

# MEDICINE UPDATE

 Passi HealthCom



Focus on  
low back  
**PAIN**

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# EDITORIAL

## Janus kinase inhibitors in rheumatoid arthritis management: Focus on Tofacitinib

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**R**heumatoid arthritis (RA) is a chronic, debilitating autoimmune disease localized mainly to the joints, and characterized by inflammation of the articular synovium, joint damage, deformity, and progressive disability. The disease has no cure and is progressive in nature; and when untreated, individuals experiencing multiple exacerbations tend to have poor outcomes with increased disability and mortality.

Treatment of patients with rheumatoid arthritis lays focus on early diagnosis and early initiation of treatment to prevent irreversible damage to the joints. Though various treatment modalities are available, and treat to target approach has been recommended, many patients do not achieve therapeutic targets either because of adverse reactions, or because of laboratory abnormalities, indicating an unmet need of additional therapies. In such patients with an inadequate response to initial conventional synthetic DMARDs in presence of poor prognostic factors, Janus kinase (JAK) inhibitor could be considered for treatment of rheumatoid arthritis.

Janus kinase family of tyrosine kinases play a vital role in regulating intracellular signal transduction of cytokines responsible for driving inflammatory processes that are associated with the pathogenesis of rheumatoid arthritis; signifying an important role of



JAK inhibitors in inflammatory diseases management. Tofacitinib, an oral JAK inhibitor, has been approved for treatment of rheumatoid arthritis that inhibits the process of intracellular signalling from the receptor to the cellular nucleus via JAK 3 and JAK 1 with a functional selectivity over JAK2. Tofacitinib is a promising therapeutic modality for rheumatoid arthritis as it suppresses cytokine/chemokine expression and the immune activation through the JAK/STAT interferon-dependent signaling pathway.

# SECTION 1

## GLOBAL UPDATE

### NEW COMPOUND SHOWS PROMISE IN TARGETING BITTER TASTE RECEPTORS FOR ASTHMA AND COPD TREATMENT

Bitter taste receptors, commonly associated with our taste buds, have been discovered in unexpected places, including the airways. These receptors offer a potential avenue for treating respiratory conditions such as asthma and COPD. In a recent development, scientists have designed a potent and selective compound that holds promise for advancing therapies targeting these receptors, according to a study published in ACS' *Journal of Medicinal Chemistry*.

Among the various types of bitter taste receptors, the TAS2R14 subtype is notably present in tissues beyond the mouth. While the specific structure of the receptor and its activating compound, or "ligand," remain uncertain, certain synthetic compounds, like the nonsteroidal anti-inflammatory drug (NSAID) flufenamic acid, have been identified as activators of TAS2R14s. However, existing compounds lack potency and structural similarity, presenting a challenge for developing improved ligands.

Building upon this foundation, a team of researchers designed and synthesized analogs based on flufenamic acid. These compounds were tested using a cell-based assay to measure receptor activation, revealing promising results. Replacing a phenyl ring with a 2-aminopyrimidine and substituting a tetrazole for a carboxylic acid group increased potency and selectivity for TAS2R14 receptors, making a new ligand six times more potent than flufenamic acid.

This heightened potency means lower quantities of the compound could achieve similar effects as the NSAID, potentially minimizing side effects.

The study's findings hold significant potential for understanding the role of bitter taste receptors in respiratory health and guiding the development of targeted therapies.

**Source:** Triggering bitter taste receptors could someday treat asthma, COPD. Available at: <https://www.sciencedaily.com/releases/2023/03/23031310119.htm>. Accessed on 09/08/2023

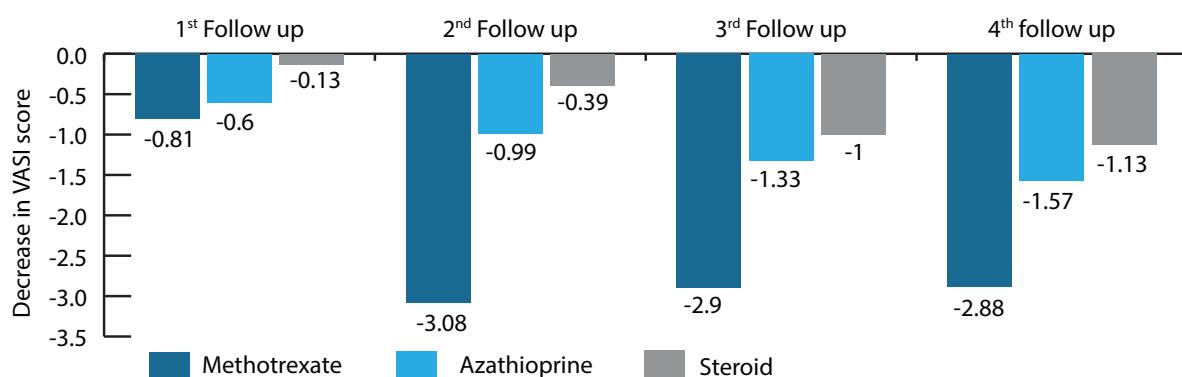


## COMPARATIVE EFFICACY ORAL CORTICOSTEROIDS, METHOTREXATE, AND AZATHIOPRINE IN PATIENTS WITH UNSTABLE VITILIGO

Vitiligo is a benign disease characterized by milkywhite well-defined macules and patches due to progressive loss of melanocytes. Therefore, the primary goal of treatment is to stabilize the disease progression and subsequent repigmentation. A study was performed to compare efficacy of oral corticosteroids, methotrexate, and azathioprine in patients with unstable vitiligo. In this retrospective analysis, a total of 319 patients with unstable vitiligo treated with 0.5 mg/kg oral corticosteroids, 0.3 mg/kg methotrexate and 1 to 1.5 mg/kg azathioprine were evaluated. Findings of the analysis were as follows:

- The most commonly observed type of vitiligo was non-segmental vitiligo (78.85%), followed by vitiligo vulgaris (7.69%).
- At the end of the study, patients in all three groups showed reduction in disease activity
- Methotrexate has an early effect, while both steroids and azathioprine have a gradual and sustained effect, as shown in figure 1.

