

# MEDICINE UPDATE

 Passi HealthCom



**Solid organ  
preservation and  
its application**

**Volume 31**

**Number 7**

**November 2023**



## CONTINUING • MEDICAL • EDUCATION

### LEADERS IN HEALTHCARE COMMUNICATIONS

CME Communications, the Continuing Medical Education arm of Passi HealthCom, which is a 28-years old organization with excellence in Healthcare Communications, now has a global presence and expertise in designing different engagement strategies to promote healthcare education.

The focus of CME Communications is to train clinical professionals to fill gaps in the areas of healthcare for best deliverance to patients.

#### • OUR ACTIVITIES

- Medical Conferences
- Accredited Live CMEs
- Seminars & Workshops
- Advisory Board Meetings
- Observerships
- Webinars
- Diploma/MSc Programs

#### • AREAS WE CATER

- CME Communications is proud to cater almost all disciplines of medicine, targeting a broad range of healthcare professionals in each specialty, ranging from General Physicians to Specialists and Super-specialist.
  - Cardiology
  - Dermatology and Cosmetology
  - Endocrinology & Diabetes
  - Gastroenterology
  - Medical Oncology
  - Nephrology
  - Neurology
  - Orthopedics
  - Pediatrics
  - Psychiatry
  - Reproductive Medicine
  - Urology

### OUR ACADEMIC PARTNERS

#### • USA

- » Cleveland Clinic
- » Mayo Clinic
- » Boston University School of Medicine (BUSM)

#### • UK

- » Royal College of Physicians (RCP)
- » University of South Wales, Cardiff
- » University of Exeter

#### • Netherlands

- » International Federation of Diabetes and Cardiometabolic Disorders (IFDCD)

### Asia & Middle East Offices

#### Delhi:

318, Virat Bhawan, Commercial Complex,  
Dr Mukherjee Nagar, Delhi - 110009  
⌚ 91-11-47029273, 45706616  
✉ info@cme.com.in [www.cme.com.in](http://cme.com.in)  
CIN : 74899DL1993PTC056229

#### Mumbai:

Unity, D-2/5, Khira Nagar,  
S.V. Road, Santacruz (W),  
Mumbai - 400054  
[www.passi.org](http://passi.org)  
⌚ 91-22-26613074, 26615445  
📠 91-22-26615445

#### Dubai:

P.O.Box No. 49245, Dubai, U.A.E.  
⌚ +971 506558239  
📠 +971 43349807

## ACTIVE DAY



## GOOD NIGHT SLEEP



In Allergy Rhinitis & Allergic Rhinitis with Asthma

Rx **MONADINE**™  
Tablets  
(Montelukast Sodium 10 mg + Fexofenadine Hydrochloride 120 mg)

**4**TIFIED ALERT... From **MON** to **DINE**



Rx **MONLEVO**®  
Tablets  
(Montelukast Sodium 10mg + Levocetirizine Hydrochloride 5mg)

**THE POWER OF FREEDOM**



FRANCO - INDIAN  
PHARMACEUTICALS PVT. LTD.  
20, Dr. E. Moses Road, Mumbai 400 011

# Contents

**EDITORIAL BOARD**

**EDITOR-IN-CHIEF**

Dr. P.S. Shankar

**MEDICAL DIRECTOR**

Dr. Sushil Kumar

**SECTION EDITORS**

**DERMATOLOGY**

Hema Jerajani

**PEDIATRICS**

A. Prema

**NEUROLOGY**

K.S. Anand

**PUBLISHER**

Sarvesh Passi

## **EDITORIAL**

- Phytopharmaceutical extracts for treatment of hair loss 6

## **SECTION 1**

### **Global Update**

- Is there any association between dietary pattern adherence and improved ovarian reserve in overweight and obese reproductive age women? 7

- Levetiracetam in epileptic seizures 8

- Does pre-treatment folate intake improve reproductive success among women undergoing assisted reproduction? 8

- Impact of antiepileptic drugs levetiracetam and valproate on platelet function 9

- Economical effect of ozenoxacin vs. other topical antibiotics in patients with impetigo 10

## **SECTION 2**

### **Clinical Update**

- Solid organ preservation and its application 11



# Contents

## ADVISORY BOARD

A.K. Agarwal  
Naresh Trehan  
S.K. Sarin  
Tamal K. Biswas  
K.B. Gupta  
A.P. Jain  
K.V. Krishna Das  
M. Panja  
Prasant Kumar Sahoo  
J.N. Pande  
P.G. Raman  
H.C. Sathya  
Suneeta Sahu  
O.P. Sharma  
M.M. Singh  
Virendra Singh  
Subhash Varma  
Vijaikumar  
S. Chandrasekharan  
V. Parameshwara  
Sukhvinder Singh

Successful alleviation of psoriatic arthritis with skin lesions localized to the scalp with apremilast

**15**

An approach to tonsillopharyngitis in clinical practice

**18**

## SECTION 3

### Medical Quiz

**21**

## SECTION 4

### Events Update

**22**

## SECTION 5

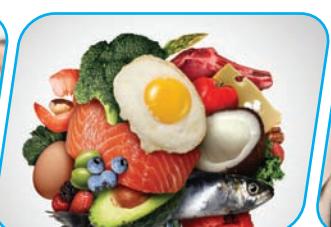
### Tech Update

**23**

## SECTION 6

### Legal Update

**25**



## EDITORIAL

# Phytopharmaceutical extracts for treatment of hair loss

**Dr. Sharmila Patil**

MBBS, DDVL, MD - Skin & VD

Dermatologist, Cosmetologist, Trichologist

Professor and Head of the Department D Y Patil School of Medicine

Consultant in Fortis Hospital, Mulund, Mumbai

**C**hronic telogen effluvium is a primary, idiopathic disease affecting middle-aged women. This condition lasts for more than six months without widening the central part of hair or follicular miniaturization. This condition is usually caused by emotional and physical stress. In telogen effluvium, according to dermoscopy, the anagen/telogen ratio is significantly reduced and more than 25% of the hair is in the telogen phase.

The most important aspect of the treatment of telogen effluvium is to educate the patient and eliminate the causative factors. No specific treatment for this disorder is currently available. Because of the fact that the standard drugs (minoxidil and finasteride) are not effective catagen inhibitors and anagen inducers, it clearly points to the need for alternative treatment options. Phytopharmaceutical extracts (Biochanin-A and Acetyl tetrapeptide-3) are considered to be the most effective and well-tolerated alternative treatments for hair loss.



These extracts can be beneficial for conditions like telogen effluvium because they stimulate anagen hair and inhibit telogen hair growth along with inhibition of 5- $\alpha$  reductase activity, reduction of inflammatory responses, and stimulation of extracellular matrix (ECM) protein synthesis near hair follicles.

# SECTION 1

## GLOBAL UPDATE

### IS THERE ANY ASSOCIATION BETWEEN DIETARY PATTERN ADHERENCE AND IMPROVED OVARIAN RESERVE IN OVERWEIGHT AND OBESE REPRODUCTIVE AGE WOMEN?

Anti-Müllerian hormone (AMH) concentration and antral follicle count (AFC), markers of ovarian reserve have been used to predict ovarian responsiveness to gonadotropins in women undergoing ovarian stimulation. There exists an inverse relationship between increasing body mass index and AMH concentration, such that overweight or obese women demonstrate reduced ovarian responsiveness to oral ovulation induction medications and gonadotropin stimulation. Evidence had shown that adherence to profertility diet (PFD) and avoidance of environmental toxins was associated with improved reproductive outcomes in women undergoing in vitro fertilization (IVF). Profertility diet is characterized by increased intake of whole grains, soy and seafood, dairy, low pesticide residue produce. Though there is considerable data highlighting the association between lifestyle and dietary patterns and reproductive outcomes, there is scarcity of data to demonstrate effect of diet on measures of ovarian reserve. A study was conducted to evaluate the association between dietary pattern and ovarian reserve in reproductive age women without a history of infertility. This study included 185 women aged 18–44 years without a history of infertility. Women were stratified based on  $BMI < 25 \text{ kg/m}^2$  and  $BMI \geq 25 \text{ kg/m}^2$  and they were subjected to four dietary patterns. Serum AMH (ng/mL) and AFC were the endpoints.

There were no significant association was seen in between western, prudent and fertility diet and ovarian reserve. In overweight and obese women with  $BMI \geq 25 \text{ kg/m}^2$ , an increased adherence to PFD was associated with a significantly higher AMH. Mean AMH concentration in women in the third and fourth quartiles of PFD adherence were 1.45 ng/mL and 1.67 ng/mL higher than women in the lowest quartile, respectively. There also existed an association between high AFC and higher adherence to PFD in women with  $BMI \geq 25 \text{ kg/m}^2$ .

