

# MEDITIME

A Medical Bulletin from TIME Pharmaceuticals (P.) Ltd.

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## Technology Transfer with Pharma Giant of Bangladesh SQUARE Pharmaceuticals

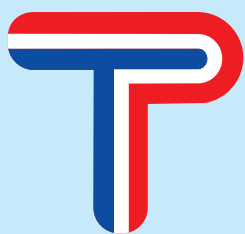


OAB Pathophysiology

Medical Management of OAB

जवान पुरुषमा देखिने क्यान्सर

*Touching Lives, Delivering Promises*



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A Medical Bulletin from TIME Pharmaceuticals (P.) Ltd.

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## Editorial



Technology transfer and international collaborations are processes regularly discussed worldwide to improve the technologies & qualities in the pharma sector. Technological differences are the primary cause of international inequalities in economic achievements. Thus, TIME Pharmaceuticals joins hand with giant multinational company "SQUARE

Pharmaceuticals" to bring the latest technologies in the premises of TIME Pharmaceuticals. The objective of technology transfer is to incorporate new technologies to improve the efficiency in productive process with robust formulation and latest analytical techniques. The final destination of TIME Pharmaceuticals is to create new industry standard, development in future technologies and finally turn into a potential source of revenue generation through export.

TIME Pharmaceuticals proudly launches new molecule Tolterodine tartrate (BRAND NAME: URODINE 2mg IR) for the first time in Nepal for the treatment of overactive bladder with the blend of technology between SQUARE and TIME Pharmaceuticals. It is the well studied molecule with long safety record and equally efficacious than other generics treated in OAB with less adverse effects. This product not only has superiority in terms of pharmacological aspect; but also has improved formulation technology. We are bringing chain of molecules by means of technology transfer. Orosis-D (Calcium & Vitamin D<sub>3</sub> in tablets) is another formulation with blended technology. Thus, now onwards, a series of molecule will be manufactured in technical collaboration with SQUARE Pharmaceuticals in order to improve quality of products. As we have invested for high quality standard in products, our mission will not be successful without your valuable support. So, we request for your valuable support in our every steps.

In this issue, we are supported with the articles related to Overactive bladders, its physiology and medical management as well as cancer in young adults, with the objective of sharing information related to it in different parts of Nepal. We feel honor to share the information from our valued doctors with our readers. I thankfully acknowledge all medical fraternities for your continuous support for our MEDITIME, and wish similar support with valuable feedback and suggestion for improvement in it.

Thank you

Sudarshan Lal Shrestha  
Editor in Chief

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## BONE HEALTH & CALCIUM



Bones increase in size and mass during periods of growth in childhood, adolescence and reaching peak bone mass around age 30. The greater the peak bone mass, the longer one can delay serious bone loss with increasing age. Everyone should therefore consume adequate amounts of calcium and vitamin D throughout childhood, adolescence and early adulthood. Osteoporosis is most associated with fractures of the hip, vertebrae, wrist, pelvis, ribs and other bones.

When calcium intake is low or ingested calcium is poorly absorbed, bone breakdown occurs as the body uses its stored calcium to maintain normal biological functions. Bone loss also occurs as part of the normal aging process, particularly in postmenopausal women due to decreased amounts of estrogen. Many factors increase the risk of developing osteoporosis, including being female, thin, inactive or of advanced age; smoking cigarettes; drinking excessive amounts of alcohol and having a family history of osteoporosis.

Various bone mineral density (BMD) tests are available. The T-score from these tests compares an individual's BMD to an optimal BMD (that of a healthy 30-year old adult). A T-score of -1.0 or above indicates normal bone density, -1.0 to -2.5 indicates low bone mass (osteopenia) and lower than -2.5 indicates osteoporosis.

Although osteoporosis affects individuals of all races, ethnicities and both genders, women are at highest risk because their skeletons are smaller than those of men and because of the accelerated bone loss that accompanies menopause. Regular exercise and adequate intakes of calcium and vitamin D are critical to the development and maintenance of healthy bones throughout the life cycle. Both weight-bearing exercises (such as walking, running and activities where one's feet leave and hit the ground and work against gravity) and resistance exercises (such as calisthenics and that involve weights) support bone health. (National Institute of Health, Office of Dietary Supplement)

## CALCIUM INTAKE & STATUS

Not all Calcium consumed is actually absorbed in the gut. Humans absorb about 30% of the calcium in foods, but this varies depending upon the type of food consumed. Other factors also affect calcium absorption including the following:

**Amount consumed:** The efficiency of absorption decreases as calcium intake increases.

**Age and life stage:** Net calcium absorption is as high as 60% in infants and young children, who need substantial amounts of the mineral to build bone. Absorption decreases to 15%–20% in adulthood (though it is increased during pregnancy) and continues to decrease as people age; compared with younger adults, recommended calcium intakes are higher for females older than 50 years and for both males and females older than 70 years.

**Vitamin D intake:** This nutrient, obtained from food and produced by skin when exposed to sunlight of sufficient intensity, improves calcium absorption.

**Other components in food:** Phytic acid and oxalic acid, found naturally in some plants, bind to calcium and can inhibit its absorption. Foods with high levels of oxalic acid include spinach, collard greens, sweet potatoes, rhubarb and beans. Among the foods high in phytic acid are fiber-containing whole-grain products and wheat bran, beans, seeds, nuts and soy isolates. The extent to which these compounds affect calcium absorption varies. Research shows, for example, that eating spinach and milk at the same time reduces absorption of the calcium in milk. In contrast, wheat products (with the exception of wheat bran) do not appear to lower calcium absorption. For people who eat a variety of foods, these interactions probably have little or no nutritional consequence and furthermore, are accounted for in the overall calcium DRIs, which factor in differences in absorption of calcium in mixed diets.

Some absorbed calcium is eliminated from the body in urine, feces and sweat.

**Groups at Risk of Calcium Inadequacy :** The following groups are among those most likely to need extra calcium:

- Postmenopausal women
- Amenorrhic women and the female athlete triad
- Individuals with lactose intolerance or cow's milk allergy
- Vegetarians

**"Adequate calcium and vitamin D as part of a healthful diet, along with physical activity, may reduce the risk of osteoporosis in later life" FDA Claims.**

**Table 1 : Recommended Dietary Allowances (RDAs) for Calcium**

Age	Male	Female	Pregnant	Lactating
0-6 months*	200mg	200mg		
7-12 months*	260mg	260mg		
1-3 years	700mg	700mg		
4-8 years	1,000mg	1,000mg		
9-13 years	1,300mg	1,300mg		
14-18 years	1,300mg	1,300mg	1,300mg	1,300mg
19-50 years	1,000mg	1,000mg	1,000mg	1,000mg
51-70 years	1,000mg	1,200mg		
71 + years	1,200mg	1,200mg		

\*Adequate Intake (AI)





प्रो. डा. अर्जुन देव भट्ट

वरिष्ठ कन्सल्टेन्ट युरोलोजिष्ट  
मेडिकेयर नेशनल हस्पिटल एण्ड रिसर्च सेन्टर लि.  
चावहिल, काठमाण्डौ

# जवान पुरुषमा देखिने क्यान्सर

## अध्ययनको औचित्य:

शुक्रग्रन्थि तीन प्रकारका कोशिकाले बनेको हुन्छ:

- ◆ बीज उत्पादन गर्ने कोशिका (Germ Cells)
- ◆ सेरटोली कोशिका (Sertoli Cells)
- ◆ लेइडिग कोशिका (Leydig Cells)

