April-June 2019
Volume 16 Issue 2

ISSN 2222-5188

Info Medicus

The essence of medical practice

Overview of sleep disorders

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Editorial Board

EDITORIAL

Dear Doctor,

We thank you for your all out support and appreciations of our previous issue of Info Medicus. We would like to be your trusted partner working together towards adding value to life. In this connection, our team has been working effortlessly to accomplish your academic quest at all times. We assure you of our best commitment to bring the most recent developments in the health segments around the globe at your desk.

In this issue, we have introduced two new fascinating sections. One is Patient Handouts that physicians can provide to their patients. The other is Update on the Medical Research. We hope that these two contemporary sections will be helpful to you in your day to day medical applications.

Recently, sleep disorder has become a leading cause of depression among people. Apart from medications mental support is also needed for such patients. Hence, we have highlighted the topic overview of sleep disorders in Review article section. Besides, the other sections are presented as usual.

Your trust in us is a motivational factor to do our best continuously. We assure you that in our upcoming issues we shall bring more up to date information that will add value to your clinical practices.

Thanking you and warm regards

(Dr. S. M. Saidur Rahman)
General Manager
Medical Services Department

(Dr. Rumana Dowla)
Manager
Medical Information & Research

Helpful tips for breastfeeding

How soon should mother breastfeed her baby?

Unless the baby needs immediate medical attention, mother should have skin to skin contact with her baby right away after giving birth. Mother should breastfeed within the first hour, even if it means breastfeeding before her baby is weighed or bathed.

How long mother should breastfeed?

Mother should breastfeed for at least the first six months of her baby's life. Mother should not give her baby other foods or liquids during this time. Mother can keep breastfeeding for as long as her baby wants, but mothers are encouraged to do it for at least one year.

Are there any reasons why mother shouldn't breastfeed?

Women who have breast implants, breast reductions, infections after delivery or who have babies who are tongue tied, have jaundice or are in intensive care can all try to breastfeed. However, mothers who have HIV should not breastfeed. If mother or her baby is having trouble breastfeeding, then she should talk to the physician right away.

What is a lactation consultant?

A lactation consultant is an expert in breastfeeding. He or she can help the mother if she is having problems (for example, if her baby has trouble latching onto the nipple, if mother has pain with breastfeeding, or if she don't make enough milk).

What if mother don't have enough milk for the baby?

If mother thinks that she is not making enough milk, then she is adviced to talk to her physician or lactation consultant. Be sure to drink 60 to 80 ounces of fluids per day and eat a healthy diet of fruits, vegetables, and proteins. Feed the baby whenever he or she seems hungry (usually 10 to 12 times a day). Each feeding can last about 20 to 30 minutes (10 to 15 minutes on each breast).

What if mother have nipple or breast pain?

The pain can be caused by the baby not latching correctly. Mother could also have pain because mother's nipples are cracked, mother's breasts are overfilling with milk, or have an infection in mother's breast. Even if mothers are having any of these problems, they should keep breastfeeding. If mother's breasts are painful because they are overfilling with milk, some medicines, massage, moist heat, or pumping out breast milk could help. If mother's have nipple pain or dryness, they can use breast milk or moisturizers to soften the nipple.

Reference: Am. Fam. Physician., 15 September 2018; 98(6)

Bleeding in early pregnancy

What causes bleeding during early pregnancy?

About one in every four pregnant women will have vaginal bleeding in the first few months. Mild cramping and light spotting can be normal in early pregnancy. But vaginal bleeding may be a sign of something more serious. Some of the most common causes are:

- Threatened miscarriage: This is when there is bleeding from the uterus but the pregnancy is still healthy. Sometimes a blood clot forms in the uterus and increases the risk of miscarriage. But most women with threatened miscarriage will have a healthy baby.
- Ectopic pregnancy: This is when the pregnancy grows outside the uterus, usually in the fallopian tubes. Symptoms include heavy bleeding, dizziness, sharp pain in the stomach or shoulder and cramps. Ectopic pregnancy is a medical emergency and can be life threatening.
- Early pregnancy loss (also called miscarriage): This is the unexpected loss of a pregnancy before 14 weeks. Most miscarriages happen because the pregnancy is not developing normally.

  Other causes of bleeding in early pregnancy include infections, hemorrhoids (swollen veins in the rectum or anus), cervical cancer and rare pregnancy related cancers.

What should patients do if they are having bleeding?

Patients should go to the physician right away. Physician can do tests to see why patients are bleeding. Patients may need a pelvic examination, an ultrasound, blood tests or urine tests. If it is still early in the pregnancy, patients may need more tests to find the cause of the bleeding.

How it is treated?

