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The 455th International Symposium on Therapy

The 455th International Symposium on Therapy was held by the Zoom Webinar on July 21, 2022. Dr. Taro Kondo, Managing Director of the International Medical Society of Japan (IMSJ), presided over the meeting.

Topics related to excretion

Introductory Message from the Chair

Taro Kondo, MD, PhD
Managing Director, IMSJ

Thank you for watching our web lecture in the midst of the 7th wave of the COVID-19 pandemic.

Setting the theme of the 455th International Symposium on Therapy as "Topics related to excretion", we have invited two doctors, one from internal medicine and the other from urology, to deliver a lecture.

Especially in actual outpatient and home health care settings for the elderly, there are many issues related to their defecation and urination. Meanwhile, in recent years, guidelines for chronic constipation have been developed and several new medications have become available, and the diagnosis, treatment, etc. of overactive bladder, which relieves urinary urgency, has come to assume a more important role not only for urologists but for internists.

In Lecture I, Takeshi Mizukami M.D, Ph.D, the head doctor, Dept. of Endoscopy Center, NHO Kurihama Medical and Addiction Center, will speak on "Pathophysiology of chronic constipation inferred from abdominal X-rays and its treatment-effects of the social situation- ", while in Lecture II, Hikaru Tomoe MD, PhD, the professor, Department of Urology, Pelvic Reconstructive Surgery Adachi Medical Center, Tokyo Women's Medical University will talk about "Treatment of urinary frequency and urinary incontinence"

Lecture I

Pathophysiology of chronic constipation inferred from abdominal X-rays and its treatment -effects of the social situation-

Takeshi Mizukami M.D, Ph.D
The head doctor
Dept. of Endoscopy Center
NHO Kurihama Medical and Addiction Center

Chronic constipation is a functional bowel dysorder, symptoms of difficult, infrequent, or incomplete defecation predominate that persists for several months.
The difficulty in treating chronic constipation is that the patients do not understand their condition.

Mechanical obstraction, medications, and systemic illnesses can cause constipation and must be excluded, especially in new onset patients. Functional constipation is caused by disordered function of the colon and requires treatment of itself.

Chronic constipation can be divided into 3 broad categories: 1) Normal-transit constipation: Idiopathic constipation, constipation-dominant irritable bowel syndrome, secondary constipation such as drug-induced constipation and symptomatic constipation, 2) Slow-transit constipation: Constipation-dominant irritable bowel syndrome, and 3) Defecatory or rectal evacuation disorders: Rectal constipation and Dyssynergia.
Above 3 different pathophysiological conditions may overlap, which makes difficult to manage. Furthermore, at present in Japan, there is no way to diagnose the pathophysiological conditions.

Exclusion of organic diseases is the most important issue in the treatment of chronic constipation, and colonoscopy is often performed.
It is well known that colonoscopy in patients with constipation is difficult, indicating that the difficulty contributes to constipation.

"Colon morphological abnormalities" such as sigmoid colon malrotation and " Colon motility abnormalities" such as non-transporting segmental movements observed with an unanesthetized colonoscope, are factors that make colonoscopy difficult.
In constipation-predominant irritable bowel syndrome, which has abdominal pain associated with bowel movements, "colon morphological abnormalities" and "colon motility abnormalities" are more frequently observed, and the cecal intubation time is twice as long in IBS patients as in asymptomatic patients.

Colon morphology abnormalities inhibits defecation as it inhibit colonoscopic insertion, and it may cause abdominal pain associated with defecation and colonoscopic insertion in constipation-predominant irritable bowel syndrome with normal-transit time.

Non-transporting segmental movements may cause abdominal pain, and prolong the colon transit time and reduce stool tightly, resulting in constipation-predominant irritable bowel syndrome with slow-transit time. The stress events such as "going on a trip" are the triggers for constipation in patients with colon motility abnormalities (Intestinal Reseach 2017). As an indication of the same phenomenon, thirty percent of constipated patients are stress-related and their abdominal X-rays showed colonic spasm and hard, reduced stools (Gastroenterology. 1949) .