बीज उत्पादन गर्ने कोशिकाको मुख्य कार्य शुक्रकीट उत्पादन गर्ने हो । सेरटोली कोशिका शुक्रकीट विकसित हुन चाहिने पुरुष हर्मोनको स्थानीय स्तर व्यवस्था गर्न चाहिने रस उत्पादन जस्ता महत्वपूर्ण कार्यमा संलग्न हुन्छ । लेइडिग कोशिका पुरुष हर्मोन उत्पादन गर्दछन् ।

शुक्र ग्रन्थिका बीज उत्पादन गर्ने कोशिकाबाट क्यान्सरको सुरुवात हुन सक्ने सम्भावना सबै भन्दा बढी हुन्छ । अरु बाँकी दुई थरीका कोशिकाबाट क्यान्सर भए पनि त्यो ५% मात्र देखा पर्दछ । शुक्रग्रन्थिको क्यान्सर ९५% बीज उत्पादन गर्ने कोशिकाहरू सँग सम्बन्धित भएकोले यो लेख त्यसैमा केन्द्रित रहने छ । पुरुषमा देखा पर्ने विभिन्न क्यान्सरको दाँजोमा शुक्रग्रन्थिको क्यान्सर ज्यादै न्यून हुन्छ । पुरुषमा हुने सम्पूर्ण क्यान्सरको १% मात्र शुक्रग्रन्थि क्यान्सरको हिस्सामा पर्दछ । विकसित देशमा यो क्यान्सर बढ्दो छ । शुक्रग्रन्थि क्यान्सर शल्य, रासायनिक तथा विकिरण उपचारबाट ९५% पुरुषहरू रोग मुक्त हुन सक्छन् । समयमै रोगको पहिचान हुन सकेका खण्डमा शल्य उपचारबाट मात्र पनि यो रोग मुक्त हुन सकिन्छ । खास गरेर सिसप्लाटिन (Cisplatin) नामक औषधि उपचारबाट मृत्यु हुनेको संख्या घट्दो छ ।

शुक्र ग्रन्थि क्यान्सर लक्षणहरू थाहा पाएर रोग पहिचान समयमै गर्न सकिने भएकोले यो रोगबारे आम जनमानसमा प्रचार बढाउनु पर्ने नितान्त आवश्यक छ । जन चेतना उच्च स्तरमा भएको खण्डमा यो रोगको निदान शुक्रग्रन्थि मै रोग सीमित रहेको अवस्थामा हुन सक्ने भएकोले त्यसैलाई केन्द्र बिन्दुमा राखेर प्रचार-प्रसारलाई उच्च प्राथमिकता दिनु पर्दछ ।

## कस्ता पुरुष शुक्र ग्रन्थि क्यान्सरको उच्च जोखिममा हुन्छन् ?

के कारणले प्रारम्भिक बीजाणु कोशिका (Primordial Cell) शुक्रग्रन्थि क्यान्सरमा स्मान्तरण हुन्छ अझै थाहा छैन । तर कस्ता पुरुष यो स्मान्तरणको उच्च जोखिममा हुन्छन् त्यो भने जानकारीमा आएको छ ।

अण्डकोष बाहिर रहेको शुक्रग्रन्थिमा क्यान्सर विकसित हुने सम्भावना १५ गुणा बढी हुन्छ । त्यस्तो अवस्थामा शुक्रग्रन्थि पेट भित्र भए क्यान्सर हुने सम्भावना २५ गुणा सम्म पनि बढी हुने केही वैज्ञानिक बताउँछन् ।

अर्को जोखिम भनेको पुरुषको उमेर हो । १८ देखि ३५/४० वर्षको उमेरमा बीज उत्पादन गर्ने कोशिका (germ cells) धेरै छिटो छिटो विभाजित हुने र वृद्धि हुने भएकाले क्यान्सर हुने सम्भावना यो उमेरमा बढी हुन्छ । तर त्यसो भन्दैमा कम वा बढी उमेरमा शुक्रग्रन्थिको क्यान्सर हुन भन्ने होइन । जस्तो कि बिरलै भएपनि ३ वर्ष भन्दा कम उमेरका बच्चामा वा १० वर्ष भित्रका ठीटाहरूमा अण्डपीतजालो संलग्न क्यान्सर (Yolk Sac) देखा पर्न सक्छ भने ६० वर्ष भन्दा माथिका पुरुषमा प्राय लिम्फोमा प्रजातिको अर्बुद देखा पर्दछ र यसले दुबै शुक्रग्रन्थिलाई समावेश गर्न सक्छ ।

जुन पुरुषको नजिकको नातेदारमा शुक्रग्रन्थि क्यान्सर देखा परेको छ उसमा पनि यस्तो क्यान्सर हुने सम्भावना ४ देखि १० गुणा उच्च हुन्छ । त्यस्तै आफ्नो अर्को शुक्रग्रन्थिमा क्यान्सर भएको थियो भने दोस्रो शुक्रग्रन्थि त्यो रोगको निम्ति बढी जोखिममा रहन्छ ।

काला जातिमा भन्दा गोरामा यो रोग ५ गुणा बढी पाइने गर्दछ । न्युजिल्याण्ड, सक्थानडिनाभियन देशका पुरुषको शुक्रग्रन्थिको क्यान्सर संसारमै सबै भन्दा बढी विकास हुने गरेको पाइएको छ ।

नेपालमा प्रत्येक वर्ष कति पुरुष शुक्रग्रन्थि क्यान्सरबाट ग्रस्त हुन्छन् त्यसको लेखा छैन । तर विश्वमा भएको सन् २०१३ को १० देशको अध्ययन अनुसार सबै भन्दा कम पुरुष भारतमा शुक्रग्रन्थि क्यान्सर

पीडित हुन्छन् । एक लाख पुरुषमा न्युजिल्याण्डमा ७.८ व्यक्ति र भारतमा ०.५ व्यक्तिमा शुक्रग्रन्थि क्यान्सर देखिन्छ । यही अध्ययन अनुसार यो रोग संसारमा बढ्ने क्रममा छ यद्यपि मृत्यु हुने बिरामीको संख्या भने घट्दो छ । भारत र नेपालको धेरै कुरामा समानता रहेकाले हाम्रो देशमा पनि भारतको जस्तै शुक्रग्रन्थि क्यान्सरको संख्या एक लाख पुरुषमा ०.५ कै दर छ भनेर पूर्वानुमान (assumption) गर्न सकिन्छ । तर अब हाम्रो देशमा आफ्नै मौलिक तथा भर पर्दो आँकडा संकलन गर्ने व्यवस्था मिलाउन अत्यन्त आवश्यक छ ।

## लक्षण:

शुक्रग्रन्थिमा पीडा रहित ठोस डल्लो देखा परे त्यसलाई यो अङ्गको क्यान्सर रोग निदानको विशेष लक्षण परिचय मान्न सकिन्छ । यस्तो अवस्थामा शुक्रग्रन्थि आफ्नो संगैको अर्को शुक्रग्रन्थिको अनुपातमा ठूलो, सारो, दर्दहीन, केही भारी तथा नितान्त पीडितको ध्यान आकर्षण गर्ने हुन्छ । त्यसको अलावा यस्तो शुक्रग्रन्थि नितान्त चोट पटक लाग्ने उन्मुख खालको हुन्छ । त्यसैले खास गरेर १८ देखि ३५/४० वर्ष सम्मका पुरुषमा अण्डकोष भित्र कुनै पनि एउटा शुक्रग्रन्थि ठूलो हुँदै आए र औलाहरूको बीचमा त्यसलाई थिच्दा पीडाको अनुभूति नभए क्यान्सरको शंका लिनै पर्दछ । यस्तो शुक्रग्रन्थिलाई टर्च लाइटको प्रकाश पठाएर वारवार हेर्न खोज्दा प्रकाश सञ्चरण (Transilluminate) नभएर भित्र कालो दाग देखा पर्दछ । क्यान्सर वृद्धिको सिलसिलामा शुक्र ग्रन्थि भित्र रक्तस्राव भएको खण्डमा पीडा अनुभव हुन सक्छ । त्यसको अलावा रोग फैलिने सिलसिलामा काछ, पेट तथा छाती भित्र क्यान्सर तन्तु फैलिएको अवस्थामा बिरामीहरू विभिन्न किसिमको पीडा अनुभव गर्दछन् ।