It was inferred that there exists an association between increased adherence to a profertility diet and improvement in ovarian reserve markers in overweight and obese women.

**Source:** Eskew AM, Bedrick BS, Chavarro JE, Riley JK, Jungheim ES. Dietary patterns are associated with improved ovarian reserve in overweight and obese women: a cross-sectional study of the Lifestyle and Ovarian Reserve (LORE) cohort. *Reprod Biol Endocrinol.* 2022;20(1):33.

## LEVETIRACETAM IN EPILEPTIC SEIZURES

Antiepileptic drugs (AEDs) play a vital role in the treatment of epilepsy as their use is associated with decreased morbidity and mortality, including sudden deaths. The objective of this study was to assess the clinical efficacy of levetiracetam in the treatment of various types of epileptic seizures, based on the clinical evidence available. Relevant data was searched to identify clinical studies conducted on Levetiracetam. Results revealed as compared to phenobarbitone, levetiracetam exerts a neuroprotective benefit, that is of significant importance in neonates since they are in process of neurodevelopment. It exerts no significant effect on bone metabolism, hence is considered safe in growing children and the elderly. Since levetiracetam monotherapy is significantly better with respect to withdrawal rates due to tolerability issues compared to the other first-line agents, it can be considered as the first line therapy in new-onset focal epilepsy or partial onset seizures in adults and elderly. Use of levetiracetam as an adjunct therapy is favourable in the treatment of refractory or drug-resistant epilepsy, as its use is associated with higher or comparable seizure cessation/freedom compared to other newer and older AEDs.



Levetiracetam is well-tolerated and possess excellent safety profile as it has a lower incidence of treatment emergent adverse effects across all ages compared to oxcarbazepine and topiramate. In children with partial seizures, levetiracetam may be a considered as a suitable option as an add-on treatment, due to its favorable efficacy and insignificant toxicity. In benzodiazepine resistance status epilepticus, levetiracetam has been considered as a potential first-choice and second-line AED. With levetiracetam, there is no associated cardiotoxicity, respiratory depression, arrhythmia. It improves the quality of life due to higher rates of seizure freedom and favorable tolerability profile. Its safety and tolerability is more apparent during pregnancy.

It was concluded levetiracetam can be considered as an effective and safe first-line antiepileptic drug in treatment of various types of epileptic seizures.

**Source:** Uppal S, Uppal S, Panchal G. Recent updates on Levetiracetam. IP Indian J Neurosci. 2022;8(1):21-30.

## DOES PRE-TREATMENT FOLATE INTAKE IMPROVE REPRODUCTIVE SUCCESS AMONG WOMEN UNDERGOING ASSISTED REPRODUCTION?

According to data available, approximately 15% of couples report to be infertile. Though there is scarcity of data with respect to effect of diet and fertility outcomes, some evidences have shown that folate is associated with improved fertility outcomes. Moreover, folate is necessary for DNA synthesis, transfer of RNA cysteine and methionine, signifying that folate requirement is greatly increased during periods of rapid cell growth, such as the peri-conceptional period. The aim of this study was to ascertain the correlation between folate intake before assisted reproductive technology and reproductive outcomes among women undergoing the treatment. This study included 232 women aged 18-46



years. Intermediate and clinical endpoints of ART were evaluated with respect to clinical pregnancy, implantation, live-birth rate and embryo quality.

Results revealed a positive and strong association was reported between higher folate intake and higher implantation, clinical pregnancy, and live birth rates per initiated cycle. In women having higher supplemental folate intake ( $>800 \times g/day$ ), live birth rates were 20% higher as compared to women having lower intake ( $<400 \times g/day$ ). Adjusted percentage of initiated assisted reproductive technology cycles resulting in a live birth for women in increasing quartiles of folate intake were 30%, 47%, 42% and 56%. Moreover, there existed a direct relationship between higher supplemental folate intake and higher fertilization rates and lower cycle failure rates before embryo transfer.

It was inferred that pre-treatment of folate is associated with favorable reproductive outcomes that includes higher live birth rates in women undergoing ART.

**Source:** Gaskins AJ, Afeiche MC, Wright DL, Toth TL, Williams PL, Gillman MW, Hauser R, Chavarro JE. Dietary folate and reproductive success among women undergoing assisted reproduction. *Obstet Gynecol.* 2014;124(4):801-809.

## IMPACT OF ANTI-EPILEPTIC DRUGS LEVETIRACETAM AND VALPROATE ON PLATELET FUNCTION

Antiepileptic drugs are known to have an effect on platelet functions and the complex coagulation system; though the mechanism underlying it remains widely unknown. Valproate (VPA), a broad-spectrum antiepileptic drug has been considered as first choice treatment option for idiopathic and symptomatic generalized epilepsies due to its marked efficacy. However, its use is associated with adverse effect such as hemorrhagic diathesis that may vary in onset and severity and occurs in 33 to 55% of patients with VPA plasma levels between 215 and 1000  $\times g/mL$ . Furthermore, VPA use is associated with reduced platelet count and aggregation and an ATP release impairment; effects may occur within few months of therapy and with plasma VPA levels within the normal range. These effects may be reversed with dosage reduction. Levetiracetam has been effectively used as monotherapy and as adjunctive therapy in all types of epilepsy. The associated adverse effects are mild to moderate, appear within the first month after treatment initiation, are not dose dependent, and mostly resolve without medication discontinuation. Its use is not associated with any hematology side-effects. A placebo-controlled, double-blind crossover study was done to compare the influence of VPA and levetiracetam on platelet functions. It included 12 healthy subjects who were given valproate 500 mg and results were compared with levetiracetam 1000 mg as a control substance and placebo. A blood sample was taken before and 90 min after medication intake. Changes in platelet, erythrocyte, and leukocyte cell count and in platelet functions [CD62 expression (P selectin), thrombin binding, and fibrinogen binding] were studied. Findings of the study stated that there were no significant differences in all cell counts were noted before and after different study drugs. Fibrinogen binding significantly decreased and the CD62 expression significantly increased after valproate intake. This resulted in decreased platelet aggregation.

In conclusion, it was inferred that levetiracetam has no relevant effect on blood cell counts and on platelet functions as measured by thrombin binding, fibrinogen binding, and P-selectin expression. Levetiracetam is not associated with increased bleeding risk.

**Source:** Olaizola I, Brodde MF, Kehrel BE, Evers S. The Impact of Levetiracetam and Valproate on Platelet Functions-A Double-Blind, Placebo-Controlled Crossover Study. *J Clin Med.* 2023 Jan 25;12(3):933.



## ECONOMICAL EFFECT OF OZENOXACIN VS. OTHER TOPICAL ANTIBIOTICS IN PATIENTS WITH IMPETIGO

Impetigo is a widespread infection of the outermost layer of the epidermis that is primarily caused by *Staphylococcus aureus* and less frequently by *Streptococcus pyogenes*. Impetigo causes contagious and readily spreadable lesions on the face, arms, or legs of the patients. The most widely used topical antibiotics for treatment of impetigo in children include mupirocin (MUP), fusidic acid (FA), and most recently approved drug ozenoxacin. It has been demonstrated that ozenoxacin, a nonfluorinated quinolone, has strong bacteriostatic and bactericidal action against the most prevalent Gram-positive bacteria associated with skin and soft tissue diseases.

A retrospective observational study was performed to investigate the clinical and economic consequences of the use of ozenoxacin vs. MUP and vs. FA for the treatment of impetigo in routine clinical practice. Patients with impetigo who initiated treatment with ozenoxacin, MUP or FA were enrolled. Treatment duration, comorbidities, systemic drug usage complications, utilization of resources and related costs were compared among regimens.

Findings of the study were as follows:

- The mean age of patients was 12.6 years; 48.6% of the population was male; the following treatments were given: 9.3% (ozenoxacin), 56.4% (MUP), and 34.5% (FA)
- Complication rates after treatment with ozenoxacin was 1.8%, MUP was 3.3%, and FA was 3.2%, respectively, with mean expenses of €158 (OZ), €265 (MUP), and €287 (FA), respectively,  $p<0.001$
- Proportion of patients discontinuing therapy after two weeks of treatment was 87.6% (ozenoxacin), 83.2% (MUP), and 82.4% (FA);  $p<0.001$ .
- Inferably, in patients with impetigo, ozenoxacin is a successful and affordable treatment approach than mupirocin and fusidic acid.



