cheaper

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- Use of Artificial Intelligence in the assay and analysis of the tests which can make the whole procedure easier. This is also being developed.

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mRNA vaccine technology

*Dr. Sabitha Baby**

- Use of vaccines has helped us to prevent many infections and to save millions of lives. Traditional vaccine approaches, such as live attenuated and inactivated pathogens and subunit vaccines, provide long lasting protection against variety of infections.

- In addition to prevention of a future infection (prophylactic vaccines), the concept of vaccines has been widened to reinforce the immune defense system to treat already existing infection or diseased states (therapeutic vaccines).

- Ideally, a vaccine should be safe, highly immunogenic, non-integrating, easy to manipulate, genetically stable and inexpensive to produce. The answer to this dilemma remains in the endless possibilities of custom-made messenger RNA(Mrna). Messenger RNA is the molecule that cells naturally use to carry DNA's instructions to cells' protein-building machinery. The self-adjuvant effect of mRNA is a double-edged sword for vaccine efficacy.

- mRNA vaccines have become a versatile technology for the prevention of infectious diseases and the treatment of cancers. For vaccines, mRNA is manufactured by chemical rather than biological synthesis, so it is much quicker than conventional vaccines to be redesigned, scaled up and mass-produced.

- mRNA vaccines have the potential for rapid, inexpensive and scalable manufacturing, mainly owing to the high yields of in vitro transcription reactions thus can rapidly generate vaccines against new diseases quicker and more economically.

- mRNA is a non-infectious, non-integrating platform, they do not integrate into the host cell genome or interact with DNA and therefore impose no mutational risk of infection to the host or insertional mutagenesis, so it is safe.

- mRNA vaccines have strands of genetic material called mRNA inside a special coating. That coating protects the mRNA from enzymes in the body that would otherwise break it down. It also helps the mRNA enter the dendritic cells and macrophages in the lymph node near the vaccination site. Direct intramuscular (IM), intradermal or subcutaneous injection of in vitro transcribed mRNA are the main delivery routes for mRNA vaccines against infectious diseases.

- To elicit an antigen-specific immune response, an mRNA-vaccine has to reach the cytosol of target cells. However, as opposed to DNA vaccines, RNA vaccines only have to cross the plasma membrane, but not the nuclear envelope which may improve the probability of successful in vivo transfection.

- The vaccine mRNA codes only for the critical fragment of the viral protein. This gives the immune system a preview of what the real virus looks like without causing disease. This preview gives the immune system time to design powerful antibodies and activating T-cells that can neutralize the real virus if the individual is ever infected.

- Instead of delivering a virus or a viral

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protein, RNA vaccines deliver genetic information that allows the body's own cells to produce a viral protein.

- Synthetic mRNA that encodes a viral protein will borrow host machinery to produce many copies of the protein. This protein will look just like the virus protein. When that protein leaves the cell, the immune system recognizes it is as a viral protein and goes to work creating antibodies against it, without posing any risk of infection.

- mRNA vaccines closely but harmlessly mimic the virus' ability to trigger the body's immune responses to infection and elicit Tcell and B cell based immunity. A variety of antigens can be expressed with high efficiency and induce potent humoral and cellular immune responses after mRNA vaccination

- There are two types of mRNA vaccines: the conventional type (non-amplifying mRNA) and RNA replicon vaccines (self-amplifying mRNA vaccines: SAMs). Both unformulated and Nano-particulate mRNA is used for direct in vivo vaccination. One drawback to mRNA vaccines is that they can break down at high temperatures. This can be overcome by lyophilization

- The COVID-19 Vaccine of Moderna and Pfizer is based on this technology and works by preparing the body to defend itself against COVID-19.

It is expected that the above vaccines will provide more than 90.0% efficacy among the people who receive the vaccine. Apart from the vaccines, it appears that mRNA technology has now reached a level where protein or gene replacement therapies based on mRNA has become conceivable.

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Robot Nurse: The Newer Trend in Nursing.

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Introduction and relevance

Robots have played a pivotal role in a wide range of fields, such as the military, mining, space, construction, agriculture and health care. In recent years, there has been an increasing interest in robots especially the cases where technology intersects with decisions about care in healthcare institutions and in home care settings. At present, the rising incidences of lifestyle diseases and growing demand for affordable healthcare, coupled with increased role of government in healthcare investment and emergence of technologies such as artificial learning, machine learning and robotics are the major driving factors in Indian healthcare industry.

Driven by the shortage of qualified nurses and the high percentage of aging populations, the past decade has witnessed a significant growth in the use of robots in nursing. The COVID 19 pandemic acted as a catalyst in introducing robots in the nursing scenario in India. Prototypes resembling "robot nurses" could have both negative and positive impact.

Common Robot Nurse in Use

- Robot Dinsow: - This is used by Thai and Japanese hospitals for patient care, which monitors elderly patients via video and sets up video chats with their relatives. It also alerts caregivers of patient activity by phone. Additionally, it provides reminders for medication and exercise and exercises alongside the elderly. Finally, it provides entertainment by offering games and karaoke.

- Robot bear: - Japanese robotics engineers at Riken and Sumitomo Riko Labs have created a robotic bear which is capable of providing care to elderly patients, which can lift a patient from standing position or from the floor, transfer a patient to a wheelchair, carry a patient from point A to B, and turn patients in bed.

- Robot Paro: - A seal-like robot which is used in hospitals world over. It stimulates interaction between patients and caregivers and helps to relax patients by imitating the voice of a baby harp seal.

  Additionally, it adapts to patient behavior in part through its five sensor types: light, audio, temperature, posture, and tactile. Overall, this robot helps to reduce patient stress, improve their relaxation and motivation, and improve their socialization with caregivers and their peers.

- Robot pepper: - A humanoid robot used in the reception area of two Belgian hospitals for greeting people and guiding patients to their proper department. It can recognize 20 languages and can identify gender, and can identify joy, sadness, anger, and surprise. It can also interpret non-verbal cues like head tilts, frowns, smiles, and shifts in vocal tones.

Robotic nurse during COVID 19 in India

- The Government Stanley Medical College Hospital had introduced the "robot nurse" to reduce the number of times a healthcare provider, especially a staff nurse, interacts with a COVID 19 patient. The robot delivered food, water and medication to patients admitted to the COVID-19 ward in the hospital. The robot was put on trial for a few days at the hospital, and a staff nurse, who was posted at the ward, was trained in operating the robot. A government hospital in Jaipur introduced the humanoid robot which made its way to assigned patients with a tray carrying food or medicines.