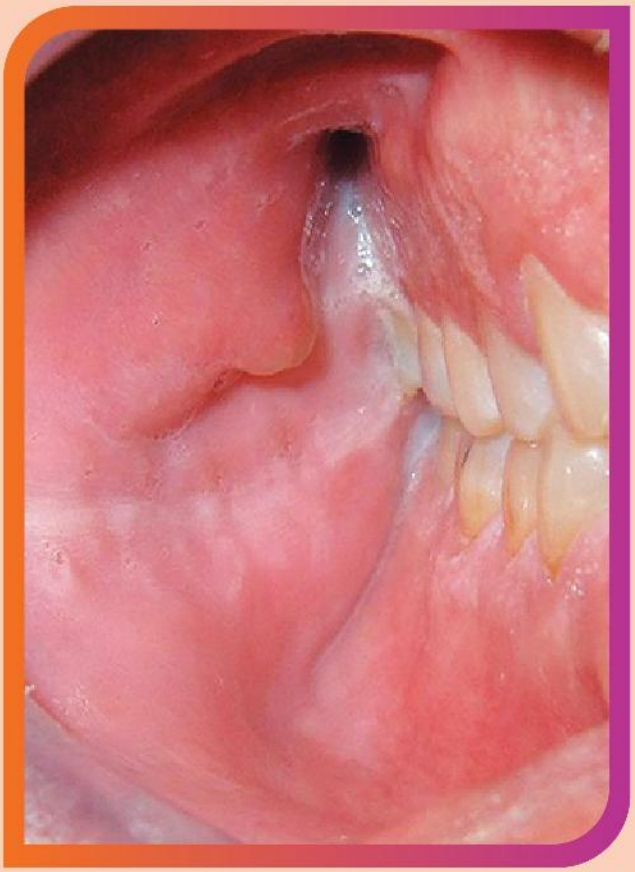
It depends on the cause of bleeding. No treatment is needed for a threatened miscarriage. Ectopic pregnancies need to be treated with medicine or surgery. After a miscarriage, the tissue may pass on its own. If not, patients may need medicine or a procedure.

What can patients do to prevent early pregnancy loss?

There is no way to prevent an early pregnancy loss after it has been diagnosed. Most women who have had an early pregnancy loss can have healthy pregnancies in the future. If patients have had two or more early pregnancy losses, she is adviced to talk to her physician about whether she needs other tests or treatment.

Reference: Am. Fam. Physician., 1 February 2019;99(3)

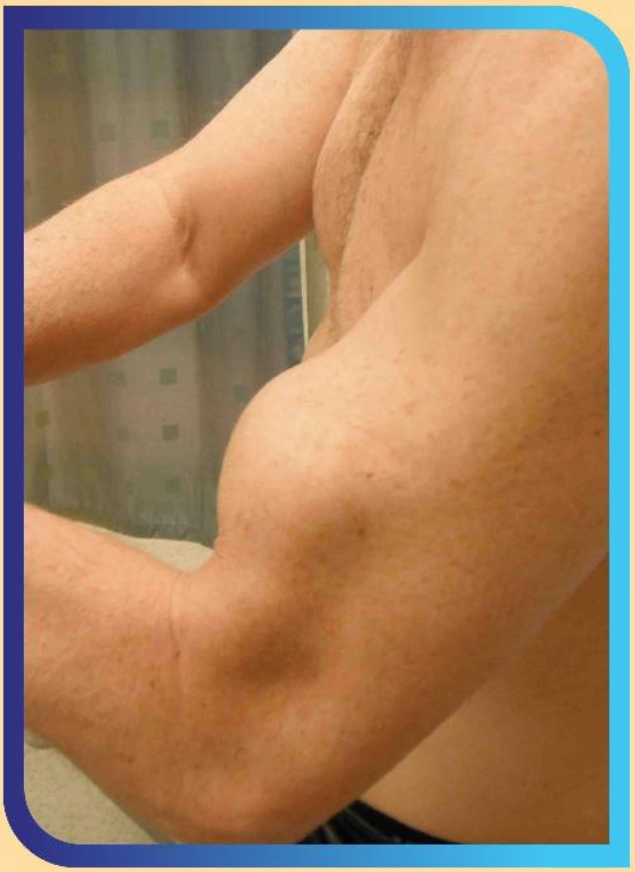
Obstructive parotitis



A 51 year old man presented to the emergency department with a 3 day history of pain and swelling on the right side of his face, fever and dry mouth. On physical examination, firm right preauricular swelling was noted with erythema of the overlying skin. An oropharyngeal examination revealed dry oral mucosa and swelling adjacent to the right parotid papilla, with no saliva expressed from the orifice. Maxillofacial computed tomography showed changes consistent with inflammation in the parotid gland and surrounding tissues, with marked dilatation of the parotid duct and a small calcified mass proximal to the duct orifice. Acute parotitis can be caused by obstruction of the parotid duct, with concomitant inflammation, resulting from bacterial super infection of the oral flora. A combination of stasis, a change in the salivary contents and infection can lead to the formation of stones in the salivary duct that can in many cases be visualized on radiography because of their high calcium content. This patient underwent surgical removal of the stones, stenting of the duct and treatment with antibiotics and his condition improved rapidly.

