# HAPPENINGS

## A KUHS PUBLICATION ON RECENT ADVANCES

**A SAMAGRAM INITIATIVE**

**Issue 4**

**January 2021**

## Message from Vice Chancellor

*I am happy to note that the Fourth 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

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## ‘Happenings’: A Publication from KUHS on Recent Advances

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| **1. Stream** | MODERN MEDICINE |
| **2. Specialty** | PATHOLOGY |
| **3. Date** | 07/12/2020 |
| **4. Title** | Next Generation sequencing – walk into personalised genetic era of personalised medicine |
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# Next Generation sequencing – walk into personalised genetic era of personalised medicine

**Relevance & Introduction:**

Genes are made of DNA which is a double helix made of sugar and phosphate with 4 types of bases – adenine (A), Thymine (T), Gnanine (G) and cytosine (C), which are linked in a specific way – A with T and C with G. The DNA molecules can make copies of itself and code for proteins, where each gene is a length of DNA that codes for a specific protein. These DNA molecules are tightly packed around proteins celled histones to make chromosomes which are 23 pairs in humans. Genome is a complete set of DNA, that includes all genes that are needed to build and maintain that organism and in humans, there are approximately 3 billion of base pair that reside in 23 pairs of chromosomes in nuclei of all cells.

A generic sequence is the complete list of nucleotides (A, C, G & T), which with the help of enzymes, m RNA and ribosomes produce and code for proteins. As these proteins make up the body structures and control chemical reaction and carry signals between cells, if a cell's DNA is mutated, an abnormal protein is produced which can lead to cancer and other diseases.

DNA sequencing is determining the exact order of the bases in a strand of DNA and there are many methods of genetic testing like PCR, Cytogenetics (Karyotyping and FISH), micro assays and gene expression profiling. DNA sequencing of which Next Generation sequencing (NGs) is a high through put sequencing method that enables sequencing of everything genomes and transcriptomes to DNA – Protein interactions. It can be paralleling sequence millions of clonally amplified molecules per run with reduced sample size in less time with low reagent cost and produce enormous amount of data.

Types and Application:

- Though the term genome was created in 1920 by Hans Winter from Germany, it was only in 1976 that Walter Fiers from Belgium established for the first two complete nucleotide sequence of a viral RNA genome (Bacteriophage MS2).
- It is one year later in 1977, that Fred Sanger completed the first DNA – genome sequence and it was in mid-1990's complete genome sequences of all three domain of life released.
- The original sequencing methodology known as ISI generation Sanger Chemistry used specifically labeled nucleotides to read through a DNA template during DNA synthesis.

This sequencing technology requires a specific primer to start the read at a specific location along the DNA template and record the different labels for each nucleotide within the sequence.

- Though after all technical innovations, the Sanger method reacted capacity to read through 1000 – 2000 base pair (bp), it cannot surpass 2 kilo base pair.
- In order to sequence longer section of DNA, a new technology called shot gun sequencing was developed during "Human Genome Project" in 2003, where generic DNA is enzymatically or mechanically broken down into smaller fragments and cloned into sequencing vectors in which cloned DNA fragments can be sequenced individually. The core philosophy of massive parallel sequencing used in Next Generation Sequencing (NGs) is adapted from shot gun sequencing, which is Venter et al 2003; Margulies et al 2005; Shendure et al 2005second degeneration DNA sequencing.
- Next Generation Sequencing like massive parallel sequencing have opened up the prospect of personal genome sequencing in a diagnostic tool and major step towards that goal was completion of the fill genome of James D Watson in 2007.
- Different methods of DNA sequencing are cloning by emulsion and bridge PCR, Ion Torrent Sequencing, Chain termination method (obtained from Sangers), Pyro sequencing, sequencing by ligation, solid phase amplification, shot gun sequencing and Next Generation Sequencing.
- NGs technology was DNA sequencing – by – synthesis repeatedly called massively parallel sequencing, where the read length is much shorter than that attained by Sanger Sequencing.
- There short reads are a major limitation in current technology as coverage is an important issue, which is number of short reads that overlap each other within a specific genomic region. Moreover, short reads can create many sequences that cannot be interpreted or wrapped to any reference DNA or be accurately assembled.
- Hence, third generation DNA sequencing which is single – Molecule long read native sequencing is under development and that will be very useful to detect epigenetic nucleotide modifications and smaller insertions and deletions.

- These new generation sequencing projects have picked up small genetic variants, single nucleotide variants (SNV), structural variants (SVS), copy number variants (CNV), deletions, duplications, insertions, inversions, translocation, repetitive sequence expansions, complex combinations, chip sequencing and cytogenetics.
- Hence the application of NGs helps in research, diagnostic and treatment settings as not only structural variants, functional variants are also detected.
- The major applications of NGs include Molecular Diagnosis for oncology and inherited diseases, whole genome sequencing, discovering non coding RNAs, defining DNA – protein interactions, Enabling metagenamics, mutation discoveries, RNA sequencing, pharmacogenomics, vaccinology and biomarker discovery.
- Few examples where NGs is useful in diagnosis & treatment is (1) EFFR mutation and ALK – EML 4 translocation in lung cancer, (2) BRAF mutation and microsatellite instability in colorectal cancer & (3) oncomine myeloid panel where hot spot genes, fill genes, fusion driver genes, expression genes and expression control genes are used which helps in picking up generic alteration and targeted therapy in myeloid malignancies like CML, AML, MDS, MPN, CMML & JMML.
- The current application of NGs in COVID – 19 testing detects 98 targets on SARS – COV – 2 for highly accurate detection and can produce 3,072 results in 12 hours on latest available platforms.

Future application of NGs:

Includes Somatic mutation detection, polymorphism in Mendelian disorders / HLA typing, targeted exome, Tumour DNA, microbial profiling, community characterisation, structural variants and the most fascinating library creation.

Conclusion:

NGs has capacity to sequence DNA at unprecedented speed and enabling unimaginable scientific achievements and novel biological applications. But the massive data produced by NGs also presents a significant challenge for data storage, analysis and management solutions. For example: It may show a genetic change or structural variation, which cannot be explained as those changes may not have been seen before. That will warrant testing of the family and long follow up of the patient and clinical significance is very difficult to explain to the clinicians.

Technical issues with NGs are we need (1) perfect bioinformatics methods for sequence alignment which need regular updation, (2) optical algorithms to detect structural variations, (3) backup Sanger sequencing as there will be several regions with inadequate coverage and (4) high upfront cost.

However, third generation sequencing will help us to compromise on diagnostic platforms which will in turn help with other treatment protocols and making personalised medicine will become a possible reality leading to personal generic era.

References:


(1) Acta Med litu 2017 – 24 (1), 1 – 11.

(2) J. Genet Genomics 2011 – March 20; 38 (3) 95 – 99.

(3) Internal Journal of molecular sciences 2011 (12).

(4) www.researchgate.net

(5) Venter et al 2003; Margolis et al 2005 and Shandure et al, 2005.

(6) Elaine R. Mardis (2008) the impact of next generation sequencing technology on genetics. Cell vol. 24 No. 3, 133-14.

(7) Elaine R. Mardis (2009): Next-Generation Sequencing Methods. Annu. Rev. Genomics hum genet. 9:387-402.

(8) Jorge S Reis-Filho (2010): Next-Generation Sequencing, Breast Cancer Research 2010, 11 (Suppl 3).

(9) Some websites – https://www.ncbi.nlm.nih.gov/pubmed

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

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|---|---|
| **12. Stream** | Modern Medicine |
| **13. Specialty** | Pathology |
| **14. Date** | 09/12/2020 |
| **15. Title** | **IgG4 –PROTECTIVE OR PATHOGENIC?** |
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# IgG4 –Protective or Pathogenic?

SOURCE: Original article

**RELEVANCE:**

IgG4-related disease (IgG4-RD) is a recently defined systemic inflammatory and fibrous condition of unknown etiology and multiple clinical presentations.

In the thyroid gland, a subcategory of Hashimoto thyroiditis (HT) with IgG4-rich inflammation was first discovered and named IgG4 thyroiditis by Yaqiong Li et al who conducted a study on the prevalence of IgG4 thyroiditis in Asian population.

Although recent studies demonstrated that IgG4 thyroiditis is a specific entity independent from IgG4-RD, recognition of this unique subset of thyroid disease has yielded important insights into understanding its pathogenesis and the development of novel therapeutic approaches.

**Introduction:**

- ✓ Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated fibro-inflammatory condition that often causes the formation of tumefactive lesions.
- ✓ One of the earliest manifestation of IgG4-related thyroiditis may be hypothyroidism, and although thyroid enlargement may not be palpable, it is visible in imaging studies. Later, the thyroid becomes enlarged and fibrous, which may even lead to compression-induced dysphagia and dyspnea. Riedel's thyroiditis and Hashimoto's thyroiditis are also part of the IgG4-RD spectrum

We present a recent case of IgG4 thyroiditis of a 47-year-old male who presented with hypothyroidism. Clinically and radiologically diagnosed as Hashimotos thyroiditis. Near total thyroidectomy was done and showed diffusely enlarged thyroid grossly which on histopathological and immunohistochemical examination diagnosed as IgG4 thyroiditis.

- ➢ IgG4-RD usually affects middle-aged to elderly individuals with a predilection for male sex. The clinical signs and symptoms are usually nonspecific, and depends on the site and numbers of affected organs and the severity of the disease.

- IgG4 antibodies are dynamic molecules that can alter their properties by spontaneous exchange of one of the two Fab fragments between individual immunoglobulin molecules.
- They can dislocate their heavy-chain dimers and subsequently bond half-molecule of one IgG4 with a different IgG4 half-molecule. This half-molecule exchange yields bi-specific antibodies that are capable to bind with two different antigens, but monovalent for each of them.
- This unique class of immunoglobulins G has been shown to play a role in inducing immune tolerance in chronic or recurrent antigen exposure.
- This property suggests a regulatory function of IgG4, but also show that specific exogenous antigens may induce a response by IgG4-positive B-cells.
- The role of endo- and exogenous specific antigens in the etiopathogenesis of IgG4-RD is currently a subject of studies and discussion.
- The response of IgG4-positive B-cells has been shown to be polyclonal, i.e. directed against multiple antigens
- Unlike autoimmune diseases, in IgG4 related diseases T helper 2 (Th2) cells and regulatory T-cells causes B-cell differentiation into plasma cells and subsequent IgG4 production
- The affected organs enlarge due to massive infiltration by inflammatory cells and, often, the formation of secondary lymphoid follicles.
- Increased immunoglobulin production by numerous plasma cells leads to hypergammaglobulinemia
- 30-50% of patients with IgG4-RD have a history of concomitant or past allergies as Th2-cells also induce an allergic response with eosinophilia and elevated serum IgE levels.
- Serum IgG4 levels exceeding 135 mg/dl are generally considered to be diagnostically significant.
- Approximately 70% of patients shows characteristic features include

1- elevated serum IgG4 levels

2- diffuse lymphoplasmocytic infiltrates rich in IgG4(+) cells

3- a “storiform” fibrosis pattern

*4*- obliterative phlebitis affecting various organs.

- Other than the typical histological appearance, immunohistochemical confirmation with IgG4 should be required as the number of IgG4+ plasma cells is more sensitive and specific than the serum IgG4 titer.
- It is also important to assess the proportion of IgG4-positive cells among all IgG-positive cells, which should be at least 40% in most organs.
- Recent studies indicate that the number of circulating CD38highCD27highCD19+CD20-CD22– plasma cells (short-lived immunoblots) is elevated in patients with IgG4-RD, including those with normal serum IgG4 levels.
- Although many experts agree to the fact that a high IgG4 level alone is no longer an independent diagnostic marker, it is still an important diagnostic clue as well as for assessment of disease activity in some patients.
- Though glucocorticoids are first-line therapy for active untreated IgG4-RD, it is observed that patients do not maintain responses as glucocorticoids are tapered. Recently rituximab a select B-cell depleting agent has been found promising in more effective disease control even in steroid-refractory cases.
- Moreover, the use of other steroid-sparing drugs has been suggested for remission induction and maintenance.

**Future:**

Despite intense studies, the pathogenesis of IgG4-RD remains unclear. A large number of IgG4(+) plasma cells can be observed in nonspecific chronic inflammatory conditions, also adjacent to neoplastic lesions with an inflammatory response, and in autoimmune inflammatory infiltrates.

Thus, the fundamental question about the role of IgG4(+) cells in the pathogenesis of inflammation, tissue damage, and fibrosis in IgG4-RD still remains unanswered.

Meanwhile, an accurate early diagnosis determines initiation of the effective glucocorticoids treatment, which helps prevent extensive fibrosis, with the resulting organ damage and, often dramatic, functional impairment.

**References:**


1- *Yaqiong Li1, Keiko Inomata2, Eijun Nishihara3, Kennichi Kakudo-IgG4 thyroiditis in the Asian population.* ***Gland Surgery, Vol 9, No 5 August 2020.***
2- *marta legatowicz-koprowska-IgG4-related disease: why is it so important?.Centr Eur J Immunol 2018; 43 (2): 204-208)*

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| | |
|---|---|
| **1. Stream** | Modern Medicine |
| **2. Speciality** | Pathology |
| **3. Date** | 27-12--2020 |
| **4. Title** | **AUTOMATED URINE SEDIMENT ANALYSERS** |
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## AUTOMATED URINE SEDIMENT ANALYSERS-the Principles/technology

- Urinalysis is one of the most common examinations performed in clinical laboratories, and it is frequently performed to screen for kidney and urinary tract diseases, as well as for cholestatic, metabolic, and hemolytic diseases.
- Manual microscopic sediment examination is time consuming, labour-intensive and lack standardisation.
- The first automated urine sediment analyser was introduced as the "Yellow Iris Urinalysis workstation" in 1985
- New generation analysers, based on different technologies, have been developed to automate microscopy. The main approaches for the auto-quantification and classification of urine particles are Fluorescence Flow Cytometry, which is based on staining particles, and the Digital Microscopic Image based technologies.
- **Three types** of instruments are on the market, each one being based on its own technology:
    1. Automated intelligent microscopy (iQ200, Beckmann)
    2. Flow cytometry (UF-1000i, Sysmex)
    3. Cuvette-based microscopy (UriSed/sediMAX)

**Particles identified** include : Erythrocytes, Leukocytes, Squamous epithelial cells, Small round epithelial cells including Renal Tubular Epithelial Cells (RTECs), Hyaline casts, Casts with inclusions, Crystals, Bacteria, Yeasts and Spermatozoa

**AUTOMATED INTELLIGENT MICROSCOPY:**

An automated microscope is focalised on a planar flow cell, in which the particles flow as a sheet, being sandwiched between two layers of an enveloping fluid. A stroboscopic lamp, firing 24 bursts/second, stops the motion of the particles passing through the camera. The stopped motion view is observed through magnifying lenses and the images are collected by a video-camera. For each particle, the background is removed for better identification and is analyzed by a neural network which contains 26,000 reference images. Each particle is isolated within one image, which is then inserted in one particle category.

The minimum urine volume required = 3 mL

Throughput: 60 samples/hour.

**FLOW CYTOMETRY:**

Passage of the sample into two laminar flow cells (one for bacteria, one for the other particles) obtained by passing a sheath liquid around the sample. Automatic staining of the particles with two dyes which emit orange and green fluorescence, DNA within the cells are stained by orange dye phenathridine and membranes are stained by green dye carbocyanin.

Irradiation of the sample with an argon laser beam done. Detection of both scattered light and fluorescence, which are converted into the 4 following parameters:

- FSC = Forward scattered light intensity
- FI = Fluorescence intensity
- Flw= Fluorescence pulse width
- Fscw = Forward scattered light pulse width

The measured parameters are converted into electric signals that allow the identification of particles.

The urine volume required = 0.8-1.2 mL and 9 µL used for analysis

Throughput: 100 samples/hour

**CUVETTE-BASED MICROSCOPY:**

A walk-away automatic urine sediment analyser which supplies black and white images of particles within whole fields of view Crystals identified are Calcium Oxalate, Uric Acid and struvite, mucus.A single-use cuvette is filled with automatically mixed native urine - volume aspirated: 2.0 mL and volume examined: 2.2 µLThe sample is centrifuged within the instrument (10 seconds at 260 g) The cuvette is forwarded to the microscope table and automatic focusing at different levels is performed. For each sample 15 images are taken.

Identification and quantitation of the particles is carried out by Auto Image Evaluation Module (AIEM), a complex artificial neural network structure which has specifically been developed for the instrument.

Throughput: 100 samples/hour

**USES**

They aid in the diagnosis of Prerenalazotemia, Acute tubular injury, Acute interstitial nephritis, Nephritic syndrome, Nephrotic syndrome, Crystalline and Osmotic nephropathy.

**Limitations** include difficulty to distinguish renal tubular epithelial cells and transitional cells in some analysers as they can identify only hyaline and non-hyaline (or pathologic) subtypes; identify only a few types of crystals and miss lipids completely.

- **Recent advances** in the world of automated urine analysers include the introduction of - Fluorescence flow cytometry with blue semiconductor laser and hydrodynamic focussing.

**REFERENCES**


1. *Corey Cavanaugh, Mark Perazella. Urine Sediment Examination in the Diagnosis and Management of Kidney Disease. Am J of Kidney Diseases. 2019;73(2):258-72.*
2. *Becker GJ, Garigali G, Fogazzi GB. Advances in urine microscopy. Am J Kidney Dis. 2016;67(6):954-964.*
3. *Fogazzi GB, Ponticelli C, Ritz E. The Urinary Sediment: An Integrated View. Milano, Italy: Elsevier Masson; 2010.*

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| | | |
|---|---|---|
| **1.** | **Stream** | Modern Medicine |
| **2.** | **Speciality** | Pathology |
| **3.** | **Date** | 11-10-2020 |
| **4.** | **Title** | USE OF NLR (neutrophil to lymphocyte ratio) in COVID 19 |
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# USE OF NEUTROPHIL-TO-LYMPHOCYTE RATIO (NLR) IN COVID-19

**ABSTRACT**

Coronavirus disease 2019 (COVID-19) is a contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) also known as novel coronavirus. It is a highly infectious disease, has been rapidly spreading all over the world and remains a great threat to global public health.

**DEFINIITION**

- The neutrophil-to-lymphocyte ratio (NLR) is the ratio of neutrophils to lymphocytes. Inflammation plays a major role in the pathophysiology of COVID-19. The neutrophil-to-lymphocyte ratio (NLR) indirectly reflect a patient's inflammatory state.

**INDICATION**

- Most patients infected with the novel coronavirus has mild and moderate illness, but some develops severe illness. In cases of critical illness, patients progress rapidly to acute respiratory failure, acute respiratory distress syndrome, metabolic acidosis, coagulopathy, and septic shock.
- For patients with mild and moderate illness, general isolation treatment is required and ICU-care is not needed unless the condition worsens. Patients with severe illness requires supportive measures.
- Early identification of risk factors for critical illness facilitates appropriate provision of supportive care and rapid access to the intensive care unit (ICU) when required.

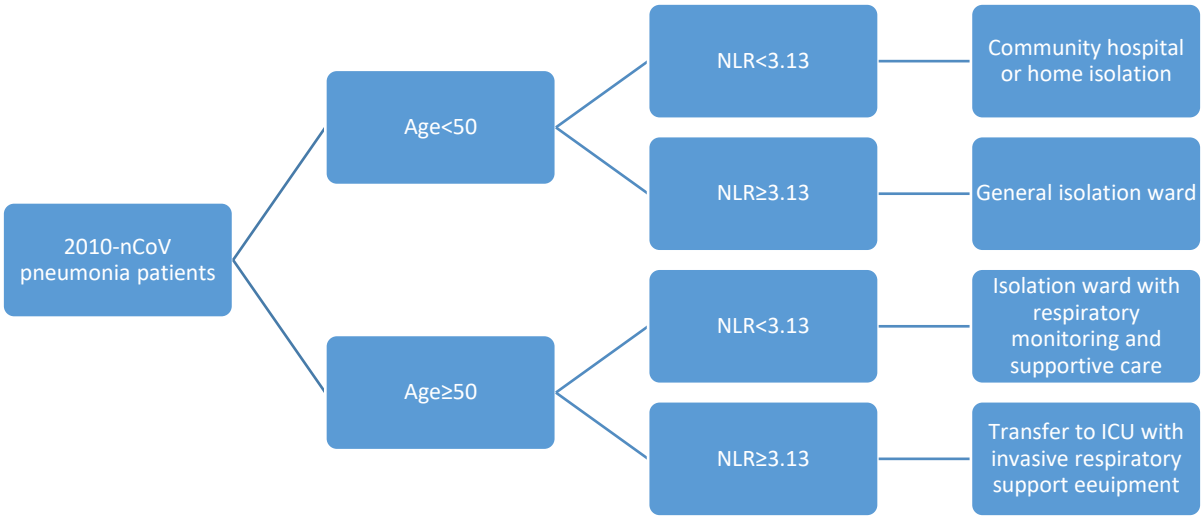
**CALCULATION**

- The NLR is calculated as the absolute neutrophil count divided by the absolute lymphocyte count.

$$\text{Neutrophil Lymphocyte Ratio(NLR)} = \frac{\text{Absolute neutrophil count}}{\text{Absolute lymphocyte count}}$$

**INTERPRETATION**

- The neutrophil-to-lymphocyte ratio (NLR) was identified as **an independent risk factor for critical illness** in patients with COVID-19 infection.




- NLR>3.13 is independently associated with more severe COVID-19.
- NLR>3.13 was associated with lower survival compared with NLR <3.3.
- In the clinical practice of treating patients with COVID-19, it is observed that the neutrophil-to-lymphocyte ratio (NLR) of severe patients is higher than that in mild patients.

**CONCLUSIONS**

- NLR is a predictive factor for early-stage prediction of patients infected with COVID-19 who are likely to develop critical illness.
- Patients aged ≥ 50 and having an NLR ≥ 3.13 are predicted to develop critical illness, and they should thus have rapid access to an intensive care unit if necessary.
- NLR can be used as an early warning signal for deteriorating severe COVID-19 infection and can provide an objective basis for early identification and management of severe COVID-19 pneumonia.
- The neutrophil-to-lymphocyte ratio (NLR) is a low-cost marker compared to cytokines and is easily accessible value that have been known to correlate with inflammation and prognosis in several conditions.
- NLR could help physicians rapidly identify high-risk patients and adopt timely intervention.

- Early prognosis prediction would help reduce mortality and alleviate the shortage of medical resources.

**REFERENCES**


- *CHAN, A. ROUT, A Use of Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratios in COVID-19. Journal of Clinical Medicine Research, North America, 12, jun. 2020.*
- *Li, X., Liu, C., Mao, Z. et al. Predictive values of neutrophil-to-lymphocyte ratio on disease severity and mortality in COVID-19 patients: a systematic review and meta-analysis. Crit Care 24, 647 (2020). https://doi.org/10.1186/s13054-020-03374-8*
- *Jingyuan Liu et al. Neutrophil-to-Lymphocyte Ratio Predicts Severe Illness Patients with 2019 Novel Coronavirus in the Early Stage, medRxiv 2020.02.10.20021584; doi: https://doi.org/10.1101/2020.02.10.20021584*
- *Liu, J., Liu, Y., Xiang, P. et al. Neutrophil-to-lymphocyte ratio predicts critical illness patients with 2019 coronavirus disease in the early stage. J Transl Med 18, 206 (2020). https://doi.org/10.1186/s12967-020-02374-0*

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| | | |
|---|---|---|
| **1.** | **Stream** | Modern Medicine |
| **2.** | **Speciality** | Pathology |
| **3.** | **Date** | 9-10-2020 |
| **4.** | **Title** | **CLEANING PROTOCOLS IN LABORATORIES DURING COVID 19 PANDEMIC** |
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# CLEANING PROTOCOLS IN LABORATORIES DURING COVID 19 PANDEMIC

**ABSTRACT**

Corona virus disease 2019 (COVID- 19) is caused by SARS-CoV-2 which spreads through respiratory droplets when the infected person breathes, coughs, speaks, sneezes or sings. It is also transmitted via contaminated surfaces. So clean surfaces, hygienic practices and proper self-protection measures could reduce its transmission to some extent. All laboratories should assess their own risks and prepare standard operating procedure for cleaning. *The Relevance of this article lies in the fact that ignoring these protocols can lead to creating hotspots for COVID 19 spread in the lab.*

**CLEANING PROTOCOLS IN LAB (Based on EHRS and CDC guidelines)**

**I. Risk assessment and preparation of SOP**

- Analyze **number of staff** that the lab can accommodate while maintaining social distancing.
- Analyze the possibility of **one-way traffic path** inside the lab to avoid collision and contact.
- Assess **commonly shared equipments and high touch areas** and make a list of it. ex: taps, bench tops, door handles, computer keyboard, door handles, switches, pen, slide trays, electronic keypads of machines, etc.
- Analyze the **supply of personal protection equipments**, gloves, face shield, soap, clean running water, sanitizers.
- Prepare **SOPs for cleaning hard surfaces, electronic equipments, and lab personnel** which will adhere strictly to the local policies as well as to the state regulations and public health guidelines.

**II. Personal Hygiene**

- Staffs should follow clean habits for coughing sneezing.
- Regular hand washing with soap and water.
- One-way traffic inside the lab and maintain social distancing (If space is not available use face shields and plastic partitions and barriers.

**III. House keeping**

- Give the housekeeping staff special guidance regarding proper use of disinfectants.

- Give special instructions for cleaning high touch areas.
- All deliveries received must be opened promptly and wash hands after removing packages.

**IV. Selection of Disinfectants**

- Environmental protection agency (EPA) has listed out the agents that can kill SARS CoV in 'list N'. ex: 10%bleach in water, 70% ethanol.
- Verify the disinfectants you are using by its name and ID number in that list.Note that all products with the name Lysol/ Clorox are not necessarily effective against COVID-19.
- DO NOT mix the cleaning chemicals together especially with bleach.

**V. How to clean**

- **Hard surfaces, handles, floor: -** Clean the organic materials and dirt with soap and water.
- Saturate clean wipes / clothes with disinfectants and apply to the surface, surface should be visibly wet after wiping.
- disinfecting agent should evaporate from the surface
- clean twice per day- start of day and halfway through work day
- **Electronics and delicate surfaces: -** 70% ethanol wipes, use lint free cloth or wipes.
- **Lab equipment:** - lab personnel should clean their equipments before and after use by themselves. This should be reminded by posters or pictures beneath every machine.
- **Personal belongings** should be disinfected by themselves like face shield, mobile, lab coat, books, goggles, etc
- **CAUTION: -**Wipes should not be in a dripping stage to avoid getting liquid into any openings of the equipment.

  **-**Also dispose wipes regularly.

  **-**Avoid spraying.

  - Do not wipe while the equipment is switched on.

**REFERENCES**


1. *Lab Cleaning and Disinfection COVID-19 Guidance EHRS. 2020;(5/13/2020).*
2. *Corona virus Disease 2019 (COVID-19) [Internet]. Centers for Disease Control and Prevention. 2020 [cited 8 October 2020]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/index.html*
3. *List N: Disinfectants for Corona virus (COVID-19) | US EPA [Internet]. US EPA. 2020 [cited 9 October 2020]. Available from: https://www.epa.gov/pesticide-registration/list-n-disinfectants-coronavirus-covid-19*
4. *Tips for Lab Safety During a Pandemic [Internet]. Corning.com. 2020 [cited 8 October 2020]. Available from: https://www.corning.com/worldwide/en/products/life-sciences/resources/stories/at-the-bench/the-rules-for-lab-safety-during-a-pandemic.html*
5. *[Internet]. Mtu.edu. 2020 [cited 8 October 2020]. Available from: https://www.mtu.edu/research/covid-19/ramping-up-research-checklist.pdf*

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Modern Medicine |
| **2. Specialty** | Pathology |
| **3. Date** | 14/12/20 |
| **4. Title** | Plasmablastic Myeloma Versus Plasmablastic Lymphoma- Recent Advances In Diagnosis And Treatment |
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| **11. Suggested Structure of Article** | 1. Facing Sheet of the Article<br>2. Article on maximum TWO sides of an A4 Page<br>3. Title of the Recent Advance<br>4. Source: Original Article / Site / Book<br>5. Contributor’s Name (To be Published)<br>6. A note on why it is relevant.<br>7. Body of the article as 10 to 20 Bulleted Points<br>8. References (2 to 3 nos.) |

# PLASMABLASTIC MYELOMA VERSUS PLASMABLASTIC LYMPHOMA- RECENT ADVANCES IN DIAGNOSIS AND TREATMENT

SOURCE: Original article

**RELEVANCE:**

Plasmablastic myeloma and plasmablastic lymphoma are two rare aggressive neoplasms that share several overlapping cytomorphologic as well as immunophenotypic features, thus posing a difficulty in the definite diagnosis.