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- V2 Buddy, the Nursing Robot, was used to assist nursing interface by checking the body temperature of Covid-19 patients, dispensing sanitizing hand rub, delivering medicines and food, and enabling the nursing staff to interact with Covid-19 patients remotely through video and audio interface from their nursing stations. A voice-enabled nursing call facility was also made available through a V2 Buddy Call through which the patients in isolation could speak to nursing staff in the nursing station whenever required for clinical support and counseling. One of the projects being undertaken at the Artificial Intelligence and Robotic Technologies Park, which has been set up at the Indian Institute of Science in a public-private model is development of 'Asha', a robotic nurse. The robot, which has a human-like face, is capable of showing real emotions — it can smile, make lip movements while talking, blink, make hand gestures and speaks in a female robotic voice.

Advantages of robot nurse

1. Robots are programmed to accomplish routine nursing tasks dictated solely by prescribed procedures, thereby reducing the human staff's perception of workload and stress.

2. Robots can perform increasingly sophisticated task (what humans do) more efficiently, quickly and at a lower cost and are quicker to train.

3. Robots can help to schedule tasks during nursing shift and prioritize care with the click of a button.

4. Robots can help with patient transfers, ambulation, and lifting which will significantly reduce physical stress on nurses and allow nurses to more efficiently use their hours at work.

5. Robots are programmed with algorithms that reduce calculation errors to virtually zero, so it will eventually be safer to double check medications with a robot – even chemotherapy and blood products.

6. Robotic nursing will be used as a platform for patient education as well. In hospitals, outpatient settings, and at home, patients will be able to access hundreds of videos outlining medication uses, side effects, disease management, support group, emotional support hotlines, and all at the blink of an eye in any language.

7. Robot nurse will be able to help with discharge planning and procedures which will make it easier and quicker.

8. Robot nurse will be integrated into all hospital technologies and monitors so that nurses and doctors can detect early and more accurately signs of patient decompensation which will lead to improved patient health outcomes.

9. Robots will have the ability to triage patients in clinics, emergency departments, and via telehealth services in order to streamline care and provide standardized approaches to symptom management with far fewer resources.

10. Robots can transcribe and store crucial medical information minimizing the possibility of error as well as helping doctors and nurses to diagnose patients and even assisting lower-skilled health workers to administer treatment to patients with less input from doctors or other higher-skilled professionals.

11. Robots have been found to help elderly combat loneliness, and with increased use, they can help stabilize mood and give support to a variety of patients with mental illnesses.

12. Robots can help older adults and chronically ill patients to remain independent, reducing the need for careres and the demand for care homes. They may

also serve as a companion to patients who have a few or no visitors by entertaining them.

13. Robots can efficiently address cognitive decline issue by reminding care-receiver when to eat, or drink or take medication, do exercise or attend an appointment.

14. With fewer burdens on nurses and improved quality of care for patients, collaboration with nurse robots will improve current trends of nursing shortages and unsafe patient ratios.

Disadvantages of robot nurse

1. Nursing is an expression of genuine caring and not just fixing a person physiologically. This is purely a human trait, and in matters of emotional support, robotic nurses can never outperform human nurses. No matter how well-programmed, robots lack common reasoning ability and empathy.

2. Robots can only do the specific algorithm built up in them, so when faced with a new unusual situation, they may put a patient's life in danger by taking time to respond or giving a wrong response.

3. A potential con of robotic nursing is the ability for intelligent online hackers to infiltrate the healthcare databases and gain access to sensitive private information.

4. Use of nurse robots is considered an invasion taking away jobs from human nurses.

Conclusion and Implications

While it need not be a case of pitting human nurses against the robotic ones, it should be more of a symbiotic relationship prioritizing the universal aspects of healthcare and wellness. Establishing a middle ground will help in maximizing the benefits for both patients and the nursing staff.

The nursing education will need to revamp its curriculum by incorporating research on the effects of technology and machine learning specific to the nursing profession, with a focus on leveraging AI technology to aid human healthcare personnel. Nurses will need to learn how to adapt to robotic co-workers and develop skills to direct and manage them. So, in the years to come, nursing education and research will undergo a transformation to encompass a metamorphosed demand for professional nursing practice with, and not for robots in healthcare.

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PPH Butterfly: a novel device to treat postpartum haemorrhage through uterine compression.

*Lt Col (Asso.Prof.) Regina**

Source: Caroline Cunningham, Peter Watt, Nasreen Aflaifel, Simon Collings, Dot Lambert, John Porter, Tina Lavender, Tony Fisher, A.n,drew Weeks, Original Article: PPH Butterfly: a novel devise to treat postpartum haemorrhage through uterine compression, BMJ Innov 2017;3:45-54

- Postpartum haemorrhage (PPH) is a significant cause of maternal morbidity and mortality. The most common cause is an inability of the uterus to contract adequately after childbirth. In bimanual compression (BMC), one hand is placed within the vagina and the other hand is on the abdominal wall to compress the uterus. It is effective, but very uncomfortable for the woman.

- We designed a device that could replicate BMC without inserting a hand vaginally, therefore being less invasive. It could also help in diagnosing the source of the bleeding.

- A multidisciplinary team developed the design, using an obstetric manikin. Clinician and consumer groups also gave input on the concept and design. A healthcare product company and prototype manufacturer provided input into strategy, design and manufacture.

- The PPH Butterfly is a single piece, plastic medical device that replicates BMC. It is designed to be easy to use and low-cost and allows for smooth insertion and removal. It is acceptable to clinicians and consumers and performs well in tests.

- Conclusions This is the first device designed to replicate BMC while being less invasive. It could potentially be an effective form of PPH management, while also diagnosing the source of the bleeding. The device will now be tested in humans.

- Postpartum haemorrhage (PPH) is an obstetric emergency that can follow vaginal or caesarean delivery. It is esti mated that each year PPH accounts for 27% of the 303 000 maternal deaths worldwide and a further 20 million women suffer long-term effects.3 Although the absolute risk of death is much lower in high-income countries (1 in 100 000 vs 1 in 1000 births in low- income countries), and in spite of marked improvements in management, PPH remains a significant contributor to maternal morbidity and mortality throughout the world.