## रोग निदानमा परीक्षणको भूमिका:

सर्व प्रथम शुक्रग्रन्थि क्यान्सरको रोग निदानमा सबैभन्दा ठूलो भूमिका स्वयं पुरुषको हुन्छ । अण्डकोष भित्र कुनै पनि शुक्रग्रन्थि एक्कासी ठूलो हुँदै आयो, त्यसलाई

औलाको बीचमा छामेर थिच्दा पीडा महसुस नभए, सधै लगाएका लुगा आफूलाई असजिलो लागे वा बीच बीचमा टक्कर लाग्ने भएका खण्डमा चिकित्सक संग परामर्श गर्नु पर्दछ । यस्ता पुरुषलाई पेट तथा अण्डकोषको अल्ट्रासोनो ग्राफी गराएर चिकित्सकहरू अरु थप परीक्षण के गर्नु पर्ने हुन्छ निधो गर्दछन् । अल्ट्रासोनोग्राफी शुक्रग्रन्थि क्यान्सर रोग पहिचानको निम्ति एउटा अती महत्वपूर्ण परीक्षण हो । सूलभ प्राय धेरैको सामर्थ्य राख्न सक्ने र बीना जटिल असर भएको परीक्षण भएकाले पनि युएसजी बार-बार दोहर्याउन पनि मिल्छ । यो परीक्षणबाट अण्डकोष भित्रका विभिन्न संरचनाहरूका रोगको सही मूल्याङ्कन गर्न सकिने भएकाले परीक्षण भइरहेको समयमा देखा परेको पुरुषको शुक्रग्रन्थिको व्याधि क्यान्सर हो वा होइन भनेर निकै मसिनो संग छुट्याउन सकिन्छ । यदि यो रोग अर्बुद हो भने त्यो काछ वा पेटको जालोको पछाडि तिर फैलिएको अवस्था छ वा छैन पनि थाहा पाउन सकिन्छ । युएसजीकै आधारमा शुक्रग्रन्थिको प्राथमिक शल्य उपचार गरिन्छ । शल्यक्रिया गर्नु अगाडि शुक्रग्रन्थि अर्बुदको सुइले तानेर वा खोलेर तन्तु निकाल्ने र त्यसको जाँच गर्दा रोग नराम्रो संग अण्डकोषको छाला तथा रक्त संचार भएर विभिन्न ठाँउ तिर फैलिने सम्भावना उच्च हुने भएकोले सुरुमै युएसजीबाट अर्बुदको संका भए एकै पल्ट शुक्रग्रन्थि तथा त्यसतिर जाने रक्त, लिम्फाटिक र शुक्रबाहिनी नलीहरूको धेरै भाग निकालिन्छ । अन्तिम रोग निदान भने शल्य विधिबाट निकालिएको अङ्गको तन्तु परीक्षण आधारमा कुन प्रकारको क्यान्सर हो त्यो यकिन गरिन्छ । त्यसपछि विकिरण, रासायनिक वा थप शल्य उपचार गर्ने वा बिरामीलाई चिकित्सकको निगरानीमा राख्न त्यसको निर्क्योल गरिन्छ ।

### अर्बुद सूचकको रक्त परीक्षण:

रक्त परीक्षणमा निम्न तीन "अर्बुद सूचक" (Tumor Markers)

- ◆ एल.डि.एच (LDH-Lactose Dehydrogenase)
- ◆ ए.एफ.पी (AFP- Alfa Fetoprotein) र
- ◆ एच.सि.जी (HCG-Human Chorionic Gonadotrophin) रक्त स्तरले रोग निदान, पूर्वानुमान (Progress), उपचारको असर (Treatment Response), शीघ्र रोग पुनराक्रन्त (Early Detection of Relapse) जस्ता थुप्रै महत्वपूर्ण पक्षमा ठूलो सघाउ पुर्र्याउँछ । अर्बुद सूचकहरू रोग वर्गीकरण र पूर्ण उपचारको निगरानीमा ठूलो महत्व राख्छन् । यी परीक्षण प्राथमिक शल्यचिकित्सा पूर्व र तत्पश्चात् पनि गर्नु अनिवार्य हुन्छ । शीघ्ररोग पुनाराकान्तको सूचना पाउन यी सूचक सय प्रतिशत सबै रोगहरूमा

र सबै प्रकारका शुक्रग्रन्थि क्यान्सरमा देखा पर्दैनन् । अर्बुद सूचक क्यान्सर पूर्ण रूपमा निराकरण भयो भएन हेर्न महत्वपूर्ण भएपनि यीनीहरूको स्तरको आधारमा मात्र "रोगको अव कुनै उपचार तथा निगरानी आवश्यक छैन" भनि पूर्ण निर्भर हुनु हुँदैन ।

### सेमिनोमा - ननसेमिनोमा (Seminoma and non-seminoma)

यो शुक्रग्रन्थि क्यान्सरको ज्यादै महत्वपूर्ण वर्गीकरण हो । यी दुवै थरीका क्यान्सर बीजीय कोशिकाबाट नै उत्पन्न हुन्छन् । तर तिनिहरूको उग्रता, घातकता र विषाक्ततामा निकै भिन्नता हुन्छ । ५०% शुक्रग्रन्थिको क्यान्सर सेमिनोमा वर्गमा पर्दछन् । ती प्राय ४० को दशकमा देखा पर्दछन् र कम घातक, ढीलो शुक्रग्रन्थि बाहिर फैलने र उपचारको हिसावले छिटो निको पार्न सकिने हुन्छन् ।

सुरु अवस्थाको सेमिनोमा शल्यक्रिया बाटै पूर्ण निको हुने सम्भावना उच्च हुन्छ । शल्य उपचार पछि पेट भित्र रोग फैलिएको देखा परे विकिरण उपचारको सहयोगबाट सय प्रतिशत बिरामीमा रोग पूर्ण रूपमा नियन्त्रण गर्न सकिन्छ । तर पनि १५% जति बिरामीमा फेरि रोग बल्फेर रासायनिक उपचार कार्बोप्लाटिन (Carboplatin) बाट गरिन्छ । यद्यपि रासायनिक उपचारबाट राम्रो उपलब्धि पाउन सकिन्छ तर पनि बिरामीले ५ वर्ष सम्म निगरानीमा रहनु पर्दछ । ननसेमिनोमाको उपचारमा विकिरणको महत्व खाँसै छैन । ननसेमिनोमा प्राय ३० को दशकमा देखा पर्दछन् र छिटै शुक्रग्रन्थि बाहिर फैलिने, बढी घातक र उपचार लामो समय गरिराख्नु पर्ने हुन्छ । ननसेमिनोमा अर्बुदमा लुकेर बसेको क्यान्सर बाँकी छ वा औषधिले सुकाएको क्यान्सर कतै फेरि पलायो कि भनेर बढी लामो समय रक्त सूचक हेर्नु पर्ने हुन्छ ।