As they show similarities in immunohistochemical markers as well as in molecular studies, the differentiation must be based mostly on clinical differences.

Though it is difficult, it is critical to differentiate between these two entities as the treatment protocols are significantly different.

INTRODUCTION:

- Plasmablastic myeloma (PBM) is rare aggressive plasma cell neoplasm characterized by presence of large plasma cells with hyperchromatic nuclei, prominent nucleoli, increased N/C ratio and increased mitotic activity.
- It can present as blood cytopenias, lytic bone lesions, bone marrow involvement, M band in serum protein electrophoresis, Bence Jones proteinuria, renal dysfunction, hypercalcemia etc.
- Plasmablastic lymphoma (PBL) is a rare variant of diffuse large B cell lymphoma characterized morphologically by large B lymphocytes and proliferation of plasmablasts/ immunoblasts with rare plasma cells.
- PBL is usually seen in immunocompromised individuals and is usually associated with EBV infection, mainly affecting extranodal sites especially oral cavity.
- Both these neoplasms show positivity for plasma cell markers like CD38, CD138, MUM1/ IRF4 and negative for B cell markers like CD20.
- They have comparable genetic alterations with some subtle differences. PBM show genetic mutations in BRAF, C-MYC, p 53, MLL, ETV6 and t (14,18). PBL shows C-MYC, PRDM1and EBER mutations.
- Both have high proliferation index and similar tumor gene expression profiles with loss of p16 and p27 and positive expression of p63.
- EBV status has been shown to be more highly associated with PBL than PBM.

- However, there is a notable correlation between EBV positive plasma cell neoplasms with the presence of plasmablastic morphological features showing aggressive clinical course compared to EBV negative plasma cell neoplasms.
- Differentiation between PBM and PBL must be based mostly on clinical differences like bone marrow involvement, paraproteinemia in blood, Bence Jones protein in urine, lytic lesions of bone or hypercalcemia/renal dysfunction favours PBM. Presence of associated lymphadenopathy and / or oral mass in absence of myeloma defining signs favoursPBL.
- Lamda light chain positivity favours the diagnosis of PBM over PBL although in few cases of PBL, lambda or kappa monoclonality can be seen.
- Identification of MYCgene rearrangement can help to distinguish PBL from PBM as MYC rearrangement is rare in latter.
- Treatment modality wise, in PBM a Bortezomib (proteasome inhibitor) based myeloma treatment plan is recommended. But in case of PBL a more aggressive therapy, that is dose adjusted EPOCH (etoposide, doxorubicin, cyclophosphomide, vincristine, prednisolone) along with Bortezomib with or without consolidation radiotherapy and hematopoietic stem cell transplantation is recommended. In those cases, where differentiation is difficult EPOCH with Bortezomib treatment is recommended.
- Recently we encountered a similar case that posed us a diagnostic difficulty. Patient was a 61year old immunocompetent male, presented with right sided obstructive nasal mass and epistaxis. Histopathology showed a aggressive neoplasm composed mainly of large atypical cells with plasmacytoid morphology. IHC showed tumor cells positive for CD138, LCA, MUM-1, lambda light chain restriction and negative for CD20, Sox-10, S-100, PAX-5, CD56 and kappa light chain. Ki 67 index was found to be high (70-75%) and EBER CSIH-positive. Serumprotein electrophoresis was negative, RFT- normal and no other lytic lesions of bone.
- Based on all these findings a diagnosis of Plasmablastic neoplasm is given with possibilities of plasmablastic myeloma and plasmablastic lymphoma, favouring more towards former in view of lambda light chain positivity.

- To conclude, though it is always a diagnostic challenge, it is important to differentiate between these two entities, as the treatment for these two diseases are significantly different.

**References:**

*1)Plasmablastic myeloma versus plasmablastic lymphoma: different yet related diseases.Hematol Transfus Int J.2018;6(1):25-28.*
*2)Epstein-Barr virus expression in plasma cell neoplasmsand its association with plasmablastic morphologic features. J Hematopathol(2013)6:213-218.*

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | DENTISTRY |
| **2. Speciality** | PERIODONTOLOGY |
| **3. Date** | 10-12-2020 |
| **4. Title** | Ozone therapy in Periodontics |
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| **10. Consent for Publication** | I hereby declare to abide by the KUHS Rules regarding publication and agree that the article contributed by me may be published in the KUHS publication on Recent Advances. |
| **11. Suggested Structure of Article** | 1. Facing Sheet of the Article<br>2. Article on maximum TWO sides of an A4 Page<br>3. Title of the Recent Advance<br>4. Source: Original Article / Site / Book<br>5. Contributor’s Name (To be Published)<br>6. A note on why it is relevant.<br>7. Body of the article as 10 to 20 Bulleted Points<br>8. References (2 to 3 nos.) |

# Title - Ozone therapy in Periodontics

- Ozone is an unstable gas and it quickly gives up nascent Oxygen molecule to form Oxygen gas. Due to the property of releasing nascent Oxygen, it has been used in human medicine since long back to kill bacteria, fungi and to inactivate viruses and to control hemorrhages.
- The use of ozone in dentistry is gaining importance in dental practice and is used in almost all dental applications. The undisputed disinfection power of ozone over other antiseptics makes its use a very good alternative or an additional disinfectant to standard antiseptics. The application of ozone in dentistry comes as a result of physico-chemical properties. The known actions of ozone in human body include immunostimulating and analgesic, antihypoxic and detoxicating, antimicrobial, bioenergetic and biosynthetic (activation of the metabolism of carbohydrates, proteins, lipids etc)

- Of these, the main application lies on its antimicrobial properties. It is effective against both Gram positive and Gram negative bacteria, viruses and fungi. The antimicrobial effect of ozone is a result of its action on cells by damaging its cytoplasmic membrane due to ozonolysis of dual bonds and also ozone-induced modification of intracellular contents because of secondary oxidant effects.

- Ozone influences cellular and humoral immune system and causes the synthesis of biologically active substances such as interleukins, leukotrienes, and prostaglandins which is beneficial in reducing inflammation and wound healing. It also improves the metabolism of inflamed tissues by increasing their oxygenation and reducing total inflammatory processes.

- It activates mechanisms of protein synthesis, increases amount of ribosomes and mitochondria in the cells. These changes on the cellular level explains the elevation of functional activity and regeneration potential of tissues in periodontium.

- Periodontal disease is a multi-factorial disease and the role of microorganisms and host response in its etiology is well established. Evidence shows that ozone has good biocompatibility with periodontal cells and gingival fibroblasts.

- According to the clinical case, different applications modalities of ozone therapy are available using ozone gas, irrigation with ozonated water and in-office use of ozonized oil as well as home use
- Ozonated water at a concentration of 0.5–4 mg/L has been proven to strongly inhibit formation of dental plaque. It can be used to irrigate the affected area during and after scaling, root surface planning, non-surgical pocket curettage, irrigant during the surgical procedure and/or as a final surgical site lavage. Sutures can be covered with a thin layer of ozonized oil and the patient can be instructed to apply the oil 3-4 times a day.
- It is an established antimicrobial agent for subgingival irrigation in patients with chronic periodontitis. and can be used as gas or in aqueous form for treating periimplantitis
- According to **Talmac etal (2020)** ozone therapy when applied in addition to periodontal therapy significantly improves clinical parameters in smokers and non-smokers
- Contraindications for ozone therapy include pregnancy, autoimmune disorder, hyperthyroidism, anemia, myasthenia gravis, alcohol intoxication, CVD, myocardial infarction, ozone allergy, hemorrhage.
- **Clinical relevance**

Ozone therapy can be used as a treatment modality for dental patients of all ages and applicable to a wide range of conditions of intra oral hard and soft tissues. Its unique properties, non-invasive nature, versatility, relatively little side effects, and adverse reactions make ozone therapy an effective tool in the treatment of gingivitis and periodontitis.

**References**


- *Talmaç, A.C., Çalişir, M. Efficacy of gaseous ozone in smoking and non-smoking gingivitis patients. Ir J Med Sci (2020). https://doi.org/10.1007/s11845-020-02271-x*
- *Sansriti Tiwari, AlokAvinash, ShashankKatiyar Dental applications of ozone therapy: A review of literature. Saudi Journal of Dental Research.2017; Vol 8 Issue1- 2:105-111*
- *Kumar A, Bhagawati S, Tyagi P, Kumar P. Current interpretations and scientific rationale of ozone usage in dentistry: A systematic review of literature.Eur J Gen Dent 2014:3:175-80*
- *Saini R. Ozone therapy in dentistry: A strategic review. J Nat Sci Biol Med. 2011;2(2):151-153. doi:10.4103/0976-9668.92318*

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### FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Dental |
| **2. Speciality** | Orthodontics |
| **3. Date** | 8-12-20 |
| **4. Title** | Platelet Rich Plasma For Accelerated Orthodontic Tooth Movement |
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| **10. Consent for Publication** | I hereby declare to abide by KUHS Rules regarding publication and agree that the article contributed by me may be published in the KUHS publication on Recent Advances |
| **11. Suggested structure of Article** | 1.Facing sheet of the article<br>2.Article on maximum TWO sides of A4 page<br>3.Title of the recent advance<br>Platelet Rich Plasma For Accelerated Orthodontic Tooth Movement<br>4.Source: Publications and review articles<br>5.Contributers name(To be published) : Dr Anjali V A<br>6.A note on why it is relevant- included in the article<br>7.Body of the article as Bulleted points<br>8.References |

# Platelet Rich Plasma for Accelerated Orthodontic Tooth Movement

**Contributor: Dr Anjali V A**

**Relevance**

A number of methods and researches are there in the field of orthodontics for acceleration of tooth movement as we can reduce long treatment time and its adverse effects and also due to increased demand in adult patients seeking orthodontic treatment. Various invasive and noninvasive methods are there for acceleration of tooth movement. The use of injectable PRP at different stages of orthodontic treatment can influence the bone quality and enhance the rate of tooth movement and thus improves the quality of treatment outcome.

- PRP has been used widely in various medical and dental procedures to enhance the bone remodeling due to various bioactive properties of platelets.
- PRP was introduced by Robert Marx in dental literature in 1998 for mandibular reconstructive procedure.
- Platelet rich plasma(PRP) is an autologous concentration of human platelets derived by gradient density centrifugation of whole blood. It comprises of the concentrate of platelets and fundamental growth factors which are actively secreted by platelets[3].
- The growth factors include
    - Three isomers of platelet derived growth factors (PDGFaa, PDGFbb, PDGFab)
    - Two of the numerous transforming growth factors-b (TGFb1, TGFb2)
    - Vascular endothelial growth factor(VEGF)
    - Epidermal growth factor(EGF)
- Also contains cytokines (ILs and TNFs), adhesive proteins, proteases, antiproteases
- PRP is an easily accessible rich source of growth factors to support bone and soft tissue healing by accelerating endothelial, epithelial and epidermal regeneration, stimulates angiogenesis, enhance collagen synthesis, osteoid production, promotes soft tissue healing.
- Orthodontic tooth movement can be described as an inflammatory process. So the presence of ILs and TNFs helps in accelerated tooth movement.

**Preparation of PRP**

- The process of preparation of PRP involves the use of centrifugation process for platelet separation from RBC and their sequestration to higher concentration without losing the platelets.
- It should be prepared by aseptic processing.
- The effect of PRP in localized acceleration of tooth movement depends on its concentration. So it's synthesis is critical for the success of the PRP in acceleration of tooth movement.
- Eric Liou et al[1] described the procedure as
    - 60ml of whole blood is drawn from the medial cubital vein of a patient using three 30 ml syringes containing 3 ml of 10% sodium citrate as anticoagulant. 1ml of blood is checked for platelet count.
    - Remaining 59ml of whole blood is centrifuged at 1000rpm for 12 min at room temperature. The blood separates into 3 basic components as RBC at bottom, buffy coat(platelets) in middle and poor platelet plasma at the top.
    - RBCs are discarded and the remaining buffy coat and poor platelet plasma are again centrifuged at 3000rpm for 8 min.
    - The poor platelet plasma is removed until 4ml remained and the remaining poor platelet plasma is mixed with buffy coat to platelet rich plasma.
    - 1ml of PRP is analyzed for platelet count.

**Regimen for use of PRP injections**

According to Liou et al

- PRP is injected submucosal through the attached gingival, 0.7ml at each target area
    - For aligning and leveling single dose at the beginning of treatment at labial and lingual/palatal site of anterior teeth.
    - For anterior retraction 2 doses, one at the beginning and another booster dose at 6months after first injection at lingual/palatal side of anterior teeth.

- For posterior teeth protraction 2 doses, one at the beginning and another booster dose at 6months after first injection at buccal, lingual/palatal and mesial sides of posterior teeth.

- The optimal PRP fold for a higher than 2-fold acceleration of orthodontic tooth movement and no pressure side alveolar bone loss is 11 -12.5
- The duration of action of PRP injection is 5-6 months with a maximum acceleration noted in 2$^{nd}$ to 4$^{th}$ month after injection.

**References**

1. *E.J.W. Liou, "The development of submucosal injection of platelet rich plasma for accelerating orthodontic tooth movement and preserving pressure side alveolar bone," APOS Trends Orthod., vol. 6, pp. 5-11. October 2017.*

*2. Marx R. E. Platelet-Rich Plasma: Evidence to Support Its Use. J Oral Maxillofac Surg. 2004;62(4):489-496.*

*3. Angaj Malandkar, Shubhangi Mani, N.G. Toshniwal, Nilesh Mote, Vishal Dhanjani. Platelet-Rich Plasma in Orthodontics- A Review. International Journal of Innovative Science and Research Technology. Volume 4, Issue 8, August – 2019*

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Dental |
| **2. Speciality** | Oral Pathology and Microbiology |
| **3. Date** | 18-12-2020 |
| **4. Title** | SMOOTH MUSCLE ACTIN IN ODONTOGENIC TUMORS |
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Source: Original Articles

## SMOOTH MUSCLE ACTIN IN ODONTOGENIC TUMORS

**RELEVANCE:**

- Odontogenic tumors comprise a complex group of lesions with diverse histopathological types and clinical behaviours. These lesions are derived from the tooth producing tissues or their remnants that remain entrapped either within the jawbones or into the adjacent soft tissues.
- They range from hamartomatous or non-neoplastic tissue proliferation to malignant neoplasm's and is most common in mandibular molar and canine area.
- Myofibroblasts (MF s) are modulated fibroblasts with smooth muscle like features characterized by presence of a contractile apparatus. Stromal myofibroblasts have the potential to facilitate progression of neoplastic epithelial lesions that could contribute to their biological behavior. Many immunohistochemical studies have been conducted to find out the role of smooth muscle actin in different odontogenic cysts and tumors.
- Ever since the Myofibroblasts (MF) were discovered by Gabbiani *et al*, in the early 1970's and shown to actively promote dermal wound contraction, this cell has been on the rise and its importance shown for different physiological and pathological processes.
- Myofibroblasts are capable of remodeling connective tissue but also interact with epithelial cells and other connective tissue cells and may thus control such phenomena as tumor invasion and angiogenesis.
- Most of the myofibroblasts express alpha smooth muscle actin (α – SMA), which is the actin isoform typically found in vascular smooth muscle cells and coordinately regulated by TGF – β1. α SMA is the actin isoform that predominates within vascular smooth muscle cells and play an important role in fibrogenesis.
- The presence of stromal myofibroblasts has been linked to the biological behavior of both benign and malignant tumors. Soluble factor secretion by stromal myofibroblasts influences tumor progression and invasion.
- Myofibroblastic differentiation features are the predominant cell type in different primary and play a central role in the deposition of collagen as well as in tissue remodeling

phenomena that are attributed at least in part to contractile forces generated in their cytoplasm.

- Myofibroblasts in tumors also expresses tissue factor, the cellular initiator of the protease blood coagulation cascade, leading to the formation of thrombin; a strong correlation between expression of the tissue factor by macrophages or myofibroblasts in close proximity to infiltrating tumor cells, and progression to invasive cancer.
- Recent studies have shown that smooth muscle fibroblasts may originate from fibroblasts within the tumor stroma or even from carcinoma cells by the process of epithelial – mesenchymal interaction.
- In a study of 24 cases of ameloblastomas by Sherlin *et al*., smooth muscle actin positivity was noted at the tumor front of the lesion which clearly indicates the pivotal role of smooth muscle actin positive myofibroblasts in tumor progression.
- Similarly, Vered *et al*., have observed similar expression and significant alpha smooth muscle actin positivity (88%) in tumor stroma.
- Lombardi and Morgan confirmed the presence of Myofibroblasts in odontogenic cyst walls and suggested that they might be part of a homeostatic response to the distension caused by cyst enlargement.
- Fregnani *et al*., suggested that abundant presence of Myofibroblasts and expression of matrix metalloproteinase – 2 (MMP – 2) in solid ameloblastomas may be associated with a more aggressive infiltrative behavior.
- The abundant presence of Myofibroblasts in the stroma of the tumors and expression of MMP – 2 in the neoplastic or stromal cells was significantly correlated with rupture of the osseous cortical, which has been considered an important prognostic marker of ameloblastoma aggressiveness.
- Along with α -SMA, staining with Desmin and Vimentin also helps to identify Myofibroblasts with greater specificity.

**CONCLUSION**

- The high frequency of myofibroblasts in known aggressive tumors suggests that they play a role in the biological behavior of these lesions.

- Further investigations and studies in this field will help in establishing the role of stromal Myofibroblasts in odontogenic lesions which will help in establishing new treatment modalities which could help in reduction of the extent of the lesion and thus aids in better surgical management.

**REFERENCES**


- *Shyam Prasad Reddy, et, al. Immunohistochemical assessment of odontogenic tumors using smooth muscle actin – A short study. Indian J Dent Adv 2012; 4(3): 892-896.*
- *Annegowda VM, Devi HU, Rao K, Smitha T, Sheethal HS, Smitha A. Immunohistochemical study of alpha – smooth muscle actin in odontogenic cysts and tumors. J Oral Maxillofac Pathol. 2018; 22(2): 188-192.*
- *J Priya, B Satish, H Bhagyalaxmi, C Madhuri, D Mahesh. Comparison of immunoexpression of α - SMA in inflamed and non-inflamed odontogenic keratocysts and ameloblastoma. International Journal of Applied Dental Sciences. 2014; 1(1): 05-10.*

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Dental |
| **2. Specialty** | Orthodontics and Dento-Facial Orthopedics |
| **3. Date** | 18/12/2020 |
| **4. Title** | Application of Cyclic Forces (AcceleDent) to Accelerate Tooth Movement in Orthodontic Patients- A Paradigm Shift? |
| **5. Name of Contributor** | Dr Ravisankar V |
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| **10. Consent for Publication** | I hereby declare to abide by the KUHS Rules regarding publication and agree that the article contributed by me may be published in the KUHS publication on Recent Advances |
| **11. Suggested Structure of Article** | 1.Filled up Facing Sheet of the Article<br>2.Article on maximum TWO sides of an A4 Page<br>3. Title of the Recent Advance- *Application of cyclic forces (AcceleDent) to accelerate tooth movement in orthodontic patients- A paradigm shift?*<br>4.Source: Original Article / Site / Book<br>5.Contributor’s Name (To be Published)<br>6. A note on why it is relevant.<br>7.Body of the article as 10 to 20 Bulleted Points<br>8. References (2 to 3 nos.) |

# Application of Cyclic Forces (AcceleDent) to Accelerate Tooth Movement in Orthodontic Patients- A Paradigm Shift?

**Relevance**

Patients seek orthodontic treatment primarily for aesthetic reasons with treatment time involving 2 or more years in fixed appliances. This lengthy duration can deter patients from receiving treatment and can result in patients aborting treatment while at the same time more likely to elicit aberrant root resorption and demineralization. With patients wanting significantly shorter treatments of only 6 to 12 months, this places significant pressure on orthodontic providers and companies to find ways to accelerate treatment (1). Treatment time depends on the rate of tooth movement, which in turn depends on the rate of alveolar remodeling. Therefore, it may be possible to increase the rate of tooth movement by accelerating the biological response of the periodontal ligament and alveolar bone. Earlier approaches attempted to accelerate tooth movement include low-energy laser irradiation, magnetic fields, pharmacological interventions with injection of prostaglandin E2 and vitamin D, corticotomy-facilitated orthodontics etc. However, adverse events, such as local pain, severe root resorption, morbidity of surgery, cost and insufficient clinical evidence were associated with these treatments (2). Shapiro suggested that orthodontic forces should not be continuous, since the piezoelectric charges are created only when stress is applied and released (1). A vibrational appliance using cyclic forces is therefore suitable for initiating these stress induced charges because forces can be applied and released at a rapid rate at the same time proved safe and painless (2)

**Cyclic Forces**

- Research has demonstrated that the use of cyclic forces increases the rate of bone remodeling compared to static forces (2). While similar in their non-constant nature, cyclic forces- sometimes referred to as pulsatile forces- are different from intermittent forces that are applied for some duration of time, removed and then reapplied.
- A static force occurs once and affects cells once; an intermittent force is still a static force; the only difference is that it is introduced episodically. In contrast, cyclic forces are oscillatory in nature and change magnitude rapidly and repeatedly, affecting the

cells with each oscillation of force magnitude. The frequency of cyclic forces is never zero. Force frequency is a concept of critical importance, but has rarely been considered in the field of orthodontics until recent years.

- Cyclic forces have been used for other parts of the body, such as Juvent system that is used to counteract lost bone and muscle in the prevention of osteoporosis. Recently, a new device has been introduced (AcceleDent, OrthoAccel Technologies) that utilizes these forces to reduce the duration of orthodontic treatment (2).

**AcceleDent Device**

- The AcceleDent device uses the application of cyclic forces to move teeth in bone faster through accelerated bone remodeling. One portion of the device is a mouthpiece similar to a sports mouthpiece, which the patient bites onto during use. The mouthpiece portion is connected to another piece that stays outside the mouth; this portion (activator) houses the components that provide the vibration. The activator includes a battery, motor, rotating weights and microprocessor for storing usage data. The patient connects the mouthpiece to the activator and uses the device once daily for 20 minutes. The applied force from the device is at 0.2N (20 grams) at 30 Hz. The activator is placed in a docking station between uses to both recharge the activator and show compliance data.
- A randomized control trial done at Texas Health Science Centre showed the low level cyclic loading of 0.25 N at 30 Hz increased the rate of tooth movement significantly (1.16mm/month for AcceleDent group compared to 0.79mm/month in the control group) when applied as an adjunct to orthodontic treatment (1).
- The results from analysis of harms and safety-related outcomes showed that the AcceleDent is safe and convenient for patient's use.
- Another study reported 2 to 3 mm of movement per month in both arches by measuring the reduction in Little's irregularity index (2).
- A retrospective study examining the rate of leveling and alignment in the mandibular arch of non-extraction subjects reported a 30% increase in the rate of movement using the AcceleDent appliance (1).

- A reduction in post orthodontic adjustment pain was also reported with AcceleDent (1).
- Vibrational loading stimulates bone remodeling, but the biological mechanism underlying this effect is not exactly understood. Further studies should address the question whether cyclic loading, as an adjunct to orthodontic stress, activates known or new signaling pathways underlying the faster tooth movement.

**Conclusion**

- Reducing the duration of orthodontic treatment increases the acceptability especially among adults. The concept of the use of static forces in orthodontics has not been challenged in more than a century of clinical practice. New technology related to the biological impact of force frequencies using cyclic forces could represent a paradigm shift in orthodontics.

**References**


1. *Miles P, Fisher E. Assessment of the changes in arch perimeter and irregularity in the mandibular arch during initial alignment with the AcceleDent Aura appliance vs no appliance in adolescents: A single-blind randomized clinical trial. Am J Orthod Dentofacial Orthop 2016;150:928-36*
2. *Pavlin D, Anthony R, Raj V, Gakunga PT; Cyclic loading (vibration) accelerates tooth movement in orthodontic patients: A double-blind, randomized controlled trial. Semin Orthod 2015; 21:187-194.*

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Dental |
| **2. Speciality** | Periodontics |
| **3. Date** | 19-10-2020 |
| **4. Title** | Updates on "POCT" in Periodontics |
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# Updates on "POCT" in Periodontics

**Source:** Original articles

**Contributor:** Dr Shahana C Mohamed

**Relevance:**

Periodontal disease, one of the most common oral diseases, is characterized by gingival inflammation and periodontal tissue destruction. Over the past few decades, though there have been significant developments in the understanding of periodontal disease pathogenesis, the methods by which they are diagnosed remains unchanged. Traditional diagnostic methods like clinical and radiographic examination helps to identify only the past tissue destruction. Hence, novel methods which helps to detect the current disease activity and predicts the future disease progression are necessary for better diagnosis and treatment planning. Biological fluids like saliva, serum, urine, gingival crevicular fluid etc has a wide array of biomarkers which aid in measuring periodontal disease activity.

- **Point of Care Testing (POCT)** is defined as medical testing conducted outside of a laboratory at or near the site of patient care, including the patient's bedside, the doctor's office, and the patient's home[1]. Saliva serves as an optimal diagnostic tool for periodontal disease due to the presence of locally produced proteins, genomic biomarkers such as DNA and mRNA, and various metabolites that originate from the host and the bacteria.[2] Saliva is readily available, can be collected by simple, safe and non-invasive methods and hence is an ideal medium for POCT. This review focuses on POC diagnostics based on saliva and its applications in Periodontics.
- **Oral fluid Nano sensor test (OFNASET)**

An ultra-sensitive, ultra-specific automated POC device designed for the electrochemical detection of multiple salivary proteins and nucleic acids. Developed by the University of California, Los Angeles Collaborative Oral Fluid Diagnostic Research Laboratory (UCLA) led by Dr David Wong[3], the intended use of the OFNASET is for detection of salivary biomarkers for oral cancer. Four salivary mRNA biomarkers (SAT, ODZ, IL-8 and IL-1b) and two salivary proteomic biomarkers (thioredoxin and IL-8) in saliva are detected with this system.

- **Electronic taste chips (ETC)**

A lab-on-a-chip system, which differentiates between healthy and periodontally diseased individuals based on the C-reactive protein (CRP) levels, developed by researchers at Rice University in Houston, Texas[3]. The ETC system is advantageous over the ELISA in having porous beads, which allows greater number of antibody molecules to capture and hence detect CRP at extremely low concentrations.

- **OraQuick**

FDA-approved oral swab in-home test for HIV-1 and HIV-2 and provides results in 20 minutes. It is a stick-like device with a fabric swab on one end which is inserted into a tube of testing fluid. The fluid to be diagnosed is mixed in a vial with developing solution and the results are displayed on a testing device.

- **Integrated microfluidic platform for oral diagnostics (IMPOD)**

A POC diagnostic test which helps in rapid measurement of levels of the collagen cleaving enzyme Matrix metalloproteinase-8(MMP-8) in saliva from healthy and periodontally diseased subjects. The hand-held IMPOD has been used to rapidly (3–10 minutes) measure the concentrations of MMP-8 and other biomarkers in small amounts (10 ml) of saliva[3].

- **My PerioPath**

My PerioPath uses DNA polymerase chain reaction to detect the type and concentration of bacteria present in the salivary sample[3]. This test requires the shipping of saliva samples to the laboratory for results.

- **Omnigene**

They are species specific DNA probes to identify eight pathogens which are known to cause periodontal disease - *Porphyromonas gingivalis*, *Prevotella intermedia*, *Aggregatibacter actinomycetem comitans*, *Fusobacterium nucleatum*, *Eikenella corrodens*, *Campylobacter rectus*, *Bacteroides forsythus* and *Treponema denticola*.