**SOURCE:** Rodríguez-Quintosa J, Ago CC, Sicras-Mainar A, Villoro R, Pérez-Román I. Clinical and economic consequences of ozenoxacin vs. other topical antibiotics for the treatment of impetigo: a real-life study in Spain. *Glob Reg Health Technol Assess.* 2022;9:133-137.

## SECTION 2

### CLINICAL UPDATE

# Solid organ preservation and its application

#### ORGAN PRESERVATION PROCEDURE: AN OVERVIEW

Organ transplantation is now the only effective therapy and is performed as the treatment of choice in patients with end-stage diseases. Through several scientific developments, organ transplantation has evolved over the past 50 years in order to access the comprehensive, integrated diagnostic service of today. Use of an organ preservation protocol is one of the most important steps in matching and transplanting the appropriate donor organ to the recipient for resumption of life-sustaining function. This has only been possible by the development and thorough knowledge of the type of donor, the effects of Ischemic reperfusion injury on donated organs and how to prevent them by using organ preservation methods.<sup>1</sup>

#### Types of donor

There are three types of donor<sup>2</sup>

- Living donor: (kidney, and part of the liver)
- Circulatory death donors (DCDs): (kidney, liver, lung and heart)
- Brain death donors (DBDs) further divided into standard criteria donor (SCD) and extended criteria donors (ECD) (Figure 1).

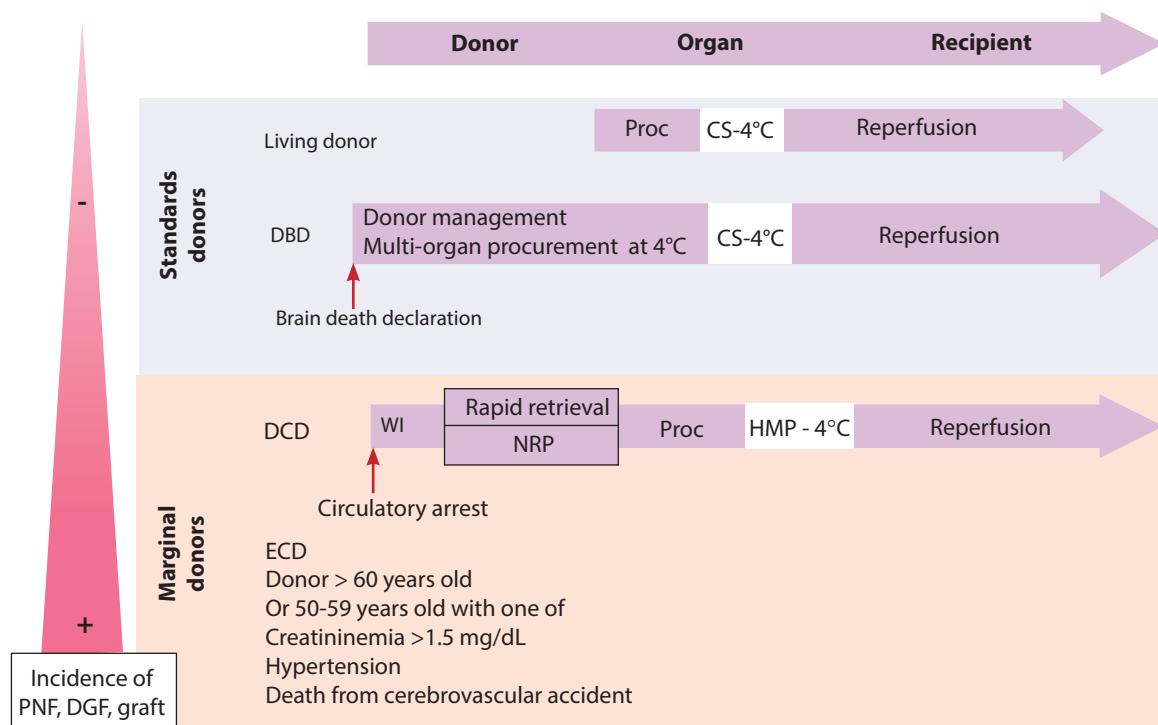
- SCD : Donor under 60 years of age
- ECD : (kidney, liver, heart, lung, pancreas and intestine)  
Donor either > 60 years or aged 50 to 59 years with at least 2 of the following three criteria: (i) cerebrovascular accident as cause of death; (ii) serum creatinine level > 1.5 mg/dL (137 mmol/L); (iii) pre-existing history of systemic hypertension

#### Ischemic – reperfusion injury

Ischemic reperfusion can lead to variety of injury mechanisms that have negative consequences on both short-and long-term consequences and it starts instantly as the organ is no longer supplied by blood and it is aggravated when the organ is re-vascularized. As a result, it is essential to alter the methods for graft preservation. On this account, organ transplantation is going through a significant changes nowadays.<sup>3</sup>

#### ORGAN PRESERVATION

In transplant procedure, organ preservation is a critical step due to scarcity of organ availability for transplant. The main objective of organ preservation is to maintain the organ and tissue functioning during storage in order to maintain graft function on re-perfusion. For the most of transplantable organs, there are primarily two methods

**Figure 1: Role of preservation in graft journey according to the type of graft (e.g kidney)**

**Abbreviations:** ECDs: extended criteria donors; DCDs: deceased donors after circulatory arrest; DBDs: brain-dead donors; DGF: Delayed graft function; PNF: Primary non-function; SC: static conservation at 4°C; NRP: normothermic regional perfusion; WI: Warm ischemia; HMP: Hypothermic conservation on perfusion machine.

**Source:** Lepoittevin M, Giraud S, et al. Preservation of Organs to Be Transplanted: An Essential Step in the Transplant Process. *Int J Mol Sci.* 2022;23(9):4989.

of preservation: static or dynamic. The basic approach for static storage is simple static cold storage (SCS) whereas dynamic preservation includes hypothermic machine perfusion (HMP) and other perfusion-based methods such as normothermic machine perfusion and gaseous oxygen perfusion. Currently, SCS and HMP are approved for kidneys, and only SCS for livers, lungs, pancreas, or heart.<sup>1</sup>

### Static cold storage and preservative solutions

Since the 1960s, static cold storage without oxygen supply has gradually become the gold standard method for organ preservation. In SCS, the donor organ is first flushed with preservative solution at 0–4 °C and then immersed in the same solution at the same temperature till transplantation. The preservative solution offers cytoprotection by reducing cellular metabolism.

**Table 1: Types of preservative solution**

<b>ICF type (low Na<sub>+</sub> and high K<sub>+</sub> concentrations)</b>	<b>ECF type (low K<sub>+</sub> and high Na<sub>+</sub> concentrations)</b>	<b>Modified (low K<sub>+</sub> and low Na<sub>+</sub> concentrations with amino acid)</b>
Collins solution	Celsior	Histidine-tryptophan-ketoglutarate (HTK)
Euro-Collins solution	LPDG (Perfadex)	Custodiol-N
UW solution	Ep4 (EP-TU)	
	ET-Kyoto	
	IGL-1	

**Source:** Jing L, Yao L, Zhao M, Peng LP, Liu M. Organ preservation: from the past to the future. *Acta Pharmacol Sin.* 2018;39(5):845-857.

Comparison of various methods used for preservation of organs				
Methods	Temp.	Merits	Challenge	Clinical application
Cold static storage	0-8°C	Low cost, simple and easy to operate	Metabolite accumulation, not for organ function assessment	Kidney, liver, lung, heart
Hypothermic machine perfusion	0-8°C	Provides oxygen and metabolic substrates	Perfusion time is limited, not for organ assessment	Kidney, liver
Normothermic machine perfusion	35-38°C	Provides oxygen and essential substrates; maintains metabolic activity and viability; good for organ assessment and repair	Perfusion time is limited for organ regeneration	Kidney, liver, lung, heart
Subnormothermic machine perfusion	20-34°C	Newly proposed technique	To be determined	
Controlled oxygenated rewarming	8-20°C	Slowly, gradually rise the perfusate temperature to mitigate ischemia reperfusion injury	To be determined	Liver

**Source:** Jing L, Yao L, Zhao M, Peng LP, Liu M. Organ preservation: from the past to the future. *Acta Pharmacol Sin.* 2018 May;39(5):845-857.