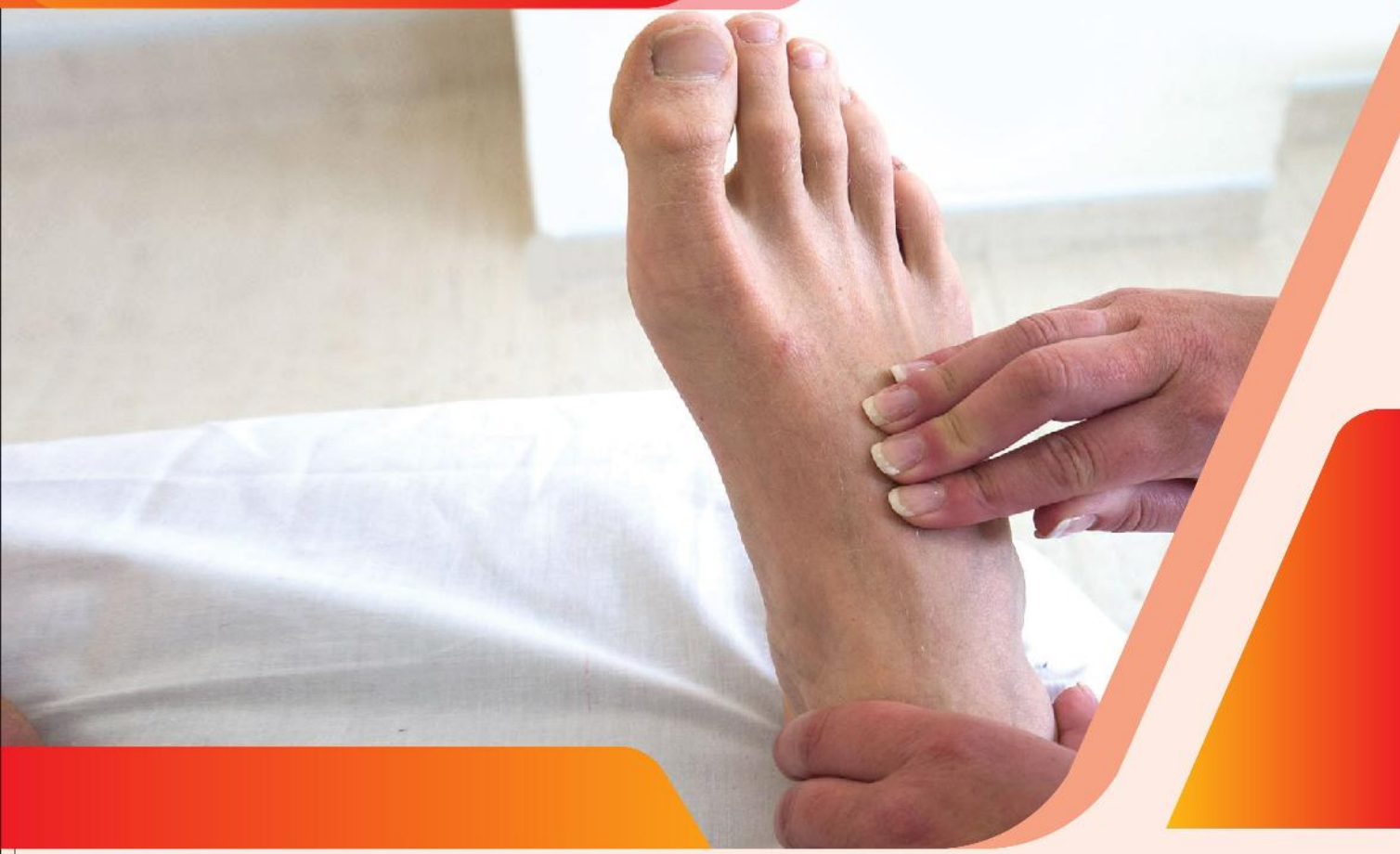
Reference: N. Eng. J. Med., 14 June 2012, Vol. 366, N. 24

Popeye sign



A 79 year old man presented to the orthopedic clinic with a large bulge on his left upper arm. The bulge had developed 2 days before presentation when he was lifting an object and felt a sudden sharp pain in his left shoulder. A physical examination revealed an obvious deformity in the anterior mid upper arm that became more pronounced during elbow flexion known as popeye sign or popeye deformity. Magnetic resonance imaging of the shoulder revealed a complete rupture of the long head of biceps tendon and is caused by bulging of the biceps muscle belly after rupture of the biceps tendon. Rupture of the biceps tendon usually occurs proximally and often occurs in older patients as a result of the shoulder joint and associated muscles, tendons and ligaments undergoing degenerative changes associated with overuse and aging. Nonoperative management is often sufficient for ruptures of the proximal biceps tendon. This patient was treated with nonsteroidal anti-inflammatory drugs. At follow up 4 months after the initial presentation, the patient's pain was reduced and no longer affected his daily life.

Reference: N. Eng. J. Med., 16 November 2017, Vol. 377, N. 20



Clinical assessment of peripheral arterial disease of the lower limbs

Overview

Arterial perfusion of the lower limbs is commonly encountered in general and specialist practice and has both acute and chronic presentations. A systematic assessment of patients with this condition is essential to prevent limb or tissue loss.

Indications

Clinical assessment of peripheral arterial disease of the lower limbs is indicated in atherosclerosis, thrombosis, embolism, traumatic damage to the arterial wall, compression of the arterial lumen (e.g., popliteal entrapment syndrome) or changes in the arterial wall (e.g., thromboangiitis obliterans), in patients with ulcers or in those who are about to undergo surgery of a lower limb.

Preparation

A Doppler probe and a blood pressure cuff should be available for the examination. Obtain consent to perform the examination. Ask how the patient is feeling and whether there is any pain or tenderness. The patient should have been instructed to remove clothing such that the lower limbs are completely exposed. Place the patient in the supine position, either lying flat or lying with the head of the bed at a 45 degree angle.

Examination

When examining a hospitalized patient, observe the bedside environment for indicators of the patient's functional status or for evidence of risk factors for vascular disease. Look at the patient's hands for tobacco stains or cyanosis and assess the temperature of the hands. Check the patient's radial or carotid pulse to rule out atrial fibrillation. Obtain blood pressure measurements in both arms.