- **My PerioID**

This test identifies the genetic susceptibility of a patient to periodontal disease by using salivary samples and helps in evaluating the patients which are at higher risk of periodontal destruction. This test requires the shipping of saliva samples to the laboratory for results.

**Challenges:**

Application of POC diagnostics in clinical setting is still questionable. These new periodontal diagnostics needs to be standardized and validated with existing methods of disease evaluation. Another drawback is the cost effectiveness of such procedures for integration into routine clinical periodontal practice.

**References**


1. Song Y, Huang YY, Liu X, Zhang X, Ferrari M, Qin L. Point-of-care technologies for molecular diagnostics using a drop of blood. *Trends Biotechnol*. 2014;32(3):132-9.
2. Ji S, Choi Y. Point-of-care diagnosis of periodontitis using saliva: technically feasible but still a challenge. *Front Cell Infect Microbiol*. 2015; 5:65.
3. Srivastava N, Nayak PA, Rana S. Point of Care- A Novel Approach to Periodontal Diagnosis-A Review. *J Clin Diagn Res*. 2017;11(8): ZE01-ZE06.

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Dental |
| **2. Speciality** | Periodontology |
| **3. Date** | 10-12-2020 |
| **4. Title** | Role of Epigenetics in periodontal therapy |
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## ROLE OF EPIGENETICS IN PERIODONTAL THERAPY

- Periodontal diseases: These are multifactorial diseases which are initiated by the interaction of pathogenic microorganisms with the host tissues which trigger a host mediated immune-inflammatory response. A disproportionate relation between the destructive and reparative responses thus created in the host leads to loss of supporting periodontal tissues leading to various periodontal diseases. This is further influenced by genetic risk factors, environmental and acquired risk factors.
- Periodontal treatment strategies: they aim in replacing the essential balance between regeneration and destruction of the supporting periodontal tissues. Tissue engineering in the field of periodontics is directed towards regeneration of lost periodontal tissues by utilizing principles of stem cell therapy, biomaterials and genetics.
  - Gene therapy: modification of cells for a desired therapeutic effect forms the backbone of gene therapy.
  - Epigenetic therapy: Yet another emerging concept includes modification of gene expression rather than changing the DNA sequence
- Epigenetics: It forms a link between the phenotype and the environment by controlling the silencing or over expression of genes causing expression of different molecules.
- Epigenetic mechanisms: DNA methylation, post-translational histone modification, and non-coding RNA. These epigenetic alterations along with other risk factors can trigger diseases like periodontitis. Moreover, pathogenic bacteria causing periodontitis may also be subjected to epigenetic alterations which may further enhance the destruction of periodontal tissues.

By understanding about epigenetics the difference in response to the periodontal therapies between individuals can be well explained. Studies show that even different tissues in the same patient showed differences in epigenetic mechanisms.

- Epidrugs: As epigenetic changes can be reversed, newer forms called epidrugs have been introduced which can inhibit enzymes like:
  - DNA methyl transferases
  - Histone deacetylases, and

- Histone methyltransferase enhancer

The following have been studied and their action as epidrugs have been very promising:

- Chaetocin (a natural fungal secondary metabolite)
- BIX01294, Anacardic acid (isolated from cashew)
- Garcinol (derived from Kokum)
- Curcumin and
- Sodium butyrate

These drugs can be introduced into scaffolds and used in tissue engineering to regenerate periodontal tissues effectively.

**Conclusion**

By understanding the epigenetic alterations, the susceptibility to periodontal diseases as well as other such immune-inflammatory diseases can be discerned and could be introduced as a diagnostic tool for identifying such diseases. Moreover, epidrugs could be made part of conventional therapies for providing better periodontal regeneration.

**References**


1. *Larsson L, Castilho RM, Giannobile WV. Epigenetics and its role in periodontal diseases: a state-of-the-art review. J Periodontol. 2015. Apr; 86(4):556-68.*
2. *Patel, Deepkumar & Lee, Yoon Ju & Chauhan, Bindi & Sidhu, Lovleen & Heck, Diane & Duck, Hong. Epigenetics- Epidisease- Epidrug: A Key Context folded inside of periodontal diseases. Enliven archive. 2019.1(1): 1-4.*
3. *Almiñana-Pastor PJ, Boronat-Catalá M, Micó-Martinez P, Bellot-Arcís C, Lopez-Roldan A, Alpiste-Illueca FM. Epigenetics and periodontics: A systematic review. Med Oral Patol Oral Cir Bucal. 2019 Sep 1;24(5):e659-e672.*

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Dental |
| **2. Speciality** | Periodontics |
| **3. Date** | 30-12-2020 |
| **4. Title** | Periodontology in the new millinnea |
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# PERIODONTOLOGY IN THE NEW MILLENNIA

The following inventions have made the way for the better management of periodontal diseases in the new era

**Laser**

- The laser is a device that emits light through an optical amplification mechanism based on stimulated electromagnetic radiation emissions.
- Lasers may be used in a centred beam for excisions and incisions and in an unfocused beam for ablation and coagulation. Some studies indicate that additional benefits can be provided by lasers used as an adjunct to scaling and root planing.
- The laser is used for caries prevention, bleaching, restorative removal and curing, cavity preparation, dentinal hypersensitivity, growth modulation and for diagnostic purposes in hard tissue application, while soft tissue laser application helps in wound healing, hyperplastic tissue removal to expose the tooth that has been damaged or partially erupted.

**Photodynamic therapy (PDT)**

- Oxygen-dependent photochemical reaction that occurs when a photosensitizing compound in the presence of light, leading to the generation of predominantly singlet oxygen species of cytotoxic reactive oxygen.
- PDT can be seen as an adjunctive to conventional mechanical therapy. Technological simplicity and active bacterial eradication are the two reasons why PDT in periodontics is extensively studied. Antimicrobial PDT may also lead to the detoxification of endotoxins such as lipopolysaccharide, in addition to the removal of bacteria.[1]

**Gene Therapy**

- Gene therapy is a procedure that is used to correct damaged genes responsible for the development of diseases.
- For the treatment of diseases, the technique utilises distilled preparations or a fraction of a gene.
- The main goal of gene therapy is to insert therapeutic material into the target cells, where it becomes active and exerts the therapeutic effect that is expected.[2]

**Piezo surgery**

- In 1998, Dr. Tomaso Vercellotti invented the Piezo surgical device for bone graft harvesting.

- Piezo surgery is used for regenerative processes in root preparation, osteotomy, osteoplasty, ridge extension, accelerated orthodontics, and bone harvesting.

**Nanotechnology**

- Nanotechnology consists of a process in which materials are isolated, consolidated and deformed by an atom or one molecule.
- The presence of nanoparticles can be used for dentin hypersensitivity treatment, tooth repair, tissue engineering scaffold.

**Tissue engineering**

- Tissue engineering, in conjunction with scaffolds, signalling molecules and cells, is a modern and advanced area of science that deals with the development of new techniques for the creation of new tissues to replace the old damaged tissues.
- The concepts of cell and developmental biology and the study of biomaterials work in this area.

**Minimally Invasive Surgery**

- The practise of using smaller incisions as minimally invasive surgery was introduced by Wickham and Fitzpatrick.
- To achieve pocket depth reduction and attachment level gain with less recession in the controlled site, this technique utilises very tiny incisions with less reflection.

**Ozone therapy**

- As an adjunctive to mechanical debridement, both gaseous and aqueous ozone are used.
- Using ozonated water flushed below the gum line and/or ozone gas infiltrated into the gum tissue and supporting tissues, can be used to cure periodontal disease.

**References**


1) *Kömerik N, Wilson M, Poole S. The Effect of Photodynamic Action on Two Virulence Factors of Gram-negative Bacteria. Photochemistry and photobiology. 2000 Nov; 72(5):676-80.*
2) *Mammen B, Ramakrishnan T, Sudhakar U, Vijayalakshmi. Principles of gene therapy. Indian J Dent Res.2007; 18(4):196-200.*
3) *Cortellini P, Tonetti MS. A minimally invasive surgical technique with an enamel matrix derivative in regenerative treatment of intra-bony defects: a novel approach to limit morbidity. J Clin Periodontol. 2007; 34(1):87-93.*

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Dental |
| **2. Speciality** | Oral Medicine and Radiology |
| **3. Date** | 03-01-2021 |
| **4. Title** | TRANSLATIONAL RESEARCH; A NEW FRONTIER IN MOVING FROM BENCH TO BEDSIDE AND BEYOND |
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# TRANSLATIONAL RESEARCH; A NEW FRONTIER IN MOVING FROM BENCH TO BEDSIDE AND BEYOND

## Relevance

Numerous research activities are happening in the field of dentistry, mostly intended to enhance clinical efficiency and perhaps treatment predictability. When basic research is aimed at the acquisition of knowledge without the obligation to apply it to practical ends, clinical research or patient oriented research often focus on major therapeutic interventions or development of new technologies. But only a fraction of them are competent enough to generate a paradigm shift in the scientific or therapeutic perspectives of dental sciences and do not reach the community at large. Where are we lacking? Working in silo often creates a wide gap between basic researcher and clinical researcher that lead to a transitional lag between implementation of discoveries from basic research into its clinical use. Here is the importance of **Translational research** – a term often used interchangeably with translational medicine or translational science or **bench to bedside** – is an effort to bridge the gap between basic scientific research to create new therapies, medical procedures, or diagnostics. It is supported by **three main pillars: bench side, bedside and community.**

- Translational research is part of unidirectional continuum in which research findings are moved from the researcher's bench to patient's bedside and community.
- It includes two areas of translation. One is the process of applying discoveries generated during research in the laboratory, and in preclinical studies to the development of trials and studies in humans.
- The second area of translation concerns research aimed at enhancing adoption of best practices in the community. Interestingly, when such basic science discoveries are applied to clinical practice, it further contributes to additional basic science discoveries.
- The translational archetype has been subdivided into three phases:
    - ✓ **T1 research** expedites the movement between basic research and patient-oriented research that leads to new or improved scientific understanding or standards of care. Examples of T1 research are drug development, pharmacogenomics, and research into new areas such as genetics, genomics, and

proteomics.

- ✓ **T2 research** facilitates the movement between patient-oriented research and population-based research that leads to better patient outcomes, the implementation of best practices, and improved health status in communities. Examples of T2 are clinical epidemiology, health services (outcomes) research.
- ✓ **T3 research** promotes interaction between laboratory-based research and population-based research to stimulate a robust scientific understanding of human health and disease. Examples of T3 are emerging disciplines such as molecular and genetic epidemiology.

- A significant barrier to translational research includes cultural differences between basic scientists and clinicians, which stem from the lack of communication, differences in education and training and different goals and reward mechanisms. Another barrier is lack of resources in terms of workforce, infrastructure, and funding.
- It requires **interaction of several disciplines** and clinicians need to think "out of the box" and training programs may be needed for researchers to excel as critical thinkers.
- As we are transforming from an empirical approach to tailored approach of **personalized medicine** and targeted therapy, translational research would serve as an excellent tool in improving disease detection, preempt disease progression, customize disease prevention strategies and avoid prescribing drugs to individuals with predictable side effects.
- We stand at the edge of a new frontier which encourages researchers and clinicians to work constructively and cooperatively towards maximizing health care.
- The constant challenges of teaching, researching, publishing and competing for limited sources of funding, coupled with pursuing career ambitions may seem as a daunting task. However, it can be an intensely satisfying and exhilarating endeavor, especially when the fruits of the laboratory studies are translated to improved healthcare strategy or generate a paradigm shift in clinical practice with subsequent benefits to our patients and societies globally.

**Reference**


1. *Sharma N, Annigeri RG. Translational research in oral cancer: "A challenging key step in moving from bench to bedside". J Can Res Ther 2018;14:245-8.*
2. *Rubio DM, Schoenbaum EE, Lee LS, Schteingart DE, Marantz PR, Esposito K. Defining translational research: implications for training. Acad Med. 2010 Mar;85(3):470-5.*

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Dental |
| **2. Speciality** | Oral Medicine and Radiology |
| **3. Date** | 07.12.2020 |
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# NANODENTISTRY

- Nanotechnology or nano science refers to research and development of an applied science at the atomic or molecular level.[1] The word “nano” is said to be derived from the Greek word which stands for “dwarf”.[2] One nanometer is 1 billionth or $10^{-9}$ of a meter. The basic concept of nanotechnology is to employ individual atoms and molecules to construct functional structures. It finds applications in medical field as in pharmacological research, clinical diagnosis, supplementing immune system, cryogenic storage of biological tissues, detection of proteins, tissue engineering, tumor destruction by heating, Magnetic resonance imaging (MRI) contrast enhancement e.t.c. The various nanoparticles include nanopores, nanocapsules, dendrimers, nanorods, liposomes and so on.
- Nanotechnology finds applications in dentistry and an emerging new field is called nanodentistry. The new treatment opportunities in dentistry include local anaesthesia, dentition renaturalization, permanent cure of hypersensitivity, complete orthodontic realignment during a single office visit, and continuous oral health maintenance with the help of mechanical dentifrobots that destroy caries- causing bacteria and even repair blemishes on teeth where decay has set in.
- Diagnosis and treatment of oral cancer

  Nanodevices can be inserted into the body to identify the early presence of a disease or to identify and quantify toxic molecules and tumor cells.[3] Tumor markers have been studied by using atomic force microscopy which employs nanoparticles. The nano electromechanical system, oral fluid nanosensor test and optical nanobiosensor can be used for diagnosing oral cancer. Nanoshells are used in cancer therapy. They have outer metallic layers that selectively destory cancer cells while leaving normal cells intact.
- Tissue engineering

  Applications of tissue engineering and stem cell research in dentistry include treatment of fractures, periodontal ligament regeneration, implant osseo integration, cartilage regeneration of the temporo mandibular joint, bone augmentation and pulp repair
- Nanorobotic dentifrices (Dentifrobots)

  Dentifrobots in the form of mouthwash or tooth paste left on the occlusal surface of teeth can cleanse organic residues by moving throughout the supragingival and subgingival

surfaces, metabolizing organic matter into harmless and odourless vapors and performing continuous calculus debridement.

- Dentinal hypersensitivity

  The dentinal tubules of a hypersensitive tooth have twice the diameter and eight times the surface density of those in nonsensitive teeth. Dental nanorobots could precisely occlude selected tubules in minutes using native logical materials effecting a quick and permanent cure for the patients.

- Digital dental imaging

  Advances in digital dental imaging are also expected with nanotechnology. The radiation dose obtained using digital radiography with nanophosphor scintillators is diminished and high quality images can be obtained

- Nanotechnology has great scope in the field of drug delivery and gene therapy in the future. But it is not without its disadvantages, the extensive application of nanomaterials in a wide range of products for human use possesses a potential risk to human health and environment. The optimal utilization of the advantages offered by nanotechnology in dentistry will facilitate improvement in oral health and revolutionize clinical dental practice.

**References**


1. *Kovvuru SK, Mahita VN, Manjun BS, Babu BS. Nanotechnology: The emerging science in dentistry. J Orofac Res. 2012;2:33-6.*
2. *Verma SK, Prabhat KC, Goyal L, Rani M, Jain A . A critical review of the implication of nanotechnology in modern dental practice. Natl J Maxillofac Surg. 2010;1:41-4.*
3. *Freitas RA, Jr Nanodentistry. J Am Dent Assoc. 2000;13:1559-65*



**Source**: Article: Nanotechnology and its applications in Dentistry by IMF Abiodun-Solanka, DM Ajayi, and AO Arigbede. Annals of Medical and Health Sciences Research.2014; 3: S171-177.

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Dental |
| **2. Speciality** | Prosthodontics |
| **3. Date** | 03-01-2021 |
| **4. Title** | **3D PRINTING: A GAME CHANGER IN MAXILLOFACIAL PROSTHETICS AND PROSTHODONTICS!** |
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## 3D PRINTING: A GAME CHANGER IN MAXILLOFACIAL PROSTHETICS AND PROSTHODONTICS!

Source: Review articles and Publications
Contributor's Name: **Dr. Adhershitha A R**

**Relevance:** Traditional methods of maxillofacial prosthetic design and manufacture are largely qualitative in nature, as the final fit and aesthetics of the prosthesis solely depends on the artistic expertise and dexterity of the clinician. Traditional processes are also highly exhaustive in terms of labor requirement and impression making procedure of the defect can be highly invasive and agonizing for the patient. To overcome these drawbacks and to potentially minimize the demands of time and efforts required to fabricate a prosthesis, digital designing and manufacturing can be an effective alternative in this field.

- Three-dimensional (3D) printing technology was first demonstrated in 1986. Additive manufacturing, rapid prototyping and solid freeform technology are synonymous to 3D printing.
- As per the American Society for Testing and Materials (ASTM) additive manufacturing is the process of making objects from 3D model data, adding materials layer upon layer, with the advantage of minimum material wastage.
- Additive manufacturing is the perfect solution to get customized items, when it applies to maxillofacial prosthesis, as it allows great authenticity and natural appearance. In the challenging field of maxillofacial prosthetics and surgery, some solutions have to be adapted to the patients. Customarily, prosthesis should be inconspicuous and have to match with the patient's morphology.
- Additive manufacturing techniques are found to be used for scaffold production in tissue engineering also. This 3D scaffold will allow fabrication of complex bone grafts with meticulous control over the internal channel networks of the scaffold, necessary for cell proliferation and eventually bone ingrowth. This will address the drawbacks of existing techniques by retaining the shape and position of the graft material during the consolidation phase.
- The primary step in 3D printing is to obtain anatomical scans using imaging techniques such as Magnetic Resonance Imaging (MRI) and Computed Tomography (CT). The image

from these modalities are then saved in a standard format such as Digital Imaging and Communications in Medicine (DICOM) and later with the help of computer-aided design (CAD) software, virtual 3D prototype with Standard Tessellation Language (STL) can be created. Final step is 3D printing and deposition of the material layer by layer to achieve the final structure.

- Various printing techniques used are fused deposition modelling (FDM), stereolithography (SLA), selective laser sintering (SLS), inkjet bioprinting, extrusion bioprinting and laser-assisted bioprinting. The created virtual 3D prototype can be printed using the appropriate technique and the printed object is subjected to post-printing modifications to obtain the final product.
- 3D printing has made the process of fabricating a prosthetic nose or any other body part as easy as pressing the print button. Polyjet multimaterial printing technology in the production of maxillofacial prosthesis allows for not only exemplary digital reproduction, but can actualize complex color combinations, simulating skin pigmentation, besides adjustable mechanical properties, to obtain the tactile feel of human tissue.
- Additive manufacturing is also capable of changing the face of dental implant surgery. It is actually possible to create a 3D model to replace a missing tooth. Undeniably, 3D printing creates more accurate replacement teeth on a faster pace than with traditional methods.
- One of the most common applications of 3D printing in dentistry is the production of crowns. It is possible to get a scan of the patient's teeth using intraoral scanners, to create virtual 3D models and to manufacture it using additive manufacturing. This process is really time-saving, and there is provision to modify and reprint the crown if there is any kind of an error.
- It is also possible to 3D print complete dentures. Indeed, even the denture base is 3D printable and can be adapted to the patient's morphology. As of now 3D printed dentures are under clinical trials, but it is expected to be a common 3D printed product in the near future.
- Application of 3D printing in the field of maxillofacial reconstructive surgeries are obtaining highly precise anatomic prototype models to aid in preoperative planning and improve postoperative facial symmetry, virtual planning and printing of pre-contoured

grafts and plates to revamp surgical outcomes and reduce operating time, provide high-accuracy and life like prostheses that can enhance the aesthetics and psychological status of patients and also for surgical planning and training.

- Poly (glycolic acid) (PGA), polylactic acid (PLA) and copolymer (PLGA) were the commonly used degradable polymers that are being used for maxillofacial defect repair. Metals (titanium), Polymers (poly (methyl methacrylate), Ceramics (calcium phosphates) are the non degradable materials used for this purpose.

**References**


1. *Aldaadaa A, Owji N, Knowles J. Three-dimensional Printing in Maxillofacial Surgery: Hype versus Reality; J Tissue Eng. 2018 Apr 20; 9:2041731418770909. doi: 10.1177/2041731418770909.*
2. *Gali S, Sirsi S.3D printing: The future technology in prosthodontics; Journal of Dental & Oro-facial Research Vol 11, Issue 1. Jan-Jun 2015*

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Dental |
| **2. Speciality** | Conservative Dentistry And Endodontics |
| **3. Date** | 5.12.20 |
| **4. Title** | Guided Endodontic Access |
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| **12. Suggested Structure of Article** | 1. Facing Sheet of the Article<br>2. Article on maximum TWO sides of an A4 Page<br>3. Title of the Recent Advance<br>4. Source: Original Article / Site / Book<br>5. Contributor’s Name (To be Published)<br>6. A note on why it is relevant.<br>7. Body of the article as 10 to 20 Bulleted Points<br>8. References (2 to 3 nos.) |

# GUIDED ENDODONTIC ACCESS

**SOURCE:** Book and Original Articles.

**RELEVANCE:**

We have come a long way in dentistry from “extension for prevention” to “prevention of extension”. A similar approach in endodontics is going to change the future of dental practice with **Minimal Invasive Endodontics (MIE)**. MIE mainly includes preservation of structural integrity of tooth, alternate access cavity designs, guided endodontic access, modern burs, cleaning and shaping, 3D irrigation and disinfection, magnification aids like loupes and dental operating microscope. Survival of an endodontically treated tooth depends mainly on its remaining structural integrity after access preparation. The concept of Conservative endodontic cavities (CEC) was introduced to preserve the pericervical dentin (PCD), which is crucial to transfer the occlusal load to the root. In traditional endodontic cavities (TEC) much of PCD is lost which reduces the fracture resistance of tooth. Guided endodontic access helps in preserving PCD and is the most conservative approach even in difficult cases like calcified canals.

- Guided endodontic access is a technologically driven approach to prepare smallest possible customized access cavity with minimal tooth structure removal for ensuring long term survival and function of endodontically treated teeth.
- Guided endodontics includes CBCT, digital impression systems, 3D printing technology, template designing software and dynamic navigation.
- 3D Guided endodontics provides safe and predictable treatment outcome even in most challenging cases compared to conventional treatment strategies. With advanced CBCT imaging and software, clinicians can not only assess the root canal anatomy, length and location but also virtually plan the access cavity design for individual tooth with 3D scanner and 3D templates.
- This virtual planning will help to preserve the tooth structure and avoid any procedural errors.
- Guided endodontics can be Static or Dynamic. **Static Guided Endodontics** uses CBCT merged with optical impression, creating platform for design of a virtual drill path with help of sleeve guide.

- **Dynamic Guided Endodontics** uses information from patients CBCT to plan access cavity, overhead tracking cameras relate the position of bur in 3D by looking at the software interface, clinician gets immediate feedback about position of bur as it relates to the position of planned access and the tooth.
- Technological advancements have enabled inter-operability between 3D imaging devices, 3D virtual planning systems and 3D printers to process, manipulate and create data for producing 3D printed guides.
- **3D Endodontic Guide** is a template fabricated to guide drills into pre-planned positions for localization and exploration of root canal orifices.
- Endodontic guides are also called Endoguide, Endodontic Template, 3D Endodontic Guide/Template.

- **Steps in 3D guide planning and designing**:

  **1**.CBCT of invoved tooth, **2**. Surface Scan: using intra-oral scanner or scanning a model made after an impression. The scan has to cover atleast one quadrant of the tooth arch to secure a stable support for the guide. **3**.Merging CBCT scan with Surface scan using software: superimposition of CBCT data and surface scan is very crucial to get accurate fit of the guide. Three to six reference landmarks or points are marked on both scan files and then software automatically merges them. **4**.Designing Endoguide: mainly done by tracing the canal, creating virtual drill path by deciding the target point, angle of the drill and diameter of the drill and finally Sleeve selection. These Endoguides are printed with the help of 3D printers.
- Studies have shown that skill or experience of clinician does not affect the accuracy of guided endodontic procedure. In addition to conserving remaining tooth structure it also reduces the chair side time compared to conventional techniques especially in difficult cases like calcified canals or developmental anomalies.
- High success rate has been seen with guided endodontic technique with a low deviation angle three dimensionally and at the tip of bur.
- Some of the limitations of Static guidance are that it will work only for straight parts of root canals, might require drill guide for each canal increasing the cost in multiple canal cases, tooth has to be stable during scan and guided drilling, presence of metallic

restorations may lead to artefacts while imaging thus resulting in inaccuracies in treatment planning, limited availability of armamentarium, requires time to prepare endoguides before procedure, and does not allow even minor changes in treatment plan.

- Dynamic guidance however can overcome this limitations as clinician can visualize the bur on screen in 3D and control the removal of tooth structure to keep it as minimal as planned. High speed drills and burs can be used, no guide rings are required, any changes in treatment plan can also be accommodated. However limited mouth opening could pose problems especially in posterior teeth.
- Research shows that Dynamic guided endodontics are more accurate than Static guided endodontics but overall guided access techniques are more accurate and safe than traditional freehand technique.
- Guided endodontics with its predictable outcome, lower risk of procedural errors and preservation of structural integrity of tooth even in most challenging cases is soon going to be the future of Endodontics.

**REFERENCES:**


1. *Kinariwala N, Samaranayake L. Guided Endodontics, Springer 2020.*
2. *Krastl G, Zehnder M S, Connert T, Weiger K, Kuw S. Guided Endodontics: A novel treatment approach for teeth with pulp canal calcification and apical pathology. Dent Traumatol. 2016; 32: 240-246.*
3. *Zubizarreta- Macho, Munoz, Deglow, Agustin-Panndero, Alvarez. Accurracy of computer aided dynamic navigation compared to computer aided static procedure for endodontic access cavities: an in-vitro study. J Clin Med 2020; 9:129.*

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Dentistry |
| **2. Speciality** | Periodontics |
| **3. Date** | 18.12.2020 |
| **4. Title** | Advances in application of platelet concentrate for periodontal regeneration. |
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## Advances in application of platelet concentrate for periodontal regeneration.

**Relevance:**

- Periodontal regeneration is defined as reproduction or reconstitution of lost or injured periodontal tissues. Conventional procedures used in periodontal regeneration offer limited potential toward attaining complete periodontal restoration. **In 1971, Robert Marx** showed evidence that platelets are reservoirs of **growth factors and cytokines** which are the key factors for bone and soft tissue regeneration. Platelet concentrates are autologous products so it eliminates the risk of any adverse reactions and disease transmission, also being economical, its low-cost regenerative modality have a promising scope in periodontal regeneration when used alone or in combination with other biomaterials
- Choukroun's pure **platelet rich fibrin (P-PRF)** is classified as a second generation platelet concentrates which have gained tremendous momentum in periodontal regeneration.
- Since PRF is **autologous, there are no associated immune reaction**.Its preparation is simple, inexpensive and there is no requirement of any additive agent. But lack of rigidity and faster degradation may limit its application in guided tissue regenerative procedures.
- The technique of preparation, transfer process, time and temperature of centrifugation and vibration are the various factors which determine the quality of the biomaterial.**Many modifications have been made in the preparation of platelet concentrates to enhance its bioactivity**.
- **Leukocyte Platelet-Rich Fibrin (L-PRF**): The L-PRFis modified PRF which contain platelets, leukocytes, growth factors and stem cells that are trapped within the fibrin network with enhanced strength. Blood should be collected quickly in 9ml glass-coated plastic tubes and centrifuged in Intra-Spin centrifuge at room temperature (2700 rpm for 12 minutes) to produce L-PRF clots.
- **Advanced Platelet-Rich Fibrin (A-PRF):** Another modification of P-PRF in which rpm is reduced while centrifugation time is increased (1300 rpm for 14 minutes). Centrifugation speed (G-force) and time influence growth factor release, cellular activity of gingival fibroblasts exposed to each PRF matrix.
- **Injectable platelet-rich fibrin (I-PRF):** Injectable form of PRF is a platelet concentrate in liquid formulation used alone or in combination with other biomaterials (3300rpm for

2minutes). It also clots and attains a gel form after about 10-15 minutes for sustained release of growth factorswith higher presence of regenerative cells in the tissue and induces expression of transforming growth factor-β and collagen-1 mRNA.