There are two types of preservative solutions, intracellular fluid (ICF) type and extracellular fluid (ECF) type (Table 1). ICF type solution prevent cellular edema by maintaining intracellular ion concentrations upon cold-induced dysfunction of Na<sup>+</sup>/K<sup>+</sup> pumps. But, the risk of hyperkalemia-induced pulmonary vasoconstriction with ICF solution led to the development of ECF type preservative solution.<sup>4</sup>

- The University of Wisconsin (UW) solution is used for abdominal organ preservation
- HTK solution developed for heart preservation, however it also led to comparable patient survival for transplants of abdominal organ
- A low-potassium dextran glucose (LPDG) solution was developed and currently used as the gold standard for lung preservation. In clinical lung transplantation in Japan, ET-K and EP-TU solutions have been used.<sup>4</sup>

## Limitations of SCS

- Prolonged hypothermic preservation led to tissue damage
- Evaluating the viability and function of donor organs can be challenging
- Injury from ischemia-reperfusion is unavoidable
- Minimal likelihood of organ repair<sup>4</sup>

## Machine perfusion

Currently, machine perfusion has become more prevalent as a result of the increasing usage of marginal organs from extended-criteria donors. Machine perfusion is a technique that helps in maintenance of microvasculature of organ, provision of oxygen and nutrients in support of tissue metabolism, and removal of toxic metabolic waste.<sup>1</sup>

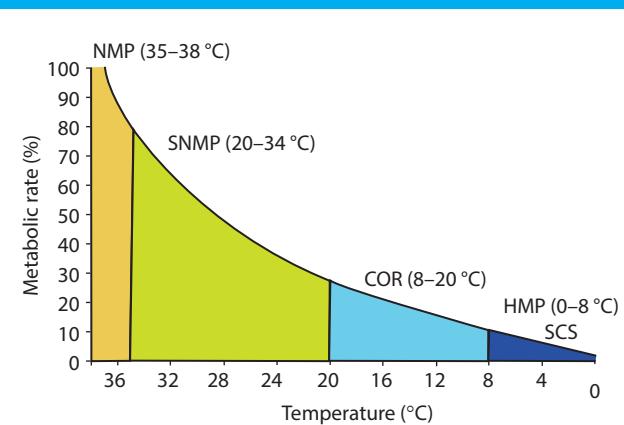
The rate of cellular respiration is proportional to the ambient temperature.<sup>4</sup> Different temperature for machine perfusion and their effect on tissue metabolism illustrated in Figure 2.

Hypothermic machine perfusion has progressed to become clinical reality and routine in several fields of solid organ transplantation especially in kidney preservation.<sup>5</sup>

## NEW DEVELOPMENTS TO IMPROVE ORGAN PRESERVATION

The extension of machine perfusion duration and establishment of an equilibrium in the condition of organ are crucial primary objectives. The current technology will probably need to be further modified in order to preserve organs for several days.

Some of the current approaches are depicted below:<sup>1</sup>

**Figure 2: Effect of temperature on tissue metabolism**

**Abbreviations:** NMP: normothermic machine perfusion, SNMP: subnormothermic machine perfusion, COR: controlled oxygenated rewarming, and HMP: hypothermic machine perfusion.

**Source:** Jing L, Yao L, Zhao M, Peng LP, Liu M. Organ preservation: From the past to the future. *Acta Pharmacol Sin.* 2018;39(5):845-857.

- Isolated perfusion at elevated temperatures
- Ischemic pre-conditioning and trophic factors in organ preservation
- Gene therapy
- Cryopreservation
- Pharmacological manoeuvres

## CONCLUSION

The best treatment for patients with end-stage disease is organ transplantation. For donor organ preservation, which is directly connected to morbidity and survival following transplantation, preservation techniques and solutions are important. Currently, SCS is the accepted technique for organ preservation. However, preservation time with SCS is constrained since prolonged cold storage raises the likelihood of early graft malfunction, which increases persistent problems. Additionally, methods for organ assessment and repair are needed due to the raising demand for the marginal donor. Current research on organ preservation is dominated by machine perfusion methods.

## REFERENCES

1. Guibert EE, Petrenko AY, et al. Organ Preservation: Current Concepts and New Strategies for the Next Decade. *Transfus Med Hemother.* 2011;38(2):125-142.
2. Lepoittevin M, Giraud S, et al. Preservation of Organs to Be Transplanted: An Essential Step in the Transplant Process. *Int J Mol Sci.* 2022;23(9):4989.
3. Eltzschig HK, Eckle T. Ischemia and reperfusion--from mechanism to translation. *Nat Med.* 2011;17(11):1391-401.
4. Jing L, Yao L, Zhao M, Peng LP, Liu M. Organ preservation: from the past to the future. *Acta Pharmacol Sin.* 2018;39(5):845-857.
5. Resch T, Cardini B, et al. Transplanting Marginal Organs in the Era of Modern Machine Perfusion and Advanced Organ Monitoring. *Front Immunol.* 2020;11:631.

# Successful alleviation of psoriatic arthritis with skin lesions localized to the scalp with apremilast

## CHIEF COMPLAINT

A 66-year-old man with dandruff and suspected to have scalp eczema presented with complaints of painful swollen joints in his right hand, right knee, and bilateral ankle joints. He experienced difficulties in walking because of the severe joint pain in his legs.

## HISTORY

- He had been treated by a general practitioner with an anti-inflammatory ointment for 2 years
- Previous therapies included topical treatments, psoralen ultraviolet A, acitretin with minimal effects
- About 4 months after the development of polyarthritis and dactylitis, the scalp skin lesions gradually spread to his face
- He remained free from any skin lesions besides those on the face and scalp
- No allergies
- No family history of psoriasis or arthritis.

## EXAMINATION

### General Examination

- Temperature:* Afebrile
- Blood pressure:* 130/90 mmHg
- Heart rate:* 70 bpm
- Respiratory rate:* 16 breaths/min
- No palpable lymph nodes, icterus or edema.

### Systemic Examination

- Chest:* Clear on auscultation
- Cardiovascular:* Normotensive; no murmurs; no added heart sounds
- Abdomen:* No distension or tenderness
- Musculoskeletal:* Swelling or tenderness in his right hand, right knee, and bilateral ankle joints.

### Dermatological Examination

- A massive amount of dandruff was observed across the scalp
- The hairline of the sideburns showed reddish borders
- The right knee and ankle joint were swollen and painful. Multiple sites of dactylitis with the appearance of “sausage digit” were observed in both hands, but skin lesions or nail involvement was absent
- With development of facial skin lesions, psoriatic arthritis (PsA) was suspected.

### INVESTIGATIONS

- Hematological examination revealed the following findings: white blood cell count = 9300/ $\times$ L; antinuclear antigen = negative; anti-SS-A/SS-B antibody = negative; c-ANCA/p-ANCA = negative; RF = negative; matrix metalloproteinase-3 = 324.4 ng/mL; C3 = 156 mg/dL; C4 = 48.2 mg/dL; CH50 = 81.9 mg/dL; and C-reactive protein = 4.59 mg/dL



Clinical pictures at baseline



After Apremilast treatment

- In hand X-ray images, distal phalanges of the 3<sup>rd</sup> and 4<sup>th</sup> fingers in left hand presented proliferative bony changes
- Scaphoid bone erosion was observed in the right hand
- Liver and kidney functions were normal.

## DIAGNOSIS

Based on the appearance of the head and facial skin lesions, psoriasis was suspected.

## MANAGEMENT

The patient was put on cyclosporine 2 mg/kg/day and slowly increasing doses of Apremilast starting from 10 mg once a day and building on to 30 mg twice daily.

## RESULTS

- About 1 month after the first hospital visit, Apremilast swiftly alleviated his scalp and facial skin lesions. In addition, joint pains in his hand and legs also disappeared, and he could walk without difficulties
- Resolution in symptoms with PASI of 7.2 was observed.