**Figure 1: Reduction in Vitiligo Area Scoring Index (VASI) score at 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> follow up after treatment with oral corticosteroids, methotrexate and azathioprine in patients with unstable vitiligo**



Although all three drugs are equally effective in controlling disease activity, the onset of methotrexate's action is early. Therefore, methotrexate can be used to stop disease activity in rapidly spreading vitiligo.

**Source:** Mittal N, Kaur T. Role of oral corticosteroids, methotrexate, and azathioprine in patients with unstable vitiligo: A comparative study. *Pigment International* 2022;9(1):33-38.

## DECODING UNEXPLAINED CHRONIC COUGH: A COMPARATIVE ANALYSIS WITH ASTHMA AND COPD

Chronic cough, a prevalent condition affecting up to 20% of the adult population, frequently persists despite medical interventions. However, diagnosing unexplained chronic cough (UCC) demands careful consideration, as numerous clinical conditions such as asthma and COPD must be excluded before arriving at a conclusion.

This study aimed to compare clinical features of patients with a primary diagnosis of UCC with those with asthma or COPD without a primary diagnosis of UCC, thus facilitating easier clinical differentiation.

The study encompassed a period spanning for >5 years, capturing an array of crucial patient information, including demographics, hospitalization and outpatient medical encounters, prescribed medications for chronic cough, lung

function tests, and hematologic parameters. Asthma and COPD were grouped together to eliminate overlap with UCC.

## Results

- Patients with UCC used more cough medications and with higher frequency than those with asthma/COPD ( $p < 0.0001$ )
- Over a period of five years, patients with UCC exhibited significantly more cough-related encounters compared to their counterparts with asthma/COPD (8 versus 3, respectively;  $p < 0.0001$ )
- Moreover, the intervals between successive encounters for UCC were notably shorter versus the asthma/COPD group (144 versus 288 days, respectively)
- FEV1/FVC ratios, residual volume%, and DLCO% were markedly higher in the UCC group versus the asthma/COPD group; whereas, bronchodilator responses favored asthma/COPD.



By elucidating the distinct clinical features that set UCC apart from asthma and COPD, the research can potentially expedite accurate diagnoses, particularly within specialized medical settings where patients with these conditions are frequently referred for evaluation and treatment.

**Source:** Singh U, Bernstein JA. Can clinical characteristics differentiate patients with unexplained chronic cough from patients with asthma and COPD? *Allergy Asthma Proc.* 2023;44(2):90-99.

## COMPARISON OF EFFECTIVENESS OF AZITHROMYCIN VERSUS CLARITHROMYCIN IN COMBINATION WITH BETA-LACTAMS FOR TREATMENT OF COMMUNITY-ACQUIRED PNEUMONIA

A study was conducted with the aim to differentiate the efficacy of azithromycin versus clarithromycin in combination with beta-lactams in treatment of community-acquired pneumonia. In this systematic review, databases such as PubMed, Google Scholar, Trip, Medline, and Clinical Key were searched to identify randomized clinical trials with patients who received azithromycin or clarithromycin in combination with a beta-lactam.

## Results

Treatment parameter	Azithromycin–beta-lactam group	Clarithromycin–beta-lactam group
Treatment success rate	87.55% (10-14 days of treatment)	75.42% (5-7 days of treatment)
Length of hospital stay (days)	8.45	7.25

Azithromycin-based combinations showed higher treatment success rate. However, clarithromycin–beta-lactam regimen achieved a shorter length of hospital stay among patients with community-acquired pneumonia.

**Source:** Al-Salloum J, Gillani SW, Mahmood RK, Gulam SM. Comparative efficacy of azithromycin versus clarithromycin in combination with beta-lactams to treat community-acquired pneumonia in hospitalized patients: a systematic review. *J Int Med Res.* 2021 Oct;49(10):3000605211049943.

## RITUXIMAB ADMINISTRATION IN PATIENTS WITH PEMPHIGUS: FOCUS ON HEALTH RELATED QUALITY-OF-LIFE

Pemphigus is a group of autoimmune disease which is clinically described by the development of painful and flaccid blisters on the skin and/or mucous membranes. The individuals affected by pemphigus exhibit remarkably compromised health-related quality of life (HRQOL). There are two major subtypes of pemphigus based on location of blister formation or the specificity of autoantibodies directed against different desmogleins. The two subtypes are pemphigus vulgaris (PV) and pemphigus foliaceus(PF). In line with this, a study was conducted to compare clinical outcomes and HRQOL through the use of disease-specific measures as well as comprehensive generic health status measures among patients with PV and PF who received Rituximab (RTX) treatment 3 months earlier (3M group)and those who received RTX in the last 2 weeks (R group).



The results revealed that there was improvement in SF-36 scores with RTX treatment in all dimensions except for mental health. There was greatest mean improvement in the role physical index (75.45 in the 3M group vs 53.04 in the R group( $P=.009$ ). There was clinically significant improvement of QOL in patients receiving RTX 3 months earlier ( $P=.005$ ). In addition to this, the PGA scores indicated that patients in the 3M group were significantly more likely to report less severe disease vs the R group ( $P=.008$ ). Conclusively, rituximab administration in patients with pemphigus can lead to rapid and significant improvement in HRQOL as well as patient- and physician-assessed measures. It has favorable safety profile along with its impact on patients' daily lives and mental health makes RTX a suitable treatment option for patients with pemphigus.

**Source:** Aryanian Z, Balighi K, Nassimi M, Hatami P, Shahandashti MI, Goodarzi A, Etesami I. Rituximab Treatment and Improvement of Health-Related Quality of Life in Patients With Pemphigus. *Cutis*. 2023 Jan;111(1):53-56.

## SECTION 2

### CLINICAL UPDATE

# Focus on low back pain

#### OVERVIEW

Low back pain cannot be termed as a disease itself, but rather a symptom with many causes. It is characterized as presence of pain near the midline in the lumbar or sacral region. It is also known as lumbar back pain, which is defined as pain in the back from the level of the lowest rib down to the gluteal fold, with or without radiation into the legs.