- **Titanium platelet- rich fibrin (T-PRF):** T-PRF may be more efficient in activating platelets than silica used within glass tubes, as silica present in the glass tube may produce hazard to patients.T-PRF is prepared in Grade IV titanium tubes at a centrifugation of 2800 rpm for 12 minutes.
- **Concentrated growth factors preparation (CGF):** CGF has a difference in centrifugation speed which permits the isolation of much larger and denser fibrin matrix richer in growth factors, platelets, leukocytes and CD34+ stem cells.
- **Autologous fibrin glue (AFG) and sticky bone:** AFG was obtained by centrifuging 20 - 60CC of blood in non-coated tubes at 2400-2700 rpm for 2 minutes. AFG mixed with particulate bone powder and allowed to rest for 5-10 minutes for polymerization and this resulted in a yellow colored mass called sticky bone.
- In **future perspectives** platelets are being proposed to be used as carriers for loading drugs or biological therapies to specific target locations due to its biocompatibility, low immunogenicity, protection of growth factors against enzymatic degradation, long-term bioavailability as well as ease of surface modification for selective targeted delivery.

**Conclusion**

The current research on platelet concentrates has shown promising results in periodontal regeneration. At the same time, there is need to evaluate its properties, which includes quantification and the number of growth factors released from PRF over time.

There are only limited studies in the literature on the effect of platelet concentrates on cell proliferation and other biologic effects. Hence more studies should be conducted which open newer strategies for the use of this platelet concentrate.

**References**


1. *Nityasri, Aromal S, Pradeep KY, et al. Role of CGF (Concentrated Growth Factor) in periodontal regeneration. J Dent Health Oral DisordTher. 2018; 9:350–352.*
2. *Ozsagir ZB, Saglam E, SenYilmaz B, Choukroun J, Tunali M. Injectable platelet-rich fibrin and microneedling for gingival augmentation in thin periodontal phenotype: A randomized controlled clinical trial. Journal of Clinical Periodontology. 2020; 47:489-499.*

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

| | | |
|---|---|---|
| **1. Stream** | Dental | |
| **2. Speciality** | Orthodontics | |
| **3. Date** | 07-12-2020 | |
| **4. Title** | **Finding the hidden orthodontic scar-External Apical Root Resorption** | |
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| **Suggested Structure of Article** | 1. Filled up Facing Sheet of the Article<br>2. Article on maximum TWO sides of an A4 Page<br>3. Title of the Recent Advance<br>4. Source: Original Article / Site / Book<br>5. Contributor’s Name (To be Published)<br>6. A note on why it is relevant.<br>7. Body of the article as 10 to 20 Bulleted Points<br>8. References (2 to 3nos) | |

# Finding the hidden orthodontic Scar-External Apical Root Resorption

**Relevance**

One of the most common undesirable side effects of orthodontic treatment is **external apical root resorption (EARR)**. 90% of patients undergoing orthodontic treatment were observed to have root resorption, as evaluated by previous histologic, experimental and radiographic studies. Severe root resorption with a range of loss of more than 2mm to half the root length has been observed in around 5% of patients undergoing orthodontic treatment and can have clinically significant consequences. There might be a reduction in long-term viability of the dentition due to a reduced crown-to-root ratio.

Root resorption observed early during orthodontic treatment is reported to be predictive of a chance of more severe resorption with continued treatment. Therefore, in the earlier phases of orthodontic treatment, it is imperative to accurately detect mild to moderate root resorption, to prevent severe root resorption and the unfavourable outcome of increased tooth mobility or premature tooth loss. It is important to identify the risk factors - both biologic and treatment related which contribute to external apical root resorption, so as to minimize the detrimental effects.

- The most popular diagnostic method to identify root resorption is using **radiographs**- the intraoral periapical radiograph and the Orthopantomogram. The main drawbacks cited include radiation exposure, problems with standardization, besides the inability to indicate whether the root resorption is on-going or inactive.
- Computerized tomography and **cone-beam computed tomography** have been shown to increase diagnostic accuracy; however, the routine use in dentistry is difficult due to the high cost and high radiation exposure. With these two methods going against ALARA, there was a need for a more sensitive and safer method for detecting root resorption.
- **Biomarkers** involved in external apical root resorption have been identified in the oral fluids- Gingival Crevicular Fluid (GCF) or saliva. Consequently, if significant tests could be created utilizing these biomarkers, it would be advantageous as it is non-invasive and easy to collect the samples. Besides, it offers a great potential for the early detection of root resorption, much before the root damage is visible on a radiograph or a cone-beam computed tomography scan.

- Quantification of the constituents of GCF is the current method to identify specific biomarkers with reasonable sensitivity. GCF analysis provides a safe and non-invasive method for identifying individuals at risk for root resorption thereby predicting subsequent clinical prognosis as well as the need for implementation of alterations in therapy. The expected impact of this research is far-reaching, considering the potential benefit to patients. However, the perceived progress is slow may be due to the difficulty in preservation and isolation of biomarkers and the cost involved.
- Isolation of Biomarkers in GCF/saliva require high-level laboratory instrumentation to perform ELISA, Western-blot, electrophoresis (SDS-PAGE) or liquid chromatographic mass spectrometry and immunoassay to quantify root resorption.
- Recent studies have revealed that small extracellular vesicles called exosomes have many clinically relevant proteins. **Exosomes** are small vesicles of endosomal origin which are released by different cell types, after fusion of multi-vesicular bodies with the plasma membrane. The odontoclasts and osteoclasts have different exosome proteome profiles and higher activity in forming resorption lacunae are exhibited by odontoclasts. Future development to utilize exosomes as non-invasive and non-radiographic diagnostic assays to monitor bone and dentin resorption *in vivo* has to be investigated further.
- The future of this field will rely on the ease of validation of specific biomarkers and their incorporation into broad clinical practice - the state-of-the-art assays that are reliable, specific, sensitive and economic.
- Ability of these tests for early detection and subsequent prevention of further damage to root structures may help develop a predictive model to prevent serious complication developing in patients susceptible to extensive EARR.

**References**


1. *Balducci L, Ramachandran A, Hao J, Narayanan K, Evans C, George A. Biological markers for evaluation of root resorption. Arch Oral Biol. 2007;52(3):203-8.*
2. *Rody WJ Jr, Holliday LS, McHugh KP, Wallet SM, Spicer V, Krokhin O. Mass spectrometry analysis of gingival crevicular fluid in the presence of external root resorption. Am J Orthod Dentofacial Orthop 2014; 145:787-98.*
3. *Rody WJ Jr, Chamberlain CA, Emory-Carter AK, McHugh KP, Wallet SM, Spicer V, Krokhin O, Holliday LS. The proteome of extracellular vesicles released by clastic cells differs based on their substrate. PLoS One. 2019; 14(7): e0219602.*

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Dental |
| **2. Speciality** | Conservative Dentistry & Endodontics |
| **3. Date** | 11-01-2021 |
| **4. Title** | Dental Operating Microscope: An inevitable tool for magnification in Endodontics |
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# Dental Operating Microscope: An inevitable tool for magnification in Endodontics

- Magnifying aids
  - Dental Operating Microscope.
  - Surgical Operating Loupe.

**Rationale**

- Though Operating Microscope have been used for decades in dentistry and other medical specialities, it was not a very popular tool in endodontics mainly because of its high cost and the need of sophisticated operating skills to work under microscope. Until recently performing endodontic therapy entailed ‘‘working blind,’’ that is, most of the effort was taken using only tactile skills with minimum visual information available. With the advent of economical low cost microscopes and with the emergence of many short term advanced micro endodontic courses, use of magnifying aids has become very popular recently in the field of endodontics worldwide.

**Significance of Dental Operating Microscope (DOM)**

- It increases resolving power of human eye 0.2mm to 0.006mm which is very essential for producing precision in endodontic treatment.
- With DOM we can achieve a magnification in the range of x3.5 – x30. Low magnification is for orientation of surgical field, mid-range magnification is for working and high magnification is for fine inspection of details.
- Effective use of operating microscope helps to maintain our posture and working distance which will be very helpful in limiting neck and back strain.
- It uses Galilean optics in which parallel beam of light reaches operators eye and helps the observer to focus at infinity, relieving eye strain.
- Microscope has enabled the clinician to do some specific treatment with more accuracy, which was not at all possible without magnification.
- Previously documentation of root canal treatment was limited to paper work and radiographs. Now with DOM video or clinical pictures of procedure with in root canal can be documented easily with accessories attached to microscope like beam splitter and video camera.

**Parts of an Operating microscope**

- Eyepieces: available in different power settings (6.3x,10x,12.5x,16x,20x) with dioptre adjustments & eye guards.
- Binocular tube: 0- $210^0$tiltable ergonomic head with interpupillary distance 50-75mm.
- Magnification changer: Manual and power zoom changers are available with 3 step or 5 step (0.4x,0.6x,1.0x,1.6x,2.5x).
- Objective lens: Lens of different focal length are available (F=300mm; f=400mm) Nuvar variable objective system with focal length varies from 300-400 mm are also available.
- Fine focus adjustment knob
- Light source: LED based illumination with 60,000 hour rated bulb life.
- Optional accessories: Beam splitter, rotoplate and proline range of camera adapters.

**Designs available**

- Ceiling mount, Wall mount, Table mount, Floor mount

**Applications of DOM in Endodontics**

- To do the endodontic treatments efficiently under microscope we need to have high definition or front surface mirrors, micro mirrors and other long shank hand as well as rotary instruments with small head. Use of rubber dam isolation is mandatory in using DOM.
- Diagnosis of cracks in tooth.
- Preparation of constricted or ninja access cavity preserving the fracture resistance of the tooth.
- Detection and management of calcified root canals, missed canals, aberrant canals, dilacerated canals and canals blocked by restorative materials.
- Helps efficiently in retreatment cases especially in gutta-percha and sealer removal, cleaning and shaping, retrieval of broken instruments, perforation repairs etc.
- Can be used in micro endodontic surgical procedure.

**References**


1. *Carr G B, Murgel C A F. The use of Operating Microscope in Endodontics. Dent Clin N Am. 2010;54:191-214.*
2. *Kim S, Baek S. The microscope and Endodontics. Dent Clin N Am. 2004;48:11-18.*
3. *Dr.Syngcuk Kim, Gabriele Pecora and Dr. Richard A Rubinstein. Color Atlas of Micro surgery in Endodontics. 1st edition 2001 by Saunders publication.*

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Ayurveda |
| **2. Specialty** | Balroga |
| **3. Date** | 28-12-2020 |
| **4. Title** | Management of developmental disorders in children – Ayurveda based integrative approach |
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# MANAGEMENT OF DEVELOPMENTAL DISORDERS IN CHILDREN – AYURVEDA BASED INTEGRATIVE APPROACH

Developmental disability in children is still a topic of research and advancements worldwide. Developmental disabilities include limitations in function resulting from disorders of the developing nervous system. 15 per cent of the world's population, or more than 1 billion people, are living with disability. As per UNICEF, there are at least 93 million children with disabilities in the world, but numbers could be much higher[1]. Although frequently addressed during pediatric rehabilitation care, problems in mobility and self-care still prevail in young adults with developmental disorders affecting their domestic and work life.

- The etiologies of these disabilities are genetic, antenatal, natal, post-natal, nutritional and environmental which are mostly preventable. Integrating the concepts of *Dinacharya*,(proper personalized daily diet and regimen) *Ritucharya*,(proper seasonal diet and regimen) and *garbhinicharya* (proper personalised daily diet and regimen of pregnant lady) along with the conventional management of pregnancy helps to improve the physical, mental and spiritual wellbeing of the mother and baby.
- Early intervention is one of the key factors in the management of developmental disorders in children. Collaborative efforts of Ayurvedic physician, developmental pediatrician, physiotherapist, speech therapist, occupational therapist and child psychologist is essential for stimulating the physical, mental and social development of disabled children.
- Injury to the developing brain is the key factor leading to disability. Drugs like *Mandukaparni*(Centella asiatica)[2]*, Brahmi*(Bacopa monnieri)*,Sankhapushpi* (Convolvulus Pluricaulis) etc have already reported neuro protective and cognitive enhancement activities which will help in the rejuvenation of the developing brain.
- The Ayurvedic treatment of developmental disorders in children starts with modalities for enhancement of digestion, absorption and metabolism, which are otherwise minimal in such children. This stabilizes the proper growth of these children.
- The external procedures like *snehana* (different methods of oleation) and *swedana*(different methods of sudation) helps to reduce the spasticity, improve the muscle tone, reduce contractures and thereby improve the range of body movements.
- Various applications in head like *Sirodhara*(pouring oil/other medicated liquid gently overhead), *Sirolepa*(applying medicated paste on head) and *Siropichu*(placing oil dipped cloth on head) helps to improve cognition, reduce hyperactivity and improve sleep pattern.

- Studies have been conducted in Ayurveda based integrative management of disorders like Cerebral palsy, Autism spectrum disorders and ADHD in various institutions throughout India[3]. Majority of the published studies are case series or have black box designs and have shown clinically significant results. In all the above studies, the diagnostic and assessment tools used were from conventional medicine and treatments were based on Ayurvedic principles. Controlled trials in the future will help to establish the results more scientifically.

**References**


1. *https://www.unicef.org/disabilities/#:~:text=Estimates%20suggest%20that%20there%20are,their%20voices%20heard%20in%20society.*
2. *Gray, N. E., Alcazar Magana, A., Lak, P., Wright, K. M., Quinn, J., Stevens, J. F., Maier, C. S., & Soumyanath, A. (2018). Centella asiatica - Phytochemistry and mechanisms of neuroprotection and cognitive enhancement. Phytochemistry reviews : proceedings of the Phytochemical Society of Europe, 17(1), 161–194. https://doi.org/10.1007/s11101-017-9528-y https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6857646/*
3. *Bhinde, S. M., Patel, K. S., Kori, V. K., & Rajagopala, S. (2014). Management of spastic cerebral palsy through multiple Ayurveda treatment modalities. Ayu, 35(4), 462–466. https://doi.org/10.4103/0974-8520.159044*
   *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4492036/*

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Nursing |
| **2. Speciality** | Medical Surgical Nursing |
| **3. Date** | 07.12.2020 |
| **4. Title** | **How Technology is impacting nursing practice in 2020** |
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# HOW TECHNOLOGY IS IMPACTING NURSING PRACTICE IN 2020

## Relevance

In the last 30 years, technological advances have transformed the medical landscape. The days of meticulous charting and manually filing records are dwindling. With emerging technologies in telehealth and electronic recordkeeping, patients have more accessibility to their data than ever before. In the nursing field, technology allows RNs to improve efficiency and communicate more effectively. The advances in information technology and new devices have improved the quality of life for patients and healthcare professionals alike. The evolving technological advances in nursing are the wave of the future in healthcare. Emerging new technologies in EHRs, AI, apps and software development are becoming increasingly popular as more hospitals and facilities integrate them into their health system. While there are drawbacks that come with telecommunication, it's clear that information technology has the potential to improve the quality of life for nurses and RNs alike.

- **Improved Accessibility**

Electronic health records (EHRs) have transformed the healthcare information technology space. An electronic health record is a digital version of a patient's medical history. It can include progress notes, providers, problems, medications, lab data, etc. EHRs can improve patient care by improving the accuracy and clarity of medical records, and making data easily accessible to healthcare providers, doctors, and patients.

Advancements in telehealth have also played a large part in improved accessibility. Telecommunication systems have made it easier for patients separated geographically to receive nursing care via remote patient monitoring, live video conferencing and mobile health apps. In today's environment, it has become easier for those in remote geographic areas to have access to quality care.

- **Decreased Human Error**

New technologies can decrease the chance of human error. Nurses who work long hours or have understaffed units are at a higher risk of making mistakes. With new medical technologies, routine procedures are simplified. For example, automated IV pumps can measure the dosage of medication given to patients. This creates a quicker process for changing drip amounts and dosage. EHRs also help with decreasing mistakes at the bedside. Since the data is readily available, EHRs can help reduce duplication of tests or delays in treatment.

- **Positive Impact on Nursing Shortage**

Nurse burnout has been a factor in the shortage of nurses in the U.S. Prolonged mental and physical exhaustion can cause nurses to feel stretched thin, which leads to nurses leaving their practice setting. Emerging technologies in telehealth can help mitigate the burden put on nurses since it takes fewer nurses to provide adequate care.

**Potential Drawbacks of Nursing Technology**

The rapid growth of technology in the healthcare space has identified potential obstacles that hospital systems may face.

- **A Threat to the Human Element**

Improved technology can threaten to replace person-to-person interaction between nurse and patient. Nurses have the role of establishing a relationship with their patients and their families; they are responsible for explaining medications, taking vitals and helping patients with daily needs. In some hospitals, nurses are required to wheel in their workstation (a computer on wheels) to record information about the patient. While typing information on a computer is perceived to be more trustworthy by patients and healthcare professionals alike, it will inevitably create less face-to-face interaction.

As a response to the aging population, robotics has become an emerging field in healthcare. In Japan, nurse robots are being manufactured and tested as a way to lessen the burden of nurses; however, these robots lack empathy and a "human touch." More research is required before understanding if these machines will improve patient care.

- **Generational Divide**

Nurse leaders understand that workplace technology integration can be largely influenced by generational differences among staff. In the nursing field, baby boomers make up roughly 50 percent of the entire RN staff. Baby boomers are perceived to be lacking in tech-savvy skills and may be slower to adapt to new devices. According to a journal published in 2015, rapid technological advances are a factor that cause older nurses to retire.

- **Data and Security Threats**

As with most any computerized information, EHRs kept in the cloud or in the form of big data are more susceptible to being hacked. Cybercrimes for hospitals are not uncommon as patient profile data can be sold on the black market ranging from $20 to $50. If an inexperienced employee accidentally clicks on malware, a whole EHR system may be at risk of being compromised. Hospitals that have a breach in data or EHR can pay hefty fines depending on the severity. Security threats to a patient's data can ultimately make a facility think twice before storing important patient records in the cloud.

**Reference**


1. *https://www.nursepractitionerschools.com/blog/important-advances-in-nursing-science/*
2. *https://www.nursepractitionerschools.com/blog/important-advances-in-nursing-science/*
3. *Scott T. Advances in nursing practice. Emerg Nurse. 2016 May;24(2):5. doi: 10.7748/en.24.2.5.s1. PMID: 27165371.*

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1.Stream** | Pharmacy |
| **2.Speciality** | Pharmaceutics & Pharmaceutical Engineering |
| **3.Date** | 07/12/2020 |
| **4.Title** | Tablet Manufacturing by 3D Printing Technology |
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| **11.Suggested Structure of Article** | 1. Facing Sheet of the Article<br>2. Article on maximum TWO sides of an A4 Page<br>3. Title of the Recent Advance<br>4. Source: Original Article / Site / Book<br>5. Contributor’s Name (To be Published)<br>6. A note on why it is relevant.<br>7. Body of the article as 10 to 20 Bulleted Points<br>8. References (2 to 3 nos.) |

# Tablet manufacturing by 3D Printing Technology

**Relevance**

The first 3D printed tablet to be FDA-approved was manufactured in 2015 by Aprecia Pharmaceuticals. Two years later, GSK completed a study using ink-jet 3D printing and UV curing to create tablets used to treat Parkinsonism. 3D printing technology is transforming the pharmaceutical industry with controlled release, short-term drugs, and the potential for on-site printing in pharmacies. Such experiments can open the door to improvements in individual medicine and clinical trials, which will benefit patients and manufacturers alike.

**Introduction to 3D printing**

With this technology, 3D computer-aided design (CAD) files build a prototype from an idea so it can be digitally controlled and customized fabricated. The technology uses a bottom-up approach in which layers of living cells, wood, alloys, thermoplastics, and metals are placed on top of each other to create the desired 3D object. Hence, 3D printing is also known as layered manufacturing, additive manufacturing, computer automated manufacturing, rapid prototyping or Solid Freeform Technology (SFF).

**3D printing in tablet manufacturing**

- First, a virtual 3D design of an object is created using digital design software such as Onshape, SolidWorks, Creo Parametric, AutoCAD, and Autodesk. Converts this digital model (. STL) to a digital file format, referred to as standard tessellation language or stereolithography. (. STL) The triangular sides provide information about the surface of the current 3D model in the file. The (. STL) file is converted to a G file by designing a series of 2D horizontal cross-sections with the help of special slicer software installed on the 3D printer. The print head is now moved along the x-y axis to form the base of the 3D object. The print head is now allowed to move on the z-axis, thereby depositing successive layers of the desired material, thus creating a complete 3D object. The maximum number of 3D printing technologies is compatible with the (. STL) file format. Some errors may occur when converting the 3D model to (. STL) digital file; Therefore, software such as Magic (Materialize) can be used to troubleshoot errors during conversion. File formats other than (. STL) are used as Additive Manufacturing File Format (AMF) and 3D Manufacturing Format (3D) format.

- In the example of Aprecia Pharmaceuticals, 3D printing was used to reformulate the anti-epileptic medication levetiracetam. The new product, Spritam, has a highly porous structure that could not be achieved with traditional manufacturing. This structure causes the pill to dissolve in seconds upon contact with saliva, helping both elderly and young patients suffering from trouble with swallowing pills, known as dysphagia.
- This innovative development was achieved through a proprietary powder bed and inkjet 3D-printing technology known as ZipDose. In manufacturing, an initial powdered layer containing the drug itself is laid down. That first layer then passes under an inkjet print head, and a binding liquid is printed at specified locations along the powdered sheet. Successive layers are then printed up to 40 times, depending on the size of the tablet. Printing the layers allows the drug to be packed more tightly. A single tablet that would normally hold 200 mg can be layered to hold 1,000 mg. The result is a high-dose medicine that is easy to swallow for epileptic patients and breaks down inside the body to administer a steady dose over time.

**Conclusion**

To date, Spritum is the only FDA-approved 3D printed pharmaceutical on the market. However, the FDA sees 3D printing as a tool to improve the quality and stability of drugs. 3D printing technology is a valuable and potential tool for the pharmaceutical industry, leading to individualized medicine focused on the needs of patients. It offers many advantages such as increased cost efficiency and faster production. Created a revolution in the way 3D printing was produced. This improves design construction and reduces lead time and equipment costs for new products.

**References**


1. *Trenfield SJ, Awad A, Goyanes A, Gaisford S, Basit AW. 3D printing pharmaceuticals: drug development to frontline care. Trends Pharmacol Sci. 2018; 39:440–51.*
2. *Bansal M, Sharma V, Singh G, Harikumar SL. 3D printing for the future of pharmaceuticals dosages forms. Int J Appl Pharm. 2018; 1–7.*
3. *https://www.pharmaceuticalonline.com/doc/3d-printing-in-the-pharmaceutical-industry-where-does-it-currently-stand-0002*

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Pharmacy |
| **2. Speciality** | Pharmaceutics |
| **3. Date** | 8-12-2020 |
| **4. Title** | Pharmacosomes: The Lipid-Based Novel Drug Delivery System |
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# Pharmacosomes: The Lipid-Based Novel Drug Delivery System

The aim for the development of novel drug delivery systems is to minimize the side effects and maintain relatively unvarying and potent levels of drug in the body. Pharmacosomes are colloidal, nanometric size micelles, vesicles or may be in the form of hexagonal assembly of colloidal drug dispersions attached covalently to the phospholipid. They act as befitting carrier for delivery of drugs quite precisely owing to their unique properties like small size, amphiphilicity, active drug loading, high entrapment efficiency, and stability2.

The advantages of Pharmacosomes3.

- Leakage of drug take place can be prevented by covalent linkage with the carrier.
- Entrapment efficiency of drug is high.
- Both hydrophilic and lipophilic drugs are suitable for Pharmacosomes.
- Direct drug delivery to the site of action can be achieved.
- Bioavailability of poorly soluble drugs can be improved
- Adverse effects and toxicity can be reduced

Components of Pharmacosomes3

**1. Drugs**: A drug having an active hydrogen atom can be esterified to the lipid, with or without spacer chain resulting into amphiphilic complexes. These synthesized amphiphilic complexes (pharmacosomes), facilitate membrane, tissue or cell wall transfer in the organism.

**2. Lipids:** Phospholipids are principal molecular building block of cell membranes. Two type of phospholipids generally used are phosphoglycerides and spingolipids.

**3. Solvent:** Organic solvent of intermediate polarity is used in development of pharmacosomes. It must be of high purity and volatile in nature. The phospholipids and the drug must be dissolved in the selected solvent. The selection of solvent depends on polarity of the drug and the lipid.

Preparation of Pharmacosomes2, 3

**1. Solvent Evaporation Technique:**

**(a) Hand-shaking method:** The drug lipid conjugate is mixed with an organic solvent, which under the conditions of vacuum deposits a thin film on the walls of round-bottom flask and yields a vesicular suspension when hydrated with aqueous medium.

**(b) Rotary evaporator**: Mixture of drug and lipid is dissolved in a volatile organic solvent. There after solvent is evaporated using rotatory evaporator in round bottom flask which leaves a thin film of solid mixture deposited on the walls of flask.

2. Ether-Injection Technique: The drug lipid complex is dissolved in an organic solvent. This mixture is then slowly injected into a heated aqueous agent, resulting in the formation of vesicles. The state of amphiphiles depends on the concentration. When the concentration is less, amphiphiles introduce a monomer state but as the concentration is increased, variety of structures may be formed, that is, round, cylindrical, disc, cubic, or hexagon type.

3. Anhydrous co-solvent lyophilization method: First of all, drug and phospholipids are dissolved in solution of dimethyl sulfoxide containing glacial acetic acid. Then mixture is agitated to get clear liquid and then freeze-dried overnight at condenser temperature. The resultant complex is flushed with nitrogen and stored at 4o C.

4. Supercritical fluid process: Drug and lipid complex are dissolved in a supercritical fluid of CO2, then mix into nozzle mixing chamber.

**Conclusion**

Pharmacosomes plays an important role in overcoming the limitations associated with vesicular drug delivery system. With the improvement in spacer groups and linkages, further drug fate and biological activity may be modified. Pharmacosomes have immense potential in improving the drug delivery in case of both natural and synthetic active constituents. Developing the pharmacosomes of the drugs has been found to improve the absorption and minimize the toxicity.

**Reference**

1. *Ajay Semalty, Mona Semalty, Balwant singh rawat, Devendra singh, M S M Rawat. Pharmacosomes: the lipid-based new drug delivery system. Expert opin drug deliv. 2009, 6(6): 599-612.*

*2. Archana Pandita, Pooja Sharma. Pharmacosomes: An emerging novel vesicular drug delivery system for poorly soluble synthetic and herbal drugs. ISRN Pharmaceutics. 2013: 1-10.*

*3. Ali Gamal Ahmed Al-kaf, Ahmad Mohammed Othman. A Review on Pharmacosomes: an emerging novel vesicular drug delivery system. Universal Journal of Pharmaceutical Research. 2017, 2(1): 21-24.*

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1.Stream** | Pharmacy |
| **2.Speciality** | Pharmaceutical Biotechnology and Nanotechnology |
| **3.Date** | 06/12/2020 |
| **4.Title** | DNA SEQUENCING USING GRAPHENE NANOPORES |
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# DNA SEQUENCING USING GRAPHENE NANOPORES

**Relevance**

Fast, cheap, and reliable DNA sequencing could be one of the most disruptive innovations of this decade, as it will pave the way to personalized medicine. A variety of nanotechnology-based approaches have been explored and established, including sequencing with nanopores. Owing to its unique structure and properties, graphene provides interesting opportunities for the development of a new sequencing technology. In recent years, a wide range of creative ideas for graphene sequencers have been theoretically proposed and the first experimental demonstrations have begun to appear.

**DNA sequencing**

- DNA sequencing is the process of determining the exact order of the bases in a molecule of DNA. By this, it is possible to give patients precise & personalized treatment developed on the basis of that patient's specific DNA sequence.
- DNA sequencing has come a long way since 1970s, when the first technique was introduced by Frederick Sanger. The technique involved 4 steps:
    - DNA amplification
    - Sequencing reaction
    - Separation and detection of the fragments
    - Assembling of the sequenced parts of a gene

**Nanopore sequencing**

- DNA strands are electrical conductors. Different nucleotide bases have different electrical characteristics. The measurement of these properties determines the DNA sequence. So, a tiny hole [nanopore] was made through a thin sheet of material and measured the amount of current passes from one side of the sheet to another. Pulled a DNA strand through the hole and measured the current again. The changes in current give the direct reading of nucleotide sequence in the strand.