## DISCUSSION

### Overview

Psoriatic arthritis (PsA) is characterized by cutaneous manifestation of psoriasis which coexists with arthritis usually in the absence of rheumatoid factor and is known to affect 20 to 30% of such patients.<sup>1,2</sup>

It is known to affect men and women between the ages of 40 and 50 years affecting peripheral and axial joints, entheses, skin, and nails. PsA is associated with comorbidities such as osteoporosis, uveitis, subclinical bowel inflammation, and cardiovascular disease.<sup>3</sup>

Though the etiology of PsA is not well understood, it involves the interaction between genetic and environmental factors that leads to immune-mediated inflammation involving the skin and joints and may involve other organs. In patients with psoriasis or PsA wherein patients are already at risk due to genetic risk factors, environmental factors such as infection or mechanical stress initiate a chronic inflammatory process primarily involving the joints and skin, resulting in the production of IL-23 which is a central cytokine in the pathogenesis of PsA and psoriasis.<sup>1</sup>

### Combating psoriatic arthritis with Apremilast

The conventional therapeutic agents for psoriasis such as methotrexate, acitretin, and cyclosporine are invariably associated with end-organ toxicities and treatment related side effects. High cost and inconvenient modes of administration and along with the possibility of iatrogenic immunosuppression further degrade their position as a treatment option for psoriasis.<sup>4</sup>

Apremilast, a phosphodiesterase-4 (PDE4) inhibitor inhibits PDE4 conversion of cyclic AMP to AMP, thus indirectly downregulating the inflammatory response through decreased inflammatory cytokine expression and increased expression of anti-inflammatory cytokines.<sup>5</sup>

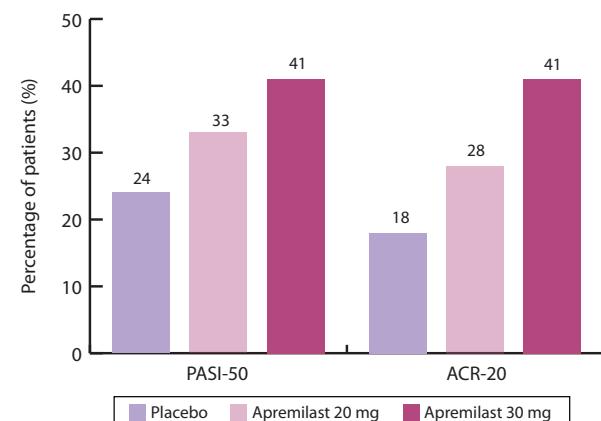
Psoriatic Arthritis Long-term Assessment of Clinical Efficacy (PALACE) phase III clinical trial was done to

assess Apremilast treatment in patients with active PsA, including current skin involvement, despite prior therapy with conventional disease-modifying antirheumatic drugs and/or biologic agents.

The study included 505 patients who were randomised (1:1:1) to placebo, Apremilast 20 mg twice daily, or Apremilast 30 mg twice daily. Rescue therapy with Apremilast was designated at week 16 for placebo patients not achieving 20% improvement in swollen and tender joint counts. At week 24, the remaining placebo patients were then randomised to Apremilast 20 mg twice daily or 30 mg twice daily. The efficacy and safety of Apremilast were assessed over 52 weeks. The results were as follows:

- Significantly more patients receiving Apremilast 20 mg twice daily (28%) and 30 mg twice daily (41%) achieved 20% improvement in American College of Rheumatology response criteria versus placebo (18%;  $p=0.0295$  and  $p<0.0001$ , respectively) at week 16 (Figure 1)
- Significantly greater mean decrease in the Health Assessment Questionnaire-Disability Index score was achieved with Apremilast 30 mg twice daily ( $-0.20$ ) versus placebo ( $-0.07$ ;  $p=0.0073$ )
- Significantly more number of patients taking Apremilast 30 mg twice daily achieved 50% reduction from baseline Psoriasis Area and Severity Index score (41%) versus placebo (24%;  $p=0.0098$ ) at week 16 (Figure 1)
- At week 52, observed improvements in these measures demonstrated sustained response with continued Apremilast treatment.<sup>5</sup>

**Figure 1: Effect of Apremilast on Psoriatic arthritis<sup>5</sup>**



This thus signifies that Apremilast is effective in improving signs and symptoms of patients affected with psoriatic arthritis.

## REFERENCES

1. Tiwari V, Brent LH. Psoriatic Arthritis. [Updated 2020 Aug 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK547710/>. Accessed on: 14-06-2021.
2. Sankowski AJ, Lebkowska UM, Cwikla J, Walecka I, Walecki J. Psoriatic arthritis. *Pol J Radiol*. 2013;78(1):7-17.
3. Ocampo D V, Gladman D. Psoriatic arthritis. *F1000Res*. 2019;8:F1000 Faculty Rev-1665.
4. Afra TP, Razmi TM, Dogra S. Apremilast in Psoriasis and Beyond: Big Hopes on a Small Molecule. *Indian Dermatol Online J*. 2019;10(1):1-12.
5. Edwards CJ, Blanco FJ, Crowley J, Birbara CA, Jaworski J, Aelion J, Stevens RM, Vessey A, Zhan X, Bird P. Apremilast, an oral phosphodiesterase 4 inhibitor, in patients with psoriatic arthritis and current skin involvement: a phase III, randomised, controlled trial (PALACE 3). *Ann Rheum Dis*. 2016;75(6):1065-73.

# An approach to tonsillopharyngitis in clinical practice

## OVERVIEW

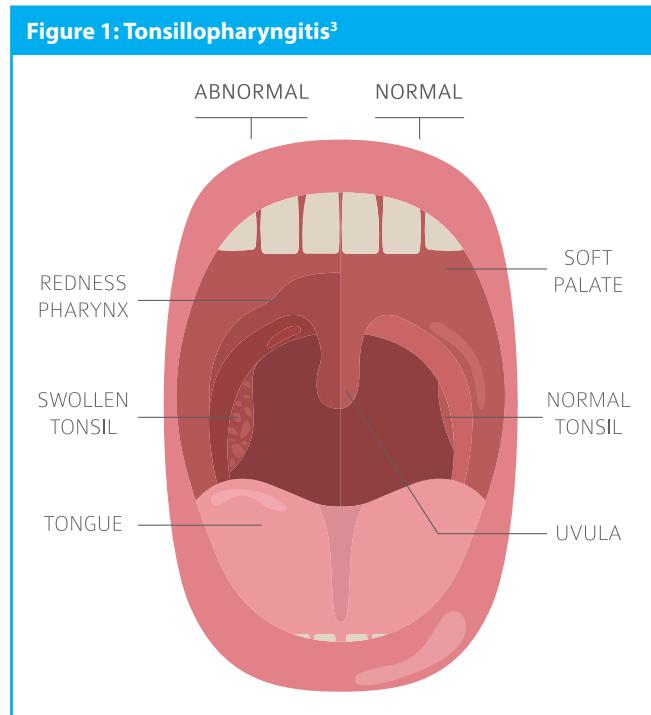
Tonsillopharyngitis, one of the common reasons for primary care visit has been accounted as common acute infection seen in adults and children.<sup>1,2</sup> It involves the mucous membranes and lymphatic tissues of the throat, usually the posterior pharynx, the tonsils and the soft palate (Figure 1).<sup>3</sup>

According to data available, it accounts for 6% of visits by children to family physicians and pediatricians, creating a burden such that children miss their school on an average of 4.5 days and parents miss 1.8 days of work in order to care for them.<sup>1</sup> Classified as infectious

**Table 1: Infectious and inflammatory tonsillopharyngitis<sup>1</sup>**

<b>Infectious tonsillopharyngitis</b>	<b>Caused by either viral or bacterial infection</b> <ul style="list-style-type: none"> <li><b>Viral causes:</b> Rhinovirus, coronavirus, adenovirus, parainfluenza, influenza, echovirus, reovirus, respiratory syncytial virus, herpes simplex virus, coxsackievirus, and Epstein-Barr virus</li> <li><b>Bacterial causes:</b> Streptococci, <i>Corynebacterium diphtheriae</i>, <i>Neisseria gonorrhoeae</i>, <i>Chlamydia pneumoniae</i>, and <i>Mycoplasma pneumoniae</i></li> </ul>
<b>Inflammatory tonsillopharyngitis</b>	Caused by laryngopharyngeal reflux, allergic rhinitis with postnasal drip, foreign body, chronic mouth breathing, mucositis, muscle tension dysphonia, vocal cord granuloma, rheumatoid arthritis, gout, pemphigus, and Kawasaki's disease

**Figure 1: Tonsillopharyngitis<sup>3</sup>**



and inflammatory tonsillopharyngitis based on the etiological factor involved, the most common cause of tonsillopharyngitis is viral infection. Table 1 describes them in detail.<sup>1</sup>

## GROUP A STREPTOCOCCAL PHARYNGITIS

*Streptococcus pyogenes*, also known as Group A Streptococcus (GAS), is the most common bacterial etiology for acute pharyngitis. According to data available, it accounts for 5 to 15% of all adult cases and 20 to 30% of all pediatric cases, with a peak incidence in winter and early spring.<sup>4</sup> The economic burden associated with GAS