It is called acute in nature, if an episode of low back pain has arisen for the first time in a patient's life, or after a pain-free interval of at least six months, and lasts no longer than six weeks.<sup>1</sup>

#### ETIOPATHOGENESIS

It is not necessary that the cause of low back pain will lie in the spine only, it can also be due to abdominal or pelvic disease. Pathophysiologically oriented diagnostic categories for low back pain are often not reproducible, and they generally have no clear-cut implications for treatment. Therefore, in the German National Disease Management Guideline for Low Back Pain, low back pain is pragmatically classified as either nonspecific or specific.

If there is no clear causal relationship between the symptoms, physical findings, and radiographic findings, then back pain is called nonspecific. Physicians should accordingly exercise caution before ordering further diagnostic tests and treatments.



Whereas in specific low back pain, by definition, a patho-anatomical relationship can be demonstrated between the pain and one or more pathological processes, including compression of neural structures, joint inflammation, and/or instability of one or more spinal motion segments. Specific diagnostic investigations and cause-directed treatments should be initiated by physicians.<sup>1</sup>

Roughly 1–4% of patients with low back pain were found to have a vertebral body fracture on their primary investigation; 0.7% had a tumor (primary or metastatic), 0.2% had ankylosing spondylitis, and 0.01% had spondylodiscitis.

**Different types of specific low back pain<sup>1</sup>**

**4%**  
Disk herniation

**3%**  
Spinal stenosis

**2%**  
Spondylolisthesis

**Few non-specific causes of low back pain**

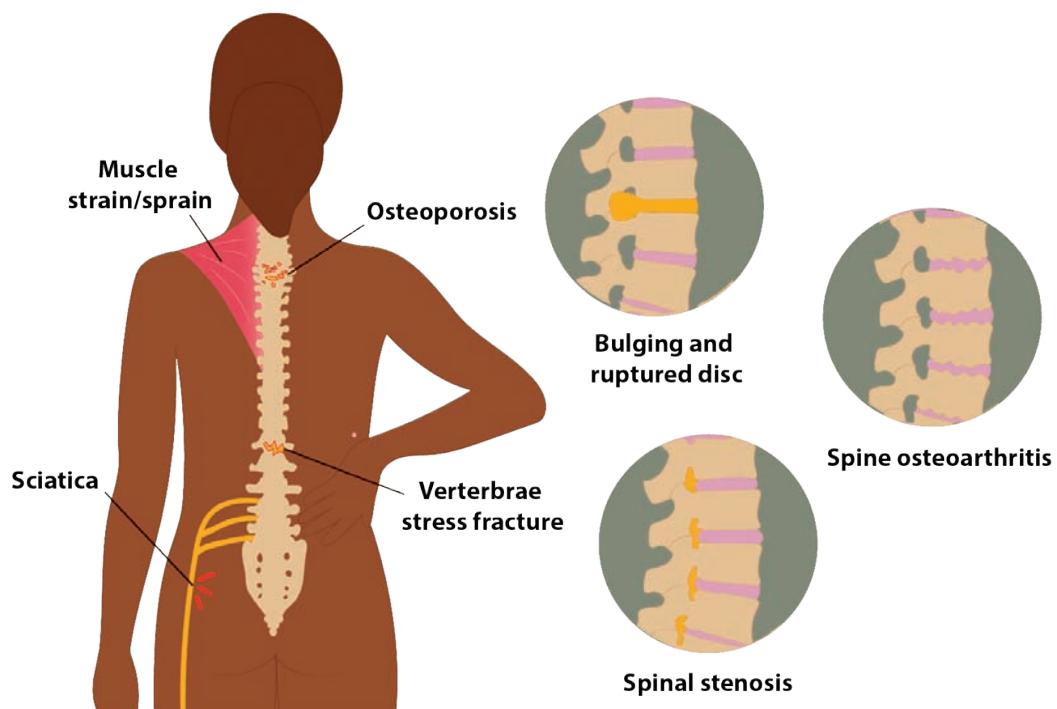
Low back pain is often caused by non-pathological functional disturbances that are best detected by physical examination and cannot be adequately demonstrated by imaging studies, especially the following<sup>1</sup>:

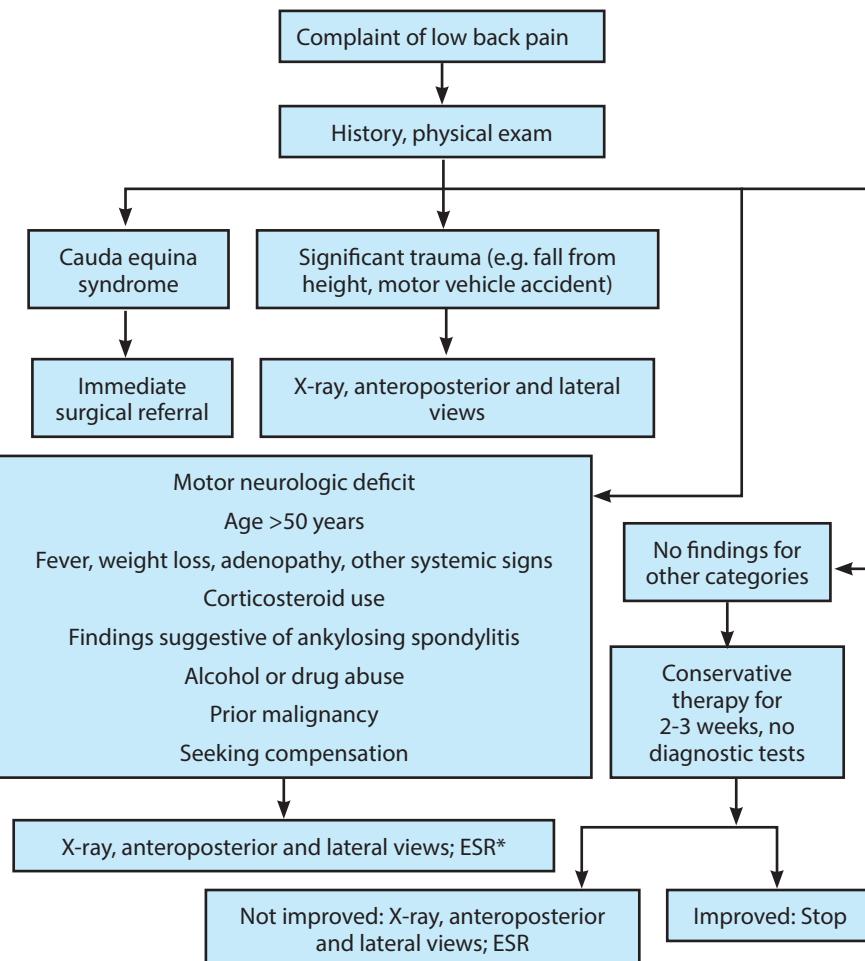
- Segmental dysfunction (e.g., “blockages”)
- Sacroiliac joint syndrome
- Altered spinal statics (e.g., straightening of the normal lumbar lordosis)

- Muscle dysfunction (e.g., shortened muscles, trigger points)
- Connective-tissue changes (e.g., swelling)
- Systemic conditions (e.g., incoordination, inadequate deep stabilization, or constant hypermobility).