- A vital step in the physiological prevention of PPH is the immediate contraction and retraction of myometrial muscle fibres during and after the third stage of labour. Uterine atony is a condition characterised by the inability of the uterus to contract adequately after the placenta has separated from the uterus. This condition is thought to be the most common cause of PPH6 7 and is often unpredictable.

- THE THEORY BEHIND THE DEVICE

- Bimanual compression (BMC) is an old technique in which the uterus is compressed between a hand on the lower abdomen and a hand inserted into the vagina and formed into a fist. Although it is highly effective, it is a very painful manoeuvre for the mother (unless she has an epidural in place) and tiring for the practitioner. The idea of the Butterfly device is to achieve the benefits of BMC without being so invasive, thus allowing it to be more widely used. It has been designed to be a slim, easily insertable

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replacement to a fist in the vagina, thus increasing acceptability of uterine compression to women and clinicians.

- The size and shape of the compression platform was based on that of a shelf pessary, an intravaginal device used for treating uterine prolapse. The depth of insertion was based on the length of a standard Cusco's vaginal speculum (figure 1—shelf pessary and Cusco's speculum combined). This should make uterine compression available for use at a much earlier stage in the PPH treatment process and provide an effective treatment without the need for medicines or advanced diagnostic skills (figure 2).

- The PPH Butterfly was invented by Professor Weeks and John Porter, with the intellectual property held by the University of Liverpool.Once inserted, the uterus is compressed against the PPH Butterfly by a hand externally on the woman's abdomen. The device will be held in place by its handle, which can be wedged against the bed, or be held by the clinician or an assistant

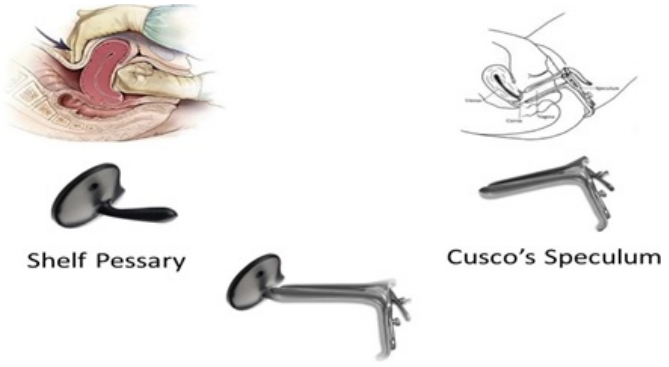
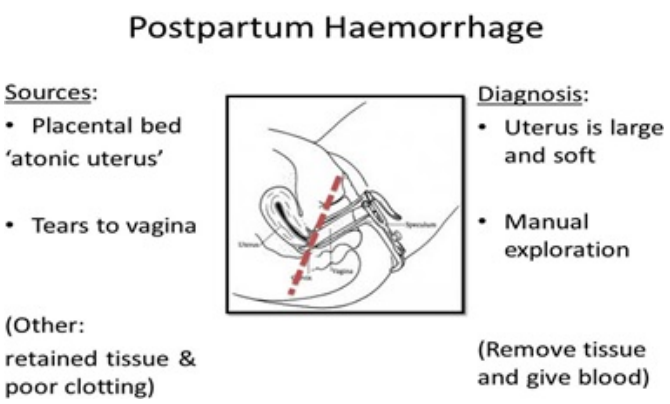


Figure 1 A composite picture combining a shelf pessary (used for the treatment of uterovaginal prolapse) and a Cusco speculum (used for vaginal and cervical examination).

Figure 2: The platform of the PPH Butterfly rests just beneath the uterine cervix (shown as a red dotted line above). Bleeding from above the red line is usually due to uterine atony and will stop abruptly with uterine compression. That from below the red line is from vaginal lacerations and blood loss will continue even with uterine compression. PPH, postpartum haemorrhage



- This is the first device designed to replicate BMC while being less invasive. It could potentially cbeing less invasive. It could potentially be an effective form of PPH management, and also in diagnosing the source of the bleeding.

Fig 3The final design of the platform.

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TRENDS IN NURSING DURING COVID 19 PANDEMIC.

*Mrs. Dixy Domini**

According to the World Health Organization (WHO), there are 20.7 million nurses worldwide. Yet that number is still not high enough. There is a global shortage of nurses and 18 million more jobs are needed to be filled by 2030 in order to meet the requirements of universal healthcare for everyone. As the nurse shortage grows steeper and the health care landscape continues to change, nurses and their leaders should be attentive to the trends that are changing the industry. With the distinguished honor of the World Health Organization deeming 2020 the Year of the Nurse and Midwife across the globe it is the time and how that will change in the future.

Self-Care for Nurses

Self-care is a deliberate activity that we do to provide for our physical, mental, and spiritual well-being. Lack of self-care can lead to errors, fatigue, and burnout, which comes at a high cost to patients, nurses and the healthcare organization. As more and more research and data come out about the physical and mental strain of nursing, healthcare leaders around the world are taking initiative to acknowledge and treat self-care as an actual responsibility. Self-care can look different for every nurse. A self-care plan should be specific, measurable, achievable, action-oriented, and time-sensitive.

Rise of the Nurse Navigator

Nurse navigators are nurses who use their medical knowledge along with their management and people skills to guide patients through their health care journey. They help patients navigate the health care system and take holistic approaches to improving their overall quality of life. The navigator specifically helps the patient with smooth transitions and care. They help patients understand what's happening to them—the tests, the diagnosis, the medicine, all of the care that they need. This role has gained importance as the population ages and chronic health conditions become more prevalent.

Expanding Entrepreneurship Opportunities

Entrepreneurship is a trend in nursing that's on the rise. There are many opportunities for nurses to set up their own businesses. Nurse navigators and nurse practitioners, who provide direct services to patients, are two examples. This is particularly important in rural areas that need services. Those areas are ripe for having nurse entrepreneurs go in and set up a business.

Traveling Nurses

As time goes on, more parts of the world become alike and nursing has become an increasingly travel-friendly profession. Nurses who enjoy adapting to different work environments and traveling to new places while taking care of people are on the rise.

The rise of Telehealth and Chat Bot Services

To aid with nurse task automation and easier access to patient care, new telehealth and chatbot technologies have become increasingly more popular. Telehealth technology allows patients to access their documents and doctors from home, giving them more control of their own health care. Online portals can be filled with test results, prescription refill requests, and appointments. Doctors or nurses can be accessed via virtual appointments, saving both patients and clinicians valuable time. Similarly, chatbot services have been introduced to give patients more ownership. Patients can schedule appointments, set reminders for medication administration and search for specialists in their area.