**Table 2: Differentiating features between bacterial and viral pharyngitis<sup>7,8</sup>**

	<b>Bacterial pharyngitis</b>	<b>Viral pharyngitis</b>
<b>Symptoms</b>	<ul style="list-style-type: none"> <li>Sudden onset of severe sore throat</li> <li>Pain on swallowing</li> <li>Fever without cough or rhinorrhea</li> </ul>	<ul style="list-style-type: none"> <li>Sore throat</li> <li>Nasal congestion</li> <li>Coryza</li> <li>Hoarseness</li> <li>Sinus discomfort</li> <li>Ear pain</li> <li>Cough</li> </ul>
<b>Clinical signs</b>	<ul style="list-style-type: none"> <li>Tonsillar erythema with or without exudates</li> <li>Anterior cervical adenitis</li> <li>Soft palate petechiae</li> <li>Red swollen uvula</li> <li>Scarlatiniform rash</li> </ul>	<ul style="list-style-type: none"> <li>Discrete ulcerative stomatitis</li> <li>Tonsillar hypertrophy</li> <li>Oropharyngeal erythema or edema</li> <li>Pharyngeal "cobblestoning"</li> </ul>

is substantial. It is associated with 0.1 million disability-adjusted life-years (DALYs) among children each year across the globe; with rheumatic heart disease (RHD), one of the significant clinical endpoints of GAS infection, being responsible for 0.5 million DALYs among 5–14 year-old children and 10.7 million DALYs among all age groups as per the data derived in 2019.<sup>5,6</sup>

Symptoms of GAS overlap with viral etiologies, complicating the problem of diagnosis. Table 2 describes the key differentiating factors between viral and bacterial pharyngitis.<sup>7,8</sup>

## SUPPURATIVE AND NON-SUPPURATIVE COMPLICATIONS

When left untreated or misdiagnosed, complications can be seen with GAS pharyngitis Box 1.<sup>1,4</sup> Retropharyngeal abscesses, affecting younger children aged between 1 and 5 years is characterized by presence of neck stiffness, dysphagia, odynophagia, and high fever following an upper respiratory infection. Based on degree of obstruction in case of airway obstruction, it can be manifested as

**Box 1: Complications of GAS<sup>1,4</sup>**

### Suppurative complications

- Tonsillopharyngeal cellulitis or abscess
- Otitis media
- Sinusitis
- Necrotizing fasciitis
- Bacteremia
- Meningitis
- Brain abscess
- Jugular vein septic thrombophlebitis

### Non-suppurative complications

- Acute rheumatic fever
- Post-streptococcal reactive arthritis
- Scarlet fever
- Streptococcal toxic shock syndrome
- Acute glomerulonephritis
- Pediatric autoimmune neuropsychiatric disorder associated with group A streptococci

muffled voice, drooling, trismus, stridor, tachypnea, or tripod positioning. Immediate consultation with an otolaryngologist and anesthesiologist is necessary given the potential for life-threatening airway compromise. CT of the neck with contrast is the modality of choice once the patient is stable. Emphasis should be laid on immediate intravenous antibiotic therapy when treating retropharyngeal abscess. Retropharyngeal abscesses <2 cm can be treated with antibiotics alone, however, if a patient fails to improve after 48 hours of therapy, incision and drainage is indicated.<sup>1</sup>

## DIAGNOSTIC CRITERIA

According to Infectious Disease Society of America (IDSA) guidelines, rapid antigen detection test (RADT) and/or bacterial culture of a throat swab has been recommended for GAS tonsillopharyngitis to distinguish GAS from viral tonsillopharyngitis.<sup>1</sup>

RADT assays are associated with certain advantages with respect to ease of use, rapid turnaround time (< 10 min), and high specificity, (95%) but have relatively low sensitivity (70–90%). Therefore, in pediatric patients, those at high risk of complications due to GAS pharyngitis, negative RADT is followed by confirmatory bacterial culture; latter being both highly sensitive and specific (90–95%) when performed correctly (Figure 1).<sup>1,9</sup>

## MANAGEMENT: ROLE OF EARLY INITIATION OF ANTIBIOTICS IN GAS PHARYNGITIS

Treatment for GAS is focused on achieving symptom relief, shortening the duration of illness, preventing non-suppurative and suppurative complications, reducing the risk of infection spread and reducing the unnecessary use of antibiotics, so as to slow the development of antibiotic resistance.<sup>1,4,5</sup>

Antibiotics have been used widely in individual with GAS pharyngitis. Their use is associated with reduced duration of illness by approximately one day, with the significant reduction in symptoms seen on the third day of treatment. It has been shown that antibiotics when given within 48 hour of the onset of symptoms are associated with improvement in symptoms and faster onset of relief. Furthermore, in individuals with GAS pharyngitis, rate of transmission is approximately 35%. Antibiotics reduce the communicability of GAS to 24 h, limiting the spread of GAS for high-risk patients.<sup>5</sup>

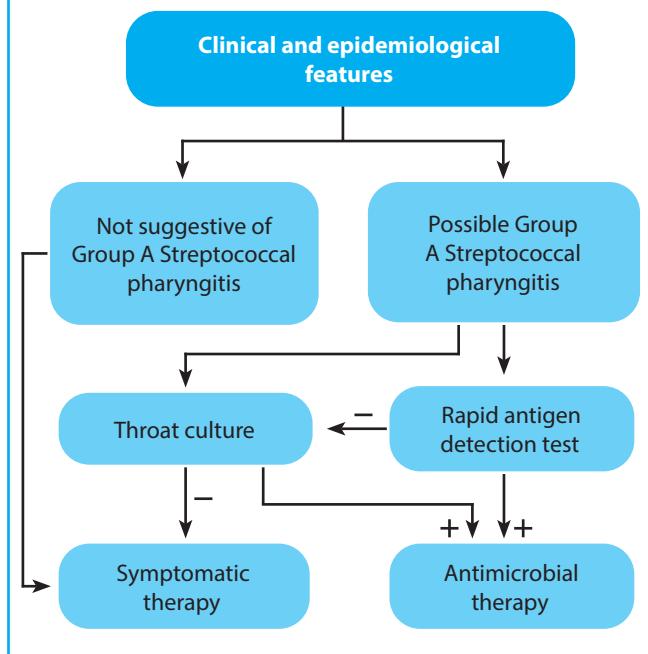
## CLARITHROMYCIN IN TONSILLOPHARYNGITIS/ GROUP A PHARYNGITIS

Clarithromycin, a second generation macrolide has been considered as a potential treatment option for patients with acute bacterial pharyngitis as it is associated with significant superior improvements over its predecessor, erythromycin, with an expanded spectrum of activity and enhanced tolerability. Furthermore, bacteriological superiority of clarithromycin over erythromycin could be accounted to be due to clarithromycin's tissue penetration ability and formation of a bacteriologically relevant 14-hydroxy metabolite. Moreover, it has lower potential for promoting the emergence of unrecognized resistant strains within an overall susceptible isolate.<sup>10</sup>

In addition to above, clarithromycin exerts anti-inflammatory and immunomodulatory effects. This could be due to the fact that it inhibits the production of microbial toxins and other virulence factors, thus weakening the pro-inflammatory host response. Moreover, it inhibits immune cell activity and regulates cytokine profile toward a less pro-inflammatory/more anti-inflammatory balance; signifying its potential use in patients with pharyngitis.<sup>10</sup>

A study<sup>11</sup> was done in individuals aged ≥12 years with symptomatic pharyngitis and a positive throat culture. It was shown that clarithromycin was effective than azithromycin with respect to eradication of streptococcal A from the pharynx (91% vs. 82%).

**Figure 2: Diagnosis of group A streptococcal pharyngitis<sup>1,9</sup>**



Therefore, 10 day course of clarithromycin is superior to 5 day course of azithromycin for eradication of group A streptococci from the pharynx of patients with acute pharyngitis.

## REFERENCES

- Hart KM. Rhinosinusitis and Tonsillopharyngitis. *Family Medicine*. 2016;519-26.
- Tewfik TL, Al Garni M. Tonsillopharyngitis: Clinical highlights. *J Otolaryngol*. 2005;34 Suppl 1:S45-9.
- Jolly DT. Acute Tonsillopharyngitis In Native And White Families. *Can Fam Physician*. 1980;26:59-66.
- Ashurst JV, Edgerley-Gibb L. Streptococcal Pharyngitis. [Updated 2022 May 8]. In: StatPearls [Internet]. Treasure Island (FL); StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK525997/>. Accessed on: 29-05-2023.
- Mustafa Z, Ghaffari M. Diagnostic Methods, Clinical Guidelines, and Antibiotic Treatment for Group A Streptococcal Pharyngitis: A Narrative Review. *Front Cell Infect Microbiol*. 2020;10:563627.
- Miller KM, Carapetis JR, Van Beneden CA, Cadarette D, Daw JN, Moore HC, Bloom DE, Cannon JW. The global burden of sore throat and group A Streptococcus pharyngitis: A systematic review and meta-analysis. *EClinicalMedicine*. 2022;48:101458.
- Sykes EA, Wu V, Beyea MM, Simpson MTW, Beyea JA. Pharyngitis: Approach to diagnosis and treatment. *Can Fam Physician*. 2020;66(4):251-257.
- Weber R. Pharyngitis. *Prim Care*. 2014;41(1):91-8.
- Luo R, Sickler J, Vahidnia F, Lee YC, Frogner B, Thompson M. Diagnosis and Management of Group A Streptococcal Pharyngitis in the United States, 2011-2015. *BMC Infect Dis*. 2019;19(1):193.
- Hoban DJ, Nauta J. Clinical And Bacteriological Impact Of Clarithromycin In Streptococcal Pharyngitis: Findings From A Meta-Analysis Of Clinical Trials. *Drug Des Devel Ther*. 2019;13:3551-3558.
- Kaplan EL, Gooch III WM, Notario GF, Craft JC. Macrolide therapy of group A streptococcal pharyngitis: 10 days of macrolide therapy (clarithromycin) is more effective in streptococcal eradication than 5 days (azithromycin). *Clin Infect Dis*. 2001;32(12):1798-802.