**HOW TO DIAGNOSE LOW BACK PAIN?**

- Based on history, examination and palpation, low back pain can be determined to be skeletal in origin.<sup>2</sup>

**What causes back pain?**

**Figure 1: Diagnosis of low back pain<sup>2</sup>**

- Figure 1 shows the methods of diagnosis of low back pain:<sup>2</sup>

## DIFFERENTIAL DIAGNOSIS OF LOW BACK PAIN<sup>2</sup>

Let's discuss special aspects of few conditions that can cause low back pain

### LUMBAR DISC HERNIATION

- A herniated disc in the spine is a condition during which a nucleus pulposus is displaced from intervertebral space
- It is a common cause of back pain

- The patients who experience pain related to a herniated disc often remember an inciting event that led to the pain
- Pain due to herniated disc is burning or stinging, and may radiate into the lower extremity
- It has been noticed that the incidence of a herniated disc is about 5 to 20 cases per 1000 adults annually
- It is most commonly seen in people in their third to the fifth decade of life, with a male to female ratio of 2:1
- Patients frequently report increased pain when sitting, which is known to increase disc pressure by nearly 40%.<sup>3</sup>

Mechanical low back pain	Non-mechanical spine disease	Visceral disease
Lumber strain	Neoplasia	Pelvic organs
<b>Degenerative disease</b>	Multiple myeloma	Prostatitis
Discs (spondylosis)	Metastatic carcinoma	Endometriosis
Facet joints	Lymphoma and leukemia	Chronic pelvic inflammatory disease
Spondylolisthesis	Spinal cord tumors	
Herniated disc	Retroperitoneal tumors	<b>Renal disease</b>
Spinal stenosis		Nephrolithiasis
Osteoporosis	<b>Infection</b>	Pyelonephritis
Fractures	Osteomyelitis	Perinephric abscess
	Septic discitis	
<b>Congenital disease</b>	Paraspinous abscess	<b>Aortic aneurysm</b>
Severe kyphosis	Epidural abscess	
Severe scoliosis	Bacterial endocarditis	<b>Gastrointestinal disease</b>
Type II transitional vertebra		Pancreatitis
	<b>Inflammatory arthritis (often HLA-B27 associated)</b>	Cholecystitis
Spondylolysis	Ankylosing spondylitis	Penetrating ulcer
	Psoriatic spondylitis	
Facet joint asymmetry	Reiter's syndrome	Fat herniation of lumbar space
	Inflammatory bowel disease	
	Scheuermann's disease (osteochondrosis)	
	Paget's disease	

**Clinical presentation<sup>4</sup>****SPINAL FRACTURES**

- There can be an injury to spine in a traumatic event involving massive force, with resulting low back pain; however, spinal fractures often arise spontaneously or after relatively mild trauma, generally because of osteoporosis
- It has been observed that the incidence of radiologically detectable fractures in 55- to 79-year-

old women is 1% per year; in men in the same age group, it is 0.6% per year

- A woman over age 50 has more than 60% chance of sustaining an osteoporotic fracture
- Plain X-ray films are in use for diagnosis and follow-up observation. MRI is the method of choice for assessing the age of a fracture, which is an important consideration in the indications for treatment.<sup>1</sup>

**Clinical presentation<sup>5</sup>**

Patients with compression fractures will typically present with acute or chronic back pain

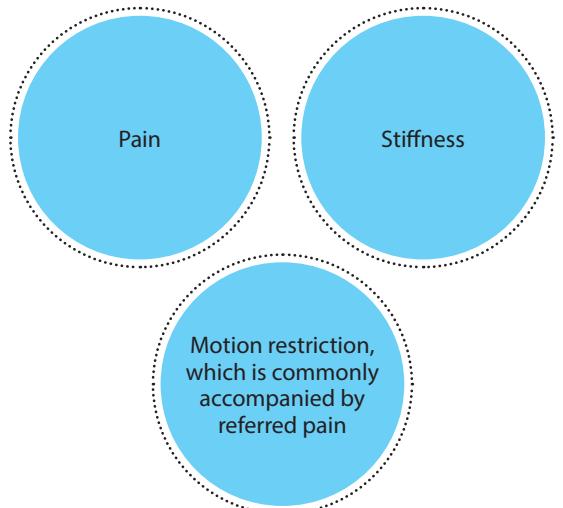
Symptoms include a sudden onset of pain that may be related to impact movements

Pain is focal at the level of disease

Pain can be increased during standing or walking or decreased while lying down

**SPINAL OSTEOARTHRITIS**

- Osteoarthritis involves articular surfaces, and can develop gradually over time into a debilitating condition, which causes pain and restriction of motion
- It has been estimated that 80% population of developed countries have an episode of low back pain during their lifetime
- In some parts of the western countries, low back pain is among the most common causes of healthcare visits.<sup>6</sup>

**Clinical presentation<sup>6</sup>**


Pain

Stiffness

Motion restriction,  
which is commonly  
accompanied by  
referred pain

Depending upon the location of pathology in spine, the distribution of a patient's pain differs

- The upper cervical complex produces pain in the occipital region and is often associated with headaches
- The lumbar spine provides pain located in the buttock and thigh region. Lumbar spine osteoarthritis can be associated with radicular pain above the knee
- Degenerative osteoarthritis causes localized and unilateral pain. This pain is reproducible upon palpation of the facet joint, relieved with flexion
- Pain from hyperextension and rotation from a standing position suggests facet joint arthropathy.<sup>6</sup>

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# A 33-year-old female with chronic endometritis treated with lactoferrin and lactobacillus

## CASE PRESENTATION

A 33-year-old lady presented to the gynecology outpatient department with complaints of altered menstrual cycles, vague pelvic discomfort on and off and increased vaginal discharge. There was no history of dysmenorrhoea or dyspareunia.