- Biological protein pores such as α-hemolysin [α-HL] and Mycobacterium smegmatis porin A [MspA] were the first nanopores. But, sensitivity of these to temperature, pH and applied voltage was a drawback. Solid state nanopores such as Silicon nitride [SiN],

Aluminium oxide [$Al_2O_3$], Silicon oxide [$SiO_2$] were exciting alternatives as they are robust and possess electrical properties. But they are 10-100 times thicker than the distance between 2 nucleotide bases. So, it's not a single nucleotide base that blocks the current flow and it makes hard to determine the sequence from any change in the current. So, the resolution is low.

**Graphene nanopore sequencing**

- Graphene is a one atom thick sheet of C-atoms, arranged in a honey comb [hexagonal] lattice with a thickness of 0.3nm. It is the thinnest & strongest known material and is very flexible. It was considered as a 'material that could not exist' since it was isolated for the first time in 2004. It is a great electrical conductor: Electrons are able to flow as fast as $1/100^{th}$ of the speed of light in vacuum. Graphene is transparent, cheap and plentiful. It is harder than diamond & 300 times harder than steel. It is stretchable up to 20% of its initial length.
- Single layer of graphene is only 0.3nm thick, smaller than the distance between 2 bases. When a DNA strand passes through it, it's a single nucleotide that blocks the pore at a moment. These makes graphene nanopore a promising device for DNA sequencing. The pores are obtained by placing a graphene sheet over a 5µm sized hole in a SiN membrane and drilling a nanosized [about 5nm] hole in the graphene using highly focused electron beam of a Transmission Electron Microscope [TEM]. Added a layer of Titanium oxide to the graphene membrane to make the hydrophobic graphene more wettable. The layer is mounted into a microfluidic flow cell, added a 1M saline solution [1M KCl, pH-8.0] on both sides of the membrane. A voltage is applied across the membrane for which the current from ion transport through pore is measured. DNA was driven electrophoretically through the nanopore as a long string. Each nucleotide obstructs the nanopore to a different characteristic degree and the amount of the current passing through the pore varies depending on the type of nucleotide. Each temporary drop in measured conductance arises from a single nucleotide that translocate through the pore. In DNA, A-T & G-C base pairs stretch to a different degree for a particular voltage because of their difference in number of H-bonding.

**Conclusion**

- It is a method of direct sequencing without the need of an intervening PCR amplification or a chemical labeling step or the need for optical instrumentation [lasers] to identify the chemical label. This low-cost, ultra-fast & accurate DNA sequencing could revolutionize both healthcare and biomedical research, and lead to major advances in drug development, preventative medicine and personalized medicine. DNA sequencing could get a lot faster and cheaper and thus closer to routine use in clinical diagnostics.

**References**


1. *Stephanie J. Heerema et al. (2016), Nature Nanotechnology, Graphene nanodevices for DNA sequencing, 11, 127–136.*
2. *Falah Awwad et al. (2018), Biosensors and Bioelectronics,* ***Graphene-based nanopore approaches for DNA sequencing: A literature review, 119, 191-203.***

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Pharmacy |
| **2. Specialty** | Pharmacognosy |
| **3. Date** | 12-12-2020 |
| **4. Title** | **ORGAN- ON- A- CHIP-A POWERFUL ALTERNATIVE TO TRADITIONAL ANIMAL TESTING** |
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| **10. Consent for publication** | I hereby declare to abide by the KUHS Rules regarding publication and agree that the article contributed by me may be published in the KUHS publication on recent advances. |
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## ORGAN- ON- A- CHIP-A POWERFUL ALTERNATIVE TO TRADITIONAL ANIMAL TESTING

- Microphysiological systems, also known as 'tissue chip', 'organ-on-a-chip', 'body-on-a-chip', or 'human-on-a-chip' have appeared over the last decade as potent systems to investigate responses to pharmaceuticals. While applicable to animals, these systems are potent in foreseeing human response prior to clinical testing of drugs or as extension of clinical studies to determine the mechanism.
- Organ-on-a-Chip a cutting-edge technology, is an interdisciplinary technique imitating *in vivo* physiology and pathology for *in vitro* disease modeling, drug screening and precision medicine. It has the ability to exemplary the details of organ physiology and also help in understanding the mechanisms of drug and chemical response.
- Body-on-a-chip systems are multi-organ systems, designed to match human physiological response to drugs and have the potential to identify efficacies and toxicities in organs. In pharmaceuticals, these systems can evaluate the chemical contact of an individual, which is a significant device in assessing the safety of chemicals, food ingredients, and cosmetics.
- The technology can be gradually incorporated into the drug development pipeline from primary stages of drug discovery to preclinical screening, testing, and translation of new drugs, which binds the gap between animal studies and clinical trials.
- Recently it was observed that research on organ-on-a-chip proved potential in studies that utilized human-induced pluripotent stem cell to developed personalized tissue or organ models. Integrated multiple organs on single chip with sophisticated representation of absorption, distribution, metabolism, excretion and toxicity process are being employed to understand drug interactions and mechanisms of action in the human body. Through this technology the scientist can predict drug efficacy and safety in a better refined manner. Hence, they are considered useful alternatives to traditional preclinical cell culture methods and *in vivo* animal studies.
- Microbiorobots in organ-on-a-chip's fluid aim to reproduce the hemodynamic flow in the microvasculature thus enables oxygen and nutrient exchange, thereby aid in Penetrating Tissue Barriers for Drug Delivery. A potential application of Microbiorobots in organs-on-a-chip established is treating pulmonary hypertension.
- Organ-on-a-chip systems are integrated mechanical, chemical, and physical inputs to generate functionally tied tissue-like structures that allow fine control over experimental

conditions. They reproduce organ function perfectly and hence can be considered as substitutes to *in vitro* tissue models or live animal models of disease. A lung-on-a-chip system was built based on integrated epithelium and endothelium and integrated respiratory mechanics to simulate the alveolar–capillary interface. The AngioChip is a porous, biodegradable, scaffold, branched, fluid channel that mimics vascularized cardiac and hepatic tissue. This system instinctively supported perfusion, promoted angiogenesis and also performed *in vivo* after surgical implantation with rat femoral vessels.

- Even though animal experiments are crucial for preclinical screening in the drug discovery, issues like ethical considerations and species differences persist. To overcome these issues, cell based assays using human-derived cells have been keenly pursued. Organ-on-a-chip, have been widely studied recently as a novel *in vitro* model as it is possible to physically and chemically mimic the *in vitro* environment by using microfluidic device technology, maintenance of cellular function and morphology, and replication of organ interactions. The functions of organs like lung, liver, kidney, and gut have been reproduced as *in vitro* models.
- To conclude, microphysiological systems holds pronounced potential in drug discovery to develop models that review patient biology beyond the boundaries of traditional cell-based assays. Scientific discoveries have enabled microenvironments that can withstand multiple different connected cell types in microfluidic devices and mimic aspects of *in vivo* biology before challenging to establish *in vitro*.

**References**


1. *Haley C. Fuller, Ting-Yen Wei, Michael R. Behrens and Warren C. Ruder. The Future Application of Organ-on-a-Chip.Technologies as Proving Grounds for MicroBioRobots. 2020; 11: 947.*
2. *Yasamin A. Jodat, Min Gyeong Kang, Kiavash Kiaee, Gyeong Jin Kim, Angel Flores Huidobro Martinez, Aliza Rosenkranz, Hojae Bae, and Su Ryon Shin. Human-Derived Organ-on-a-Chip for Personalized Drug Development. Curr Pharm Des. 2018; 24(45): 5471–5486.*
3. *Hiroshi Kimura, Yasuyuki Sakai, Teruo Fujii. Organ/body-on-a-chip based on microfluidic technology for drug discovery. Drug Metabolism and Pharmacokinetics. 2018; 33: 43e48.*
4. *Malcolm Haddrick, Peter B. Simpson Organ-on-a-chip technology: turning its potential for clinical benefit into reality. Drug Discov Today. 2019;24(5):1217-1223.*

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Pharmacy |
| **2. Speciality** | Pharmacy Practice |
| **3. Date** | 05/12/2020 |
| **4. Title** | **CLINICAL PHARMACIST- CHANGE FROM PRODUCT FOCUSED SERVICE TO PATIENT CENTERED APPROACH** |
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## CLINICAL PHARMACIST- CHANGE FROM PRODUCT FOCUSED SERVICE TO PATIENT CENTERED APPROACH

Pharmaceutical care is, the responsible provision of drug therapy for the purpose of achieving definite outcome that improve or maintain a patient's quality of life. For years, there is a trend for pharmacy practice to move away from its original focus on medicine supply towards a more inclusive focus on patient care. The role of pharmacist is changed from a compounder and supplier of pharmaceutical product to some one that of a provider of services and information on pharmaceutical products and to improve patient care. The pharmaceutical industry in India is growing at a rapid rate with its new medicines are being introduced. Very often with the ever evolution of medicines, for the better treatment output, the pharmacist must respond positively to health service changes. The pharmacists must contribute all their efforts by ensuring that prescriber's intensions are translated into safe, effective and economic use of medicines, so that maximum benefit is available for the patient from their treatment.

Demographic and epidemiological changes, challenges of ageing populations, changes in the disease profile and pattern have imposed demands in health service provision. Along with this the advancements in the technology, scientific breakthroughs, and development in the medical field which must be adopted by the hospital for the better patient care, changed the role and responsibility of clinical pharmacist. Complications of medical management is more in hospital set up, as hospital pharmacist work with doctors, nurses and other health care professionals. So in a patient oriented service the hospital pharmacist has to do the following duties.

1. The patients from various backgrounds may not ask all the aspects of medication to the doctors. In such cases the pharmacist should be approachable. He can provide more assistance and would be able to advise on administration of medicine with dose, frequency, contraindications, possible side effects, when to be taken, how long to be taken, special storage condition if any etc. Such enquiries from other health care department also can be handled by the clinical pharmacist.
2. All medicines have side effects, and some of them are known, while many are still unknown, even though those medicines may have been in clinical use for several years. Rapid introduction of new chemicals to the market made difficulty in monitoring ADR. Since ADR reduces the therapeutic output and arises some economic burden to the patient, there is a

need to train our hospital pharmacists in a well-structured manner to build synergies for monitoring ADR. Many of the hospital pharmacy department follows the program. This helps in improving treatment outcome.

3. The changing responsibilities of hospital pharmacist include prescription analysis/audit, which is helpful to analyze and report use and misuse of drugs in the hospital. Irrational use of antibiotics, which is the major reason for antibiotic resistance, drug-drug interactions in the prescription can be properly analyzed and rectified. A modern pharmacist is always alert about the prescriptions. When judging the appropriateness of the prescription other factors also come in to play, including the effectiveness of the drug, its cost, and the effect on quality of life of the patient.
4. Education of the patient and other health professionals is another key role of the hospital pharmacist. Medicines are changing and developing all the times and pharmacists need to keep constantly an update on changes in the use of medicines as well as keep a tab on new medicines which have been launched.

   Therefore, the hospital authority should have the responsibility to update their hospital pharmacist with latest happenings and improvements in the field of hospital pharmacy practice. The innovations that come with technological advances require the adaptations of health system and enhancement of pharmacist knowledge base. The hospital adopts a practical approach that is based on National Accreditation Board for hospitals and Health care providers (NABH) standards. This helps in building confidence and improving commitment of the pharmacist towards compliance to NABH criteria, thereby improving the efficiency of pharmacy services.
5. The hospital can make use of the services of the pharmacist in wards. Along with ward pharmacy services, the pharmacist can attend ward rounds and can make suggestions on initiation, alteration, and ending of treatment. This does have other advantages in helping pharmacist to understand complexities of therapeutic decision making and in helping clinicians to consider wider aspects of drug treatment.

   Therapeutic drug level monitoring, helps in reporting the concentration of drug in blood using pharmacokinetic calculations to recommend a new dose and frequency. This can be practiced as a part of pharmacy services. Unfortunately, all these activities are largely undocumented and unrecognized. All these show that the pharmacy practice has moved from historical

orientation of product focused service to patient oriented approaches and enhanced the treatment output.

**REFERENCES**


1. *Skledar S.J et al; "Training and recruiting future pharmacist through a hospital based Student internship programme." Am J Health Syst Pharm; 2009 Sep 1; 66(17):1560-4.*
2. *Clark.B.E,Mount.J.K: "Pharmacy Service Orientation- A measure of organizational culture in pharmacy practice sites." Res Social Adm Pharm; 2006 Mar; 2 (1):110-28.*
3. *N Barber, F Smith, and S Anderson; "Improving quality of health care: the role of pharmacists." Qual Health Care; 1994 September; 3(3): 153–158.*

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Allied Health Sciences |
| **2. Speciality** | Microbiology |
| **3. Date** | 28/12/2020 |
| **4. Title** | **Multi-system inflammatory syndrome in children (MIS-C) and COVID-19** |
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| **11. Suggested Structure of Article** | i) Facing Sheet of the Article<br>j) Article on maximum TWO sides of an A4Page<br>k) Title of the RecentAdvance<br>l) Source: Original Article / Site /Book<br>m) Contributor’s Name (To bePublished)<br>n) A note on why it is relevant.<br>o) Body of the article as 10 to 20 BulletedPoints<br>p) References (2 to 3nos.) |

## Multi-system inflammatory syndrome in children (MIS-C) and COVID-19

**Relevance**

As severe acute respiratory syndrome corona virus 2 continues to spread globally, there have been increasing reports from Europe, North America, Asia, and Latin America specifying children and adolescents with COVID-19-associated multi-system inflammatory conditions. However, the association between multi-system inflammatory syndrome in children and COVID-19 is still unknown.

In the past 5 months, there have been reports from various countries describing children and adolescents with COVID-19-associated multi-system inflammatory conditions, which develops after the infection rather than during the acute stage of COVID-19. The clinical characters of these pediatric cases are both similar and apparent from other well described inflammatory syndromes in children, including Kawasaki disease, Kawasaki disease shock syndrome, and toxic shock syndrome.

**Preliminary case definition**

Children and adolescents 0–19 years of age with fever $\geq$ 3 days and two of the following conditions:

- Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammatory signs (oral, hands or feet).
- Hypo tension or shock.
- Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),
- Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
- Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).

AND

- Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin.
- No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.
- Evidence of COVID-19 **(**RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.

**Distinctions between Kawasaki Disease**

There are several important features of MIS-C that differentiate it from Kawasaki disease. Recent data suggests that coronary artery dilation in patients with MIS-C is mild and transient, similar to

that seen in some other febrile illnesses of childhood, including systemic onset juvenile idiopathic arthritis.

Another important difference between the diseases is in the epidemiology; the highest attack rate and most severe consequence of Kawasaki disease occur in infants, whereas the median age of MIS-C appears to be about 9 years of age, with infants relatively spared. Finally, marked lymphopenia is a common laboratory finding in MIS-C, but it is not a feature of Kawasaki disease.

**Classification**

Recently, the CDC published initial findings of 570 children in the United States who were reported to fit its quite broad case definition of MIS-C. The study divided patients into three groups based on latent class analysis, a statistical modeling technique that divides cases into groups by underlying similarities. Patients in Class 1, which had the highest degree of organ involvement and higher prevalence of shock and lymphopenia, were judged to have little overlap with patients with Kawasaki disease. In contrast, patients in Class 3 more commonly met the criteria for Kawasaki disease. Patients in Class 2 had the most respiratory symptoms and highest prevalence of nasopharyngeal RT-PCR positivity for SARS–CoV-2, and likely had acute COVID-19. It should be remembered that acute COVID-19 can affect multiple organ systems, and that the presence of multiple organ involvement does not necessarily indicate the diagnosis of MISC.

**Pathogenesis**

The pathogenesis of MIS-C is unknown, and a post-infectious etiology has been hypothesized but not proven. SARS–CoV-2 antibodies arise in the second week after the infection, but their presence does not indicate resolution of infection. A recent study reported that inefficient and reduced neutralizing antibody activity against SARS–CoV-2 in patients with MIS-C, compared with adults with severe COVID-19 causing acute respiratory distress syndrome (ARDS) and adults who recovered from mild disease, suggesting a reduced protective serological response. The virus is generally not detected in the respiratory tract of patients with MIS-C, but other compartments such as the gastrointestinal tract have not yet been investigated.

Although the presence of SARS–CoV-2–specific T cells in the peripheral blood of recovered and COVID-ARDS (cute respiratory distress syndrome) adult patients has been recently reported, no such reports exist among children yet, and the biological significance of SARS–CoV-2–reactive T cells, whether protective or even detrimental, is still unclear. A direct effect of SARS–CoV-2 Spike

protein structure on immune activation has also proposed. Indeed, recent data suggest that the SARS–CoV-2 Spike protein has a superantigen-like element with sequence and structure similar to Staphylococcal Enterotoxin B, which could initiate the hyper inflammation seen in MIS-C and in adults with severe COVID-19 and cytokine storm.

**Management of MIS-C**

To date, there are no widely accepted guidelines on the management of MIS-C, but several organisations have published their own guidelines. Physicians at various centers have created treatment protocols based on symptoms, previous treatment of similar conditions such as Kawasaki disease, or COVID-19 treatment guidelines for adult patients. If MIS-C is suspected or diagnosed, a multidisciplinary team approach should be taken, including a pediatric infectious diseases unit, and cardiology, immunology, rheumatology, and intensive care unit teams to consider antiviral therapy (if PCR positive for SARS-CoV-2) or immunotherapy, or both. General supportive care is crucial, especially attention to vital signs, hydration, electrolytes, and metabolic status. Few children present with respiratory compromise or hypoxia, but they should be closely monitored for potential compromise.

**References**


1) *Li Jiang MD,Prof Mike Levin,Prof Karen Wilson,Shaun K Morris,Oman Irfan. COVID-19and multisystem inflammatory syndrome in children and adolescents. The Lancet-Volume 20, Issue 11 E276-E 288.*
2) *Anne H Rowley,Stanford T,Shulman and Moshe Arditi, Immune pathogenesis of COVID-19–related multisystem inflammatory syndrome in children. The Journalof clinical investigation.*
3) *Multisystem inflammatory syndrome in children and adolescents with COVID-19, WHO/2019-nCoV/Sci_Brief/Multisystem_Syndrome_Children/2020.1.*

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Allied Health Sciences |
| **2. Speciality** | Microbiology |
| **3. Date** | 28/12/2020 |
| **4. Title** | **The Rising Supremacy of *Shigella sonnei*** |
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# The Rising Supremacy of *Shigella sonnei*

Shigellosis, is a major global agent of bacillary dysentery. Out of the four species of *Shigella,Shigella sonnei* (serogroup c) has become the most prominent serotype causing Shigellosis in Asian countries recently.

Historically *S.sonnei* has been more commonly isolated from developed countries but now an unparalleled expansion occurs across the industrializing regions in Asia, Middle East and in Latin America. The precise reason for this epidemiological distribution is unclear.

**INTRODUCTION**

Shigellosis is a severe and occasionally life threatening diarrheal infection. Around the world Shigella spp are the most common cause of acute dysentery and are responsible for a significant proportion of the burden of morbidity and mortality associated with diarrheal disease.The genus Shigella consists of four species.*S.dysenteriae* (serogroupA), *S.flexneri* (serogroup B), *S.sonnei* (serogroup C) and *S.boydii* (serogroup D),in which *S.sonnei* has only one serotype.

***S.sonnei: an emergent pathogen***

Reasons behind the dominance of *Shigella* sonnei in industrialized countries remains unclear but it may be due to 3 major environmental pressures.

- First natural passive immunisation with the bacterium *Plesiomonas shigelloides* is hypothesized to protect populations with poor water supplies against *S.sonnei.P.shigelloides and S.sonnei* share an identical lipopolysaccharide (LPS) O side chain which is thought to be the major surface antigen targeted by adaptive immune system during shigella infection. These surface antigens are cross -reactive and due to this cross reactive nature Sack and Colleagues suggested that exposure *to P.shigelloides* serotype 017 leads to protection against infections with *S.sonnei*. In areas with poor quality of water supplies exposure to *P.shigelloides* occurs frequently and so the disease due to *S.sonnei* is very rare as the population is naturally immunized. *P.shigelloides* is found in water and environmental samples in both industrialized and industrializing countries but water treatment practices prevent frequent exposure in regions with adequate sanitation. The phenomenon of passive immunisation in under developing

countries would explain at least in part why *S.sonnei* is more commonly isolated in developed countries.

- Secondly, *Acanthamoeba* (most common amoeba found globally) can act as an environmental host for a variety of intracellular pathogens including *Helicobacter pylori,Vibrio cholerae* and also various *Shigella* species. Cyst of *Acanthamoeba* is resistant to chlorine treatment. Uptake of bacilli into amoebic cyst allows the bacteria to persist in antipathetic environmental conditions including desiccation, starvation and a variety of chemical and physical agents. After phagocytosis *Shigella* species are localized in *A.castellanii* vacuoles and gradually in the cyst and has survivability for three weeks or more. In addition, lateral gene transfer may also facilitate genetic adaptation. Thus from all available evidence it suggests that protozoa may play an important role in the epidemiology of *S.sonnei* in industrializing regions.

- Finally, a strong selective pressure from localized use of antimicrobial agents appears to have a dramatic impact on the evolution of *S.sonnei* populations. All contemporary infections are mainly due to a small number of clones that disseminated globally from Europe within 500 years. Four different lineages of *S.sonnei* were discovered in which lineage III is most prevalent globally, prevailing in Asia, South America and Africa. *Shigella sonnei* with lineage III is characterized by the presence of class II integron which shows resistance to Trimethoprin, Streptomycin and Streptothricin. *Shigella.sonnei* acquired Class II integron during mid-20$^{th}$ century after that the clone spread internationally. Horizontal gene transfers of genetic elements (plasmids, transposons, and integrons) is an important factor of bacterial evolution. Transfer of genetic elements between the members of the family Enterobacteriaceae is responsible for the spread of resistant genes and in the emergence of multi-drug resistant Gram -negative bacteria worldwide. Through horizontal gene transfer *S.sonnei* acquire plasmid and chromosomal -mediated resistant genes from both pathogenic and commensal bacteria that are circulating locally which increases its ability to establish infection, prolong shedding and out-competing antimicrobial susceptible bacteria. In areas with unregulated antimicrobial use *S.sonnei* have an abundant opportunity to acquire locally derived resistant genes.

In conclusion *S.sonnei* is now becoming a threat to the public health globally. Due to the

efforts for worldwide water and sanitation improvements, population level immunization against *Shigella sonnei* is declining. With ongoing improvements in the international quality of water supplies and rapid development of antimicrobial resistance, the burden of *S.sonnei* is likely to grow substantially which demands a vaccine in the near future that can be administrated to most vulnerable populations particularly for young children in rapidly industrializing countries.

**References**

1. *Corinne N ThompsonPham Thanh Duy, Stephen Baker (2015) The Rising Dominance of Shigella sonnei: An Intercontinental Shift in the Etiology of Bacillary Dysentery.PLOS Negl Trop Dis /doi:10.1371/journal.pntd.0003708 2015 Jun 11,2015.*

*2. Abhishek Gaurav, S P Singh, J.P.S. Gill, Rajeev Kumar and Deepak Kumar (2013), Isolation and identification of Shigella spp. from human fecal samples collected from Pantnagar, India.doi:10.5455/vetworld.2013.376-379.*

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **12. Stream** | Allied Health Sciences |
| **13. Speciality** | Humanities |
| **14. Date** | 13-10-2020 |
| **15. Title** | **The Importance of Health Humanities for Health Care Professionals** |
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| **21. Consent for Publication** | I hereby declare to abide by the KUHS Rules regarding publication and agree that the article contributed by me may be published in the KUHS publication on Recent Advances. |
| **22. Suggested Structure of Article** | 1. Facing Sheet of the Article<br>2. Article on maximum TWO sides of an A4 Page<br>3. Title of the Recent Advance<br>4. Source: Original Article / Site / Book<br>5. Contributor’s Name (To be Published)<br>6. A note on why it is relevant.<br>7. Body of the article as 10 to 20 Bulleted Points<br>8. References (2 to 3 nos.) |

# The Importance of Health Humanities for Health Care Professionals

**Abstract**: Health humanities are an interdisciplinary field of study that draws on aspects of the arts and humanities in its approach to healthcare, health and well-being. It involves the application of creative or fine arts and humanities to questions on human health and well-being.

Medical humanities are mainly concerned with training medical practitioners, while health humanities links health and social care disciplines with arts and humanities.

## The medical/health humanities

- The term medical/health humanities were coined by Moore in1976.
- Literature was used in teaching undergraduate medical students at University of Melbourne, Australia.
- Medical humanities course can be designed such that students can learn from their peers, patients, caregivers and families.
- **It is now a part of the curriculum of many health professional schools, either integrated into core curricula or offered as an elective.**

## Teaching - learning modalities – Health for Humanities

1. **Didactic lectures:**
    - In this method of teaching, teacher gives instructions to the students and the students are mostly passive listeners.
2. **Interactive discussions:** focused on interaction between the teacher and the student
3. **Role plays :**
    - Allows students to explore realistic situations by interacting with other people in a managed way in order to develop experience and try different strategies in a supported environment.
    - Eg: patient – doctor course at University of Irvine
4. **Literature excerpts:** We can also make use of excerpts from philosophy, history and literature to illustrate and illuminate teaching in medical education.
5. **Writing and Reflective writing assignments:**
    - Reflective writing encourages one to make observations about their own experiences and beliefs and link those with theoretical learning
6. **Music and painting**: Can help health professionals to develop deeper awareness and better communication skills that will give them access to the stories of patients and provide a face and a context to a medical problem.

**Advantages of learning health humanities**

- Refocus knowledge and medicine in relation to understanding of what it means **to be 'human'**
- More **emotional support** for students
- Increases **clinical acumen**
- **Attention** in particular improves
- Practicing **Empathy** becomes frequent
- Improves **reflective skills** and improve **self-awareness** of the students

**REFERENCES**


1. *Bleakley A. Medical humanities and medical education. London: Routledge; 2015.*
2. *Blease C. In defense of utility: the medical humanities and medical education. Med Humanit. 2016; 42(2):103–8.*
3. *Ousager J, Johannessen H. Humanities in undergraduate medical education: A literature review. Acad Med. 2010; 85:988-998.*
4. *Jones T, Blackie M, Garden R, Wear D. The almost right word: The move from medical to health humanities. Acad Med. 2017;92:932-935.*

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream:** | Allied Health Science |
| **2. Specialty:** | Pathology, cytology, cytogenetics, regenerative medicine |
| **3. Date:** | 17-12-2020 |
| **4. Title** | **Severe acute respiratory syndrome associated corona virus 2** |
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| **11. Suggested Structure of Article** | 1. Facing Sheet of the Article – attached the current page<br>2. Article on maximum TWO sides of an A4 Page – 5 pages<br>3. Title - Severe acute respiratory syndrome associated corona virus<br>4. Source: review articles and publications<br>5. Contributor’s Name (To be Published) : Dr Deepa R<br>6. A note on why it is relevant – included in the article as initial 2 paragraphs<br>7. Body of the article as 10 to 20 Bulleted Points - yes<br>8. References (2 to 3 nos.) – 3 relevant reference given at the end of write up |

# Severe acute respiratory syndrome associated corona virus 2

**Relevance:** The pandemic **CoVID-19** caused by Severe Acute Respiratory Syndrome Associated Coronavirus 2 (**SARS-CoV2**), has spread worldwide with about 70 million confirmed cases and more than 1.5 million deaths till now, as per WHO. Understanding the basic structure, pathogenesis and laboratory diagnosis of SARS-CoV-2 is important for getting novel insights to restrain the spread of the disease.