सेमिनोमा विकिरणबाट तुरुन्त प्रभावित हुने हुन्छ । तर रोग निरोधक उपचार (Prophylactic Treatment) को रूपमा विकिरण उपचार र प्रयोग गर्नु सुरक्षित हुन्छ । किन भने विकिरण उपचारको १०/२० वर्ष पछि पनि त्यसले मुटु तथा धमनीमा नराम्रो असर गर्न सक्छ । त्यो बाहेक विकिरणको कारणबाट वर्षौ पछि शरीरका विभिन्न अङ्गको क्यान्सर हुने सम्भावना रहन्छ । त्यसैले सेमिनोमाका बिरामी जसमा रोग शुक्रग्रन्थि बाहिर रहेको यकिन छैन त्यस्ता बिरामी चिकित्सकको निगरानीमा रहनु पर्दछ । सेमिनोमा फैलिएको देखा परे रासायनिक उपचारबाट पनि पूर्ण निको पार्न सकिन्छ । सेमिनोमाको उपचार विभिन्न विधिबाट सफलताका साथ उपलब्ध गर्न

सकिन्छ । पछिल्लो समयमा सेमिनोमा पहिलो वा दोस्रो जुन सुकै अवस्थामा भए पनि शल्य उपचार पछि विकिरणको सट्टामा सोभै रासायनिक उपचारलाई प्राथमिकतामा राख्ने पनि चलन छ ।

ननसेमिनोमा प्रथम अवस्थामा भएका मध्ये भण्डौं २०% देखि ५०% सम्म बिरामीको रोग पेटको जालोको पछाडि (Retroperitoneal Space) तिर फैलिसकेको हुन्छ । तर पनि तिनीहरू मध्ये ९५% बिरामी उपचारबाट पूर्णरूपमा क्यान्सर रहित अवस्थामा पुग्न सफल हुन्छन् । यस्तो उच्च स्तरिय सफलता दिलाउने रासायनिक औषधि ब्लेवोमाइसिन (Bleomycin), इटोपोसाइड (Etoposide) र सिसप्लाटिन (Cisplatin) को प्रयोग साथै पेट भित्रको सबै गिर्खा निकाल्ने दोस्रो शल्यक्रियाबाट सम्भव हुन्छ ।

### उपचार:

शुक्रग्रन्थिको क्यान्सर उपचार शल्यक्रियाबाट सुरु हुन्छ । निकालिएको अङ्ग तन्तु परीक्षण गरेर कुन वर्गको क्यान्सर हो त्यो छुट्याएपछि रासायनिक वा विकिरण विधिबाट बिरामीको पूर्ण उपचार हुन्छ । उपचारको सिलसिलामा विभिन्न परीक्षण दोहर्न्याएर गरिराख्नु पर्ने हुन्छ । औषधि उपचारले फैलिएका क्यान्सर गिर्खाहरू पूर्ण रूपमा हराएर नगएको अवस्थामा दोस्रो विस्तृत शल्यक्रिया कार्यन्वयन गर्नु पर्ने हुन्छ । अन्ततोगत्वा ९५% बिरामीहरू पूर्ण रूपमा क्यान्सर मुक्त हुन सक्छन् ।

### निचोड:

शुक्रग्रन्थिको क्यान्सर दुर्लभ मध्ये नै गनिन्छ । तर २५ वर्ष देखि ३५ वर्षका पुरुषमा देखा पर्ने प्रमुख क्यान्सर शुक्रग्रन्थि कै हो । सामान्य अवस्थामा रोग नै नहुनु पर्ने उमेरमा यस्तो रोग हुन सक्ने तर थोरै सतर्कता र ज्ञानबाट यसको निदान तथा पूर्ण उपचारमा महत्वपूर्ण सहयोग हुन सक्ने भएकोले आम जनमानसमा यसको चेतना जगाउन महत्वपूर्ण हुन्छ ।

के कारणले शुक्रग्रन्थिको क्यान्सर हुन्छ वैज्ञानिकहरू किटेर भन्न सक्ने अवस्थामा छैनन् । तर कुन पुरुषमा यो रोगको सम्भावना उच्च हुन्छ, त्यो भने यकिन थाहा छ । खास गरेर शुक्रग्रन्थि अण्डकोष भित्र नभएर पेट तिर भए वा नजिकका नातेदारमा यो रोग भएको रहेछ भने त्यस्ता पुरुषमा यो रोगको सम्भावना बढी हुन्छ ।

अण्डकोष भित्र एउटा शुक्रग्रन्थि एक्कासि ठूलो हुँदै आए, त्यो सारो तर नदुःखे भए क्यान्सरको शंका गर्नु पर्दछ । यो क्यान्सरको उपचार शल्य, रासायनिक र विकिरण बाट हुन्छ र प्राय ९५% बिरामी पूर्ण निको हुन्छन् ।

# OVERACTIVE BLADDER

## Pathophysiology



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### Overactive Bladder (OAB)

**Definition (ICS)** : Urinary urgency, usually with frequency or nocturia, with or without urgency incontinence, in the absence of UTI or other pathology

**Synonyms** : OAB syndrome, urge syndrome or urgency frequency syndrome

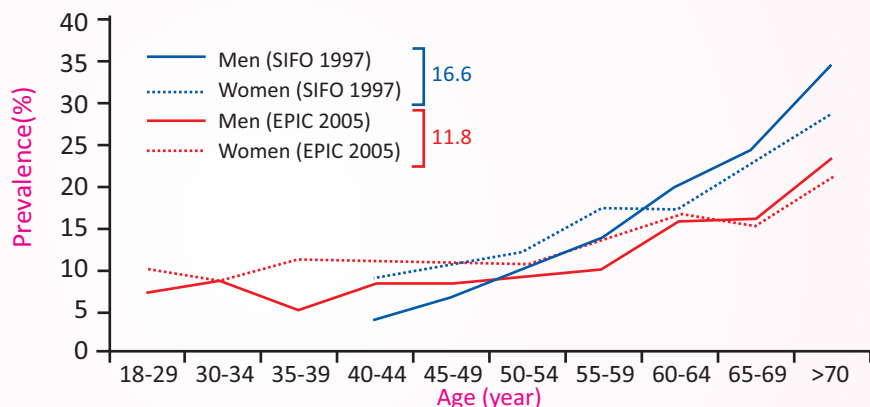
### Some terminologies

Terms	Definition
Urgency	Sudden compelling desire to pass urine that is difficult to defer
Frequency	Patient considers that he/she voids too often by day Normal is < 8 times per 24 hours
Nocturia	Waking to urinate during sleep hours Considered a clinical problem if frequency is greater than twice a night
Urge urinary incontinence	Involuntary leakage accompanied by or immediately preceded by urgency
OAB "wet"	OAB with UII
OAB "dry"	OAB without UII

### Prevalence

OAB Symptoms Are as Prevalent in Men as in Women and Increase with Age  
Population-based prevalence studies:

Comparison of data from the SIFO study (1997)\*1 and the EPIC study (2005)†2

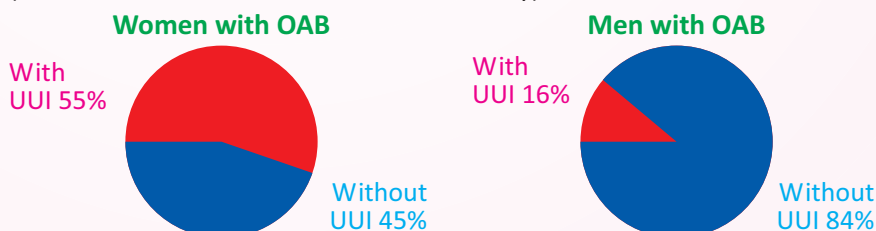


SIFO: Sifo/Gallup telephone survey

\* N = 16,776 interviews (6 European countries)-SIFO 1997

† N = 19,165 interviews (4 European countries and Canada)-EPIC 2005

**Urgency Leading to Urgency Incontinence:** More Prevalent in Women (National Overactive Bladder Evaluation Study)



This concludes prevalence of OAB increases with age in both male and female while female are more prone to OAB with Urge Urinary Incontinence (UII)

### Why is OAB important?

OAB has impact on the following aspects of life, which has direct connection to Quality of Life (QoL).