Inspection

In general, inspection of the lower limbs focuses on changes in the skin (including color, scars, and ulcers), swelling or wasting of the soft tissue and deformity of the bones.

Skin: Examine the abdomen for scars resulting from previous surgery to the aorta or iliac vessels. Look for scars on the legs resulting from previous procedures. Carefully examine the groin by stretching the skin folds open. Assess the medial aspect of the legs for scars caused by lower limb bypass surgery, such as a femoral

popliteal or femoral distal bypass procedure. Always assess the color of the skin. Look for pallor or cyanosis which may indicate hypoperfusion.

In contrast, erythema may be caused by an underlying infection such as cellulitis or an abscess. Purulent discharge through a wound or sinus is suggestive of a deep, infected collection. Also identify areas of darker skin which may represent dry or wet gangrene. Look for thin skin, hair loss, and hypertrophic changes in the toenails, which may indicate chronic ischemia. An ulcer is a break in the epithelial surface of the skin or mucosa. Identify any leg ulcers, making sure to inspect the heels and the skin between the toes. Note the location, size, edges and base of any ulcers that are present.

Soft tissue: Inspect the legs for swelling or wasting of the soft tissues. Swelling may be caused by infection, abscess formation, lymphedema or pathologic venous conditions such as deep vein thrombosis. A unilaterally swollen leg should be viewed as having an underlying pathologic vascular condition unless proved otherwise. The patient should also be examined for a wasting condition. Wasting can be a sign of ischemia, neurologic injuries or long term inactivity resulting from pain or a generally poor functional state.

Bones: Lower limb amputations can be a marker of end stage arterial disease or previous trauma. Also examine the limbs for the presence of deformities or fractures that may compress and occlude arteries and thus lead to ischemia.

Palpation

Skin and soft tissues: Feel the patient's skin with the back of the hand to assess the temperature. Use the fingers and palms to palpate for tenderness. Inquire about pain, during palpation of different areas and note the patient's facial expression to identify signs of discomfort. In patients with acute ischemia or trauma, be aware that compartment syndrome may be developing and it can occur even in the presence of palpable pulses.

Pulses: Begin by palpating the aorta. Use two hands to palpate the aorta above the umbilicus and slightly to the left of the midline (Figure-1). Palpate the common femoral pulse just below the groin crease at the level of the midinguinal point. The midinguinal point is the middle of an imaginary line running from the anterior superior iliac spine to the pubic symphysis. With the patient's knee slightly flexed and relaxed in the hands, palpate the popliteal pulse which is not always readily palpable. It is easiest to feel this pulse by placing the index and middle fingers of both hands deep in the popliteal fossa (Figure-2).

Identify the dorsalis pedis pulse by asking the patient to lift the great toe upward. This pulse will be found lateral to the extensor hallucis longus tendon which becomes visible when the great toe is in dorsiflexion (Figure-3). Palpate the posterior tibial pulse behind the medial malleolus. This pulse is located halfway between the malleolus and the Achilles' tendon (Figure-4).

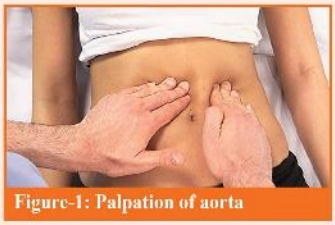


Figure-1: Palpation of aorta


Figure-2: Palpation of popliteal pulse


Figure-3: Palpation of dorsalis pedis

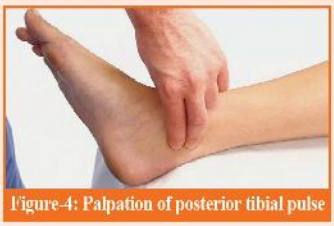


Figure-4: Palpation of posterior tibial pulse

Capillary refill time: Assess capillary refill time by gently pressing on the pulp of the toe or the nail bed for 3 seconds and counting the time needed for reperfusion to occur. A refill time that is longer than 3 seconds is abnormal.

Bones: Palpate the bones of the legs and feet, checking for tenderness, step deformity, and abnormal mobility. Deformities or fractures may compress and occlude arteries and lead to ischemia.

Special tests

Buerger's test: The test of leg elevation known as Buerger's test is used to detect poor blood flow in a critically ischemic limb. Ask the patient to lift one leg off the bed. Support the straight leg at a 45 degree angle from the bed and observe it for the development of pallor. In a patient with normal arterial anatomy or only moderate atherosclerosis, the color in the leg will not change. If leg elevation leads to pallor, place the leg in a dependent position and as reperfusion occurs, observe the leg for reactive erythema or dependent rubor.

Doppler ultrasonography: The flow of blood in the common femoral, popliteal, dorsalis pedis, and posterior tibial arteries and in any prosthetic or venous bypass grafts can be assessed with the use of Doppler ultrasonography. Healthy arteries produce a triphasic flow signal. As the severity of arterial stenosis increases, the waveform becomes biphasic and then monophasic and is eventually absent.

Summary

When performing a vascular arterial assessment of the legs, bear in mind the underlying arterial anatomy and its effect on perfusion of the skin, soft tissues, and bones. If the patient has signs of peripheral arterial disease, obtain a rapid consultation with a vascular specialist.