- Genome sequence of SARS-CoV2, whose intermediate host is still unclear, shows more similarity to (96%) bat coronavirus than to (79%) Severe Acute Respiratory Syndrome Associated Coronavirus (**SARS-CoV**) and (50%) Middle Eastern Respiratory Syndrome coronavirus (**MERS-CoV**) which had caused an earlier outbreak in China (2002) and Middle East (2012) respectively. SARS-CoV2 is more contagious than SARS-CoV and MERS-CoV which have civet cats and camel respectively as the intermediate hosts.
- **Taxonomy** - The coronavirinae subfamily, coming under the coronaviridae family (both belong to the Nidoviales order or superfamily) has 4 genera - alphacoronavirus, betacoronavirus, gamacoronavirus (mainly infecting whales and birds) and deltacoronavirus (virus isolated from pigs and birds). The alphacoronavirus consists of many animal virus and human virus, HCoV-229E and HCoV-NL63. The **betacoronavirus** genus includes prototypes of mouse hepatitis virus (HMV) and the human viruses such as the HCoV-OC43, SARS-HCoV, HCoV-HKU1, MERS-CoV, SARS-CoV and SARS-CoV-2 capable of causing mild to severe respiratory infections.
- **Viral genome & structural proteins** - The coronavirus has the largest genome (28 to 32kb) among all RNA viruses, having similarity to eukaryotic mRNA with a 5'caps and 3' poly (A) tails at its either ends, allowing expansive coding capacity and gene expression strategies. The gene coding for replicase is towards the 5' end whereas those coding for the structural genes like **S** (spike), **N** (nucleoprotein), **M** (membrane) and **E** (envelop) are clustered at 3'end of the RNA. The RNA complexed with N forms the helical capsid structure is situated inside the E. The S glycoprotein is embedded in the E giving the virus a crown like (or **corona**) morphology. Another salient feature of the coronavirus is the presence of multiple Open Reading Frames (**ORFs**). Several accessory proteins of SARS-CoV is supposed to have evolved from mutation through duplication and scavenging of ORFs. The SARS-CoV isolated in 2002 was interestingly found to have 29 nucleotides missing from the previous reported animal

isolates, probably due to fusion of ORFs 8a and 8b into a single ORF 8 while the virus *jumped* from animal to human.

- **Viral entry & non-structural proteins** - The S trimer of the SARS-CoV is cleaved by a trypsin-like host transmembrane serine protease (TMPRSS) into S1 and S2 domains. The viral entry is mediated via binding of S1 domain to the angiotensin-converting enzyme 2 (**ACE2**) receptor present on the host cell resulting in conformational changes in S2 domain, leading to the fusion of virion and host cell membrane. Unlike MERS-CoV and SARS-CoV, the S protein in novel SARS-CoV-2 exhibit a peculiar insertion in its furin like cleavage site which is speculated to be the reason for its high rate of transmission. After viral entry into host cell the nucleocapsid and viral genome are disassembled. The ORFs 1a and 1b at the 5' end of the genome RNA are translated into polypeptides (**pp1a and pp1ab**) via a frameshift mechanism and co-translational proteolytic processing along with the aid of the virally encoded main protease (Mpro) or chymotrypsin like protease (3CLpro) and one or two papain like protease resulting in production of 16 nonstructural proteins (designated as **nsp 1** to **nsp 16**), each of which have specific roles in the viral replication and assembly. The viral assembly occur in the endoplasmic reticulum golgi intermediate compartment complex and the progeny are released outside the cells via exocytosis. Another possible receptor for SARS-CoV2 entry is CD147 seen on RBCs, platelets and endothelial cells.
- **Pathogenesis** - The viral transmission is by close person to person contact, through infectious droplets and fomites. The SARS-CoV-2 infection mainly progress through three phases corresponding to different clinical stages after onset. The 1$^{st}$ asymptomatic stage may last for 1 to 3 days. Here, the inhaled virus attaches to the respiratory cells and undergo replication but with limited innate immune response. During the next stage the virus propagates along the respiratory tract triggering a more robust immune response in the conducting airways, however majority of the infected persons might show mild to moderate symptoms during this phase. Clinical manifestations range from fever, sore throat, myalgia, fatigue, diarrhea, unproductive cough to severe pneumonia. The third stage progresses to pulmonary destruction with hypoxia and acute respiratory distress syndrome (**ARDS**). The infiltrated lung and damaged alveoli shows multinucleated giant cells containing macrophages and cells of epithelial origin along with numerous characteristic syncytium like formation. CT scans of Covid patients shows '**ground glass opacities**' mostly involving

multiple lobes with a peripheral and subpleural distribution in majority of cases and a "**white lung** appearance" in severe cases.

- Clinical investigations also showed highly elevated C-reactive protein, pro-inflammatory cytokines, serum ferritin, lymphopenia and D-Dimers. There is marked hemophagocytosis and in some cases hepatic involvement, atrophy of white pulp in spleen, lymphadenopathy suggesting wide systemic spread along with copious viral shedding in respiratory and excretory secretions. Cardiovascular complications with tachyarrhythmia and thromboembolic events characterized by troponin rise are also common. The viral replication and dissemination induces endothelial damage, apoptosis, and necrosis, leading to immune cell recruitment and activation, which in turn exhibited a strong destructive and uncontrolled hyper-inflammatory reaction. Elevated levels of pro-inflammatory cytokines like IL-6, IL-1β, IL-2, IL-8, IL-17, G-CSF, GM-CSF, IP-10, MCP-1, CCL3 and TNFα, directly correlated with the severity of the disease suggestive of hyper-inflammatory response in some patients. The hypercytokinemia or '**cytokine storm**' triggers various pathological events such as vascular permeability, plasma leakage, disseminated vascular coagulation accounting for life threatening respiratory symptoms and multi-organ failure.
- **Specimen Collection and Transport** – Mainly nasopharyngeal (NP) and/or oropharyngeal (OP) swabs using dracon or polyester swabs are collected in sterile containers from the upper respiratory tract while sputum or bronchoalveolar lavage (BAL) or endotracheal aspirate from lower respiratory tract. The RNA of SARS CoV2 is detected more from NP swabs (63%) than in OP swabs (32%) and hence NP swab is preferred. WHO recommends collecting OP and NP swabs in same the tube to increase detection rate. Other specimens including rectal swabs, stool, urine and blood in appropriate sterile containers as recommended by the WHO. The source of specimen, severity of disease and various underlying factors like diabetes, heart disease determine the shedding of RNA virus and the detection rate in the specimen. Paired sera during acute (1$^{st}$ week of illness) and convalescent phase (2 or 3 weeks later) should be collected for serological assay whenever possible. Specimens in viral transport medium should be immediately shipped after triple packaging maintaining proper cold chain. It can be maintained at refrigerated temperature for up to 72 h or frozen at −70°C or below in case longer transport is expected.

- **Serological assays** are cheaper, require lesser analytical time and have greater productivity as far as automated instruments in hospitals and laboratories are concerned when compared to the molecular tests. These assay helps in serological surveillance, epidemiologic studies and to assess cross reactivity and long term immunity. Enzyme-linked immunosorbent assays (**ELISA**), rapid antibody immunochromatographic tests, point-of-care tests (**POCT**) - fluorescence assays and chemiluminescence immunoassays (**CLIA**) detects viral antigens or antibodies against the viral antigens in the specimens. The viral antigens mostly used are the N protein, S protein and RBD of the S protein. Sensitivity would be higher if N and S proteins are used together. Viral antigen particles directly detected by immunochromatographic assay, uses antibodies against the nucleoprotein of the virus pre-coated in a line over a membrane strip with colloid gold conjugate impregnation. The specimen applied at one end flows laterally over the membrane and if there is viral antigens in the sample, a visible band is formed on the test line indicating the antibody–antigen–antibody gold conjugate complex deposit. Even though rapid and easy to perform, false negative results may occur depending on variable viral load in different samples.
- **Molecular assays** - The detection of viral RNA using nucleic acid amplification tests such as **RT**-**PCR** require approved laboratory facilities and standardizations. The viral load is highest during the initial phase in NP swabs requiring lower pre-specified Ct value and fewer replications cycle than when viral load is lower. Primers for gene encoding the structural proteins, accessory proteins and RNA dependent RNA polymerase are provided by WHO and different countries follow different protocols. Other molecular methods such as loop-mediated isothermal amplification or LAMP (e.g. **Chitra GeneLAMP-N** developed by SCTIMST), multiplex isothermal amplification followed by microarray detection and clustered regularly interspaced short palindromic repeats or CRISPR based assays are being evaluated. The FnCas9 Editor linked Uniform Detection Assay or **Feluda,** resembling a home pregnancy paper strip is a faster and cheaper alternative to RT-PCR. Named after the fictional Bengali detective with an ability to solve a crime quickly in Satyajit Ray's novels, Feluda launched by the Tata group, indigenously developed by **CSIR**-**IGIB,** India is based on **CRISPR-Cas9** technology.
- Interpretation of results is subject to accuracy of test, time of specimen collection, type of specimen collected, the type of antibodies or antigen (in case of serology) and the probe (in

case of RT-PCR) used in the assay. In RT-PCR, if two targets sequence (N and S) tests positive then the disease can be confirmed if the Ct value is less than 40 for both. Low Ct value indicating high viral load is an indication of transmissibility. A positive RT-PCR along with direct antigen test also confirms a current infection. However, a negative tests has to be carefully interpreted in the current pandemic scenario. A single negative assay in a symptomatic patient should not be relied upon to exclude the disease. In case of serological tests, the aspect of long term immunity through sero-conversion should also be taken into clinical consideration along with critical evaluation of previous infection or exposure, as a false interpretation could lead to either false reassurance resulting in inappropriate behavior encouraging community spread or unwanted panic and isolation.

- Symptomatic treatment includes oxygen therapy, ventilation and ICU support in case of respiratory failure and anticoagulant therapy to reduce thromboembolism. Corticosteroids like dexamethasone, antiviral drugs such as lopinavir/ritonavir, remdesivir, oseltamivir, flavipravir and arbidol, immune-modulatory drugs like chloroquine, hydroxychloroquine, and inflammatory inhibitors like Acalabrutinib, and serotherapy (antibodies from blood of convalescing patients) and cytokine (IL6, IL1 and GM-CSF) targeting therapies like tocilizumab, sarilumad (mAb against IL6 receptor) are some of the current treatment strategies used with varying degree of success. Novel drugs are under investigations as scientists are racing against time to find a definitive cure for the disease.
- **Preventive measures** such as frequent hand washing, avoidance of public gathering especially by elderly and immune-compromised persons, avoidance of unprotected contact with farm animals, wearing masks, patient isolation, contact tracing, infection control, strengthening of emergency medicine departments are some of the current approaches to limit the spread of infection. Healthcare workers caring for infected should adopt precautionary measures to utilize PPE such as N95 or FFP2 masks, eye protections, gowns and gloves to prevent disease transmission.
- BNT162 (mRNA based vaccine) from Pfizer/BioNTech is the 1$^{st}$ Covid vaccine to be cleared by the US regulators for public use. About 45 other developed **vaccines** are under different phases of clinical trials on humans. Ad5-nCov (recombinant adenovirus), AZD1222 (replication deficient viral vector), CoronaVac, **Covaxin** (inactivated vaccine developed by **ICMR**-**NIV** collaboration set to be launched by Bharat Biotech India by June 2021) BBIBP-

CorV (inactivated vaccine), JNJ-78436735 (formerly known as Ad26 CoV-2S), mRNA-1273 (mRNA based vaccine), NVX-CoV2373 (Nano particle vaccine), ZyCoV-D, AG0301-COVID19, GX-19, INO-4800 (DNA vaccines), EpiVacCorona (peptide vaccine) are some of the prospective vaccines in the phase III/ phase II trials. Furthermore, multiple potential candidates (around 190 under investigation) are in the preclinical and developmental stages as researchers world-wide are working around the clock to find new vaccines for CoVID-19.

**Reference**


1. *Loeffelholz MJ, Tang YW. Laboratory diagnosis of emerging human coronavirus infections–the state of the art. Vol. 9, Emerging Microbes and Infections. 2020.*
2. *Deepa R. Pathogenesis, immune response and laboratory diagnosis of severe acute respiratory syndrome associated Coronavirus-2, Open Journal of Biological Sciences. 2020.*
3. *Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. Features, Evaluation and Treatment Coronavirus (COVID-19) - NCBI Bookshelf. StatPearls. 2020.*

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Allied health science |
| **2. Specialty** | Basic microbiology and Immunology |
| **3. Date** | 09.12.2020 |
| **4. Title** | Biomarkers may predict ZIKA related birth defect |
| **5. Name of Contributor** | Mrs.Anju M M |
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| **11. Suggested Structure of Article** | 1. Facing Sheet of the Article<br>2. Article on maximum TWO sides of an A4 Page<br>3. Title of the Recent Advance<br>4. Source: Original Article / Site / Book<br>5. Contributor’s Name (To be Published)<br>6. A note on why it is relevant.<br>7. Body of the article as 10 to 20 Bulleted Points<br>8. References (2 to 3 nos.) |

# BIOMARKERS MAY PREDICT ZIKA RELATED BIRTH DEFECT

**RELAVENCE**

ZIKA virus infection remerged as a global health issue due to serious clinical complications, development of specific serological assays to detect and differentiate ZIKV from other circulating flaviviruses for accurate diagnosis remains a challenge. To date approximately 800,000 cases of suspected and confirmed ZIKA virus infections have been reported in world wide. Most people infected with the ZIKA virus experiences no symptoms or mild illness with low grade fever. However, fetus exposed to ZIKA in the womb are at risk for devastating neurological defects. One of those defects, microcephaly, a smaller than usual head size gained prominence in 2015 with Brazil reporting an unusual number of cases in babies born to mothers infected with the virus.

- **ZIKA Virus**-Has recently gained attention due to recent large out breaks that occured in 2015-2016 worldwide. It is an Arbo virus; possess ssRNA, belongs to family flaviviridae. Transmitted by *ADES EGYPTI* mosquito, other modes include –mother to child transmission, rarely through sexual contact, blood transfusion and organ transplantation. Monkeys are the reservoirs. Its named after its place of discovery (1947), ZIKA forest in Uganda.
- **Epidemiology**-Till date, a total of 87 countries have had evidence of ZIKV infection. Outbreaks have been recorded in Africa, America, Asia and the Pacific. Largest out breaks occurred in 2015-2016 in Brazil. In February 2016, the who declared the ZIKA virus out break a public health emergency of international concern.in 2018 about 290 cases were reported in India, which include out breaks in Rajastan (153cases) Madhya Pradesh (130 cases) and one case from Gujarat.
- **Differential Expression of Inflammatory Cytokines and Chemokines Elicited by Acute ZIKV Infection During Pregnancy**.

  To characterizes immune responses during acute ZIKV infection, revealing deregulated expression of 47 cytokines specially 22 inflammatory cytokines and 11 chemokines were significant. whereas those of 5 inflammatory cytokines (IL1B, IL2, IL16, IL26, IFNG) and 9 chemokines (CCL11, CCL19, CCL13, CCL21, CCL7, CXCL8, AND CXCL12) were detectably repressed. Ingenuity pathway analysis(IPA)indicated that a panel of cytokines (IL10, CCL8, CCL15, CXCL9, TSLP, CCL23, CCL1, CCL2, CXCL10, and CX3CL1) induced in ZIKV + sera

associated with the activation of chemotaxis of Monocytes and NK cells. In contrast, the repression of IL16, CCL21, CCL19, CCL20, CXCL12, CCL11, CCL3, CXCL8 and IFNG cytokines in ZIKV+ sera were predicted to associate with the inhibition of chemotaxis of Tcells and B cells

- **Immune mediators involved in symptomatic onset of ZIKV + pregnancy**

  To identify cytokines specifically associated with symptomatic ZIKV infection during pregnancy. (CXCL10, TNFRSF8, CCL8, CCL2, CXCL11) were induced and 21 cytokines (MIF, IL8, CXCL12, CXCL13, CCL20, CCL7) were repressed in symptomatic ZIKV + patients.

- **Distinct ZIKV Associated Immune Signature During Different Trimesters of Pregnancy**

  ZIKV infection of blood in the 1st & 2nd trimesters of pregnancy enhance viral replication & immune suppression. In each trimester observed a unique cytokine profile increased CCL23 &

  decreased TNFSF12 in the 1st trimester increased CXCL6, TNFRSFIA, PTX3 & IFNA2 & decreased ILI2B, in the 2nd trimester and increased IL22, MMPI, IL20, IL27p28 &CCLI & decreased CCLI3, GMCSF, CXCL5 & ILIP in the 3rd trimester. In addition,10 cytokines were commonly affected by ZIKV infection in all 3 trimester of pregnancy CCL8, TNFRSF8, TNFRSF1B, TNFSF 14 & CX3CLI were significantly increased, whereas CCL20, IFNG, CCL7, CXCL13 and MIF were decreased.

- Extensive multiplexing analysis of 69 cytokines revealed that CXCL10, CCL2 AND CCL8 chemokines were specifically associated with symptomatic ZIKV + infection during pregnancy. The high level CCL2 and its inverse correlation with CD163, TNFRSFIA and CCL22 levels was apparently associated with ZIKV induced abnormal birth.
- These findings identified a panel of biomarkers which may potentially be useful in predicting ZIKA associated fecal outcomes regardless of pregnant stages, simply by evaluating the mother's blood.

**REFERENCES**

*1. Lab Medica Internationalism 1068-1760, Vol.36 no.4.6-7/2019*

*2. Sin Foo Susan et al (2018):" Biomarkers And Immunoprofiles Associated With Fetal Abnormalities Of ZIKV Positive Pregnancies".The journal of Clinical Investigation Insight,vol 3(21) :e124152,November2.*

*3. Sastry Apurba ,Sandhya Bhut "Essentials Of Medical Microbiology"Third Edition,Page No:798.*

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Allied Health Sciences. |
| **2. Speciality** | Microbiology |
| **3. Date** | 14/12/2020 |
| **4. Title** | Crispr Cas 9 A Novel Weapon To Fight With Infectious Diseases. |
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| **10. Consent for Publication** | I hereby declare to abide by the KUHS Rules regarding publication and agree that the article contributed by me may be published in the KUHS publication on Recent Advances. |
| **11. Suggested Structure of Article** | 1. facing Sheet of theArticle<br>2. Article on maximum TWO sides of an A4 Page<br>3. Title of the Recent Advance<br>4. Source: Original Article / Site / Book<br>5. Contributor's Name (To be Published)<br>6. A note on why it is relevant.<br>7. Body of the article as 10 to 20 Bulleted Points<br>8. References (2 to 3nos.) |

# CRISPR Cas 9 A NOVEL WEAPON TO FIGHT WITH INFECTIOUS DISEASES.

**Relevance**

Infectious diseases remain a worldwide threat contributing to excess morbidity and mortality annually. The recent development of the clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated protein 9 (Cas9) system is a genome editing technique used for the gene modifications in both pathogen and host cells that enables the analysis of molecular mechanisms involved in pathogenesis of infection. Better understanding of the pathogenesis of microorganisms along with rapid diagnosis and treatment of human infections, is important to prevent infectious diseases worldwide.

- **CRISPR Cas** 9 is originally identified as adaptive immune system of bacteria against invading viruses and foreign plasmid DNA, the CRISPR/Cas9 system can now reprogrammed in order to fight bacterial pathogens "with their own weapons." It is often utilized to characterize the function of genes and study prospective targets for antibiotics in bacteria providing useful information for novel therapeutic strategies.
- The CRISPR system is classified into two classes with six types and twenty-one sub types. CRISPR class I systems use multiple Cas proteins to degrade foreign nucleic acids, class II systems use a single large Cas endonuclease. The type II CRISPR/Cas9 system requires only two components that is, the Cas9 DNA endonuclease and a small guide RNA (sgRNA). This simplicity permits its application to almost every organism.
- The CRISPR/Cas9 works through the action of the Cas9 endonuclease, which is targeted to a specific locus in the genome by a sequence-specific sgRNA. Once a DNA double strand break is induced, repair processes in the cell are triggered to seal the break by two processes called non-homologous end joining (NHEJ) or homology-directed repair (HDR). During this process, bases are additionally inserted or deleted into the genomic DNA at the break, causing the so-called insertion/ deletion mutants, which often result in frame shift mutations and thereby knockout of the gene of interest.
- CRISPR Cas 9 **marketing companies** are CRISPR therapeutics, Biosciences, Editas medicine and CRISPR Cas 9 **software data bases** are Add gene, GeCKO, E- CRISP, Cas Finder

- **For bacterial infections-** The emergence of an increasing number of multidrug-resistant strains underscores an immediate need for novel therapeutic options such as chemotherapy, as well as improved vaccines.

- CRISPR/Cas9 screens used to elucidate host—pathogen interactions in infectious diseases like Clostridium septicum α-toxin, Diphtheria and chimeric anthrax toxins, Staphylococcus aureus α-hemolysin toxin, Clostridium difficile toxin B Vibrio parahaemolyticus toxicity mediated by T3SSs, Cholera-diphtheria toxin Bacillus subtilis essential genes and whole-genome interaction networks.

- CRISPR interference (CRISPRi) in the CRISPR/Cas9 system has the highest potential tool providing tailored antimicrobials for the treatment of multidrug-resistant bacterial infections.

- The CRISPR/Cas9 system show great potential to spot novel and possibly targetable host pathogen interactions that could translate to therapeutics for bacterial infections.

- **For Viral infections-** The CRISPR/Cas9 system originally evolved in bacteria to specifically target invading viruses and foreign DNA, it seems self-evident that this gene-editing tool might be used as a therapeutic tool against viral infections.

- CRISPR/Cas9 technology is used to elucidate host—pathogen interactions in Hepatitis C virus host factors, West Nile virus-induced cell death, Dengue virus and hepatitis C virus host factors, Flaviviridae host factors and Zika virus host factors
- CRISPR/Cas9-derived activator systems as targeted approaches to induce activation of dormant HIV-1 proviral DNA, were ready to antagonize HIV latency, and it can be used for efficient antiviral therapy also.
- CRISPR/Cas9-mediated gene editing has also been achieved in the Flavi virus vector Aedes aegypti, paving the way for further functional genomics related studies in this mosquito species.
- The CRISPR Cas 9 technique is used in the detection and preparation of vaccine against SARS CoV2.
- **For Parasite and fungal infections-** The CRISPR/Cas9-system could be utilized to introduce "gene drives" that suppress mosquito populations to levels that do not support malaria transmission. Studies on Plasmodium falciparum have shown that the parasite itself also can be targeted using CRISPR/Cas9 to further understand pathogenesis and drug resistance.

- Recently, a wide genome CRISPR/Cas9 screen in Toxoplasma gondii identified essential genes during infection of human host cells and provided proof for the possibility of CRISPR/Cas9-based screening platforms to expand the horizon

  anti-parasitic interventions.

- The CRISPR/Cas9 system has been recently applied in genome editing of Candida albicans, Aspergillus and Cryptococcus and has the potential to further uncover the molecular basis of fungal infection and resistance to antifungals.
- CRISPR-based therapies hold promise for the treatment of cancer and inherited red cell disorders such as sickle cell anemia and for the prevention and treatment of other infectious diseases.
- **Advantages:** Simple design and preparation, cost effective method, easy to use and time required to modify target gene is low.
- **Disadvantages**: Off target effects, Mosaic effects, immune toxicity, editing in human embryos and ethical dilemma (genetically modify human embryo) and concern.
- **Conclusion:** The rapid advance in the area of CRISPR/Cas9 as a genome-editing technology has enabled application to infectious disease research and identification of preventative and therapeutic interventions globally. Still there is challenges but they are daunting, they are not invincible, suggesting that a future infectious disease community might routinely integrate CRISPR technology into daily practice.

**References**


1. *Doerflinger M, Forsyth etal CRISPR/Cas9 The ultimate weapon to battle infectious diseases? Cellular Microbiology. 2017; 19: e12693. doi: 10.1111/cmi.12693*
2. *StrichJRetal2019.CRISPRCasbiologyanditsapplicationtoinfectious diseases. JClinMicrobiol57: e01307-18. https:// doi.org/10.1128/JCM.0130*

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## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Allied Health Sciences |
| **2. Speciality** | Physiotherapy |
| **3. Date** | 14/12/2020 |
| **4. Title** | PHYSIOTHERAPY REHABILITATION IN POST COVID-19 |
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# PHYSIOTHERAPY REHABILITATION IN POST COVID-19

**Introduction**

Covid-19 has been reported worldwide as a global pandemic and virus figures are increasing. Various degrees of complications reported in post covid-19 patients' breathlessness, weakness, fatigue, decreased exercise tolerance and impaired quality of life. The role of physiotherapy rehabilitation is an essential component for post Covid-19 patients in facilitating maximum functional recovery but effectiveness still unclear critical covid-19 patients. Rehabilitation services can be planned outpatient programs (via tele monitoring and video instructions) later continuation of the clinical rehabilitation phase. Assessment and evidence based treatment of these patients include prevention, reduction of adverse consequences in immobilization. A variety of techniques and modalities applied according to stages of the diseases, co morbidities and level of patient's cooperation" The statement, which was first released in May 2020, can be found on the WCPT website as part of their 2020 World PT Day information resources. Patients that have been discharged from the hospital often receive the advice to gradually increase their activities of daily living, and are given functional physical exercises to perform at home.

**Post-covid-19 patient assessment by the physiotherapist**

- Patient Specific Functioning Scale (PSFS)
- Before, during and after physical activity oxygen saturation and heart rate frequency
- Before, during and after physical activity, the Borg Scale CR10 for Shortness of Breath and Fatigue

**Physiotherapy consists of:**

- Respiratory force and adequate coughing techniques
- Improving general fitness and Increase mobility- early mobilization (passive and active mobilization, muscle-strengthening exercises, mobilization out of bed, standing, walking, ADL)
- Patients positioning
- Prevent loss of function: contractures, pulmonary complications and decubitus
- Insight/coping due to reduced energy

**Conclusion**

Although many questions are still unanswered, time and experience will help us identifying the specific needs of the post-COVID-19 patient within the field of physiotherapy. The importance of sharing experiences within local and international physiotherapy communities will help finding new insights and tailor made treatments for the post-COVID-19 patient.

*1. Persistent Symptoms in Patients After Acute COVID-19 – Angelo Carfi, MD; Roberto Bernabei, MD; Francesco Landi, MD, PhD; for the Gemelli Against COVID-19 Post Acute Care Study Group - JAMA. 2020;324(6):603-605. doi:10.1001/jama.2020.12603*
*2.KNGF position statement: Physiotherapy recommendations in patients with COVID-19. Royal Dutch Society for Physiotherapy (KNGF)*
*3.WPTD2020_InformationSources.pdf (*https://world.physio/sites/default/files/2020-07/WPTD2020_InformationSources.pdf*)*

# Articles from
# Best Teacher Award Winners

## ‘Happenings’: A Publication from KUHS on Recent Advances

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|---|---|
| **1. Stream** | Dentistry |
| **2. Speciality** | Prosthodontics |
| **3. Date** | 10-12-2020 |
| **4. Title** | **Changing trends in Dentistry** |
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# Changing trends in Dentistry

The last few decades witnessed an explosion of knowledge in the field of dentistry. Globally, dentists were keen to incorporate the recent advances in science and technology in an effort to upgrade their practice. In the recent past, it is seen that the rate of progress has accelerated considerably due to the extreme competition among the dentists. Some of the major developments in dentistry and the changing trends that will have a great impact on dental practice are discussed here.

**1.Oral Medicine and Radiology**

**Artificial Intelligence (AI) and its role in Dento-maxillofacial imaging**

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. Dentistry produces an enormous amount of data routinely. It involves scheduling of appointments, recording of treatment procedures, review appointments etc. Such a huge data can be used to gain deeper insight on patient patterns, research papers, routine tasks etc by means of AI. It can also ease the tasks of dentists around the world by reducing the overall work load, streamlining the procedures enabling stronger dentist-patient relationship.

Radiology is deemed to be the front door for AI into Medicine as digitally coded diagnostic images are more easily translated into computer language. Though most of the proposed machine learning algorithms in Dental Radiology were developed using two-dimensional (2D) diagnostic images such as periapical and panoramic radiographs, the increasing use of three-dimensional (3D) imaging techniques in dentistry has boosted the development and use of AI systems for various clinical applications such as automated interpretation of dental radiographs, caries detection, computer-assisted image analysis etc. Cone beam computed tomography (CBCT) and intraoral/facial scans are potential sources of image data to develop 3D image-based AI systems for automated diagnosis, treatment planning, and prediction of treatment outcome.