#### Physical

- ◆ Limitations/cessation
- ◆ Disturbed sleep
- ◆ Difficulties concentrating
- ◆ Tiredness
- ◆ Overeating

#### Sexual

- ◆ Avoidance of sexual contact

#### Domestic

- ◆ Specialized underwear, bedding
- ◆ Precautions with clothing



#### Psychological

- ◆ Depression
- ◆ Lack of self-esteem
- ◆ Lacking bladder control
- ◆ Urine odor

#### Social

- ◆ Reduction in social interaction
- ◆ Rely on toilet accessibility

#### Occupational

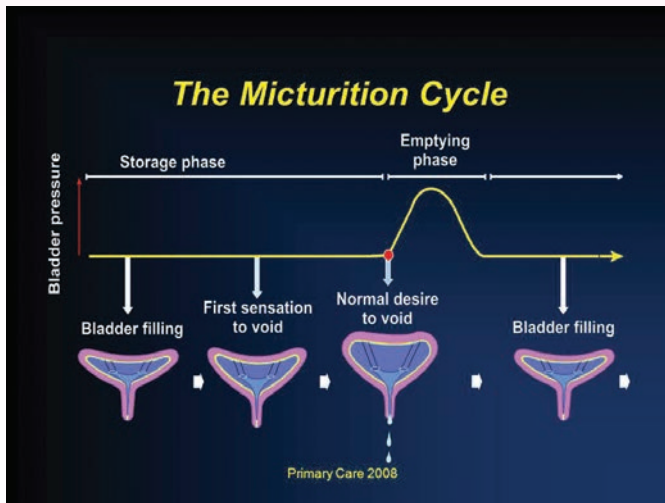
- ◆ Absence from work
- ◆ Decreased productivity
- ◆ Early retirement

## Micturation Cycle:

It comprises of two phases which are neurally controlled.

- Storage Phase
- Emptying phase

In OAB there is defect in filling phase.



## Pathology of OAB

There are many hypotheses for OAB.

### Classical theory :

#### I. Neurogenic theory:

- Inappropriate generalized nerve mediated detrusor contraction during filling

#### II. Myogenic theory

- Increased spontaneous detrusor excitation
- Enhanced propagation

#### III. Integrated theory

- Various triggers generate localised detrusor contractions (micromotions) which can spread in the bladder wall via various pathways leading to distortion in bladder wall resulting in urgency
- These micromotions are exaggerated in OAB and if excessive results in DO

## OAB vs DO (Detrusor Overactivity)

- OAB: Syndrome; Diagnosis based on symptomatology; only 40-60% of OAB patients are associated with DO.
- DO : Characterized by urodynamically demonstrable involuntary detrusor contractions during the filling phase that may be spontaneous or provoked; 80% of patients with DO have features of OAB.

## Phenotypic Pathophysiology of OAB

According to pathological factors	According to DO
Metabolic	Myogenic
Affective disorders	Urotheliogenic
Sex hormone deficiency	Urethrogenic
Urinary microbiota	Supraspinal
Functional GI disorder	Urotheliomyogenic: detrusor underactivity
ANS dysfunction	

## OAB pathophysiology according to DO:

### a) Myogenic - Same as classic theory

### b) Urotheliogenic

- OAB due to abnormal detrusor sensory function
- Urothelial and suburothelial dysfunction resulting

in increased sensitivity mediated via urothelial/suburothelial fibroblasts

- Abnormal contraction of muscularis mucosae
- c) **Urethrogenic : Urethrovesical reflex**
- Entry of urine into the proximal urethra in patients with stress urinary incontinence (SUI) may stimulate urethral afferents, inducing and/or increasing DO
  - Prolapse – inadequate support to bladder neck/urethral stretch receptors – decrease tone
  - Urethral sphincter instability

### d) Supraspinal hypothesis: brain OAB

- Decreased ability to functionally integrate afferent impulse or reduced supraspinal inhibitory control

### e) Detrusor underactivity

- Symptomatology has been shown to overlap with OAB
- Urgency most common symptom – 50% due to
  - Functional reduction in bladder capacity
  - UTI
  - Change in urothelial microbiota due to chronic retention
  - Myogenic
  - Urothelial

## Phenotypes based on pathological factors involved

### a. Metabolic syndrome

- Associated with obesity
- Proposed mechanism –heightened sensory afferent stimulation
  - Oxidative stress
  - Inflammation
  - Chronic pelvic ischemia
  - Insulin resistance – urothelial dysfunction

### b. Affective disorders:

- Increased risk in patients with anxiety/depression and affective disorders
- Bidirectional association

### c. Sex hormone deficiency

- Estrogen and progesterone receptors are found in LUT
- Onset of UI with menopause and vaginal atrophy
- Improvement UI – estrogen cream
- Estrogen deficiency – proposed to increase detrusor contractility through various pathways
- Not so with males

### d. Urinary microbiota

- Presence of commensal in UB – prevent growth of more virulent strains
- Bacterial DNA and higher load of bacteria detected in patients with UUI
- Predict response to conventional therapy – low number associated with better response

### e. Functional GI disorder

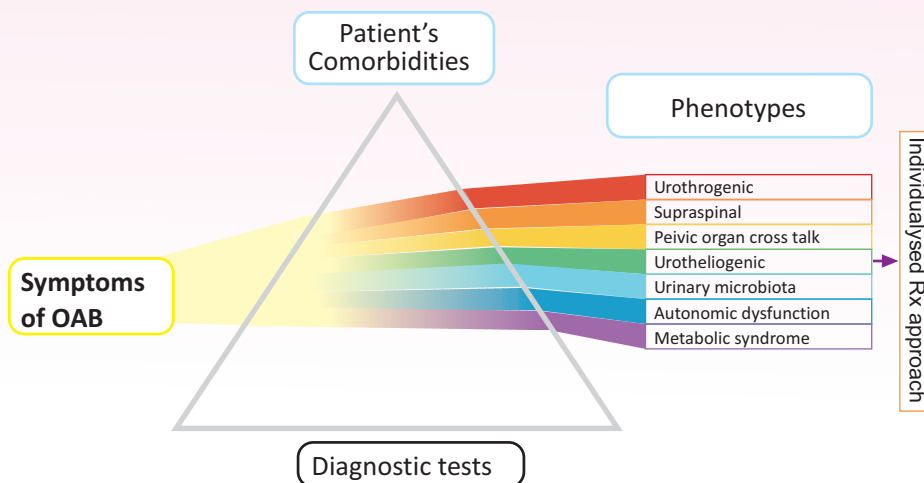
- Organ cross talk : Local cross sensitization – central sensitization
- Common embryological origin
- Common neural pathway
- Association with IBS
- May be associated with psychological or physical stress