# SECTION 3

## MEDICAL QUIZ



**Q1.** Dysfunction of one of the following lobes of the brain is most likely responsible for the seizure, which causes tingling and numbness in the left leg?

- A. Frontal
- B. Temporal
- C. Parietal
- D. Occipital

**Q2.** Anticonvulsant therapy is most likely required for patients with which of the following types of seizure?

- A. Febrile seizure
- B. Initial seizure
- C. Recurrent seizure
- D. Seizure due to alcohol withdrawal

**QQ3.** People who excrete too much calcium in their urine (hypercalciuria) should follow which of these dietary measures?

- A. Try to eliminate calcium in the diet.
- B. Consume a low-sodium, high-potassium diet.
- C. Consume a low-calcium, high-sodium diet.
- D. Decrease water consumption to conserve calcium.

**Q4.** A 75-year-old woman being investigated for recurrent urinary tract infections (*Proteus* on culture) has a staghorn calculus on CT. What is the most likely stone composition?

- A. Cysteine
- B. Uric acid
- C. Struvite
- D. Calcium oxalate

# SECTION 4

## EVENTS UPDATE

### MAYO CLINIC PEDIATRIC DAYS 2024

January 14 - 18, 2024  
Koloa, United States

### 2024 PERINATAL MEDICINE CONFERENCE

January 29 - February 1, 2024  
Lahaina, United States

### 24<sup>th</sup> ANNUAL WINTER CONFERENCE ON PEDIATRICS

February 20 - 24, 2024  
Big Sky, MT, United States

### 15<sup>th</sup> INTERNATIONAL NEWBORN BRAIN CONFERENCE (INBBC 2024)

February 28 - March 2, 2024  
Cork, Ireland

# SECTION 5

## TECH UPDATE

### LOW-COST SMARTPHONE-BASED HEARING SCREENING FOR NEWBORNS AND CHILDREN

Hearing tests for newborns are crucial to ensure early detection of hearing impairments, enabling timely intervention. However, in many parts of the world, this essential assessment remains inaccessible due to the prohibitive cost of screening devices. Recently, a team of researchers at the University of Washington has developed an innovative, cost-effective alternative using smartphones and inexpensive earbuds. This innovative hearing screening system replaces costly specialized equipment with a smartphone and affordable earbuds. The research team, led by experts from the University of Washington, successfully tested this device on 114 patients, including 52 infants up to 6 months old and pediatric patients with confirmed hearing loss. The results of their study, published in the journal *Nature Biomedical Engineering*, demonstrate the efficacy and accuracy of their novel approach. The technology relies on the mechanics of the ear because newborns cannot communicate whether they can hear specific sounds. When external sounds are played, hair cells within the inner ear vibrate, generating a nearly inaudible sound detectable by instruments. This sensitive screening process helps identify potential hearing issues, leading to referrals for more in-depth assessments with specialists.



Traditionally, expensive screening devices use specialized speakers to emit two different tones without interference. The breakthrough in the University of Washington's solution lies in using affordable earbuds, each emitting one of two different tones, attached to a microphone-equipped probe inserted into the ear. This microphone captures the ear's sounds and transmits them to a smartphone for processing. Importantly, the smartphone employs advanced algorithms to enhance signal detection, mitigating background noise and patient movement, ensuring accurate results.

This innovative system maintains the sensitivity required for hearing assessments, ensuring that individuals with potential hearing issues can be identified promptly and referred for specialist evaluation. The cost-effectiveness and accessibility of this approach make it a potential game-changer for regions lacking access to expensive hearing screening equipment.

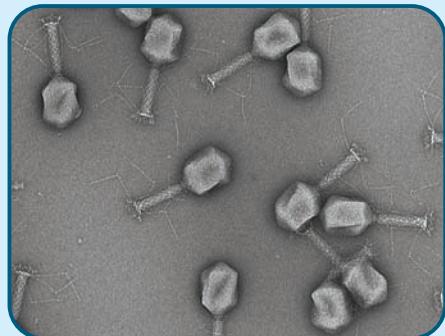
The researchers conducted tests at three hearing clinics in the Puget Sound area, ranging from young infants to 20-year-old participants, assessing various frequencies as standard for these screenings. With the potential to revolutionize global hearing screening, this smartphone-based solution offers a ray of hope for millions of children worldwide, ensuring that hearing issues can be identified and addressed early, promoting better outcomes for those affected by hearing loss.

**Source:** How low-cost earbuds can make newborn hearing screening accessible. Available at: <https://www.washington.edu/news/2022/10/31/low-cost-earbuds-can-make-newborn-hearing-screening-accessible/>. Accessed on 29-11-2023.

## BACTERIOPHAGES TO DIAGNOSE AND TREAT BLADDER INFECTIONS

With the increasing bacterial resistance, treatment of infections including that of bladder has become challenging. Bacteriophages are viruses that infect bacteria and represent a different way to treat infections, wherein these viruses have a high specific ability to target only one type of bacterium, unlike antibiotics which have a broader spectrum of activity. Researchers have developed a dual diagnostic/antibacterial bacteriophage system that can both diagnose and kill three of the most common bacterial species involved in bladder infections: Escherichia coli, Klebsiella, and Enterococci.

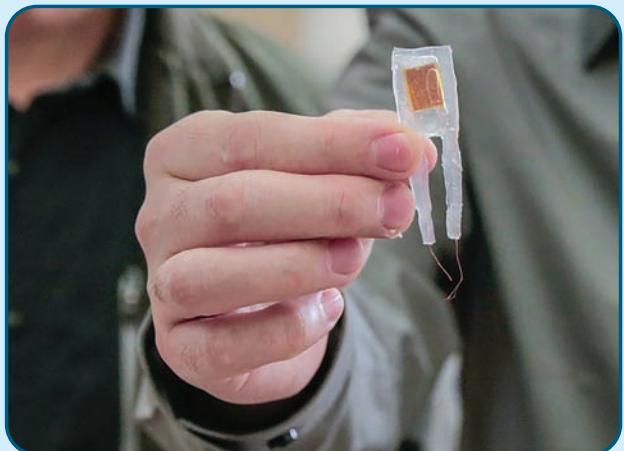
The bacteriophages have been turbo-charged by modifying them genetically so that they are more effective at killing bacteria, and also they will express a bioluminescent signal in the presence of their target bacteria. Several hours after being administered to patients with a suspected bladder infection, the researchers can collect a urine sample and then analyze it for the bioluminescent signal that the phages have been engineered to express when they encounter their target bacterial species. The phages have also been engineered to kill the bacteria more effectively, and will release antibacterial proteins that can kill other bacteria in the bladder that are not so easily targeted otherwise.



Source: Bacteriophages to Diagnose and Treat Bladder Infections. Available at <https://www.medgadget.com/2023/08/bacteriophages-to-diagnose-and-treat-bladder-infections.html>. Accessed on: 29.11.2023.

## AN IMPLANT DEVICE TO COMBAT OBESITY

Obesity has become a global epidemic and millions of clinicians are in search of a strategy to combat this problem. The same quest has resulted in development of a probable, technological, drug-free solution to the issue of obesity by researchers at University of Wisconsin-Madison. They have developed a tiny battery-free implant, about one centimetre across, which functions by stimulation of vagus nerve, and in turn the brain. The implant is attached to the stomach, which it can sense moving, that is, the peristalsis that occurs when food enters from esophagus into the stomach. Since these implants have built-in tiny nanogenerators, the device produces its own power from being shaken by the peristaltic movements of the stomach. Upon detecting peristalsis, it electrically stimulates the vagus nerve and does it for a longer duration than the stomach would naturally do. This gives brain the impression that more food is entering the gastrointestinal tract than the actual quantity, thus satisfying the hunger with “virtual” food. In trials on experimental models, the implant resulted in about 40% weight loss in comparison to controls. In addition, the surgical procedure is simpler compared to procedures like gastric bypass. It is expected that these trials might progress to provide an efficient non-pharmacological treatment option for weight loss.