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Online nursing education programs will become more popular

Because of the demand for nursing, there is high job security in the profession and a high need for further education. More colleges and universities are providing online education programs, specifically in nursing. An online education provides a way for nurses to obtain a degree while working full-time and provide a way for nurses to access higher education set at their own schedule.

Salaries and benefits will need to increase

Because of the global shortage of nurses, employers want to learn what nurses value and what keeps them satisfied. Salaries and benefits will continue to increase in order for employers to retain employees and attract potential candidates.

Bilingual nurses will be in more demand

Specifically, in the U.S., bilingualism is becoming increasingly valued. More than 350 languages are spoken across the states. Nurses who speak a second language, especially Spanish, are increasingly in demand in 2020.

Holistic Care will become more popular

As patients become more educated, they become more in charge of their health. This has resulted in a growing demand for nurses who provide holistic services. Educated nurses who are trained in providing care and managing health procedures are an ideal candidate for providing holistic services to patients.

Nurses will need to be technology savvy

Every day new health care technologies enter the market. Nurses are required to adapt to these technologies in order to improve patient care. Technology is introduced to reduce administration time, increase accuracy all keeping clinician satisfaction and the patient experience in mind. Nurses are expected to use computer technology to document and obtain patient information, and even look up treatment options when necessary. Intuitive workstation on wheels are becoming increasingly more popular.

Value-based care is the new model

The goal of value-based care is to improve health outcomes at a lower cost. The patient experience and what they value is at the forefront. Because of this, facility resources are allocated to the health outcomes delivered by the system. Quality, safety, and patient experience will greatly be taken into consideration while making decisions.

Patients will become more educated

Patients more educated about their health. Patients know the importance of a good diet and exercise. They have the World Wide Web at their fingertips and day in and day out hear from pharmaceutical companies on which medications could work for them. Nurses are faced with the challenge of being able to take this information and communicate with more educated patients.

Increased Specialization and Career Path Options

Healthcare needs are becoming increasingly complex. As a result, the scope of specializations that nurses are able to practice is widening. A nurse who specializes is in higher demand than the lower ones. As the world continues to grow, and more research and technological advancements come out, nurse career path options become endless.

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Innovative Utilization of Augmented Reality and Simulation to Promote Nursing Practice

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Relevance

The health challenges facing the nation have shifted dramatically during Covid 19 pandemic. Many of the modes of education for nursing that were predominant during the 20th century is no longer considered adequate to address the realities of health care in the 21st century. As patient needs and care environments have become more complex, nurses need to attain requisite competencies to deliver high-quality care.

Currently there are no realistic training facilities for certain procedures, for eg. obstetric forceps delivery, newborn cannulation etc. Dummy models do exist but do not exhibit sufficient realism hence novices are forced to receive crucial training on patients. A feasible alternative to the current training procedures is the use of either simulation or augmented reality technology in combination with haptic feedback.

Simulation

- Simulation is an activity or event replicating clinical practice using scenarios, high-fidelity manikins, medium-fidelity manikins, standardized patients, role playing, skills stations, and computer-based critical thinking simulations"-has become an integral part of nursing education and practice.

- Simulation helps to develop competences for professional practice.

- The use of human patient simulation as an instructional strategy can enhance patient safety and optimize outcomes, providing a means of allowing nursing students to "practice" critical thinking, clinical decision making, and psychomotor skills in a safe, controlled environment, without potential risk to a live patient.

- Scenarios using simulation provide important lessons about the importance of documentation, particularly in fast-moving critical care cases.

- Students who have the opportunity to develop clinical practices in a simulated environment report an increase in confidence as they were able to transfer significantly the knowledge learned in the classroom to the simulated environment.

Augmented Reality

- Augmented reality (AR) is the real-time use of information in the form of text, graphics, audio, and other virtual enhancements integrated with real-world objects.

- Augmented reality bridges the gap between the real and the virtual in a seamless way. This allows for additional information about the object or environment to be provided to the user.

- It supports enhanced self-learning, automated tutoring, widespread deployment and accessibility, cognitive decision making, and communication through dialogues.

- AR-enabled, tablet-based simulations of different patient scenarios allow nurses to better connect with patients (e.g., SimMan) and handle daily work situations requiring a combination of social, technical, and team skills.

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Health Care-Focused AR Apps

- AccuVein uses augmented reality by using a handheld scanner that projects over skin and shows nurses where veins are in the patients' bodies.

- Google Glass might help new mothers struggling with breastfeeding.

- EyeDecide — Uses a smartphone camera to simulate the impact of various disorders on a person's vision to educate patients with cataracts and age-related macular degeneration.

- Virtuali-tee T-shirt, through which you can see the inner parts of the human body through realistic holograms.

- HoloAnatomy to visualize the human body in an easy and spectacular way.

- Anatomy 4D — Gives medical professionals, students, and teachers an interactive, 4D understanding of the human anatomy with respect to spatial relationships of organs, skeleton, and muscles.

- With the help of AR, patients can see how the drug works in 3D in front of their eyes instead of just reading long descriptions on the bottle.

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Effectiveness of structured training program on prevention of female foeticide

*Dr.Sr.Merly **

Relevance

Contemporary Indian society professes a profound faith in every individual's right to life and dignity. The rights relating to the weaker and vulnerable sections of Indian society especially women and girl children are violated. The rejection of the unwanted girl children begin even before their birth. Female feticide is a reality in many societies and in such societies the unborn females are subjected to silent deaths inside the womb itself. The present study is carried out to evaluate the effectiveness of structured training programme regarding the prevention of female feticide on knowledge and attitude of nursing personnel and Accredited Social Health Activists (ASHAs).

- The study was conducted in primary health centres of Faridabad district of Haryana among 326 nursing personnel and ASHAs (160 in control group and 166 in interventional group).

- The instruments of data collection include a self developed self administered knowledge questionnaire to assess the knowledge regarding female foeticide and a likert attitude scale to assess the attitude of participants towards female foeticide.

- The structured training program include teaching regarding different aspects of prevention of female foeticide focusing on its consequences and a short film – 'JEENANNIDHI'- which was prepared by the investigator inorder to sensitize the nurses and ASHA workers regarding prevention of female foeticide. An in-depth interview was conducted for every 10th participant to assess the perceptions of nursing personnel and ASHA workers regarding female foeticide. All the measurements were carried out once before and twice after the structured training program.