## PAST MEDICAL HISTORY

On eliciting further history; in the last 3 years she had experienced three early pregnancy losses. Following these, she had difficulty in conceiving and had undergone multiple unsuccessful procedures elsewhere. She has had several episodes of pelvic discomfort which had been treated symptomatically.

## EXAMINATION

- PR: 86/min
- Temperature: Normal
- BP: 126/76 right arm, sitting
- Patient not in acute discomfort
- Abdominal examination: No masses/no tenderness
- Pelvic examination: Minimal greyish, non-smelly vaginal discharge noted. Cervix was normal in appearance.
- Bimanual examination showed no masses or tenderness.

## INVESTIGATIONS

- Hb: 10.8 gms
- TLC and peripheral smear: Normal
- IL- $\beta$ : 16 pg/mL; IL-6: 10 pg/mL; TNF- $\alpha$ : 20 pg/mL

- Cervical swab: Negative
- Vaginal swab: Negative for trichomonas, clue cells, or monilia
- Pelvic ultrasound: In uterus - normal myometrium, endometrium-thin, loculated endometrial fluid, small amount of free fluid in the cul-de-sac, adnexa normal
- In view of the fluid, and history of recurrent pregnancy loss and subfertility, decision made to proceed with diagnostic hysteroscopy
- Hysteroscopy revealed increased vascularity, strawberry appearance, and micro polyps.

## DIAGNOSIS

The pathology was confirmed by histopathological examination which revealed the presence of plasma cells and ruled out tuberculosis. Hence, the pathology was chronic endometritis.

## TREATMENT AND FOLLOW-UP

- The patient had previous adverse events like subfertility which was secondary to the chronic infection. Therefore, she was treated with repeated courses of antibiotics such as doxycycline, ciprofloxacin, amoxicillin and clavulanic acid
- Prebiotic and probiotics combination needs to be given simultaneously in order to replace the abnormal microbiota with normal microbiota. A combination of lactoferrin 50 mg BD and lactobacillus was co-administered for a period of three months
- There was reduction in inflammatory biomarkers such as interleukin (IL- $\beta$ ) and tumor necrosis factor (TNF- $\alpha$ )

- The patient conceived spontaneously a few months later and continued to have an uneventful pregnancy and delivered a normal baby at term.

## DISCUSSION

Chronic endometritis (CE) is defined as a persistent, long term infection of the endometrium resulting primarily in a local inflammation. It is a low grade inflammation with no systemic inflammatory signs or symptoms such as fever, pelvic pain, significant discharge. This chronic infection can result in a range of reproductive disorders - from repeated implantation failures (RIF) to recurrent early pregnancy losses, preterm labour, preterm prelabour rupture of the membranes (PPROM) and chronic deciduitis.<sup>1-5</sup> The reported prevalence of CE ranges from 8% to 72% in women of reproductive age.<sup>2</sup> Several micro-organisms such as *E. coli*, *Streptococcus*, *Enterococcus*, *Staphylococcus*, *Mycoplasma* spp, *Urea plasma urealyticum*, *Gardnerella vaginalis*, *Proteus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Corynebacterium*, Yeasts (*Saccharomyces* and *candida*

*spp*), and *Mycobacterium tuberculosis* can be found in endometrium in patients of CE.<sup>1</sup>

Chronic endometritis is clinically asymptomatic. However, occasionally symptoms such as abnormal uterine bleeding, pelvic pain, dyspareunia, leucorrhoea, pelvic discomfort, spotting are reported along with complaints of hypomenorrhoea, secondary amenorrhoea and infertility.<sup>1,2</sup> Histopathologically, it is characterized by superficial endometrial edema, abnormal increase in stromal cell density, asynchronous maturation of stroma and endometrial invasion by epithelial plasma cells, elevated inflammatory cytokines, such as TNF- $\alpha$ , IL-1 and IL-6, in menstrual blood.<sup>1,6</sup> Inflammation associated with CE adversely affects pregnancy outcomes, causing miscarriage and preterm birth. Kimura et al. reported that the prevalence of CE in infertile women is 2.8–56.8%, 14–67.5% in women with RIF, and 9.3–67.6% in women with recurrent pregnancy loss.<sup>2</sup> The risk factors associated with occurrence of CE are previous history of prolonged menstrual bleeding episodes, an abortion history, and a history of fallopian tube obstruction.<sup>7</sup>

## Lactoferrin and Lactobacillus: Potent solution for chronic endometritis

### Salient features and properties of lactoferrin<sup>8-11</sup>

- Associated with anti-inflammatory effects as it acts by preventing the development of inflammation and subsequent tissue damage caused due to release of pro-inflammatory cytokines and reactive oxygen species
- Protective effect of lactoferrin → reduced production of some pro-inflammatory cytokines such as TNF- $\alpha$  or IL-1 $\beta$  and IL-6

### Salient features and properties of lactoferrin<sup>8-11</sup>

- A recent study also concluded that the expression of inflammatory cytokines in endometrial stromal cells are suppressed by bovine lactoferrin which embarks its administration for management of CE
- Exhibits antibacterial activity
- Defense mechanism against the invasion of intracellular bacteria such as enteroinvasive *E. coli*, *Staphylococcus aureus*, *Streptococcus* and many more
- Administration of lactoferrin also suppresses preterm birth and rarely leads to adverse effects
- Lactoferrin contributes to improvement in prognosis of preterm infants by promotion of intestinal flora maturation, downregulation of pro-inflammatory cytokines, regulation of host immune response, direct action on bacteria and inhibition of biofilm formation
- Prevention of genital tract infections and its consequences including endometritis
- Anti-inflammatory activity prevents fetus infections
- Prevention of miscarriage
- Probiotic action thereby protecting the lower genital tract and preventing the consequences of inflammation both during pregnancy and before pregnancy
- Aids fertility.