Reference: N. Eng. J. Med., 3 May 2018, Vol. 378, N. 18

Reversible dilated cardiomyopathy as a complication of adrenal cortex insufficiency

Addison's disease, also known as primary adrenal insufficiency, is a disorder that occurs when the body produces insufficient amounts of cortisol and aldosterone. The failure of adrenal glands is most commonly the result of autoimmune disease. Other causes include tuberculosis, cancer or its treatment and bleeding into the adrenal glands. It is associated with nonspecific symptoms such as fatigue, weight loss, skin hyperpigmentation, hypoglycemia and nausea. Cardiovascular manifestations of Addison's disease include hypotension, arrhythmias and syncope. In extremely rare instances, Addison's disease can be complicated with dilated cardiomyopathy. Here a case of Addison's disease associated with dilated cardiomyopathy which responded to treatment with corticosteroids has been described.

Case

An 11 year old girl presented with a two month history of diffuse abdominal pain, yellowish vomiting after meals, a low grade fever that responded to anti pyretic medications, malaise, and polyuria. A physical examination on admission revealed mild pallor, light pigmentation on the lips and a body mass index (BMI) of 17.9 kg/m^2. On clinical examination her blood pressure was 80/50 mm of Hg, temperature 37°C, heart rate 100 beats/minute, and respiratory rate 20 breaths/minute. There was no jugular venous distention, no lymphadenopathies and no organomegalies, heart and lung auscultation were normal. She had no signs of peripheral edema. Her mini mental state examination score was 26/30 and her Glasgow Coma Scale (GCS) was 15/15. Her muscle strength, tone, and reflexes were all normal. Sensory examination and cranial nerves were normal. She had been treated with nitrofurantoin for recurrent urinary tract infections. Her medical history included no other medications. There was no significant family, social, or environmental history.

On investigation, complete blood count showed reduced white blood cells of 3940 cells/mm^3 with neutrophils/lymphocytes of 52/26, Hb 9 g/dl, platelets 240,000/mm^3, and mean corpuscular volume 77 fl, sodium 129 mEq/l, potassium 4.53 mEq/l, creatinine 0.97 mg/dl, chloride 105 mEq/l, ionized calcium 1.25 mmol/l, alkaline phosphatase 223 IU/l, fasting glucose 97 mg/dl, glycated hemoglobin (HbA1c) 4%, C-reactive protein (CRP) 19.6 mg/l, and ESR 112 mm/hour. TSH and free thyroxine (FT4) were within normal

range. Serial measurements of serum glucose were within normal limits. A blood smear showed hypochromic microcytic anemia. Widal, wright, and tuberculin tests were negative. Abdominal and pelvic ultrasonography was normal. An upper gastrointestinal endoscopy revealed erosions in the fundus and body of the stomach. A chest X-ray showed increased cardiothoracic ratio (Figure-1). An echocardiogram indicated dilated left ventricle where left ventricular dimensions were 55 × 44 mm, decreased fractional shortening and ejection fraction of 26%, paradoxical septal movements, pulmonary blood flow of 0.7 m/second, and grade 2 mitral valve insufficiency. The right chambers were within normal range. Urine culture revealed growth of *Klebsiella* species. Voiding cystourethrogram revealed no abnormal findings.

Based on her physical examination she was euvolemic. To correct the euvolemic hyponatremia, water intake was restricted to 75% of the calculated daily need. Despite this, hyponatremia did not resolve. A cardiac ultrasound suggested dilated cardiomyopathy so cardiomyopathy management protocol such as digoxin, furosemide, spironolactone, and captopril was initiated with no remarkable improvement. She was also started on trimethoprim or sulfamethoxazole for the urinary tract infection until urine culture became negative. Her history along with the physical examination findings and laboratory evaluation suggested adrenal insufficiency. She underwent tests for the adrenal cortex function. Her random serum cortisol was 4.25 mcg/dl, adrenocorticotropic hormone 1500 pg/ml, and 17-hydroxyprogesterone 0.7 ng/ml. Hyponatremia, low cortisol, and high ACTH along with her symptoms suggested primary adrenal cortex insufficiency. She was treated with 100 mg/m² intravenously administered hydrocortisone which was gradually reduced to 20 mg/m² orally administered hydrocortisone before discharge. Remarkable improvement was noted within days of starting treatment. A heart echocardiogram before discharge (dimensions were 53 X 42 mm, ejection fraction (EF) 42.6% and fractional shortening (FS) 21.2%) showed considerable improvement.