- The comparison of the mean score of the knowledge of the nursing personnel and ASHAs in the control and interventional group during the pre and the post-assessments show that the 't' value calculated was significant during post- I ($t= 20.816$, $p<0.001$) and post-II ($t=36.307^{**}$, $p<0.001$). This shows that the training program is effective in improving the knowledge of the nursing personnel and ASHAs regarding the prevention of the female feticide.

- There was statistical difference between the pre and post assessments of attitude of nursing personnel and ASHAs and it shows that the training program was effective in changing the mindset of the participants towards the prevention of female foeticide.

- Thematic analysis was done to analyze the perceptions of nursing personnel and ASHAs regarding prevention of female foeticide. All the participants had the opinion that the main reason for son preference is that the 'boy carries the name of the family'. Among the participants, 50% of them opined that the reason for female feticide is dowry.

- Among the suggestions given by the participants for preventing the female foeticide, 87.5% of the participants opined that the doctors should stop the detection of the sex of the baby and (87.5%) expressed the need for providing awareness to women. The response of

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56.25% of the participants reveal that they wish to stop female foeticide at any cost.

- The short film, 'JEEVANNIDHI' prepared by the investigator was broadcasted in Good TV channel on 15th August in consecutive years after getting the permission of the investigator. It is uploaded in the YouTube channel named 'Laverna Waves'.

- The Medical officers from the other PHCs and CHCs, which were not included in the study, requested to impart this training program in their centres too. The investigator trained a team of experts from the local area to implement this project, providing the tools and instruments of the study and they implemented the program. The short film was used to sensitize the people in many states of India by many missionaries and village health workers especially in rural areas of M.P and U.P.

- The training programme is effective in making a change in the knowledge and mindset of the nursing personnel and ASHAs towards female feticide.

Qualitative analysis of Nursing personnel and ASHAs regarding their perception about female foeticide reveals that they are sensitized about this pressing issue and are ready to become the channel of communication to the public for the prevention of female foeticide.

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COVID-19 Vaccines: Virus Evolution and Objective Truths

*Sisamma Sebastian**

Introduction: The World Health Organization declared the COVID-19 outbreak a pandemic in March 2020. The novel corona virus pandemic has left an indelible mark on humanity of all ages and has severely ravaged health systems affecting economic as well as social progress globally.

- **Evolution of the virus:** Since the SARS-CoV-2 the virus that causes COVID-19 have been identified, variants have emerged and been identified in many countries around the world. An early mutation was called **Alpha** which spreads at least 50% faster than earlier circulating lineages. Around the same time another mutation-laden variant called **Beta** was traced. Not long after, a highly transmissible variant called Gamma, was tracked. Whatever their origins, all three variants seemed to be more infectious than the strains they displaced. But Beta and **Gamma** also contained mutations that blunted the potency of infection-blocking 'neutralizing' antibodies triggered by previous infection or vaccination. The **Delta** variant identified was about 60% more transmissible than Alpha. **Omicron** variant that caused heavy death stall was largely due to its ability to infect people who are immune to Delta through vaccination or previous infection.

- **Vaccines for COVID-19:** Since the outbreak of COVID 19 the prominent countries have been making strenuous effort to develop vaccines for active immunization to prevent COVID-19 and for equitable protection of people.

  SARS-CoV-2, the virus that causes COVID-19, contains four structural proteins, that include spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins. Each type of vaccine prompts our bodies to recognize this protein and protect us from the virus that causes COVID-19.

Virus vaccines: These vaccines use the virus itself in a weakened or inactivated form.They contain dead virus, incapable of infecting people but still able to ***instruct*** the immune system to mount a defensive reaction against an infection.

Viral-vector vaccines: Viral vector vaccines use a modified version of a different virus (the vector, **not** the virus that causes COVID-19, but a different, harmless virus) to deliver important instructions to our cells. The viral-vector once inside our cells, make genetic material to give cells instructions to make required protein extensively which prompts our bodies to build T-lymphocytes and B-lymphocytes that will **remember** how to fight that virus if we are infected in the future.

Nucleic-acid vaccines: In these vaccines, nucleic acid (DNA or RNA) is inserted into human cells which produce copies of the virus protein and develop an immune response.

Protein-based vaccines: There are two types of protein-based vaccines against corona virus viz. protein-subunit vaccines and virus-like particle vaccines which use virus protein fragments or protein shells which are injected directly into the body. Protein-subunit vaccines include harmless pieces (proteins) of the virus that cause COVID-19 instead of the entire germ. Once vaccinated, our immune system recognizes that the proteins do not belong to the body and begins making T-lymphocytes and antibodies. Memory cells will recognize and fight the virus in any future possible infections too.

Vaccines produced and used in India

- BBV152or Covaxin: It is made up of killed

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corona virus, making it safe to be injected into the body. The vaccine can be stored at 2°C to 8°C.The two doses of 0.5 ml are given four weeks apart.

Side effects of covaxin vaccine may include injection site pain, swelling, redness and itching, stiffness in the upper arm and weakness in injection arm, body ache, headache, fever, malaise, weakness, rashes, nausea and vomiting. Covaxin can rarely cause severe allergic reactions signs of which include difficulty in breathing and fast heartbeat, swelling of the face and throat, rash all over the body, dizziness and weakness.

- Covishield: It is a viral vector vaccine known as ChAdOx1 nCoV-19 based on a weakened version of a common cold virus or the adenovirus that is found in chimpanzees. The Covishield vaccination course consists of two separate doses of 0.5 ml each. The second dose should be administered between four to six weeks after the first dose.The vaccine can be stored at 2°C to 8°C. Side effects with the covishield vaccine can be tenderness, a possible lump with pain, warmth, redness, itching, swelling or bruising etc. at the injection site, overall a feeling of unwellness, tiredness (fatigue) and nausea, headache and joint pain or muscle ache, flu-like symptoms such as chills, high temperature, sore throat, runny nose, cough and chills.

- **Sputnik** V: It uses a weakened virus to deliver small parts of a pathogen and stimulate an immune response. The product is administered intramuscularly. The vaccination is carried out in two stages: first, component I at a dose of 0.5 ml, then after 3 weeks component II at a dose of 0.5 ml. After the vaccine is administered, the patient should be monitored by a healthcare professional for 30 minutes.