## CLINICAL UPDATE

### Salient features and properties of lactobacillus<sup>12</sup>

- Causes restoration of the normal vaginal flora and acidic pH
- Reduces chances of preterm delivery
- Shifts the anti-inflammatory state to a pro-inflammatory state in the third trimester, which is essential for labor.

### Lactoferrin and lactobacillus

As mentioned above, salient features and properties of lactoferrin and lactobacillus are suggestive of effective management of chronic endometritis.

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# Escitalopram: An effective treatment strategy for depression with comorbid diabetes

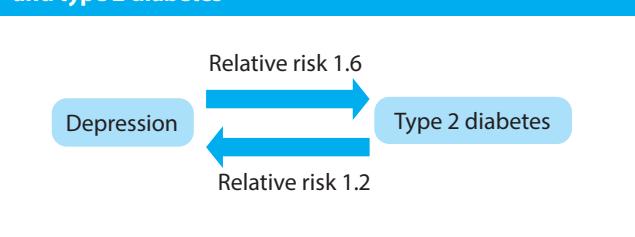
## COMORBID DEPRESSION AND DIABETES: A SHORT PREVIEW

Over the past decade, considerable interest has been generated on co-association of mental health disorders with chronic metabolic diseases, particularly due to their complex pathophysiological mechanisms and associated treatment challenges. Depression and type 2 diabetes are two frequently comorbid disorders with serious ramifications.<sup>1</sup> There is a considerable body of evidence to show that diabetes and depression share a bidirectional association, with diabetes increasing risk of depression, while pre-existing depression also increases risk of type 2 diabetes.

According to available data, the relative risk for developing type 2 diabetes in patients with depression is 1.6, while the relative risk for development of depression in type 2 diabetes has been noted to be about 1.2 (Figure 1).<sup>2</sup> Based on this data, depression appears to be a stronger risk factor for diabetes. Depression has a persistent and recurrent course in patients with diabetes.<sup>2</sup> Comorbid depression and diabetes appears to deteriorate patient outcomes.<sup>3</sup> Given the poor outcomes that are seen in patients with these co-existing disorders, the significance of early detection and optimal management of depression in patients with diabetes cannot be overemphasized. However, notwithstanding availability of a wide range of screening tools, detection rates of depression in patients with diabetes remains abysmally low.

Treating depression in diabetic patients is challenging. The co-morbidity needs to be managed with a combination of antidiabetic and antidepressant drugs; however cardiometabolic complications, weight gain and increase in appetite associated with the use of certain antidepressants – all factors that can potentially

**Figure 1: Bidirectional association between depression and type 2 diabetes<sup>2</sup>**



worsen glycemic control – calls for a careful selection of the antidepressant drug with good efficacy and a beneficial or at least neutral effect on the blood glucose profile.<sup>4</sup>

## IMPACT OF DEPRESSION IN DIABETES

Comorbidity of depression and diabetes appears to worsen outcomes of the affected patients. Depression predisposes to poor self-care, low adherence to lifestyle changes and anti-diabetic treatment.<sup>5</sup> These factors appear to increase risk of poor glycemic control, micro- and macrovascular complications, disability, and deaths in patients with depression and comorbid diabetes.<sup>2,3,5</sup> There is also some data to suggest that depression in patients with diabetes may affect cognition, although this has not been unequivocally proven.<sup>2</sup> Concomitant occurrence of the two disorders also has a negative effect on health-related quality of life (Table 1).<sup>6</sup>

## EFFECTIVELY MANAGING DEPRESSION IN DIABETES WITH ESCITALOPRAM

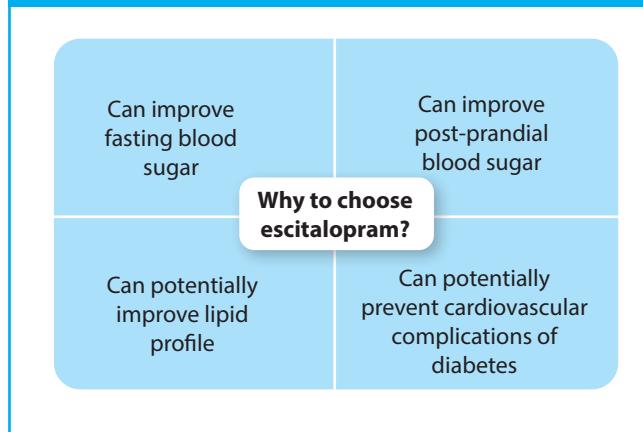
Despite being a commonly comorbid mental health disorder in patients with diabetes, effective management of depression remains suboptimal. The primary

<b>Table 1: Impact of comorbid depression with diabetes<sup>2,3,5,6</sup></b>
Poor self-care
Low adherence to lifestyle modifications and treatment
Poor health-related quality of life
Poor glycemic control
Increase in diabetic complications
Increase in disability
Increase in mortality

objective of antidepressant management in these patients is to effectively manage depressive symptoms while avoiding unwanted effect on glycemic control, reduction of diabetes-related complications and premature mortality.<sup>2,3</sup> Given the fact that many antidepressants possibly interfere with glucose metabolism, correct choice of antidepressant in these patients is crucial for patients' outcomes.<sup>4</sup> The selective serotonin reuptake inhibitors (SSRI) are among the front-line antidepressant therapy primarily owing to its superior tolerability compared to the tricyclic antidepressants (TCA). Their antidepressant effect is a result of selective inhibition of serotonin reuptake.<sup>7</sup>

Escitalopram is an effective SSRI antidepressant with proven efficacy in moderate to severe major depression. It is a proposed antidepressant for management of depression with comorbid diabetes, particularly owing to its potential beneficial effects on glucose and HbA1c levels.<sup>7</sup> In one study, when administered to patients with depression and co-occurring diabetes, escitalopram has shown the potential to lower fasting and post-lunch blood sugar in 47% of the patients which was deemed clinically and statistically significant.<sup>8</sup> These benefits of escitalopram were vindicated in another study which also evaluated this antidepressant in patients with diabetes with comorbid depression. Expectedly, escitalopram improved depression scores from 3 weeks onward underlining its antidepressant efficacy, but notably also reduced mean fasting plasma glucose at 6 weeks and post-prandial plasma glucose at 12 weeks, along with reduction in HbA1c at 12 weeks.<sup>9</sup> An additional benefit of using escitalopram as a favorable antidepressant in diabetic patients comes from report of its potential to possibly improve lipid derangements and prevent