Summarizing these colon-related findings of endoscopy, abdominal X-ray, and interview,
(1)Slow transit constipation: Stress-related constipation-predominant irritable bowel syndrome and idiopathic constipation (spastic constipation).
From abdominal X-ray, the stool is hard and small, sometimes colonic spasms are observed.
(2)Normal transit constipation: Constipation-predominant irritable bowel syndrome. Colon morphological abnormalities inhibit the bowel

movement and cause pain.
From abdominal X-ray, sigmoid colon malrotation and universal mesenterium commune are observed and the stool is not so hard and small.
(3)Defecatory or rectal evacuation disorders: Rectal constipation due to decreased rectal perception, avoiding defecation leads to stool retention in the rectum and reduces rectal perception. Dyssynergia is a defecatory disorder that causes constipation symptoms due to a failure to effectively empty the rectum because of an inability to coordinate abdominal, rectoanal, and pelvic floor muscles.
From abdominal X-ray, stool retension in rectum without bowel movement is observed (Rectal constipation), stool retension in rectum with feeling of residual stool is observed (Dyssynergia),

Rendering a confident diagnosis, while providing both education and reassurance, is the essence of treatment.
(1) Slow transit constipation reduces the stool due to stress. Teach them not to stress itself.
(2) Normal transit constipation causes difficulty in defecation and abdominal pain. Instruct stretching and exercise in order to improve the passage of stool regardless of colon morphological abnormalities.
(3) Defecatory or rectal evacuation disorders is mainly caused by reduced rectal perception. Acting on the call to defecate and scheduling visits to the toilet are suggested. Dyssynergia requires special treatment in the proctology department.

Behavioral restrictions and psychosocial stress in the recent situation affect the above-mentioned pathophysiology of chronic constipation. Present a case and explain the above pathophysilogy of it.

Lecture II

Treatment of urinary frequency and urinary incontinence

Hikaru Tomoe MD, PhD
Professor
Department of Urology, Pelvic Reconstructive Surgery
Adachi Medical Center, Tokyo Women's Medical University

A large epidemiological survey on lower urinary tract symptoms (LUTS) in Japan showed that nocturia and increased daytime urinary frequency are the most common LUTS in both men and women. The second most common LUTS in men is slow stream.
The incidence of urinary incontinence in women increases with age. The percentages of women aged ≥ 20 years and ≥ 40 years with this condition are 25% and 40%, respectively; however, the percentage of patients who receive treatment is low (around 30%). Stress urinary incontinence (SUI) accounts for 49% cases of urinary incontinence.
SUI can be defined as urine leakage that occurs when abdominal pressure exceeds urethral pressure like during coughing, sneezing, or exercise. Pregnancy, delivery, and obesity are known to weaken the pelvic floor, causing urethral hypermobility and intrinsic urethral weaknesses, and ultimately leading to SUI. Pelvic floor muscle training (PFMT) and weight loss protocols are effective therapeutic strategies. Radical surgical therapeutic techniques include midurethral sling operations (such as tension-free vaginal tape and transobturator tape operations).
Overactive bladder (OAB) syndrome is characte rized by subjective symptoms such as urgency, increased daytime frequency, nocturia, and urgency urinary incontinence (UUI). OAB affects 12.4% of individuals aged ≥ 40 years, and its prevalence is known to increase with age. The percentages of patients with OAB and concomitant UUI were 41% and 64% in men and women, respectively. This condition negatively affects the patient's quality of life. Avoiding

excessive fluid intake to control urine output is the standard treatment in these patients. Pelvic floor muscle training (PFMT) and bladder training are also effective strategies. Pharmacological therapy using anticholinergic agents remains the mainstay of treatment for patients with OAB and concomitant UUI. However, these medications are associated with adverse drug reactions such as constipation, mouth dryness, and visual accommodation disorders, and may also lead to cognitive decline. Therefore, β_3-adrenoceptor agonists are considered the first-line drugs, particularly in older adults. Both patients who cannot tolerate high doses of OAB drugs due to adverse drug reactions and patients who don't respond well to the drugs after 8- to 12-weeks are diagnosed with refractory OAB. Intravesical injection of botulinum toxin A, which can be performed in an outpatient setting, is effective in such cases. Another treatment option for refractory OAB is sacral neuromodulation implant placement; however, this technique is more invasive than the intravesical injection of botulinum toxin A and requires hospitalization.