**f. Autonomic dysfunction:**

- Major role in regulating function
- Altered in various neurological diseases associated with OAB eg parkinsonism, multiple sclerosis
- Upcoming concept of subclinical autonomic dysfunction – idiopathic OAB
  - Sympathetic dysfunction > parasympathetic
  - Better response to  $\beta 3$  agonist
- Less likely to have DO

**Summary**

- Symptom based diagnosis is vital for the proper treatment.
- Storage / afferent pathway defect are causes of OAB.
- Pathophysiology:
  - Still incompletely understood
  - Multifactorial
- Use Paradigm shift to understanding or approach or diagnose OAB



**Fig: Paradigm shift: Prism approach**

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# Product Information

Brand Name: URODINE-2

Generic Name: Tolterodine Tartrate

Strength: 2 mg IR Tablet

Pack Size: 10 × 15 Tablets

Dosage : 2 mg IR BID

Therapeutic Category: Antimuscarinic drug



**PHARMACOLOGY**

**Pharmacodynamics**

Tolterodine is a potent and competitive specific muscarinic receptor antagonist. Tolterodine acts on M<sub>2</sub> and M<sub>3</sub>, subtypes of muscarinic receptors. It targets the bladder more than other areas of the body. Tolterodine and its active metabolite (5-hydroxymethyltolterodine), act as competitive antagonists at muscarinic receptors. This antagonism results in inhibition of bladder contraction, decrease in detrusor pressure and an incomplete emptying of the bladder.

Non-selectivity property of tolterodine offers more complete suppression of detrusor overactivity. The prevention of Ach binding with M3 receptor prevents bladder contraction due to decrease in cytosolic calcium, whereas with M2 receptor causes relaxation.

**Pharmacokinetic**

**Absorption:** Tolterodine immediate release is rapidly absorbed and maximum serum concentrations typically occur within 1 to 2 hours after dose administration with Bioavailability being 77%. Food intake increases the bioavailability of tolterodine (average increase 53%)

**Distribution:** Tolterodine is highly bound to plasma proteins, primarily  $\alpha 1$ -acid glycoprotein. The volume of distribution 113 ± 26.7 L

**Metabolism:** Tolterodine is extensively metabolized by the liver following oral dosing. The primary metabolic route involves the oxidation of the 5-methyl group and is mediated by the cytochrome P450 2D6 (CYP2D6) and leads to the formation of a pharmacologically active 5-hydroxymethyl metabolite

**Elimination :** Half-life: Parent drug, as it is 1.9-3.7 hrs; active metabolite

(5-hydroxymethyl), 3 hr (8.7 hr in cirrhosis); Total body clearance: 5.7 L/kg/hr; Excretion: Urine (77%), feces (17%)

**INDICATIONS :** Urodine is indicated for the treatment of Overactive Bladder with symptoms of Urge Urinary Incontinence, Urgency, Frequency & Nocturia.

**CONTRAINDICATED:** Urinary retention, gastric retention or uncontrolled narrow-angle glaucoma. URODINE is also contraindicated in patients who have demonstrated hypersensitivity to the drug or its ingredients.

**Pregnancy Category : C**

"Tolterodine is rapidly effective in improving symptoms of OAB, producing maximum effect within 2 weeks of the treatment initiation."

*J. Am Urology, 1999.*

WHEN CONTROLLING URINE IS MAJOR PROBLEM

# URODINE

Tolterodine Tartrate 2 mg IR Tablets



**Time in Nepal with  
International Standard**

Under Collaboration with Square Pharma

**1**

**Less  
anticholinergic  
side effect**

**2**

**Safe & effective  
in both gender**

**3**

**Optimum used  
in developed  
country like USA**



Manufactured in  
Technical Collaboration  
with Pharma Giant

**SQUARE PHARMA**



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MBBS, MO, Lahan



**Dr. Barun Shrestha**  
Gastroenterologist, Bharatpur



**Dr. Sudeep Kaudel**  
Obs & Gynae, Bharatpur



**Dr. P.K. Sultania**  
General Physician, Kathmandu

**URODINE**

Tolterodine Tartrate 2mg IR Tablets

*Touching Lives, Delivering Promises*

Advancement In Technology with Square Pharmaceuticals

# Orosis-D



Calcium Carbonate 500 mg + Vit D3 200 IU Tablets



Manufactured in  
Technical Collaboration  
with Pharma Giant  
**SQUARE PHARMA**



## Product Information

Brand Name: OROSIS-D

Composition : Calcium Carbonate BP Equivalent to Elemental Calcium 500mg & Vitamin D<sub>3</sub> as Colecalciferol BP 200 IU Tablets

Pack Size: 10 × 10 Tablets

Therapeutic Category: Calcium Supplement

Dose: Twice a day

### PHARMACOLOGY:

Calcium is a mineral that is necessary for life. 99% of the calcium in our bodies is in our bones and teeth. Calcium/Vitamin D<sub>3</sub> prevent or treat negative calcium balance. It also helps facilitates nerve and muscle performance as well as normal cardiac functions. It is a bone mineral component: cofactor in enzymatic reactions, essential for neurotransmission, muscle contraction and many signal transduction pathways. Every day, we lose calcium through our skin, nails, hair, sweat, urine and feces. Our bodies cannot produce its own calcium.

Vitamin D is a fat soluble vitamin synthesized in body. Skin makes vitamin D in reaction to sunlight and

stores it in fat for later use. In OROSID-D Vitamin-D<sub>3</sub> plays role of enhancing calcium absorption from Intestine. It is necessary for the regulation of calcium and phosphate homoeostatic and bone mineralization. It also reduces bone loss. Clinical studies have shown that calcium and Vitamin D has synergist effect on bone growth as well as in Osteoporosis and fracture prevention.

### PHARMACOKINETICS:

Calcium carbonate has the bioavailability 25-35%. Whereas, Vitamin D is fat soluble and requires bile. It is absorbed in small intestine. Calcium is 40-45% protein bound. Vitamin D is hydroxylated hepatically to calciferol (25-hydroxyvitamin D),

then renally to the active metabolite calcitriol (1,25-dihydroxyvitamin D). 80% calcium is excreted as unabsorbed calcium in feces and 20% urinary via urine.

### INDICATIONS:

OROSIS-D is a calcium supplement that may be helpful in preventing deficiency. It may also be helpful in the treatment of high blood phosphorous levels in , low blood calcium levels, and proven.

"The FDA has approved calcium supplements for the treatment and prevention of calcium deficiency, which can lead to an increased risk of rickets, Osteomalacia, or Osteoporosis."



# MEDICAL MANAGEMENT OF OAB



**Prakash Chhetri**  
MCh Resident  
NAMS, Bir Hospital

## What is Overactive Bladder

Overactive bladder (OAB), as defined by the International Continence Society (ICS), is characterized by a symptom complex including urinary urgency with or without urge incontinence, usually associated with frequency and nocturia. In Asia, the prevalence of OAB is reported at 53.1%. In about 75%, OAB symptoms are due to idiopathic detrusor activity; neurological disease, bladder outflow obstruction (BOO), intrinsic bladder pathology and other chronic pelvic floor disorders are implicated in the others. OAB syndrome is a very common condition that affects people of all ages and may cause a severe impact on quality of life. OAB can be diagnosed easily and managed effectively with both non-pharmacological and pharmacological therapies.

## Healthy Bladder Functioning

A healthy bladder is free of bacterial infection or tumours and stores urine without discomfort at low pressure with intermittent signals of filling. Normal functional bladder capacity in adults ranges from approximately 300 to 400 ml.