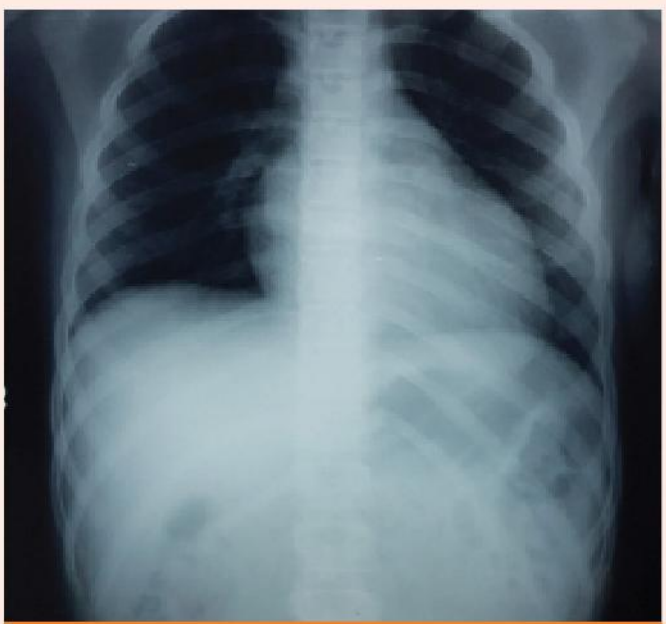


Figure-1: Posteroanterior chest -X ray showing increased cardiopulmonary index

During the 6 months after discharge, she was followed up to observe the clinical, laboratory, and radiologic improvements. Serial echocardiograms showed gradual restoration of cardiac function to near normal status. There were no signs of chronic mucocutaneous candidiasis or autoimmune hypoparathyroidism if present it would suggest autoimmune polyglandular syndrome type 1 (APS1). Since autoimmune polyglandular syndromes, congenital adrenal hyperplasia, bleeding into the adrenals, and tuberculosis were excluded and she had no history of glucocorticoid therapy, the cause of her adrenal insufficiency is mostly autoimmune. Immunologic tests to confirm this were not available.

Discussion

A case of adrenal insufficiency in an 11 year old girl which was complicated with dilated cardiomyopathy was presented. Glucocorticoid replacement therapy led to near complete restoration of normal cardiac function. Primary adrenal insufficiency is rare in children. Dilated cardiomyopathy is an extremely rare complication of adrenal insufficiency. Despite having a low EF, patient did not present with edema, possibly due to the impaired renin-angiotensin-aldosterone system caused by Addison's disease. Therefore, it is important to note that Addison's disease could mask the accompanying heart failure. There are several reports of cardiomyopathy associated with secondary adrenal insufficiency, which suggest that a hypocortisol state may be the cause of cardiomyopathy regardless of its etiology. In this case cardiomyopathy preceded the treatment with corticosteroids and improved after it. Adrenal insufficiency has also been associated with transient left ventricular apical ballooning known as Takotsubo cardiomyopathy. This type occurs exclusively in adult patients. It is known that glucocorticoid deficiency down regulates the expression of adrenergic receptors resulting in cardiovascular collapse.

Summary

The case presented, underscores two important issues, one is the rare cardiac manifestation of Addison's disease in the form of dilated cardiomyopathy and the other one is reversibility of this cardiomyopathy if the underlying disease is treated.

Reference: J. of Med. Cas. Rep., 2018, Vol. 12, N. 345

Baby born from deceased donor's transplanted uterus

The world's first baby was born to a woman who had a uterus transplant from a deceased donor. A 6 pound baby girl was delivered by C-section to an unidentified young woman who had been born without a uterus. Dr. Dani Ejzenberg who led the transplant team and practices at the University of Sao Paolo said that the birth shows that pregnancies involving a uterus from a deceased donor are viable. Doctors said that such transplants can be successful. The first uterus transplants from live donors were a medical milestone, creating the possibility of childbirth for many infertile women with access to suitable donors and the needed medical facilities. Dr. Ejzenberg stressed that it is rare that living women are willing and eligible to donate a uterus to a family member or close friend. That is why the new report is so important. Dr. Ejzenberg said in a news release that the use of deceased donors could greatly broaden access to this treatment, and the results provide proof of concept for a new option for women with uterine infertility. There have been 10 other uterus transplants from deceased donors performed, but this one is the first to result in a live birth. Dr. Ejzenberg's team reported, the recipient in this case was a 32 year old woman who was born without a uterus, and the donor was a 45 year old woman who died of a stroke. The recipient received five immunosuppression drugs (needed to prevent rejection of the new uterus by the body), antibiotics, anti-blood clotting treatment and aspirin while in hospital. Immunosuppression therapy continued after she left the hospital until the time of her baby's birth. The baby girl was born at 35 weeks and three days. The mother and baby were discharged from the hospital three days after birth. At the age of 7 months and 20 days, the baby continued to breastfeed and weighed 15 pounds, 14 ounces.

Dr. Tomer Singer, who directs reproductive endocrinology at Lenox Hill Hospital in New York city said that success in this case really could be a breakthrough. Up to 15% of couples suffer from infertility and every year thousands of women are using gestational carriers in order to conceive. He says, uterine transplantation can help many couples in achieving their dream of parenthood, and using a uterus from a deceased organ donor increases the number of donors available significantly. Singer added that it also eliminates the main challenge, which is finding a matching donor and risking the lives of live donors who have to otherwise undergone a major surgery to remove their uterus.