Source: Weight Loss Implant Simulates Food Inside Stomach. Available at: <https://www.medgadget.com/2018/12/weight-loss-implant-simulates-food-inside-stomach.html> Accessed on: 29.11.2023.

# SECTION 6

## LEGAL UPDATE

### The medico-legal aspects of anesthesia

#### OVERVIEW

Anesthesiology is a high-risk speciality; however, the public at large is not aware of the risks involved in it. Arguably, anesthesiology is the most litigation-prone subject amongst all disciplines of medicine. Moreover, since the present system of anesthesia practice in India does not offer much scope for interaction between the patient and the anesthesiologist, there is hardly any understanding between them. Consequently, in case of any adverse event, the patient/relatives react in a hostile manner towards the anesthesiologist.<sup>1-3</sup>

#### TYPES OF CASES

An anesthesiologist can be summoned to court either in a criminal or a civil case. A criminal case happens only when the offense is of a serious nature, and the idea of judicial proceeding is punishment for the lapse on the anesthesiologist's part. In a civil case the aggrieved party per se approaches the court to seek compensation for the harm caused by the action of the anesthesiologist.<sup>2</sup>

#### LEGAL PROCEEDING OF PROBLEMS

In medical practice, the bulk of serious legal problems fall within the sort of negligence.<sup>4</sup>

#### Principle related to medical negligence

Negligence is an act of commission (should not do) or an act of omission (must do), which a responsible professional with average skill, knowledge and expertise would not do (Table 1).<sup>1</sup>

#### Elements of negligence

To be successful in a suit for medical negligence, the patient (plaintiff) must prove four things:<sup>2,4</sup>

- Duty: That the anesthesiologist owed a duty of care
- Breach of Duty: That the anesthesiologist failed to fulfil his/her duty
- Damages: That actual damage resulted due to the acts of the anesthesiologist
- Causation: That a reasonably close causal relationship exists between the anesthesiologist's acts and the resultant injury.

**Table 1: Principle related to medical negligence<sup>1</sup>**

Principles related to act of commission	Principles related to act of omission
<ul style="list-style-type: none"><li>• Requisite skill and knowledge</li><li>• Expert advice</li><li>• Undue risks</li><li>• Medication error</li><li>• Carelessness</li></ul>	<ul style="list-style-type: none"><li>• Care and precaution</li><li>• Responsibility of the staff</li><li>• Informed consent and record</li></ul>

## Burden of proof

The burden of proving negligence falls on the plaintiff - ordinarily the defendant does not have to prove that he acted with sufficient care and skill as it is for the plaintiff to prove that the defendant failed to comply with the accepted standard of duty of care. However, if the damage is quite obvious, such as pre-anaesthetic evaluation not performed, unexpected cardiac arrest occurring under anaesthesia, then term 'Res Ipsa Loquitur' - things speak for themselves is applied, and the burden of proof falls on the defendant. The standard of proof is based firmly on the balance of probabilities - a standard, it should be noted which is lower than that demanded in criminal trials.<sup>1,2,4</sup>

## What does not constitute negligence?

The basic principle that governs the medical negligence cases is the BOLAM'S RULE. According to it, 'If there are two treatment practices available, doctor may use any of them and if subsequently any complication occurs with that method, then doctor cannot be held responsible for not using the second method'. A breach of duty which does not result in a damage does not, however, constitute negligence.<sup>1,4</sup>

## Standard of care

The standard of care is judged by the standard of an ordinarily careful and competent practitioner of that class. The practitioner must bring to his task a reasonable degree of skill and knowledge and must exercise a reasonable degree of care. The anesthetist will be found to be negligent if he/she had failed to make a

proper preoperative assessment of the patient; failed to check equipment; failed to monitor the patient's blood pressure and/or heartbeat in the course of surgery; or if, an inevitable accident having occurred, the anesthetist fails to invoke adequate resuscitation measures.<sup>4</sup>

## Defences

The following defences may be pleaded by the anesthetist:<sup>1</sup>

- Deny the charges: If the anesthetist is confident of not doing anything wrong, supported by written documents
- Plead contributory negligence by the patient: If patient fails to follow doctor's advice
- Plead error of judgement in treatment
- Well-informed consent: Treatment was initiated after well-informed consent, explaining the side effects of the treatment
- Damage during life saving treatment: Rib fracture during cardiopulmonary resuscitation
- Beyond limitation period: There is a limitation period for filing cases; in adult patients it is 3 years and for children this may extend till they become major. Beyond this period, this defence could be pleaded.

## REFERENCES

1. Attri JP, Momin S, Kaur G, Sandhu KS, Bala N, Channa SS. Anaesthesia provider's perception of law: Focus on preventive measures. *Indian J Anaesth.* 2015;59(2):73-78. doi:10.4103/0019-5049.151342
2. Parakh SC. Legal Aspects of Anaesthesia Practice. *Indian Journal of Anaesthesia.* 2008; 52 (3):247-257
3. Ali MR, Rahman J, Khatun R, et al. Modern Anesthesia and Its Medico-Legal Aspects. *KYAMC Journal.* 2017;7(2):806-809.
4. Krishna SR. Medico-legal aspects of anaesthesia practice. *Med J Malaysia.* 1991;46(4):320-328.



## Trust-Meter of Grilinctus

# Grilinctus®

The Trusted Brand for more than 4 decades

The Companion in Cough Management

### Grilinctus®

(Dextromethorphan HBr 5 mg, GPM 2.5 mg,  
Guaiifenesin 50 mg and NH<sub>4</sub>Cl 60 mg / 5 ml)



### Grilinctus-BM®

(Terbutaline Sulphate 2.5 mg + Bromhexine Hydrochloride 8 mg / 5 ml)



### Grilinctus®-L

(Levocloperastine Fendisolate Eq. to Levocloperastine HCl 20 mg / 5 ml)



### Grilinctus®-LS®

(Levalbuterol Sulphate 1 mg + Ambroxol Hydrochloride 30 mg + Guaiifenesin 50 mg / 5 ml)





## CONTINUING • MEDICAL • EDUCATION

### LEADERS IN HEALTHCARE COMMUNICATIONS

CME Communications, the Continuing Medical Education arm of Passi HealthCom, which is a 28-years old organization with excellence in Healthcare Communications, now has a global presence and expertise in designing different engagement strategies to promote healthcare education.

The focus of CME Communications is to train clinical professionals to fill gaps in the areas of healthcare for best deliverance to patients.

#### • OUR ACTIVITIES

- Medical Conferences
- Accredited Live CMEs
- Seminars & Workshops
- Advisory Board Meetings
- Observerships
- Webinars
- Diploma/MSc Programs

#### • AREAS WE CATER

- CME Communications is proud to cater almost all disciplines of medicine, targeting a broad range of healthcare professionals in each specialty, ranging from General Physicians to Specialists and Super-specialist.
  - Cardiology
  - Dermatology and Cosmetology
  - Endocrinology & Diabetes
  - Gastroenterology
  - Medical Oncology
  - Nephrology
  - Neurology
  - Orthopedics
  - Pediatrics
  - Psychiatry
  - Reproductive Medicine
  - Urology

### OUR ACADEMIC PARTNERS

#### • USA

- » Cleveland Clinic
- » Mayo Clinic
- » Boston University School of Medicine (BUSM)

#### • UK

- » Royal College of Physicians (RCP)
- » University of South Wales, Cardiff
- » University of Exeter

#### • Netherlands

- » International Federation of Diabetes and Cardiometabolic Disorders (IFDCD)

### Asia & Middle East Offices

#### Delhi:

318, Virat Bhawan, Commercial Complex,  
Dr Mukherjee Nagar, Delhi - 110009  
📞 91-11-47029273, 45706616  
✉️ info@cme.com.in [www.cme.com.in](http://cme.com.in)  
CIN : 74899DL1993PTC056229

#### Mumbai:

Unity, D-2/5, Khira Nagar,  
S.V. Road, Santacruz (W),  
Mumbai - 400054  
🌐 passi.org  
📞 91-22-26613074, 26615445  
📠 91-22-26615445

#### Dubai:

P.O.Box No. 49245, Dubai, U.A.E.  
📞 +971 506558239  
📠 +971 43349807