- **Corbevax:** It is a recombinant protein sub-unit vaccine, developed from a component of the spike protein on the virus's surface, which helps the body build the immune response against the virus. Corbevax vaccine is administered through an intramuscular route with two doses of 0.5ml, scheduled 28 days apart and is stored at 2 to 80 C.

- **Prevention of COVID-19:** Infection from COVID-19 can be prevented by avoiding exposure to the virus. The virus spreads mainly from person-to-person through close contact. COVID-19 also spreads by asymptomatic people. The basic preventive measures include physical distancing, wearing of masks properly, hand and respiratory hygiene, prompt self-isolation, self testing and vaccination.

Relevance of the article

This article is intended to provide accurate scientific clarifications to the various anxieties prevailing among the public regarding COVID-19 vaccines which help increase their preparedness to welcome vaccinations.

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SCRUB TYPHUS

*JISHA P MOHAMMED**

Scrub typhus is **a mite-borne disease caused by Orientia tsutsugamushi** (formerly Rickettsia tsutsugamushi). Symptoms are fever, a primary lesion, a macular rash, and lymphadenopathy.

Who gets scrub typhus fever?

Scrub typhus fever occurs in people exposed to areas with scrub vegetation where rodents live, such as forest clearings, riverbanks, grassy areas, deserts, and rain forests, especially in parts of Asia and Australia. It is not seen in the U.S. except in travelers returning from areas where the disease is found

How is scrub typhus fever spread?

Scrub typhus fever is not spread from person-to-person. Disease is spread to people by the bite of a mite (also called a “chigger”) infected with the bacteria that causes scrub typhus fever.

What are the symptoms of scrub typhus fever?

Symptoms may include a sore on the skin with a “punched out” appearance (skin ulcer that becomes dark in the center) at the site where the mite attached. Several days after the appearance of the ulcer, other symptoms may develop which include fever, headache, sweating, blood-shot eyes, swollen lymph nodes, rash, lung infection, vomiting, and diarrhea. Symptoms can worsen and complications develop.

How soon after exposure do symptoms appear?

Symptoms usually appear within 10 to 12 days after exposure, but may appear anywhere from 6 to 21 days after exposure.
Could scrub typhus fever be used for bioterrorism?

Rickettsia prowazekii, the bacteria that causes a different form of typhus (epidemic typhus fever), is considered an agent that could be used for bioterrorism.

How is scrub typhus fever diagnosed and treated?

The diagnosis of scrub typhus fever is based on signs and symptoms of illness, as well as laboratory tests. It is important to tell your healthcare provider about travel to any countries where scrub typhus fever may occur. Scrub typhus fever is treated with antibiotics. Healthcare providers choose the antibiotic based on the patient’s symptoms and the results of laboratory tests.

Is there a vaccine for scrub typhus fever?

There is currently no commercially available vaccine for scrub typhus fever.

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What can be done to prevent scrub typhus fever?

When visiting or working in areas where the disease occurs, take steps to avoid being bitten by a mite, such as by wearing long sleeves, not sitting directly on the grass, keeping your clothes off the grass, and using insect repellents applied to the skin and clothing containing dibutyl phthalate, benzyl benzoate, diethyl toluamide. In certain rare circumstances, antibiotics might be prescribed to prevent scrub typhus in areas where the disease is more common.

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Covid-19 and Cytokine Strom.

*Sherin A**

1. Covid-19 was first reported in the Wuhan province of China. Due to the massive outbreak of the disease, WHO announced that Covid-19 is a pandemic. Like SARS and MERS, SARS CoV-2 is a highly pathogenic coronavirus.

2. The ability of the coronavirus to establish a hyperimmune response called cytokine storm in the host is characterized by systemic inflammation, hyperferritinemia, hemodynamic instability, multi-organ failure CNS abnormalities and even death.

3. Cytokine storm became an immediate subject in 2020 after 10 years of its initial narration with chimeric antigen receptor (CAR)-T cell therapies for leukaemia and lymphoma, due to Covid-19.

4. Cytokine storm is a life-threatening aggressive immune response. It is due to elevated levels of cytokines, chemokines and immune cell hyperactivation which may be due to infections or challenging the immune systems with an organ transplant or therapies.

5. Conditions like juvenile idiopathic arthritis with or without macrophage activation syndrome, Still's disease, systemic lupus erythematosus, sepsis-associated with Influenza, Covid-19 & Epstein Barr virus and hereditary diseases like familial hemophagocytic lymphohistiocytosis are some conditions that cause cytokine storm.

6. SARS Cov-2 attacks alveolar type -2 endothelial cells which have high expression of angiotensin-converting enzyme II (ACE2) proteins on its surface and uses these receptors for cell entry.

7. ACE 2 proteins are also found in vascular endothelial cells, intestinal epithelial cells, cardiomyocytes and renal proximal tubule cells. This wide distribution helps to worsen cytokine storm by producing large quantities of inflammatory mediators.

8. The spike protein priming is done by Transmembrane serine protease (TRMPSS2) and the endosomal cysteine proteases cathepsin B and L (Cat B/L). Invitro experiments show that SARS Cov-2 will not bind with cells which are lacking ACE-2 receptor.

9. After the priming, the ACE 2 receptor-spike protein complex is endocytosed into the cell. This process will reduce the number of ACE 2 proteins on the surface.

10. ACE 2 converts Angiotensin 2, a vasoconstrictor as well as a proinflammatory cytokine, into Angiotensin 1-7 (vasodilators). Binding and endocytosis cause the downregulation of ACE 2 protein. This increases the serum concentration of Angiotensin 2.

11. Angiotensin II binds with Angiotensin II type1 receptor (AT1R). This complex causes the activation of nuclear factor (NF-κB), disintegrin & metalloprotease 17(ADAM17). ADAM 17 induces the production of other two NF-κB activators-mature from of Epidermal Growth Factor Receptor (EGFR) and Tumour Necrosis Factor Alpha (TNFα).

12. ADAM 17 mediates the conversion of membrane form of interleukin-6α (IL-6α) to soluble interleukin-6α (sIL-6α). Formation of the IL-6α- sIL-6α complex is mediated by glycoprotein 130(gp130) and

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(STAT3) in nonimmune cells like fibroblasts, endothelial cells, and epithelial cells.