Although the ICS defines urinary frequency as the perception by the patient that he/she voids too often. Epidemiological studies suggest that the normal micturition rate is approximately 8 micturitions per day and 1 or fewer episodes per night. As such, small volumes with increased micturition frequency suggest abnormality. Nerve fibers respond to increasing filling and micturition is prompted at or near bladder volume

## Drugs Used in the Treatment of Lower Urinary Tract Symptoms (LUTS), Overactive Bladder (OAB) and Detrusor Overactivity (DO): Assessments According to the Oxford System

	Level of Evidence	Grade of Recommendation
<b>Antimuscarinic Drugs</b>		
Atropine, hyoscyamine	3	C
Darifenacin	1	A
Fesoterodine	1	A
Imidafenacin	1	B
Propantheline	2	B
Solifenacin	1	A
Tolterodine	1	A
Trospium	1	A
<b>Drugs with mixed actions</b>		
Oxybutynin	1	A
Propiverine	1	A
Flavoxate	2	D
<b>Drugs acting on membrane channels</b>		
Calcium antagonists	2	D
Potassium channel openers	2	D
<b>Antidepressants</b>		
Imipramine	3	C
Duloxetine	2	C
<b>α-Adrenergic Receptor Antagonists</b>		
Alfuzosin	3	C
Doxazosin	3	C
Prazosin	3	C
Terazosin	3	C
Tamsulosin	3	C
Silodosin	3	C
Naftopidil	3	C

	Level of Evidence	Grade of Recommendation
<b>β-Adrenergic Receptor Antagonists</b>		
Terbutaline (b2)	3	C
Salbutamol (b2)	3	C
Mirabegron (b2)	1	B
<b>Phosphodiesterase Type 5 (PDE5) Inhibitors*</b>		
Sildenafil, tadalafil, Vardenafil	1	B
<b>Cyclooxygenase (COX) Inhibitors</b>		
Indomethacin	2	C
Flurbiprofen	2	C
<b>Toxins</b>		
Botulinum toxin (neurogenic)	1	A
Botulinum toxin (idiopathic)	1	B
Capsaicin (neurogenic)	2	C
Resiniferatoxin (neurogenic)	2	C
<b>Other Drugs</b>		
Baclofen	3	C
<b>Hormones</b>		
Estronogen	2	C
Desmopressin	1	A

Table shows that: Derifenacin, Fesoterodine, Solifenacin, Tolterodine and Oxybutynin; antimuscarinic are categorized as A grade for OAB.

capacity (approximately every 3–4 h based on volume of liquid consumed). Voiding typically occurs via initial relaxation of the pelvic floor muscles and the bladder neck followed by voluntary contraction of the detrusor muscle. Healthy voiding occurs promptly with strong continuous flow and complete emptying without pain or blood in the urine.

Changes in the adult bladder and pelvic floor muscles with ageing also include decreased bladder sensation, decreased contractility during voiding, decreased muscle tone in pelvic floor muscles and increased residual volume.

There is saying "your bladder is healthy if it is empty and even bladder is healthier if your bowel is empty"

### ◆ Muscarinic Receptors

Acetylcholine activates muscarinic receptors on detrusor myocytes and is the main contractile transmitter in the bladder. Five subtypes, of Muscarinic receptors ( $M_1$ – $M_5$ ), encoded by 5 distinct genes are identified. In the human detrusor smooth muscle  $M_2$  and  $M_3$  subtypes predominate, with  $M_3$  as the most important for detrusor contraction.

### ◆ Antimuscarinic Agents

For many years antimuscarinic drugs have been the gold standard for the treatment of OAB. As the name implies, they selectively block the muscarinic receptors in the detrusor muscle, thereby decreasing the ability of the bladder to contract.

They mainly act in storage phase, when there is normally no parasympathetic input to the LUT and results in decreasing urgency and increasing MCBC.

They are competitive antagonists, i.e. both the agonist and antagonist bind for the same site/receptors.

### Darifenacin Hydrobromide

- ◆  $M_3$  receptor antagonist
- ◆ Tertiary amine
- ◆ Three main circulating darifenacin metabolites – UK148993, UK 73689 and UK88862
- ◆ Controlled-released formulation; OD administration
- ◆ Dose – 7.5 and 15 mg/day
- ◆ Metabolized in the liver - <7.5 mg/day in moderate hepatic impairment
- ◆ Peak plasma time - 7 hrs
- ◆  $T_{1/2}$  = 13 - 19 hrs
- ◆ Pregnancy - Category C

### Tolterodine Tartrate

- ◆ Tertiary amine
- ◆ Rapidly absorbed and extensively metabolized by the cytochrome P450 system
- ◆ The major active 5-hydroxymethyl metabolite (5-HMT) has a similar pharmacologic profile as the mother compound and significantly contributes to the therapeutic effect of tolterodine
- ◆  $T_{1/2}$  - 2-3 hrs
- ◆ Urinary excretion
  - Tolterodine: 1 – 2.4 % of the dose
  - 5-HMT: 5 - 14 % of the dose
- ◆ No selectivity for muscarinic receptor subtypes
- ◆ Low incidence of cognitive side effects
- ◆ Oral high dose (6.4 mg) had a powerful inhibitory effect on micturition and also reduced stimulated salivation 1 hour after administration of the drug

(Stahl et al, 1995)

- ◆ Available in immediate release (TOLT-IR; 1 or 2 mg; twice daily) and extended release (TOLT-ER; 2 and 4 mg; once daily)
- ◆ Pregnancy – Category C

### Fesoterodine Fumarate

- ◆ Non-subtype selective muscarinic receptor antagonist
- ◆ Orally active prodrug that is converted to the active metabolite 5-HMT by nonspecific esterase
- ◆ Metabolized in the liver but a significant part (>15%) is excreted renally without additional metabolism
- ◆ Bioavailability ~ 25%, independent of food
- ◆  $T_{1/2}$  = 7-9 hrs
- ◆ Starting dose – 4 mg/day
- ◆ Can be used in patients with moderately impaired renal or hepatic function
- ◆ Pregnancy – No data

### Solifenacin Succinate

- ◆ Tertiary amine
- ◆ Modest selectivity for  $M_3$  over  $M_2$  (and  $M_1$ ) receptors
- ◆  $T_{1/2}$  45-68 hrs
- ◆ Undergoes significant hepatic metabolism
- ◆ Pregnancy – Category C

### Oxybutynin Chloride

- ◆ Tertiary amine
- ◆ Antimuscarinic effect and direct action on bladder muscle via blockade of voltage-operated  $Ca^{2+}$  channels
- ◆ Undergoes hepatic metabolism via cytochrome P450 system into multiple metabolites
- ◆ The primary metabolite, N-desethyloxybutynin (DEO) – pharmacological properties similar to those of the parent compound
  - Occurs in much higher concentrations after oral administration
  - Major cause of troublesome side effect of dry mouth
- ◆  $T_{1/2}$  = 2 hrs; but has wide inter-individuals variations
- ◆ Pregnancy – No data

### Mirabegron

- ◆  $\beta_3$  agonist
- ◆ Rapidly absorbed after oral administration
- ◆ Circulates in plasma as the unchanged form
- ◆ 55% is excreted in urine, mainly as unchanged form and 34% is recovered in feces, almost as unchanged form
- ◆ Highly lipophilic
- ◆ Metabolized in the liver via multiple pathways, mainly by cytochrome P450 and 2 D6
- ◆  $T_{1/2}$  = 23 – 25 hrs
- ◆ Pregnancy – No data

### ◆ Conclusion:

The number of antimuscarinics available is increasing and placebo-controlled, double-blind, randomized clinical trials have shown efficacy in OAB. Antimuscarinic agents are the first line treatment for OAB symptoms. Main adverse effects of antimuscarinic agents include dry mouth, constipation and headache.  $\beta_3$  agonist can be the alternative options where antimuscarinic side effects are concerned. We can individualize OAB treatment by working with each patient to identify the most effective and best tolerated agent.