**2. Oral and Maxillofacial Surgery**

**Navigation systems and their clinical applications**

The oral and maxillofacial region is characterised by complex anatomy and the presence of several critical organs, complex network of nerves and blood vessels. Navigation systems involve

the integration of imaging with the surgical field, which allows simultaneous visualization of different types of images to reveal structures that are normally visible only intraoperatively and permits navigation in areas of anatomical sensitivity. Surgical procedures in maxillofacial region have become more predictable with the application of navigation assisted surgery.

The two major types of navigation systems are optical and electromagnetic. An optical system uses infrared sensors in combination with light-emitting structures or light reflectors that are fixed to the patient's head and to a hand-held probe. Both the light-emitting structures and instruments will be detected by the system camera or computer for tracking the position of the instruments within the surgical field. Meanwhile, electromagnetic systems use electromagnetic fields and reference points on a device attached to the patient's head and a wired instrument that the surgeon uses within the surgical field.

**Clinical applications**

- **Maxillofacial trauma**: Repair of orbital or complex midfacial fractures by computer-assisted surgery can be performed using 3D repositioning with a mirroring technique of the bones in a virtual environment.
- **Removal of foreign bodies**: The removal of foreign bodies from the cranio-maxillofacial region can be risky due to the proximity to vital structures and access difficulties. Navigation systems could provide an accurate means to locate a foreign body in a 3D space.
- **Dentoalveolar surgery**: Extraction of supernumerary teeth or deeply impacted teeth can be challenging. Navigation systems help to accurately locate deeply impacted teeth so as to have minimum bone loss and trauma during surgery.
- **Orthognathic Surgery**: Navigation helps to perform orthognathic surgery with a definite plan preventing damage to critical structures.
- **Tumor surgery**: The use of navigation reduces the need for resection of vital structures and provides reliable mapping of the lesions at the skull base.

**3.Prosthodontics and Implantology**

Technological developments have a significant impact in the field of Prosthodontics and Implantology. Digitisation has become an important part of contemporary prosthodontics.

Patient management, making impressions, recording jaw movements, shade selection, fabrication of prostheses etc. are becoming digital. Digitization and technology can be used both in clinical and laboratory procedures such as CAD-CAM technology, intra oral scanners, spectrophotometer, stereolithography, rapid prototyping etc. Introduction of PEEK, PECK, TRINIA in the field has also led to the improvement in aesthetics and mechanical properties of dental prostheses.

In many counties, dental laboratory procedures are increasingly becoming automated. The global market of digital dentistry is expected to grow about 8.1% annually from 2020-2030. In 2013, it was estimated that, 5-16% of US dentists were using digital impression systems. It is predicted that 80% of dentists will be using digital impression in the coming 10-15 years. The number of dentists adopting digital impression system is growing annually at a rate of 2-2.5%. Even though automation is getting popular in India, it is much slower due to the high cost associated with it.

**3D Printing**

3D printing or rapid prototyping involves an additive manufacturing approach that builds objects layer by layer to form an object. It is set to revolutionize the prosthodontic practice in the coming years. Based on the data obtained from CBCT, anatomical replica can be produced for the fabrication of prostheses using a 3D printer. 3D printing can also be used in the fabrication of crown copings and removable partial denture frameworks. This technology is expected to revolutionize the future of dentistry particularly prosthodontics and implantology.

**4.Orthodontics and Dentofacial Orthopedics**

Orthodontics and Dentofacial Orthopedics as a speciality has evolved to the current stage by the tremendous progress in research. The important areas where this progress has achieved can be described under three headings. (i)orthodontic diagnosis and treatment planning, (ii)application of computer technology and (iii) development of biomaterials and their characterization.

**(i)Diagnosis and Treatment Planning**

Over the years, Orthodontic diagnosis and treatment planning has been transformed from conventional approach to problem oriented approach. Dento-facial esthetics is a major concern among the general public. This led to the progress of orthodontic diagnosis and treatment planning to a goal oriented approach where the positive esthetic attributes of the individuals are

maintained. When the “Evidence based medicine and dentistry” became popular in 2003, a new era was opened for successful treatment outcome. Developments in the area of biomedical imaging technology, growth and development of craniofacial region, molecular biology especially genetic engineering, genome applications and gene editing expanded newer avenues in orthodontic diagnosis and treatment planning to an individualized level. So the future of orthodontic diagnosis and treatment planning will be on “evidence based approach in an individualized manner”.

**(ii)Computer technology**

The application of computer technology and internet has revolutionized orthodontics from simple office procedures to digitization, consolidation, integration of data 3-dimentionally and creation of virtual images for the manufacture of individualized appliances and brackets using CAD-CAM technology and 3-D printing by medical grade biocompatible materials.

**(iii)Orthodontic biomaterials and characterization**

The contemporary wire and bracket materials for orthodontic purpose have evolved from metallic to non-metallic type and the future of wires is shape memory polymers, self-healing materials to prevent breakage of brackets and wires etc. Self-cleaning materials to reduce formation of biofilm around brackets and biometric bonding adhesives are other future developments in orthodontic materials. With the advancement in technology, newer approaches in material research and instrumentations are developed to study their properties.

**5.PERIODONTICS**

Accurate assessment of individual risk is considered to be one of the most important aspects of periodontal examination, diagnosis, treatment planning and prognosis. It is now evident that in addition to plaque, other risk factors such as opportunistic pathogens, environmental influence, genetic factors, host responses and connective tissue metabolism are critical to the clinical manifestation of periodontitis. In the future, identifying individual risk factors within the paradigm of personalized medicine will become central to periodontal practice. The emerging field of genomics will play an increasingly important role. Epigenetics has great potential to impact scientific understanding of periodontitis and how environment and genes interact in the clinical manifestation of disease. Precision dentistry is a relatively new concept in the field of oral

health that uses patients' risk factor data including genetic and environmental rather than clinical presentation alone so as to redefine traditional categories of health and disease.

3-D printing coupled with cone beam computed tomography can make a periodontist's diagnosis more precise. Cell-based tissue engineering for periodontal regeneration is emerging area of Periodontics. Recent developments in the delivery of cell based regeneration like biocompatible scaffolding looks promising. Collaborative efforts involving bioengineers, nanotechnologists, cell biologists and molecular biologists is required to develop a more predictable treatment protocol in the management of periodontal diseases.

**Conclusion**

The unprecedented advances in science and technology leave us with mixed feeling of modesty and gratitude. Despite the advances that exist today, we must realize that dentistry is an ever changing field of endeavour. What we consider to be sound scientific technique today may not be considered tomorrow. Research will dictate the technique of the future.

The ever-increasing cost of dental treatment is a major cause of concern for the common man. Development of indigenous materials, equipment and technology must be promoted for limiting the cost of treatment. Integrated research involving the health care professionals, biomedical engineers and other related scientists is the need of the hour. Let us be optimistic that in the near future, dentistry will reinvent itself and assume a role that will satisfy the expectations of different strata of our society.

**Acknowledgements for academic contribution:**

1.Dr Sreejith Kumar G , Professor and HOD of Orthodontics

2.Dr Tinky Bose, Professor and HOD of Oral Medicine and Radiology

3.Dr Santhoshkumar S, Professor of Periodontics

4.Dr Sarath SS, Assistant Professor of Oral and Maxillofacial Surger

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Homoeopathy |
| **2. Specialty** | MATERIA MEDICA |
| **3. Date** | 8/12/2020 |
| **4. Title** | **HOMOEOPATHY AND ITS PROMISING DEVELOPMENTS** |
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# HOMOEOPATHY AND ITS PROMISING DEVELOPMENTS

Homoeopathy is a therapeutic method for treating diseases by applying those medicines which is capable of producing similar symptoms as that of the disease from which the patient suffers. Homoeopathic treatment is pro pound by Christian Friedrich Samuel Hahnemann in the late 18th century. It is based on the fixed law that is “Similia Similibus Curentur” which means “Let like be cured by like”.

Being a Doctor of Medicine by profession, Dr. Hahnemam had also deep knowledge in various languages and hence highly interested in translating various medical books. In the year 1790, while translating Cullen’s Materia Medica, Hahnemann came to know about the therapeutics indications of Peruvian bark (Cinchona Officinalis) that it is bitter in taste & cures Intermittent fever. Hahnemann dissatisfied with this explanation & by way of experiment he took the medicine himself twice a day (about four drams). Eventually, he noticed symptoms very similar to ague of Malaria fever. This unexpected result set up in his mind a new train of thoughts & he conducted similar experiments on himself & other individuals with other medicines whose curative actions in certain diseases had been well established. On the basis of such successive experiments, Hahnemann came to the conclusion that medicines cure diseases because they can produce similar diseases in healthy individuals.

The whole system is based on easily comprehensible principles such as Law of Similia, Law of Simplex, Law of Minimum, Doctrine of Drug Proving, Doctrine of Drug Dynamization, Theory of Vital Force and Theory of Chronic Disease.

**The Source of medicines**

Homoeopathic medicines are basically extracts of plant kingdom, animal kingdom and also prepared from Mineral Kingdom, Sarcodes (It includes healthy endocrine or ductless glands or normal secretions of living human organs & lower animals, the secretions are mostly hormones), Nosodes (It includes disease producing agents or diseased parts of human beings, lower animals or plants), Imponderabilia (It includes the natural or artificial substances which have no perceptible weights).

**The Application of Medicine**

An individualised homeopathic prescription consists of a 'constitutional' medicine, prescribed mostly on the basis of mental and general features, in a relatively high dilution (30c or higher). Initially, the medicines are used as doses similar or somewhat smaller than those used in contemporary conventional medicine, but gradually reduced the size of doses to include 'ultramolecular dilutions' which are the focus of most of the argument. Homeopathic medicines are now used in both low dilutions, where the original substance is materially present, and in high dilutions, in which material quantities of the starting substance are much less likely to be present.

Dilutions are prepared by a process known as potentization which involves repeated dilutions, usually in steps of 1:10 or 1:100, with succession (vigorous shaking) between each dilution. Dilutions are denoted for instance 5x (in the Anglo-American convention) or 5dH (European convention) for the 5th decimal (i.e. 5 times1:10 dilutions) or 30c/cH for the 30th centesimal (1:100 dilutions). 'H' denotes the Hahnemannian method, in which clean glassware (test tube and pipettes) is used for each step of dilution.

The value of Avogadro's constant, the number of particles (atoms or molecules) in a mole of a pure substance, is 6.022 $\times 10^{23}$. Thus dilutions above 23x/dH or 12c/cH (corresponding to dilutions of $10^{-23}$ and $10^{-24}$ respectively) are very unlikely to contain a molecule of the starting substance. Homeopathic medicines in which a molecule of the starting substance is unlikely to be present are referred to as 'ultramolecular' or ultra-low dilutions (ULD), or BRAN (Beyond the Reciprocal of Avogadro's Number).

**The Mode of Administration**

A patient receives the medicine as Oral Method, Parenteral, Mucosal Absorption Method and Skin Absorption Method.

**Case Taking**

The data gathered from the history and examination of the patient is synthesised into a 'picture', focused with unusual symptoms and strong or unusual mental or general features. These

symptoms are then repertorised to get a suitable medicine which will be finalised with the knowledge in Materia Medica.

**PROMISING DEVELOPMENTS OF HOMOEOPATHY**

Today Homoeopathic treatment is widely accepted in all sorts of the society. Apart from common diseases, focus in life-style disease, skin care, palliative care, Disability management in children, women welfare programme, counselling for drug addicts, Tribal developmental programme and; Developmental research studies are progressing in various selected fields such as agricultural and veterinary.

- **Life- style Disease**

Life style diseases are very much advent in current days. These are the diseases which are resulting out of an improper relationship that has been built between nature and man. With an aim to eradicate and resist these life style diseases, Homoeopathic medicine link with naturopathy and yoga to form a new mode of treatment termed as “Ayushman Bhava”. In order to provide a healthy mind and body for a prosperous life, Homoeopathy department successfully implemented the project named “Ayushman Bhava”.

- **Skin care**

People come up with so many problems like Acne, Pigmentation, Eczema, Psoriasis, Hair fall, Scar marks etc. For all above complaints, conventional medicine does give relief but many times patients face recurrence. For this, Homoeopathy has a tremendous scope as it not only considers the disease from the diagnosis point of view but will go to the root of disease, finding the underlying cause and treat man as a whole.

- **Palliative care**

The Department of Homoeopathy has started palliative care units in all district level hospitals which are also secondary referral units. The palliative care units in each hospital has a team which comprises of Doctors, palliative nurses and other staff members. Home care support is an integral part of the Palliative care activities of each hospital.

**Palliative Care offers**

- support for all terminally ill patients including patients bed ridden with residual symptoms of stroke, neurological conditions, spinal cord injuries and cancer.
- Take care of physical, psychological and holistic aspects of health
- Focuses on cost effective homoeopathic treatment with medicinal and accessory support.
- Free of cost supportive care and free medical treatment by a team comprising of trained doctor and palliative nurse.
- incorporates homoeopathic treatment with other treatment modalities.

- **Disability management in children**

The Sadgamaya learning disability of children is a wide network of dispensaries and hospitals and in collaboration with Gramapanchayats and education department is spreading awareness and helping the children and families with proper management including homoeopathic medication, counselling, behaviour management and corrective teaching methods, focuses mainly on managing health problems, behavioural and learning disorders of children.

- **Women welfare programme**

Homoeopathy Department, Govt. Of Kerala is launching the first gender based programme for women Health care – **'Seethalayam'** to empower women's mental, physical and social health. The main aim of the project is to provide aid for suffering women in the society. The majority of ladies are facing physical and mental torture in domestic and social environment.

After consultation and detailed interrogation, the lady Homoeopathic Physician identifies the actual route cause of the problem and gives necessary treatment and counselling (with the help of a psychologist), if needed, treatment is also extended to the family members. In essential cases the person can be admitted in the hospital for strict Homoeopathic care. Along with treatment, 'Seethalayam' is committed to provide the multi-dimensional supports from the Social and Family Welfare Departments, State Women's Commission, Home department and other NGOs etc.

- **Infertility Clinic**

The setting up of **Ammayum Kunjum** (Mother & Child) in 2012 in Kannur District, **'Janani'** – a dream initiative of Homoeopathy Department received wide acclaim within a very short period. It has become a ray of hope in many. By 2013, Department has started infertility treatment centres at Thiruvananthapuram and Kozhikode also. The success of these three centres paved the way setting up such centres in all districts at district hospitals. Thousands of childless couples sought their solace in these centres and in turn, their dream of bearing a child has fulfilled. More than a thousand children are born in these centres.

Glancing through the Janani case records certify that cases like repeated abortions, PCOD, endometriosis, fibroids and related problems etc, which are some of the reasons for female infertility, can be best dealt with intervention through homoeopathic medicines. Similarly, the causes of infertility in male viz. Oligospermia, motility problems of sperms etc. also are successfully treated by homoeopathic medicines.

Janani is a dream come true for those who were totally hopeless of their dream of having a child even after undergoing ten or fifteen years of treatment like IVF, ICSI.

- **De-addiction**

Deaddiction clinics Under Seethalayam project of Dpt. Of Homoeopathy started working in all districts of Kerala since August 2012.These clinics provide cost effective treatment for Alcoholism and related illnesses and other substances use disorders. The treatment methods included Homeopathic medicinal therapy, Individual and family counselling, Yoga therapy. Since its inception these clinics had treated thousands of patients in OPD and hundreds in IPD with alcohol use disorders, tobacco and other substances use disorders. After that they are returned to productive and creative family life. These patients prefer this treatment as Homoeopathic medicines help them to be de-addicted with minimal withdrawal symptoms and smoothening relief. Other major activities of these clinics include awareness classes on De-addiction for adolescent students in schools and colleges, Residence associations and public. Cases are referred to these clinics from GHDs, Women cell of police, school jyagratha samithies, Alcoholic anonymous and other NGOs.

- **Tribal developmental programme**

The Tribal Mobile Medical Unit (TMMU) of Homoeopathy is functioning among the tribal settlement areas in marayoor, kanthalloor and chinnakanal panchayats in Idukki district. The study revealed that they are illiterate and very poor, totally ignorant of basic principles of health, sanitation and hygiene. The use of alcohol, tobacco and other drugs are common. Hence, the medical team proposed to conduct a large scale campaign in the settlement areas under the supervision and guidance of an expert homoeopathic physician with a medical team to improve their social status.

- **Research studies**
  - **Agrohomoeopathy**

Agrohomoeopathy is one of the newest approaches in agricultural research. In recent years' various scientific studies showed that potentised homeopathic medicines can alter physiological activities of plants. It can alter the rate of enzymatic activities, total sugar, protein and chlorophyll contents in plants. Eradication of biotic and abiotic stresses up to some extent also made possible by the use of homeopathy. In case of biotic stresses - antifungal, anti-microbial, anti-insecticidal etc activities of various homeopathic drugs has been reported. Sometimes other path of abiotic stress (salt stress, drought stress, Cold Stress, Metal toxicity, Mechanical Damages etc.) Control are costlier or less efficient. But proper selection of homeopathic drugs can be cost effective and very efficient in terms of abiotic stress tolerance in various crop species.

  - **Veterinary homeopathy:**

Homeopathic Medicines are effective in the healing of animals as it does in healing humans. A qualified homeopathic veterinary doctor can often show good results even in chronic and acute ailments for pets, such as dogs, cats and birds. The Kerala Veterinary and Animal University established by the Govt. of Kerala in December 2010, propose further education, research and extension in these areas.

- **Research in Homoeopathy**

In homeopathy, Research programmes are progressing in full swing in graduate and post graduate level. Moreover, faculty level Research in various Health Universities all over India are progressing with a hope to reveal and establish the alarming effectiveness in treating different diseases.

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Nursing |
| **2. Speciality** | Medical Surgical Nursing |
| **3. Date** | 22-12-2020 |
| **4. Title** | Nurse Navigation Model in Cancer Care |
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| **11. Suggested Structure of Article** | q) Facing Sheet of the Article<br>r) Article on maximum TWO sides of an A4Page<br>s) Title of the RecentAdvance<br>t) Source: Original Article / Site /Book<br>u) Contributor’s Name (To bePublished)<br>v) A note on why it is relevant.<br>w) Body of the article as 10 to 20 BulletedPoints<br>x) References (2 to 3nos.) |

# Nurse Navigation model in Cancer Care

## Introduction

Cancer is a huge global health burden; touching all region and people from different socioeconomic level.[1] Continuum of cancer care spans a lengthy trajectory from initial diagnosis through treatment.[2] Cancer care is complex and usually requires a team based approach from multiple health professionals to ensure quality and continuity in care. Coordination of cancer care has gained increased attention recently because it can critically and positively affects patient safety as well as care quality across different services and settings. [3] Nurses have a major role in cancer patients' care and many specific nursing roles in cancer services are expanding and evolving. Certain specific nursing roles and its application in cancer care have been tested in a few countries. Despite this evidence, no specialist positions remain relatively in developing countries. A primary literature search reveals lack of published literature/studies from India. This article is organized under the following headings.

- **Concept of patient navigation**

The word navigate is derived from two Latin words Navis (ship) and agree (to drive). The meaning of word navigate is to travel over or through safely. [4] Navigation is a process whereby a patient is given personalized care and support across the continuum of cancer care.[5] The first patient navigation programme was created by Harold P. Freeman at Harlem Hospital, New York in 1990 and thereafter the model continues to evolve and expand.[6] The model focuses on meeting the needs of patients such as providing disease and treatment related information and support and linking with other health care professionals. Services provided include detection of cases, identification of barriers to care, development and implementation of care plan and tracking throughout treatment and its completion.[7]

- **Role of oncology nurse in cancer care**

For many years' nurses are considered at the centre of patient care and they significantly influence the quality of care provided to the patients and patient outcomes. Oncology nurses provide ongoing counseling, information and support related to all the aspects of cancer care. They are best suited for this role, because they have greater knowledge and understanding about all the aspects of oncology care. Patients need information and guidance from a qualified

oncology nurse about their treatment plans and disease management.[8, 9] The roles of oncology nurse vary from primary roles like patient assessment, patient education, care coordination, direct patient care, symptom management and supportive care to advanced nursing practice roles like cancer nurse specialist, oncology certified nurse practitioner, case manager in cancer care and oncology nurse navigator.[10, 11]

- **Oncology nurse navigator**

Nurse navigation is a relatively new concept and a nursing role which has originated in United States. The Oncology Nurse Navigator is a professional whose clinical nursing expertise guides patients, families and their caregivers in informed decision making; collaborating with a multi-disciplinary team, allow for timely cancer screening, diagnosis, treatment, and supportive care across the cancer continuum.[12] Navigators oversee the treatment process, provide information and support to the patient, link with other professionals in treatment process and act as a single, constant contact. It is a more widely used term in addressing problems related to integration, coordination and continuity of cancer care, and is fit in with the concept of a holistic approach that centres on the quality of life of the person with cancer. Nurse navigator role has been implemented in different health care settings and is helpful to the multidisciplinary team for continuum of patient care from diagnosis to survivorship.[13] Specific roles of nurse navigator is illustrated below.

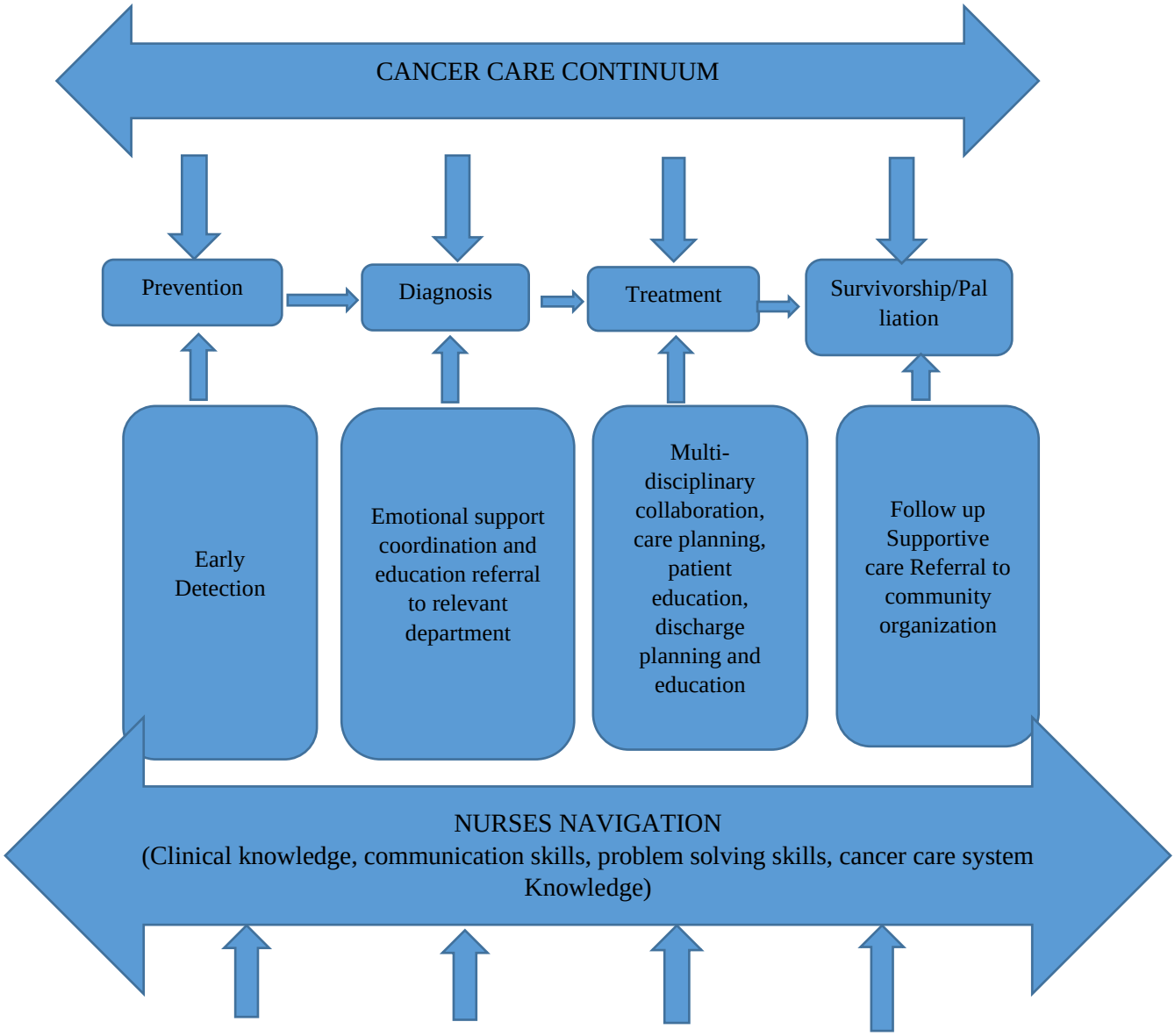


Figure 1. : Schematic Representation of Nurse Navigator's role in cancer care

- **Future Directions and Implication for Nursing Practice**

Nurse navigator programme is a promising resolution for patient care inadequacies, effective means for reducing barrier in oncology care and increase patient satisfaction and quality of care. This model has been already implemented in most of the developed countries. Interventions need to be developed in developing countries like India to enhance treatment adherence, since noncompliance with treatment due to increasing cost is a major problem. Research based evidences are lacking on use of an appropriate conceptual framework for implementation of a Nurse Navigation Programme. Further studies are warranted in evaluating patient satisfaction using nurse navigation in various types of cancers as well as in different populations of patients. Specific tools to test and validate patient navigation programmes are lacking, so identification of key components and its relevant evaluation tools to test effectiveness of navigation programme

is essential. Replication of studies exploring various patient outcomes and nurse navigation will offer the necessary evidence base to trend in oncologic nursing.

**Conclusion**

Navigation is a process by which encompasses assessment of patient needs, development of a plan for education, coordination, communication, support and implementation of same for effective transition through the illness and evaluation of its effect on patient, family and care givers. Patient navigation using nurses is viewed as an effective strategy to improve standard of oncology care as well as to achieve organizational outcomes.

**References**


*1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA: a cancer journal for clinicians. 2019 Jan;69(1):7-34.*

*2. Doll R, Barroetavena MC, Ellwood AL, Fillion L, Habra M, Linden W. The cancer care navigator. Toward a conceptual framework for a new role in oncology. Oncology Exchange. 2007;6(4):28-33.*

*3. Lee T, Ko I, Lee I, Kim E, Shin M, Roh S, Yoon D, Choi S, Chang H. Effects of nurse navigators on health outcomes of cancer patients. Cancer Nursing. 2011 Sep 1;34(5):376-84.*

*4. Hopkins J, Mumber MP. Patient navigation through the cancer care continuum: an overview. Journal of oncology practice. 2009 Jul;5(4):150-2.*

*5. Case MA. Oncology nurse navigator: ensuring safe passage. Clinical Journal of Oncology Nursing. 2011 Feb 1;15(1):33.*

*6. Freeman HP, Muth B, Kerner J. Expanding access to cancer screening and clinical followup among the medically underserved. Cancer practice. 1995;3(1):19. July 2, 2014.*

*7. Willis A, Reed E, Pratt-Chapman M, et al. Development of a framework for patient navigation: delineating roles across navigator types. Journal of Oncology Navigation & Survivorship. 2013;4(6):20-26.*

*8. Lantz PM, Keeton K, Romano L, DeGroff A. Case management in public health screening programs: the experience of the national breast and cervical cancer early detection program. Journal of Public Health Management and Practice. 2004 Nov 1;10(6):545-55.*

*9.Curran CR. Navigating the chaotic health care system. Nursing Economics. 2003 Nov 1;21(6):261-2.*

*10. Braun KL, Kagawa-Singer M, Holden AE, Burhansstipanov L, Tran JH, Seals BF, Corbie-Smith G, Tsark JU, Harjo L, Foo MA, Ramirez AG. Cancer patient navigator tasks across the cancer care continuum. Journal of health care for the poor and underserved. 2012 Feb 1;23(1):398.*

*11. McMullen L. Oncology nurse navigators and the continuum of cancer care. InSeminars in Oncology Nursing 2013 May 1 (Vol. 29, No. 2, pp. 105-117). WB Saunders.*

*12. Freund KM, Battaglia TA, Calhoun E, Dudley DJ, Fiscella K, Paskett E, Raich PC, Roetzheim RG, Patient Navigation Research Program Group. National cancer institute patient navigation research program: methods, protocol, and measures. Cancer. 2008 Dec 15;113(12):3391-9.*

*13. Darnell JS. Patient navigation: A call to action. Social Work. 2007 Jan 1;52(1):81-4.*

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Pharmaceutical Sciences |
| **2. Speciality** | Pharmaceutical Chemistry |
| **3. Date** | 23.12.2020 |
| **4. Title** | Prodrug Based Drug Design |
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# PRODRUG BASED DRUG DESIGN

## 1. INTRODUCTION

Prodrug technology has been successfully utilized to develop therapeutics and treat patients for more than 100 years. Approximately 12% of all drugs approved globally are prodrugs. The term prodrug was first coined by Albert. Elegant in concept, prodrugs are inactive, bioreversible derivatives of active-drug molecules that must undergo an enzymatic or chemical transformation to release the parent drug, which can then elicit its desired pharmacological effect in the body. Thus, the main objectives of a prodrug design are, to have active drugs to their active sites, to show the required pharmacological effects while minimizing adverse effects, to get the desired clinical and therapeutic activity of those drugs which have some undesirable properties, and to prevent the co-administration of two drugs so that the same pharmacological activity is obtained with minimum side effects (Fig 1). The prerequisites of ideal prodrugs include

- It should be pharmacologically inert.
- It should have fast transformation, by chemicals or enzymes.
- It should be a non-toxic metabolic component.