13. Another pathway to release proinflammatory cytokines is through the activation of T helper 1 lymphocytes. These cells can induce the secretion of granulocyte-macrophage colony-stimulating factor (GM-CSF) and IL-6.

14. CD14+ and CD 16+ cells secrete IL-6, Tumour Necrosis Factor-α (TNF-α) and other inflammatory cytokines mediated by GM-CSF.

15. Another type of immune response is triggered by the activation of membranous receptors like Toll-like receptors and Fc receptors producing a shattered immune response.

16. All the above steps activate 1l-6 amplifier (IL-6 Amp), which activates different cells to produce proinflammatory cytokines, chemokines and induce the migration of T lymphocytes, macrophages and neutrophils. All these attributes of hyperimmune response leads to cytokine release syndrome.

17. Inflammation of the lung epithelium causes acute respiratory distress syndrome (ARDS), hemodynamic instability causes disseminated intravascular coagulation, multi-organ failure and death.

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CELL MEMBRANE-BASED NANOPARTICLES (CMBNPs) IN CANCER THERANOSTICS.

ABDUL VAJID K*

Relevance

Cell membranes are endlessly imitated and used for the modification of nanoparticles (NPs) to enhance NP biological properties. Cell membrane-coated NPs, where core nanoparticles are wrapped with cell wall vesicles, show high biocompatibility, targeting specificity and low facet effects. Compared with typical ways, this novel approach directly leverages intact and natural functions of cell membranes, rather than replicating these options via artificial techniques. This top-down technique bestows NPs with increased biointerfacing capabilities with potential within the diagnosing and treatment of cancer, infection and different diseases.

Introduction

In the early Eighties, cells were exploited as carriers to deliver medication or nanoparticles, which considerably increased the retention and targeting potency of those medications. Though the employment of live cell-based carriers flourished, some deficiencies stayed. One among major concerns is that the activity of traveler medication, since medication is also digestible by the lysosomes of the cell carrier. Moreover, it's troublesome to regulate the discharge of drugs, which can be leaked or exocytosed throughout transport. Confronted with these issues, scientists have recently found a clue from nature to design biomimetic, cell membrane-based nanoparticles (CMBNPs).

Initially, the first CMBNPs were made-up from a red vegetative cell (RBC) membrane shell and a poly (lactic-co-glycolic acid) (PLGA) core, via a co-extrusion method, forming a core-shell structure. Afterwards, numerous CMBNPs are explored with the flexibility of selecting completely different membrane materials and different nanoparticle cores. The translocation of a natural cell wall to a synthesized NP will mix the benefits of a biomimetic cell wall surface and therefore the tailored flexibility of fabric chemistry. One among the foremost necessary profits is that the CMBNPs will be disguised as autogenic cells, thus on escape system elimination and prolong the circulation time within the blood that is very necessary for the improved porousness and retention (EPR) impact for growth targeting.

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Types of CMBNPs

1. Red vegetative cell membrane-coated nanoparticle
2. White blood corpuscle membrane-coated nanoparticle drug delivery system
3. Neoplastic cell membrane-coated nanoparticle
4. Blood platelet membrane-coated nanoparticle

Applications

Since the NP cores are artificial materials, these will be custom-made to be used as theranostic materials to function vehicles that carry imaging and therapeutic moieties.

1. Diagnosing Cancer Imaging
2. Phototheranostics
3. Therapy Drug Delivery
4. Cancer Nano vaccines

Conclusions

The CMBNP has shown the potential to considerably improve the operation of current nanoparticle systems in cancer medical aid. It will possess each distinctive function exhibited by totally different cell sorts and versatile styles derived from numerous cores. CMBNPs aren't restricted to the four

sorts that we have a tendency to review on top of. Microorganism membranes, vegetative cell membranes and different bio-functional membranes are explored for making ready CMBNPs in succession. The development of recent kind CMBNPs could further enrich targeting methods.

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Alternatives to Animal Experiments in Education and Research – An Update

Dr.Sutharson.L *

In Drug discovery approaches Animal studies are highly inevitable during 19th and 20th century. The first Nobel Prize in 1901 in medicine was for serum therapy and research involving use of horses. The latest 2014 Nobel laureates in physiology or medicine also worked on animals (1). Earlier, In India Medical colleges and Pharmacy colleges for both UG and PG Pharmacology Practical students are allowed to use animals like rodents mice, rats, rabbits and guinea pigs as per curriculum. But In 2011 University Grants Commission (UGC) followed by in 2014 Pharmacy Council of India (PCI) and Medical Council of India (MCI) made complete ban on animal experiments and recommended alternatives for Education and Research where ever possible(2). The Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) is a statutory Committee, which is established under Chapter 4, Section 15(1) of the Prevention of Cruelty to Animals Act 1960 regulating the usage of animals for research in India.

Alternatives to Animal Experiments:

4R principles are the basic ethical guidelines **R**eplacement, **R**eduction, **R**efinement and **R**ehabilitation and of animals used in experimentation.

Replacement: Replace animals wherever possible with other alternatives like tissue culture, Computer assisted

Reduction: Methods to minimize the no of animal usage by better study design and statistical analysis and modern imaging techniques, avoiding repetitions of tests.

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Refinement: It means improved control of pain which minimize actual or potential pain, suffering and distress using appropriate anesthetic and analgesic regimes for pain relief

Rehabilitation: Rehabilitation of the animals after their use

Steps in designing valid alternatives:

Step 1: Defining an alternative
Step 2: Developing the alternative
Step 3: Validating the methods
Step 4: Acceptance in scientific community

Examples for Alternatives:

1. In-vitro studies: Tissue culture/Cell culture, The Organization for Economic Cooperation and Development (OECD) has approved several tissue culture methods which measure the rate of chemical absorption by the skin

2. Computer Assisted (In-silico): Computer models can simulate different experiments within minutes compared to tedious animal models although with some shortcomings. Quantitative structure-activity relationship (QSAR) models are easier to use as compared to wet laboratory processes.

3. Microorganisms:
   Prokaryotes
   Escherichia coli- Model for molecular and genetic studies
   Bacillus subtilis- Model for cellular differentiation
   Fungi
   Neurospora crassa -Model for genetic study, circardian rhythm and metabolic regulation studies
   Saccharomyces cerevisiae,Schizosaccharomyces pombe - Model for molecular and genetic studies

4. Invertebrate animals: The most used invertebrate species are Drosophila melanogaster, a fruit fly and Caenorhabditis elegans, a nematode worm. Drosophila melonogaster is a classic model used for detecting mutagenicity, teratogenicity and reproductive toxicity.