Reference: www.medicinenet.com

Overview of sleep disorders

Introduction

Sleep disorders are brain disorders that cause interruptions in sleep patterns. They prevent people from getting enough sleep. The brain regulates sleep and is the only organ known to require or benefit from sleep. Not getting enough sleep can affect quality of life. Sleep is defined as the optimal amount of sleep required for an individual to remain alert and fully awake so that he or she can function adequately throughout the day. Getting enough sleep depends on psychological and physiological needs or state. Environmental factors, such as light and darkness, normally synchronize one's sleep pattern in accord with the prevailing day-night cycle. That is, the existence of environmentally autonomously generated rhythms suggests that we have an internal biological clock that determines how long we sleep. This internal clock is located in the suprachiasmatic nuclei (SCN) of the hypothalamus above the optic chiasm. The neurons in the SCN are responsible for generating circadian rhythms implicated in many physiologic processes, including the sleep wake cycle, body temperature and neuro-endocrine secretion processes. Melatonin, secreted mostly during the night, reaches its maximum value between 3:00 AM and 5:00 AM after which it decreases to low levels during the daytime. It helps to regulate sleep and wakefulness and functions as an antioxidant as well as an anti-inflammatory agent. However, these functions can be altered by factors such as traveling to different countries that have different seasons, different time zones or different climates. In addition, a change in the amount of noise that is experienced, the presence of intrusive thoughts, excess heat or cold, or an increase or change in the work hours can disrupt the daily sleep routines. However, one's work schedule clearly affects one's physiological and psychological functions, including the circadian rhythm, and those who do not adjust well to this situation may be more clearly at risk for health issues than those that do.

Physiology of sleep

Sleep is a fundamental necessity that is required by all of us. In general the average requirement of sleep for a healthy adult is between seven and eight hours per night. Sleep is divided into two types. Rapid eye movement (REM) sleep and non-rapid eye movement (non-REM) sleep. REM sleep, as the name suggests, is characterized by rapid movements of the eyes, while in non-REM sleep there is little or no movement of the eyes and any eye movement is slow.

There are five stages of sleep
Stage 1 is superficial sleep and only lasts for about 5-10 minutes. It is the transition from being awake to going to sleep. Body movement slows down, there is some loss of muscle tone and there may be twitching or sudden myoclonic jerks. During this time it is easy to be aroused.
Stage 2 is light sleep and accounts for around 50% of sleep in adults. Muscle movement decreases, eye movements stop, heart rate slows and the body temperature can drop. This stage lasts about 20 minutes.
Stage 3 is the start of deep or slow wave sleep. Brain waves during this stage are called delta waves due to slow speed and large amplitude.
Stage 4 is also deep or slow wave sleep, lasts for around 30 minutes and is the restorative period of sleep. During this stage it is hard to be aroused and if woken then a period of disorientation and sedation often occur.
Stage 5 is REM sleep. It occurs rapidly after stage 4 and accounts for around 25% of sleep in adults. During REM sleep, there is increased brain activity and dreaming occurs. It is believed that processing and consolidating of information and emotions occur while in REM sleep. During this time, heart rate and respiration increase and atonia occurs causing a temporary paralysis. These five stages of sleep make up the sleep cycle, which lasts for about 90 minutes. This cycle is generally repeated 5-6 times each night.

Classification

As per international classification of sleep disorders, most sleep complaints can be categorized into five namely:

- Hypersomnia
- Insomnia
- Circadian rhythm disorders
- Parasomnias
- Sleep problems associated with other disorders

Hypersomnia

The most common cause of day time sleepiness is volitional sleep deprivation during previous nights. Sleepiness, not explained by volitional sleep deprivation, can be due to sleep disorders like obstructive sleep apnea and narcolepsy.

Obstructive sleep apnea (OSA): Obstructive sleep apnea is one of the most common medical disorders causing day time hypersomnia, affecting over 2% of adult women and 4% of adult men. Though OSA is more frequent among middle aged, overweight males, it may be seen even in children (3% of all children) and thin individuals. It is seen primarily in people who are loud snorers and is characterized by collapse of the upper airway during sleep. This upper airway collapse may be associated with a fall in the blood oxygen level and results in repetitive arousals (up to 100/hour of sleep) to re-establish upper airway airflow. These brief arousals are not usually perceived by the individual, but the sleep disruptions result in excessive day time sleepiness. Obstructive sleep apnea is a risk factor for heart diseases and type 2 diabetes.

Narcolepsy: Narcolepsy is a neurological disorder affecting one in 2,000 individuals. It is characterized by the tendency to fall asleep during day time, despite having obtained an adequate amount of sleep the preceding night. Other symptoms of narcolepsy include cataplexy (sudden brief spells of muscle weakness), hypnagogic (occurring at the onset of sleep) or hypnopompic (occurring at the end of sleep) hallucinations, sleep paralysis and automatic behavior. It has shown that wakefulness and sleep are not mutually exclusive states, and that one state can intrude into the another, often resulting in striking consequences. Narcolepsy has a clear genetic component, with over 90% of individuals with narcolepsy carrying the HLA-DR2/DQ1 (current nomenclature HLA-DR15 and HLA-DQ6) gene (found in less than 30% of the general population).

Insomnia

Insomnia is the most prevalent sleep complaint in general population. It can be described as the inability to obtain sleep that is long enough to give a feeling of being rested or refreshed the following day. Although some insomnia may be constitutional in nature, there is evidence that untreated insomnia is a risk factor for the development of psychiatric problems, such as depression or substance abuse. Depression may cause insomnia, and insomnia may cause depression. Insomniacs experience an overall increase in arousal and cortisol secretion.