**Figure 2: Potential favorable effects of antidepressant escitalopram in comorbid diabetes<sup>9,10</sup>**



associated cardiovascular complications of diabetes.<sup>10</sup> Given its undeniable antidepressant efficacy, along with meritorious effects on metabolic derangement and ability to possibly prevent cardiovascular complications, escitalopram should be strongly considered for the management of depression with comorbid diabetes (Figure 2).<sup>9,10</sup>

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# SECTION 3

## MEDICAL QUIZ



**Q1. Which of the following is not an idiopathic generalized epilepsy?**

- A. Juvenile absence epilepsy
- B. Epilepsy with seizures on awakening
- C. Childhood absence epilepsy
- D. Lennox-Gastaut syndrome

**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

**Q3. A patient came to the clinic with asthmatic attack, his body did not respond to the drugs and it is found that he had hypoxemia. What do we call this condition?**

- A. Chronic bronchitis
- B. Pneumonia
- C. Heart attack
- D. Status asthmaticus

**Q4. Which of the parameters is measured in spirometry?**

- A. Residual volume
- B. Total lung capacity
- C. Functional residual capacity
- D. Forced expiratory volume

# SECTION 4



## EVENTS UPDATE

### 109<sup>th</sup> SCIENTIFIC ASSEMBLY AND ANNUAL MEETING, OF THE RADILOGICAL SOCIETY OF NORTH AMERICA RSNA 2023

November 26-30, 2023  
Chicago, Illinois

### INTERNATIONAL STROKE CONFERENCE 2024

February 7-9, 2024  
Phoenix, Arizona



### AMERICAN EPILEPSY SOCIETY (AES) 2023 ANNUAL MEETING

December 1-5, 2023  
Orlando, Florida

### 71<sup>st</sup> ANNUAL CONFERENCE OF NEUROLOGICAL SOCIETY OF INDIA (NSICON)

December 14-17, 2023  
Bhubaneswar Odisha, India

# SECTION 5

## TECH UPDATE

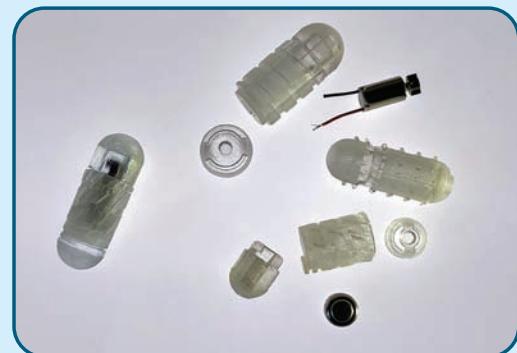
### INNOVATIVE PROTEIN DRUG DELIVERY WITH THE HELP OF ROBOTIC CAPSULES

A robotic drug delivery capsule has been developed by engineers in collaboration that aim at delivering delicate protein drugs, such as insulin, through the wall of the intestine. This was developed because of the fact that proteins were not well suited for oral therapy owing to destruction/metabolism by the low pH in the intestine. Moreover, proteins are not able to pass through the mucus layer that lines the gastrointestinal tract.

Therefore, to protect proteins from the acidic environment and create a way to travel through the mucus layer, these capsules were developed. The capsule can be loaded with the protein and then once swallowed, it becomes activated by the low pH in the intestine. The capsule has a studded cap at one end that begins to spin, tunneling through the mucus until it reaches the epithelium and deposits its drug payload.

In patients with diabetes, insulin injections are required at regular intervals, which are very painful and cause inconvenience. Though oral administration of insulin would be much useful in such patients, till date no-one has developed an effective means to achieve this. A robotic pill "RoboCap" covered in gelatin coating and size of a multivitamin manually drills down through intestinal mucus to access the underlying epithelium, offering a means to deliver proteins orally. This capsule breaks down when it reaches a specific pH on reaching small intestine. It includes a reservoir at one end that contains the protein drug and a drilling mechanism at the other end. Spinning cap, powered by motor and studded to brush away the mucus starts rotating on reaching specific pH and once the capsule drills through the mucus layer and reaches the epithelium, it releases the protein payload. Furthermore, the gelatin coating of the capsule can be fine tuned so as to break this down at different pH levels, signifying that it can be used to deliver drugs to other parts of the gastrointestinal tract that have different levels of acidity, such as the stomach.

**Source:** Robotic Capsule Drills Intestinal Mucus to Deliver Protein Drugs. Available at: <https://www.medgadget.com/2022/10/robotic-capsule-drills-intestinal-mucus-to-deliver-protein-drugs.html>. Accessed on: 27.10.2023



### AN AT-HOME DIGITAL SPIROMETER

Respiratory health has witnessed immense attention in the recent times, especially due to the COVID-19 pandemic. In sequence, research is being continuously intensified to address unmet needs at all diagnostic and therapeutic levels, and thus facilitate enhance outcomes for patients with respiratory illnesses. In clinical practice, it is often seen that for patients with chronic lung diseases, such as chronic obstructive pulmonary disease (COPD) and

asthma, an important way to keep track of lung health is to use aspirometer to check how well air can moves in and out of the lungs during forced breathing. However, this evaluation requires the patient to visit a lung specialist, which is often inconvenient and can preclude regular monitoring.

Aluna, a medical start-up, has brought a solution to this limitation of inconvenience and accessibility through their latest technology. The company has created a portable at-home digital spirometer device, which is easy to use, and can be used by the patient for daily monitoring of their respiratory functions and lung health. The concept looks similar to the home blood-glucose testing used by patients with diabetes to keep track of their glucose levels.

In order to increase the patient compliance, and to make the Spirometry process more fun especially for children, the system includes computer games that incentivize the patient to use the device regularly. Furthermore, the real-time data generated can be shared with the clinician to facilitate timely decision making and intervention including treatment modification. The device is FDA-cleared, and has hospital level accuracy along with machine learning technology, with ability to collect a broad set of data (medications, symptoms, environmental factors) for broad home health monitoring of the lung function.