A cystocele is a form of pelvic organ prolapse (POP). In addition to dysuria and defecation disorder, patients with POP experience concomitant OAB symptoms. The risk factors for POP include advanced age, pregnancy, vaginal delivery, obesity, and hysterectomy. There are few reports that show that PFMT is effective in mild cases (i.e., stages below stage II); however, it has virtually no effect on severe cases. Pessary is also useful for treating POP. However, the continuation of pessary is difficult in many cases because it occasionally slips down unintentionally and the insertion is not suitable in patients with vaginal erosion. Transvaginal mesh surgery and laparoscopic sacrocolpopexy, which enable uterine prolapse repair without hysterectomy, have recently been performed. Robotic-assisted sacrocolpopexy was covered by the health insurance in April 2020 in Japan. Approximately 50% of patients with POP concomitantly experience OAB; however, OAB symptoms usually disappear or improve in approximately 60% of these patients if the POP is repaired using pessary or by surgery. This is because POP is usually accompanied by bladder outlet obstruction. The mechanism underlying this concomitant disease is similar to that underlying the relationship between OAB and benign prostatic hypertrophy (BPH).

BPH is typically a condition with hypertrophy of prostate, BOO and LUTS. The prevalence of BPH increases with age. BPH is associated with not only micturition and post-micturition symptoms, but also OAB which is one of storage symptoms. As medical treatment, there are a1 blocker, 5a-reductase inhibitor and PGE5 inhibitor, and surgical therapy is performed in cases in which the effect of the medical treatment is insufficient. OAB induced by BPH disappears or improves when the BOO is released by a1 blocker or surgery, but if OAB symptom does not improve, the drug for OAB is administered.

Nocturia is the most frequent symptom for both men and women, and it is the most influential symptom in daily life. The causes of nocturia include polyuria, nocturnal polyuria, bladder urinary storage disorder, and sleep disorder. Of these causes, nocturnal polyuria is the most common, and nocturnal polyuria occurs in about 80% of patients with nocturia. Most of the causes of nocturnal polyuria come from medical disorders such as obstructive sleep apnea syndrome, occult congestive heart failure and lower limb edema. After these diseases are treated, nocturnal polyuria will decrease and nocturia will also improve.

Discourse

Introduction of the speaker of discourse

Taro Kondo, MD, PhD
Managing Director, IMSJ

Mr. Taisuke Abiru, Senior Research Fellow, The Sasakawa Peace Foundation, will give a lecture titled "Ukrainian war and the world after that".
On February 24, about 5 months before the setting of this project, Russia launched missile attacks. This war is still going on, and now takes on the aspect of a proxy war by the West providing new weapons to Ukraine in addition to an invasion of Ukrainian territory by Russia. The world economy has become unstable due to many difficult issues, including energy problems represented by oil and natural gas, food problems resulting from the halt of wheat exports, and the problems of accepting refugees. Why did Russia decide to invade? What will happen in the future? We would like to hear his answers to those questions.

Discourse: Ukrainian war and the world after that

Taisuke Abiru
Senior Research Fellow
The Sasakawa Peace Foundation

Looking back to the Cold War era, there was originally a Cold War structure between the Soviet Union and the West in Europe then.
At that time, the North Atlantic Treaty Organization (NATO) and the Warsaw Pact Organization were facing off against each other. However, after the end of the Cold War and the collapse of the Soviet Union, while the Warsaw Pact Organization disappeared, NATO continued to expand eastward.
The Soviet Union has been dismembered, and now even Ukraine has started to think about joining NATO.
And, why President Putin has now launched a military invasion against Ukraine? He gives three reasons:

- Ukraine has been becoming a military fort by NATO. The possibility of future Ukrainian membership in NATO is posing an essential threat to Russia.
  →National security issue
- The Ukrainian government has no intention of implementing the Minsk Protocol (on ceasefire/peace in the civil war in eastern Ukraine). Instead, it is committing genocide against people living there.
  →Humanitarian issue

- Historically, Russia and Ukraine are inseparable. The independence of Ukraine leads to the total denial of the past since the Russian Empire. Ukraine has never been a true nation.
  →Historical issue

There are probably various ways to resolve this military invasion if it is really only a security and/or a humanitarian issue, but, if it is a war based on the historical view, there is probably no room for compromise between the two sides.
In the process leading up to this military invasion, President Putin has published papers and made statements externally that quite emphasize historical issues:

- In July 2021, President Putin published a paper on the historical unity with Ukraine.

- On June 9, 2022 (the 350th anniversary of the birth of Peter the Great), President Putin made the following statement:
  "What Peter the Great did was to take back (our lands) and strengthened. The same task is imposed on us."
  →President Putin's goal is not solely to prevent Ukraine from joining NATO, but to bring Ukraine back under Russian influence.

Assuming President Putin's view of history, the goal of this war would not be reached unless at least Russia completely controls the Novorossiya region, which has a large Russian-speaking population,

including the Donbass region.
I have recently traveled to America and discussed with an expert, sharing the view that this battle is very unlikely to be overwhelmingly won by either side and will probably be extended further and further. The only positive prospect is that Russia will only be able to continue the battle at the current pace for a few more months, and after that, it may have to stop battling at least once in order to supply soldiers and weapons. There could be a temporary cease-fire, for example, by the end of the year, but it would not mean a permanent peace, and Putin would continue to battle with setting his eyes on Novorossiya and other regions.

This battle also has implications for the global economy as detailed below:

● Energy
Russia is the world's largest exporter of natural gas. It is also the world's second largest oil exporter, and the world's third largest coal exporter. Further, Russia is the world's largest supplier of enrichment services for nuclear fuel used in nuclear power plants. (Probably around 20% of nuclear fuel used in American nuclear power plants is provided from Russian uranium enrichment services.)

● Agriculture
Russia is the largest exporter of wheat in the world. It is also a major producer of nitrogen, phosphorus, and potassium - the three major components of fertilizer. In addition, Russia is the world's second largest exporter of sunflower oil and safflower oil.

● High-tech products/services
Russia produces palladium more than any other countries in the world (32%), which is essential for semiconductors and electric vehicle batteries. It accounts for 11% of the world's share of nickel production as well. Russia and Ukraine make up 40-50% share of neon gas for semiconductor production.

● Metal
Russia is the world's third largest exporter of steel. Also, Russia and Ukraine are the world's largest exporters of pig iron. Russia is the world's second largest producer of aluminum after China. Additionally, Russia is a major producer of cobalt and copper.

● Aerospace/Aviation
Russia is the third largest titanium producer in the world. The airspace over Russia is a major air route.

Given the above, it would be quite difficult to completely eliminate Russia from the global economy, and Russia has not been completely eliminated yet. Since Russia is well aware of this situation, it is putting pressure by tactically taking the global economy as a hostage including energy and food issues.

Prospecting how the world will be going forward, we tend to picture a confrontational structure between the Western bloc imposing sanction on Russia and China/Russia, but the Global South countries take the stance of not entirely sanctioning Russia, not entirely on the side of the West, or not actively supporting Russia.
From a larger historical perspective, whereas the former Cold War structure was one in which the U.S. and the Soviet Union divided the whole world in two, the world after this Ukraine war is not so simple. Specifically, although the Western bloc versus China and Russia have emerged as one axis of conflict, the rest of the countries, the Global South, play a very large part. Which side will take in such countries has become a key point, and this would be a long battle because it will not be settled so easily.
Japan was troubled even just by China and North Korea in terms of its national security, but now that having imposed economic sanctions on Russia, it will have to squarely consider these three countries from now on and is likely to face a very difficult situation.