डा. विभूति शाही  
स्त्री तथा प्रसूति रोग विशेषज्ञ  
सुखी परिवार क्लिनिक, कालिमाटी

# लेप्रोस्कोपिक सर्जरीको माग बढ्दो

## ◆ लेप्रोस्कोपिक अप्रेसन के हो ?

पेटमा ठूलो घाउ नबनाई नाइटोको तल तथा नाइटोको छेउछाउमा दुई-तीनवटा प्वाल बनाई औजार छिराएर गरिने उपचार विधिलाई लेप्रोस्कोपिक सर्जरी भनिन्छ । यसलाई दूरबिन शल्य चिकित्सा पनि भनिन्छ । यो अत्याधुनिक शल्य चिकित्सा पद्धति हो । यसमा पेटको अप्रेसन सानो घाउ बनाएर सम्पन्न गर्न सकिन्छ ।

## ◆ यो किन गरिन्छ ?

पाठेघर निकाल्नुपर्ने अवस्था, पाठेघरको ट्युमर निकाल्ने तथा पाठेघरको डिम्बमा पानीको फोका भए नभएको थाहा पाउन लेप्रोस्कोपिक गरिन्छ । बाँभोपनमा पाठेघरको नली खुल्ला छ कि छैन हेर्न पनि यसको प्रयोग गर्न सकिन्छ । अहिले पत्थरी निकाल्न पनि यसको प्रयोग गरिन्छ ।

## ◆ लेप्रोस्कोपिक किन उपयोगी छ ?

नेपालमा अहिले धेरै ठाउँमा यसको प्रयोग हुन थालेको छ । यसमा ठूलो घाउ हुँदैन ।

उमेर धेरै नभएको अवस्थामा यो विधि निकै उपयोगी छ । सौन्दर्यका हिसाबले पनि चिरेको दाग बस्दैन । पीडा तथा रक्तस्राव पनि कम हुन्छ ।

## ◆ लेप्रोस्कोपिक गरेपछि कुन कुरामा ध्यान दिनुपर्छ ?

अरु अप्रेसन गरेजस्तो यो अप्रेसन गरेपछि धेरै दिन आराम गरेर बस्नुपर्ने आवश्यकता रहँदैन । बढीमा १ हप्ता आराम गरे पुग्छ । भारी काम गर्ने अथवा गह्रौँ सामान उठाउने काम भने डेढ महिनासम्म गर्नुहुँदैन । सामान्य खाना खान सकिन्छ ।

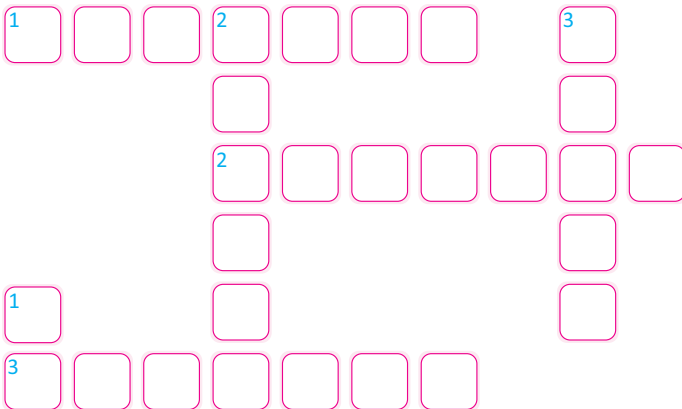
## ◆ यसको साइडइफेक्ट कतिको छ ?

नेपालमा यसको प्रयोग त्यति भएको छैन । अहिले धेरै मानिस सचेत हुन थालेकाले यसको लोकप्रियता बढ्दै गएको छ । यसको साइडइफेक्ट खासै छैन । कहिलेकाहीँ भने अप्रेसन गर्दागर्दै पिसाबथैली तथा आन्द्रामा घाउ हुन तथा प्वाल पर्न सक्छ । त्यसले गर्दा रक्तस्राव हुनसक्छ ।

## ◆ टिप्स

- ◆ लेप्रोस्कोपिक अत्याधुनिक सर्जरी भएकाले बिरामीले धेरै समय आराम गर्ने जरूरत पर्दैन ।
- ◆ यो सर्जरीपछि बिरामी छिट्टै ठीक हुन्छन् र आफ्नो नियमित काममा फर्कन सक्छन् ।
- ◆ यसलाई कसैकसैले होल सर्जरी तथा पिन होल सर्जरी पनि भन्छन् ।
- ◆ लेप्रोस्कोपिक सर्जरीमा सानो प्वाल मात्र बनाइन्छ ।
- ◆ इन्फेक्सनको सम्भावना कम हुन्छ । रक्तस्राव पनि कम हुन्छ ।
- ◆ धेरै छिटो रिकभरी हुन्छ । अस्पतालमा धेरै दिन बस्नुपर्दैन ।
- ◆ ठूलो एवं भद्दा चिराइबाट छुटकारा पाइन्छ ।
- ◆ बच्चा निकाल्नेबाहेक अरु कुरामा यो पद्धतिबाट उपचार गर्न सकिन्छ । पाठेघरको ट्युमर, पाठेघरको नलीमा शिथु बस्दा, डिम्बाशयमा सिस्ट पलाउँदा तथा पत्थरी आदिको उपचारमा यो विधि उपयोगी हुन्छ ।

Time, Square, Sinex, Crossid, Uroline, Rabepira



## MEDITIME

## CROSS-WORD

### Down:

- 1) What is the Brand name of Trimetazidine manufactured by TIME Pharma (5)?
- 2) To which Pharma Giant, TIME Pharma has recently collaborated (6)?
- 3) Star anticold tablets (5).

### Across:

- 1) Brand name of Calcium supplement with Vitamin D<sub>3</sub> of TIME Pharma (7).
- 2) First molecule of TIME Pharma manufactured in technical collaboration with Square Pharma, indicated for over active bladder (7)?
- 3) Brand of Rabepazole (7).



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TIME Pharmaceuticals

# Winner Pictures



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**Dr. Lalita Shah**  
Gynaecologist, Mirchiya



**Dr. Nirmal Lamichhane**  
Psychiatric, Pokhara



**Dr. Umesh Thapa**  
Dermatologist, Bharatpur

TIME Pharmaceuticals (P) Ltd. welcomes your comments/suggestions/inputs for coming issue of this bulletin.

Last date of "Cross Word" answers Submission : 15<sup>th</sup> Aswin 2076 (2<sup>nd</sup> Oct. 2019)

## RESPONSE FORM

Name : \_\_\_\_\_

Speciality : \_\_\_\_\_

Contact No. : \_\_\_\_\_

Birthday : \_\_\_\_\_ Anniversary Day: \_\_\_\_\_

Comments : \_\_\_\_\_

Clinical Address : \_\_\_\_\_

Email Address : \_\_\_\_\_

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# MOMENTS IN TIME



*Launching of URODINE*



*Participation in Dr. YB Rokka Book Launching Programm*



*Launching of URODINE*



*Transplant Conference*



*Drawing Competition for World Environment Day 2019*



*Awards for Annual Closing Function 2075-76*



*Team Work Game at GVR*



*Group Click at GVR*



## *Touching Lives, Delivering Promises*



We at **TIME Pharmaceuticals** believe in caring and healing our fellow citizens by delivering quality medicines with easy accessibility at affordable prices.



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