5. Rapid developing vertebrates: Zebra fish has proven to a very good model for toxicity testing

6. Micro dosing: Microdosing studies enable potential new drugs to be tested safely in humans using ultra sensitivity of accelerator mass spectrometry in Phase 0 Trail.

Currently, over 50 alternative methods have been validated and approved by regulatory authorities. In a recent study conducted shows the students preference of computer-simulated model (CSM) than live animal experiments (LAE)(3). Human Organoids consist of so-called epithelial cells -- a cell layer serving as barrier between the content of the bowels including the enteric flora, scientifically known as "microbiota," and the inside of the body. In the recent studies, how the transport of nutrients and drugs and the subsequent metabolic changes can be measured in organoids has been evaluated successfully (4). In the Current scenario Pharmacology Practical experiments of UG, PG and Drug Discovery Research in the scientific arena move towards alternatives to animal experiments in the ethical perspective as well as for cost effectiveness.

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Cell-Penetrating Peptide – Oligonucleotide hybrids for antisense therapy

*Mrs. Ayswarya K**

Relevance

- Over the past 2 decades, the antisense technology has emerged as a valid approach to selectively modulate gene expression. Antisense Oligonucleotides (AONs) are used to treat diseases such as cancer, viral infections, inflammatory and genetic disorders etc. Pharmacological applications of AONs have been hindered by the inability to effectively deliver these compounds to their site of action. One solution is peptide-ON hybrids in which a receptor-specific cell targeting peptide is attached to the AON. The investigation of Cell Penetrating Peptides (CPPs) as delivery vectors for AONs is still in its infancy and peptide-ON hybrids are soon likely to become a mainstay of therapy and will soon be available for the routine care of patients and are expected to prove to be effective, specific agents with favorable therapeutic profiles.

Introduction to oligonucleotide based antisense therapy

- Oligonucleotides (ONs) are chemically modified, short, single-stranded DNA molecules resulting from a linear sequence of 13-25 nucleotides in length, designed to be complimentary by Watson-Crick hybridization to a specific mRNA, thus inhibit its expression & block the transfer of genetic information from DNA to synthesize a protein. They down regulate the expression of disease causing proteins by inhibiting gene expression at the level of mRNA. It is first effectively used in plants to alter the levels of enzymes, plant pigments etc.

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'Science' journal recognized it as runner-up in the 'molecule of the year' award in 1992. They represent promising therapeutic tools for cancer, viral infections, inflammatory and genetic disorders. First AON was fomivirsen (Vitravene) for CMV-induced retinitis in 1998. A growing number of companies are developing ON-based pharmaceutical products, majority of which are in various stages of clinical trials. AONs are designed with the right complementary genetic code to bind to a specific sequence of its mRNA target to form a short area of double strand. Produce 80-95% down regulation of gene expression. Classic drug based therapies target and block enzymes and receptors. Since one mRNA leads to several copies of the same protein, inhibiting mRNA should be more efficient than inhibiting the resulting protein.

Why CPP-ON hybrids?

- ONs are prone to degradation by nucleases and are also large and highly charged, and are not easily absorbed through cell membrane. The sugar-phosphate backbone has been modified to confer or enhance nuclease resistance so that ONs will remain intact longer to reach the target. An alternative is PNA (synthetic DNA analogues) in which sugar-phosphate backbone is replaced with 2-aminomethyl glycine linkage giving rise to a flexible, uncharged backbone. One of the major obstacles for antisense therapy is efficient delivery to and uptake into the target cells due to poor membrane permeability. Localize in endosomes/lysosomes. One solution to enhance the delivery is to conjugate ONs to appropriate CPPs.

- Advantages: Efficient blockade of protein synthesis, low doses are sufficient,

enhanced uptake into target cells, high specificity, fewer side effects.

Cell Penetrating Peptides (CPPs)

- Most work has concentrated on peptides designed to increase cellular uptake or confer nuclear delivery. Choice of peptide influences efficiency of conjugation and subsequent yield. They consist of 10-30 amino acids; possess basic amino acids causing a net positive charge at physiological pH. ONs can covalently or non-covalently bind to CPPs.

- Can be broken into 3 groups:

- Naturally occurring CPPs: originated from naturally occurring proteins.

- Chimeric CPPs: created through the joining of two or more genes which originally coded for separate proteins.

- Model CPPs: developed according to structure - function relationships.

References

1. Graham McClorey et al. (2018), Biomedicines, Cell-Penetrating Peptides to Enhance Delivery of Oligonucleotide-Based Therapeutics, 6(2), 51.

2. TaaviLehto et al. (2016), Advanced Drug Delivery Reviews, Peptides for nucleic acid delivery, 106 (part-A), 172-182.

Table 1. Sequences of selected classical CPPs.

Peptide	Sequence
Tat^{48-60}	GRKKRRQRRRPPQ
penetratin ($Antp^{43-58}$)	RQIKIWFQNRRMKWKK
transportan	GWTLNSAGYLLGKINLKALAALAKKIL
TP10	AGYLLGKINLKALAALAKKIL
Oligoarginine (R_8)	RRRRRRRR
MAP	KLALKLALKALKAALKLA
MPG	GALFLGFLGAAGSTMGAWSQPKKKRKV
MPGα	GALFLAFLAAALSLMGLWSQPKKKRKV

Table 2. Sequences of selected new CPPs.

Peptide	Sequence
hCT^{9-32}-br	LGTYTQDFNK*FHTFPQTAIGVGAP (-AFGVGPDEVKRKKKP; attached to K*)
SAP	$(VRLPPP)_3$
$S4_{13}$-PV	ALWKTLLKKVLKAPKKKRKV
mPrPp	MANLGYWLLALFVTMWTDVGLCKKRPKP
bPrPp	MVKSKIGSWILVLFVAMWSDVGLCKKRPKP
M918	MVTVLFRRLRIRRACGPPRVRV
CPP5s	VPMLK, PMLKE (human), VPTLK (mouse), VPALR (rat)
EB1	LIRLWSHLIHIWFQNRRLKWKKK

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Basic Tenets of KUHS

- Always Go by Rule Book
- Observe Sanctity of Examinations
- Be Student Friendly at all times
- Acknowledge the Right to be Heard
- Always Give Respect and Take Respect