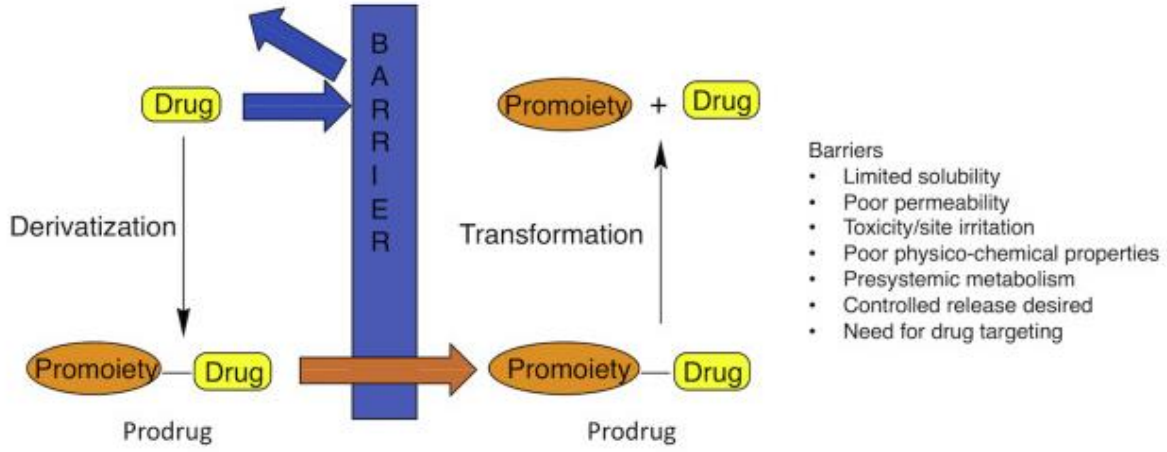


**Fig. 1: Schematic representation of prodrug based drug design**

The therapeutic rationale of a prodrug is to improve the physicochemical, biopharmaceutical, or pharmacokinetic properties of an active pharmaceutical ingredient. The prodrugs seek to modify the key properties such as Absorption, Distribution, Metabolism, and Excretion with the

end goal being the creation of a new chemical entity that optimizes the performance, utility, and potential life-cycle management of the parent drug. The prodrug approach creates enhanced versions of a parent drug by overcoming the barriers by means of increasing solubility, enhancing lipophilicity, improving bioavailability, extending half-life, imparting an extended-release profile, reduced inter-patient variability, and targeted tissue/organ delivery. In short, prodrugs work by making good drugs better.

## 2. FACTORS CONSIDERED FOR PRODRUG DEVELOPMENT

Several crucial factors must be carefully considered when designing a prodrug. These include:

- **Parent drug selection**. Not all drugs/drug categories are suited for prodrug development. The parent drug must be "chemically receptive" and present an advantageous need-solution opportunity.

- **Ligand or promoiety identification**. Ideally, the ligand that is combined with the parent drug to form the prodrug conjugate should be safe and rapidly excretable from the body. The choice of ligand should also be considered with respect to the disease state, dose, and duration of therapy.

- **Parent Vs. prodrug dynamics.** The ADME properties of both the parent drug and prodrug need to be thoroughly understood and researched to determine where and to what degree the prodrug will enable the desired improvements.

- **Degradation.** The ideal prodrug is one where the parent and ligand cleave cleanly, and the active agent is absorbed (providing its therapeutic benefit) while the ligand is rapidly excreted. This process does not always happen perfectly—chemical or enzymatic reactions can sometimes produce unexpected results—so an understanding of degradation by-products that may impact stability is of paramount concern in prodrug discovery and development.

  Based on these factors, prodrug development has proven effective with several functional groups including carboxylic, hydroxyl, amine, phosphate/phosphonate, and carbonyl. Prodrugs produced via the chemical modification of these groups include esters, carbonates, carbamates, amides, phosphates, and oximes. Of these, esters are the most

common prodrugs, with approximately 49% of all marketed prodrugs being activated by enzymatic hydrolysis.

## 3. CLASSIFICATION OF PRODRUGS

The broad classification of prodrugs is shown in Fig.2

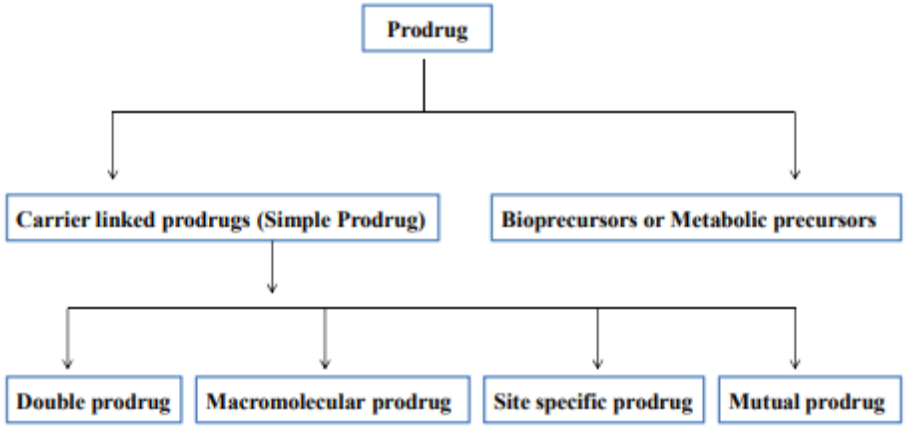


**Fig.2: Classification of prodrug**

Carrier linked prodrug (Fig.3) has an inert carrier or transport which is coupled covalently with active drug. They have ester or amide linkage and gets bio-transformed chemically or enzymatically to release the active drug. They must be non-toxic, and may mask the unwanted side effects. They alter the physiochemical properties of active drug.

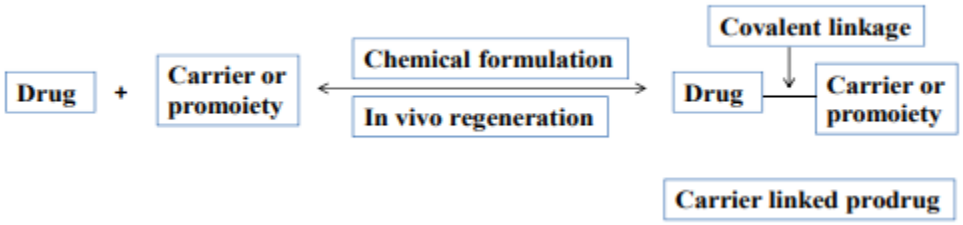


**Fig. 3 Schematic representation of carrier-linked prodrug**

Biopercusers are obtained by redox transformation through enzymes. The prodrugs result by chemical modification of parent drug without altering the lipophilicity.

## 4. PHARMACEUTICAL APPLICATIONS

Prodrug approach has a significant role in drug designing. Some drugs when given by intramuscular injection causes pain, which may be due to weakly acidic nature or poor aqueous solubility. For example, Clindamycin hydrochloride solution and Phenytoin solution causes pain

on injection. This can be overcome by formulating their salts i.e. clindamycin phosphate and phenytoin phosphate. The prodrug concept may be utilized to alter the solubility of a drug. For example, Ester prodrugs of chloramphenicol have good aqueous solubility, as chloramphenicol succinate and chloramphenicol palmitate. However, for the steroidal drugs such as Cortisol, its phosphate esters may be used.

Taste is one of the important parameter of patient acceptability. The bitter taste of drug can be moderated by prodrug designing, for example, chloromphenicol palmitate. Lipophilicity is another important parameter that governs absorption and distribution of drugs. So bioavailability can be improved on altering the lipophilicity, e.g. Pivampicillin, a prodrug of Ampicillin showed good absorption. Glycerol ester of Naproxen produced lesser gastric troubles and had greater plasma concentration. Another prodrug of Naproxen with propylphenazone is synthesised with the view to improve therapeutic index that masks the GI troubles.

The prodrug approach is used in drug design to deliver the drug at a specific site. For example, Estramustin consists of a phosphorylated steroid, coupled to a normustard through a carbamate linkage. Prodrug concept can be useful for those drugs which have small biological half-lives. Also, ester-prodrugs of glucagon-like peptides, steroids (Testosterone cypionate and propionate, Estradiol propionate and Fluphenazine, enanthate and deaconate) are used as depot injections.

Despite enormous work carried out on the development of Novel anti-inflammatory agents, their clinical usefulness is still restricted by their side-effects. The need of safe NSAIDs is still there. The prodrug and mutual prodrug concept has been used to overcome GIT side-effects of NSAIDs and other undesirable properties associated with it. A mutual prodrug is synthesized with aspirin and paracetamol linked through ester linkage thereby reducing the gastrointestinal toxicity. The toxicological and pharmacological profile is evaluated with ibuprofen guiacol ester. The synthesized ester had lesser gastrointestinal toxicity in comparison to pure ibuprofen.

The mutual prodrug is synthesized consisting of acetylsalicylic acid and paracetamol. This prodrug did not hydrolyze in the gastric juice and was slowly absorbed than either acetylsalicylic acid or paracetamol. It has been hydrolyzed quantitatively to the parent drugs. Thus there was reduced risk of irritation of gastric mucosa and paracetamol inhibited the erosion action of acetylsalicylic acid by stimulating the stomach prostraglandin synthetase.

The prodrug synthesized with a novel indomethacin ester prodrug, 2-[N-[3-(3-(piperidinomethyl) phenoxy) propyl] carbamoylmethylthio] ethyl 1-(p-chlorobenzoyl)-5-methoxy-2-methyl-indole-3-acetate. The compound showed antiinflammatory acitivity similar to indomethacin. On the molar basis, the gastric lesioning properties of prodrug was near one hundred times less than indomethacin, result in twenty times improvement in the anti-edema activity and ulcerogenicity. Nitroxybutyl esters of flubiprofen and ketpprofen was synthesized and evaluated for anti-inflammatory activity and gastrotoxicity and showed improved GIT and pharmacological actions than the parent drugs. Table 1 summarizes the prodrugs and purpose of modification.

**Table 1: Prodrug and the purpose of modification.**

| Parent Drug | Prodrug | Reason of Modification |
|---|---|---|
| **Amoxicillin** | Sarmoxicillin | Increase distribution |
| **Ampicillin** | Bacampicillin, Pivampicillin, Talampicillin | Increase distribution |
| **Ampicillin** | Hetacillin Enhance Bioavailability | Increase stability |
| **Carbencillin** | Carfecillin, Carindacillin | Enhance Bioavailability |
| **Chloramphenicol** | Chloramphenicol palmitate ester | Improve Taste |
| **Chloramphenicol** | Chloramphenicol succinate ester | Water solubility |
| **Clindamycin** | Clindamycin palmitate ester | Improve taste |
| **Clindamycin** | Clindamycin 2’ phosphate ester | Decrease pain on injection |
| **Cefamandole** | Cefamandole nafate ester | Stability |
| **Cycloserine** | Pentizidone | Stability |
| **Diethylstilbesterol** | Fostestrol | Decrease gastric distress |
| **Dopamine** | L-dopa | Delivery to brain |
| **Epinephrine** | Dipirefrin | Corneal penetration |
| **Erythromycin** | Erythromycin ethylsuccinate | Gastric stability |
| **Estradiol** | Estradiol cypionate | Extend duration |

| | | |
|---|---|---|
| **Elilefrine** | Elilefrine stearate ester | Bioavailability |
| **Fluphenazine** | Fluphenazine decanoate | Long acting depot injections |
| **Formaldehyde** | Methenamine | Urinary tract delivery |
| **Metronidazole** | Amino acid esters | Water solubility |
| | Benzoyl derivative | Mask taste |
| **Naloxone** | Mono and disulphate ester | Extend duration |
| **Nitrogen Mustard** | Amide derivative | Delivery to neoplastic tissue |
| **Salicylic acid** | Salsalate | Gastrointestinal tolerance and bioavailbility |
| **Sulfisoxazole** | Acetyl esters | Improve taste |
| **Testosterone** | Testosterone propionate | Extend duration |
| **Triamcinolone** | Acetonide | Increase topical activity |

During the years 2008–2017, a total of 249 new molecular entities were approved by FDA, of which 31 were prodrugs and is shown in Table 2.

**Table 2 Novel prodrugs granted FDA approval during 2008–2018.**

| Year | Trade name | Prodrug | Active form | Activation mechanism | Prodrug strategy/gain | Indication/use |
|---|---|---|---|---|---|---|
| **2008** | Toviaz | Fesoterodine fumarate | 5-hydroxymethyl tolterodine | Hydrolysis by nonspecific esterase | Avoid variability in CYP2D6 activity. | Overactive bladder |
| | Lusedra | Fospropofol disodium | Propofol | Conversion by alkaline phosphatase | Increased aqueous solubility for IV injection by phosphorylation | Anaesthesia |
| | Emend | Fosaprepitant dimeglumine | Aprepitant | Dephosphorylation by phosphatase | Increased aqueous solubility by phosphorylation | Prevention of chemotherapy induced nausea and vomiting |
| **2009** | Effient | Prasugrel | R-138727 | 2 steps:<br>(1) Hydrolysis by esterase.<br>(2) CYP450 metabolism | Faster and more efficient conversion of parent molecule compared to Clopidogrel, Increased potency | Prevention and reduction of thrombotic and cardiovascular events |
| | Istodax | Romidepsin | Metabolite with free thiol group | Activation by intracellular glutathione | | Cutaneous T-cell lymphoma |
| **2010** | Gilenya | Fingolimod | fingolimod-phosphate | Phosphorylation by sphingosine kinase | SAR based design to optimize activity. | Multiple sclerosis |
| | Pradaxa | Dabigatran etexilate | Dabigatran | Hydrolysis by esterase | SAR based design to optimize activity. | Thromboembolism |
| | Teflaro | Ceftaroline fosamil | Ceftaroline | Plasma phosphatase | N-phosphonoprodrug | Acute bacterial skin and skin |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | to improve aqueous solubility. | structure infections and community acquired pneumonia |
| **2011** | Edarbi | Azilsartan medoxomil | Azilsartan | Hydrolysis by esterase during absorption | | Hypertension |
| | Horizant | Gabapentin enacarbil | Gabapentin | Hydrolysis by esterase | Transport by intestinal monocarboxylate transporter type 1 and sodium dependent multivitamin transporter, Hydrolysis in tissues. | Restless leg syndrome and post-herpetic neuralgia |
| | Zytiga | Abiraterone acetate | Abiraterone sulfate and N-oxide abiraterone sulfate | 2 steps: (1)Hydrolysis by esterase (2)Metabolism CYP3A4 and SULT2A1 | | Hormone refractory prostate cancer |
| **2012** | Zioptan | Tafluprost | Tafluprost acid | Hydrolysis by esterase | Good corneal penetration, Better activity, Lesser pigmentation | Glaucoma |
| **2013** | Tecfidera | Dimethyl fumarate | Monomethyl fumarate | Hydrolysis by esterase | | Multiple sclerosis |
| | Sovaldi | Sofosbuvir | GS-461203 | Intracellular metabolism by: (1) CathepsinAcarboxyl esterase 1 (2) Histidine triade nucleotide-binding protein 1 (3) Uridine monophosphatecytidine monophosphate kinase. | Phosphoramidate prodrug to bypass first step phosphorylation required by nucleoside analogs. | Hepatitis C infection |
| | Aptiom | Eslicarbazepine acetate | Eslicarbazepine | Hydrolysis during first pass metabolism | Avoid the formation of epoxide following metabolism. | Epilepsy |
| **2014** | Northera | Droxidopa | Norepinephrine | Decarboxylation by L-aromatic-amino-acid decarboxylase | | Neurogenic orthostatic hypotension and intradialytic hypotension Parkinson's disease (off-label) |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Sivextro | Tedizolid phosphate | Tedizolid | Dephosphorylation by plasma phosphatase | SAR design, Increased monoamineoxidase inhibitory profile, Improved aqueous solubility and bioavailability | Acute bacterial skin and skin infections |
| **2015** | Aristada | Aripiprazole lauroxil | Aripiprazole | 2 steps: (1)Hydrolysis by esterase (2)Non-enzymatic hydrolysis | Increase lipid solubility, Prolonged action for IM injection. | Schizophrenia |
| | Xuriden | Uridine triacetate | Uridine | Deacetylation by esterase | Catabolism resistance, Enhanced absorption | Hereditary orotic aciduria |
| | Entresto | Sacubitril | LBQ657 | De-ethylation by liver carboxylesterase 1 | | Heart failure |
| | Ninlaro | Ixazomib citrate | Active boronic form | Rapid hydrolysis post administration | Improved affinity | Multiple myeloma |
| | Cresemba | Isavuconazonium sulfate | Isavuconazole | 2 steps: (1)Hydrolysis by esterase (2)Intramolecular cyclization leading to N-dealkylation | Improved aqueous solubility | Invasive aspergillosis and invasive mucormycosis |
| **2016** | Emflaza | Deflazacort | 21-desacetyldeflazacort | Hydrolysis by esterase | | Duchenne muscular dystrophy |
| | Xermelo | Telotristat ethyl | Lp-778902 | Hydrolysis by carboxylesterase | Improved bioavailability | Carcinoid syndrome diarrhoea |
| **2017** | Austedo | Deutetrabenazine | Mainly α-dihydrotetrabenazine and βdihydrotetrabenazine | CYP450 metabolism | Deuterated to retard hepatic metabolism | |
| | Ingrezza | Valbenazine tosylate | Mainly α-dihydrotetrabenazine | CYP450 metabolism | Improved pharmacokinetics | Tardive dyskinesia |
| | Benznidazole | Benznidazole | Various electrophilic metabolites | Reduction by Trypanosoma cruzinitroreductase | | Chagas disease |
| | Solosec | Secnidazole | (Active metabolite) | Reduction by bacterial nitroreductase | | Bacterial vaginosis |
| | Vyzulta | Latanoprostene bunod | Latanoprost acid Butanediol mononitrate | Hydrolysis by corneal esterase | Good corneal penetration, Delivery of NO releasing species | Glaucoma |
| **2018** | Xofluza | Baloxavir marboxil | S-033447 | Hydrolysis by esterase | | Influenza A and B |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Krintafel | Tafenoquine | 5,6 ortho-quinone tafenoquine | Bioconversion by CYP2D6 | | Malaria |
| | Akynzeo | Fosnetupitant | netupitant | Dephosphorylation by plasma phosphatase | Phosphorylation for IV injection | Chemotherapy induced nausea and vomiting |

## 5. CONCLUSION

Although the prodrug approach is advancing and reaching successes in providing effective medications to a variety of diseases, it still needs the utilization of sophisticated computational methods for drug design. Kinetics and thermodynamics for biological systems that have biomedicinal interests have been intensively researched and have been proved to be fruitful. Today, quantum mechanics, such as *ab initio*, semiempirical, and density functional theory, and molecular mechanics including docking are increasingly being utilized to characterize active sites of receptors and enzymes. These widely used methods have proven as successful tools for providing structure-energy calculations for an accurate prediction of potential drugs. Though significant expertise is required to successfully identify and develop prodrug candidates, the overall risk-reward profile can be highly attractive. For this reason, prodrugs continue to garner attention by scientist, researchers and companies across the pharmaceutical spectrum.

## REFERENCES


1. *Arun Rasheed and Ashok C.K., Novel Approaches on Prodrug based Drug Design, Pharmaceutical Chemistry Journal, 2008, 42 (12): 677-686.*
2. *JP Peesa, PR Yalavarthi, Arun Rasheed, VBR Mandava, A perspective review on role of novel NSAID prodrugs in the management of acute inflammation, 2016, Journal of Acute disease.*

## ‘Happenings’: A Publication from KUHS on Recent Advances

## FACING SHEET OF ARTICLE

| | |
|---|---|
| **1. Stream** | Allied Health Sciences |
| **2. Speciality** | Physiotherapy |
| **3. Date** | 05-12-20 |
| **4. Title** | Impact of Moderate Aerobic Exercises on Immune System |
| **5. Name of Contributor** | Shri. Subin Chungath |
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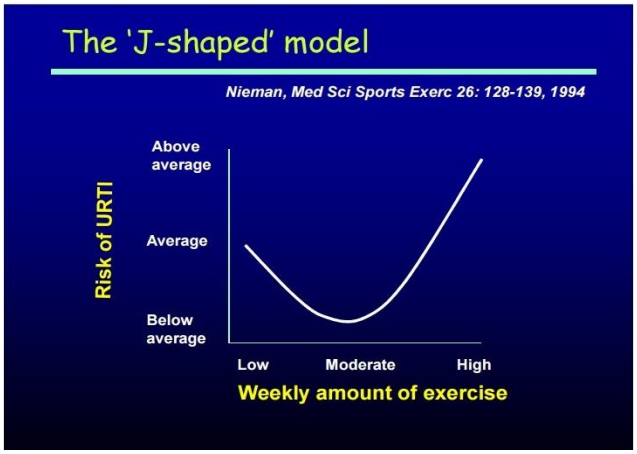
# Impact of Moderate Aerobic Exercises on Immune System

**Introduction**

Studies worldwide has proved that exercise has either a desirable or undesirable effect on immunity. These effects mainly depend on the nature, effectiveness, and extent of exercise.

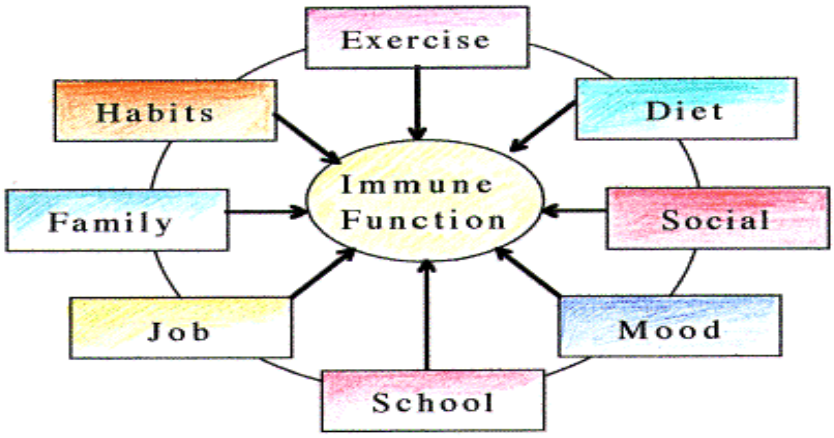
Exercise is very essential for an overall fitness of our body. According to "J" Shaped curve concept of David C Nieman- (*Appalachian State University North Carolina Research campus*) Sedentary and strenuous exercise lifestyle will impair the immune system however moderate exercise will enhance immunity. In this article I would like to focus on the impact of moderate aerobic exercise on immune responses.




This article presents an overview of moderate exercise and explains some basic concepts about immunity. According to WHO *"Immunity is the balanced state of having adequate biological defences to fight infections, diseases or other unwanted biological invasion while having adequate tolerance to avoid allergy and autoimmune diseases*."

The immune system is the collection of cells, tissues and molecules that protect the body from numerous pathogenic microbes and toxins in our environment. Our immune system provides a line of defence against invading bacteria, parasites, viruses and tumour cells. This system depends on the actions of specialized cells such as lymphocytes, granulocytes, and macrophages. The defence against microbes has been divided into two general types of reactions of innate immunity and reactions of adaptive immunity.

**Immunity at a glance**




One of most serious consequences of over training is the adverse effect on our body. According to David Neiman in his J-Shaped inverted curve explains this factor in a theoretical manner. From this J-Shaped model it is evident that moderate exercise will reduce the risk of upper respiratory tract infection.

All aerobic exercise has been designed to support the natural movement of the digestive system and increase circulation, which can also boost lymphatic and venous flow, improving your general health.

Easiest forms of physical activity are those that can be incorporated into everyday life, for example, walking, cycling, gardening, housework. The modern scientist's emphasis short term effect of moderate exercise boosts the immune functions and host defences for up to several hours and enhances the natural killer cell activity.

**The Exercise prescription for moderate level recommended by ACSM CPT 5th Edition**

| | |
|---|---|
| Warm up -purpose is to slowly elevate the pulse to an aerobic level by engaging in 5 minutes of slow aerobic activity. | |
| Aerobic session (moderate) | |
| FITT- VP guidelines | |
| F= Frequency (sessions/week) | 3 – 5 days |
| I= Intensity (% of heart rate) | 60 – 89%<br>Based on Karvonen's heart rate formula for training zone |
| T =Time (minute/session) | 30 - 35 minutes |
| T = Type | Walking, Jogging, running, cycling, Swimming, Aerobic exercise |
| V= volume | Moderate exercise level 300 minutes/week |
| P= Progression | Depends on health status |
| Warm down –purpose is to slowly decrease the heart rate by engaging in slow aerobic activity for at least 5 minutes. | |

## DISCUSSION

Exercise is known to have a profound impact on the normal functioning of the immune system. Each bout of exercise, particularly whole-body dynamic cardiorespiratory exercise, instantaneously mobilizes literally billions of immune cells, especially those cell types that can carry out effector functions such as the recognition and killing of virus-infected cells. Exercise also releases various proteins that can help maintain immunity.

### Exercise during pandemic stage using digital platform


Currently, the greatest risk of COVID-19 infection is exposure. It is paramount that we find creative ways to exercise while maintaining social distancing and proper hygienic countermeasures. While exercise may not prevent us from becoming infected if exposed, it is like that keeping active will boost our immune system to help minimize the deleterious effects of the

virus, ameliorate our symptoms, expedite our recovery times and lower the likelihood that we can infect others with whom we come into contact.

**Reality of immunity**

*"There is no elixir to improve immunity".*

For improving immunity, we need a holistic approach which includes aerobic exercises and a well-balanced diet. Studies worldwide emphasise the importance of exercise in different age group like in geriatric, adolescent, pregnancy and even in infertility. This concept can be extended to the immunosuppressive disease like cancer, HIV and even in depression. We can approach this concept in geriatric population to find the relationship between aging and moderate exercise.

Future Scope

In a developing country, a huge parity is seen on spending money on medicines vs health fitness and wellness. Instead, if we can equally spend money on conducting evidence based scientific research on biochemical and pathophysiological changes while exercising that would help to change the trajectory of the entire community in preventive aspects.

**14. References**


- *ACSM for fitness training 5 $^{th}$ edition and ACSM journals*
- *Katch and Katch, William D. McArdle, Frank I Katch, Victor L Katch (Exercise Physiology: Nutrition, Energy, and Human Performance)*
- *David C Niemen-Appalachian State University North Carolina Research campus (exercise Testing and Prescription- A health related approach)*
- *Jack H Wilmore, David L Costly – Physiology of Sports and exercise.3$^{rd}$ edition page no: 386.*
- *Carlo Gimmattei, Riccardo Banducci, Giuliapierami and Alberto Tomsai - Acute effects of exercise on immunity ASPETER SPOTRS MEDICINE JOURNEL*
- *Moderate level aerobic exercise endorphin release TED talk by Dr. Wendy A. Suzuki is a Professor of Neural Science and Psychology in the center for Neural Science at New York University.*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