**Source:** FDA-Approved At-Home Spirometer: Interview with Charvi Shetty, Co-Founder and CEO at Aluna. Available at: <https://www.medgadget.com/2022/10/fda-approved-at-home-spirometer-interview-with-charvi-shetty-co-founder-and-ceo-at-aluna.html> [Accessed on: 27.10.2023]



## NEUROMARK: AN INNOVATIVE IN-OFFICE TREATMENT FOR CHRONIC RHINITIS

An Irish medtech company has developed the NEUROMARK system, which offers a simple in-office procedure to treat chronic rhinitis by targeting the nerves responsible for common symptoms. Conventional therapies for chronic rhinitis involve long-term medication use, which may have mixed success and require repetitive administration. NEUROMARK presents an alternative approach by precisely targeting the hyperactive parasympathetic nerves driving congestion and rhinorrhea—the core symptoms of chronic rhinitis. This targeted therapy aims to preserve the integrity of surrounding nasal tissue while effectively treating the underlying cause of symptoms. This innovative treatment option for chronic allergic and non-allergic rhinitis is conveniently administered in an ENT physician's office with the use of a topical anesthetic, allowing patients to immediately resume normal activities. The NEUROMARK system enables clinicians to treat multiple nerve segments in a single procedure, utilizing algorithms that determine the optimal therapy dosage. NEUROMARK's algorithms and biofeedback monitoring ensure safe and precise disruption of the nerves associated with underlying inflammation. By tailoring the therapy to each patient's individual needs, NEUROMARK offers an effective and personalized approach to treating chronic rhinitis, revolutionizing patient care in this field.



**Source:** In-Office Treatment for Chronic Rhinitis: Interview with Brian Shields, Neurent Medical CEO. Available at: <https://www.medgadget.com/2021/02/in-office-treatment-for-chronic-rhinitis-interview-with-brian-shields-neurent-medical-ceo.html>. Accessed on 26/05/2023.

# SECTION 6

## LEGAL UPDATE

### Medicolegal aspects of consent in clinical practice

**C**onsent form is described as an integral part of patient treatment and management. The concept of informed consent arises from the fundamental ethical principle of autonomy and right of self-determination.

Sec 13 of the Indian Contract Act 1872 defines that, 'two or more persons are said to consent when they agree upon the same 3 things in the same sense.'

Relation between the physician and patient is a contract, hence it is essential to take consent before starting any procedure for patient. It may take as an assault to examine or treat a patient without taking his consent.

#### IMPORTANCE OF CONSENT

- Consent represents the right of a patient to make a decision regarding his/her medical treatment
- Consent means voluntary participation of the patient in his own treatment by a physician or any health care institute
- Consent is mandatory for all diagnostic and therapeutic procedures that have risk/adverse effects or complications
- Consent is very much essential in all medicolegal cases.

#### TYPES OF CONSENT

- Implied consent
- Expressed consent
- Blanket consent

Giving sufficient amount of information to a patient regarding his or her treatment is a primary concern of an informed consent with the aim that an individual can take a decision about the drug, device or procedure proposed for him in the course of treatment. Moreover, it gives a right to refuse the proposed treatment if he or she wants. In legal terms, treating a patient without his or her valued informed consent may take as an act of negligence.

#### ELEMENTS OF INFORMED CONSENT

##### a). *Disclosure of information*

It includes the following:

1. A doctor should explain to his patient the exact nature of the disease or the ailment.
2. A patient must be explained the need and nature of the treatment along with the likely chances of success
3. Patient should be made aware of other alternative treatment regime and benefits or adverse effects of alternative and proposed treatment.

4. Patient has a right to choose or refuse any of treatment procedure.

*b). Free and voluntary consent*

Consent should be given voluntarily by patient without any external force and misrepresentation of facts. Nobody is authorized to give consent on behalf of the patient.

*c). Capacity to decide*

Consent is given by patient who is mature enough to understand, analyse and assess the nature of the act and logical consequences of the act. A competent person must fulfil following criteria's,

1. He should be of sound disposing mind.
2. He should be legally competent to do so.
3. He should have proper reasoning for his decision.
4. He should be able to understand the implications of his consent.
5. He should be at least 12 years of age.
6. The informed consent will be legally valid when all the above-mentioned components of informed consent are met.

**For consent to be legally valid it must fulfil following criteria :**

- Person who's giving a consent should be of sound disposing mind
- Consent should be given voluntarily without any external pressure or misrepresentation of facts, etc.
- It should be clear, fair and direct
- Should be well informed
- Consent should be taken before starting the any procedure either therapeutic or diagnostic
- Consent should be complete and specific
- It should be given by a person who is well matured and able to understand the nature and consequences of the act

- There should be a third person as witness.

Examination of victim and accused in all medicolegal cases can be performed only after providing the full written expressed informed consent. Nobody can force both victim or accused, if he or she refuses. Procedure for examination and an accused and victim is done as per sec 53 and sec 54 of CrPC (Criminal Procedure Code).

**Sections of IPC and CrPC related to 5 consent**

- Sec 87 IPC - A person above 18 years of age can give valid consent to suffer any harm, which may result from an act not intended or not known to cause death or grievous hurt.
- Sec 88 IPC - A person can give valid consent to suffer any harm that may result from an act, not intended or not known to cause death, done in good faith and for its benefit.
- Sec 89 IPC - Act done in good faith for benefit of child or insane person, by or by consent of guardian.
- Sec 90 IPC - Consent to be given under fear or misconception.
- Sec 92 IPC - Act done in good faith for benefit of a person without consent.
- Sec 53 CrPC - Examination of accused by medical practitioner at the request of police officer.
- Sec 54 CrPC - Examination of arrested person by medical practitioner at the request of the arrested person.

**CONCLUSION**

Informed consent is mandatory to take in all medicolegal cases and for the subjects participating in clinical trials. Moreover, it is essential to express consent in written information in beyond routine medical examination of a patient. Hence, it act as a best defence for physician against the charges of negligence.

**Source:** Patil AM, Anchimane VT. Medico legal aspects of consent in clinical practice. *Bombay hospital J.* 2011;53:2.



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