Restless legs syndrome: Restless legs syndrome (RLS) is one of the most common causes of severe insomnia. It is a neurological sensory or movement disorder affecting 5% to 15% of the general population. The condition is characterized by four essential features: (1) the intense urge to move the legs, usually accompanied or caused by uncomfortable sensations (e.g., creepy crawly, aching) in the legs (2) symptoms that begin or worsen during periods of rest or inactivity (3) symptoms that are partially or totally relieved by movements such as walking or stretching and (4) symptoms that are worse or only occur in the evening or at night. Restless legs syndrome is also characterized by a vague and difficult to describe unpleasant sensation in the legs. Patients often have difficulty in describing the unpleasant sensations. Restless legs syndrome sensations are unlike any experienced by unaffected individuals. This discomfort appears particularly during the transition from wake to sleep. Patient's exhibit "restlessness of their legs" as movement of the legs relieves these distressing sensations. There is a susceptibility gene locus, which would explain why RLS is often found to be familial.

Circadian rhythm disorders

Daily rhythm of rest activity cycles of all living creatures is linked to the geophysical light dark cycle. The primary symptom of circadian rhythm disorders is the inability to sleep during the desired sleep time. The individual's biological clock finds it difficult to adjust to the demands of the geophysical environment. Wake sleep schedule disorders could be primary, where there is malfunction of the biological clock per see or it could be secondary, which results from environmental effects upon the underlying clock. Delayed sleep phase syndrome (DSPS) and advanced sleep phase syndrome (ASPS) are the common primary circadian rhythm disorders. In DSPS, the patient falls asleep late and rises late. Individuals suffering from ASPS fall asleep early and awaken earlier than desired. Human genetic studies have identified specific genes associated with both advanced and delayed sleep phase syndromes.

Parasomnias

Parasomnias are defined as the unpleasant or undesirable behavioral or the experimential phenomena that occur predominantly or exclusively during sleep. The common parasomnias result from an overlap of "awake behavior" during sleep. The admixture of wakefulness and NREM sleep result in the most common NREM parasomnia called "disorders of arousal" such as sleep walking or sleep terrors. Admixture of wakefulness and REM sleep result in REM sleep behavior disorder.

NREM parasomnias: The disorders of arousal are the most impressive and most common, of the NREM sleep parasomnias. They occur during stages III and IV of NREM sleep. As these sleep stages are present in abundance during the first third of the sleep cycle, the disorders of arousal are also more common during this period. They are common in childhood, usually decreasing in frequency with increasing age. Occurrences of stages III and IV of NREM sleep also decrease with advancing age. Disorders of arousal include confusional arousals, somnambulism (sleep walking) and sleep terrors. Confusional arousals are often seen in children and are characterized by movements in bed, occasionally thrashing about or inconsolable crying. Sleep walking is prevalent in childhood (1%-17%), peaking at 11-12 years of age, and is common in adults (nearly 4%). The sleep terror is the most dramatic disorder of arousal, frequently initiated by a loud, blood curdling scream associated with extreme panic, followed by prominent motor activity such as hitting the wall, running around or out of the bedroom, even out of the house, resulting in bodily injury or property damage.

REM sleep parasomnias: The most common REM sleep parasomnia is the REM sleep behaviour disorder (RBD). In patients with RBD, somatic muscle atonia which is one of the defining features of REM sleep is absent, permitting the acting out of dream mentation, often with violent or injurious results. REM sleep behaviour disorder in humans occurs in both acute and chronic forms. The acute form is often due to undesirable side effects of antidepressant medicines, like serotonin reuptake inhibitors. The chronic form of REM sleep behaviour disorder is usually either idiopathic or associated with neurological disorders.

Sleep problems associated with other disorders

A large number of mental, neurological and other medical disorders are associated with disturbances of sleep and wakefulness. The division into mental and medical categories is somewhat arbitrary. Most mental disorders can have an associated sleep disturbance. Psychoses, mood disorders, anxiety disorders, panic disorders and alcoholism are commonly seen in patients presenting with sleep complaints. Most psychotic patients experience some degree of sleep disruption during exacerbations of their illness. Neurological disorders that are commonly associated with sleep disturbance are degenerative disorders, epilepsy and headaches.

Cerebral degenerative disorders, dementia and Parkinson's disease are commonly recognized neurological disorders that are associated with sleep disturbance. Epilepsy may be exacerbated by sleep disturbance and may occur predominantly during sleep. Therefore, the term "sleep related epilepsy" is used to denote those forms of epilepsy that are highly associated with the sleep state. Electrical status epilepticus of sleep has a high degree of association with non-REM (NREM) sleep. Headaches, particularly migraine and cluster headaches, can occur predominantly in sleep. Sleeping is one disease, which is rare outside the continent of Africa. Sleeping sickness is a parasitic disease, caused by the protozoa *Trypanosoma*. The symptoms include disturbed sleep cycle, with day time slumber and night time insomnia.

Diagnosis

The first step in assessing a patient with a sleep disorders must be clinical based on history and physical examination before laboratory tests are done.

History and physical examination

The history should include details about sleep habits; history of current or previous medical, neurological and psychiatric illnesses; drug and alcohol consumption as well as family history. The entire 24 hour span must be included in brief history and not just symptoms occurring at sleep onset or during sleep at night. It is important to conduct an interview with the patient's bed partner or care giver (or parent in case of a child) for diagnosis of abnormal movements and behavior as well as breathing disorders during sleep. The bed partner may also be in a position to answer questions about the patient's sleeping habits, history of drug use, history of stress at home, work or school and changes in sleep habits.

Completing a sleep questionnaire or keeping a sleep log or diary

over a 2 weeks period may give important indications of sleep habits and sleep hygiene. Family history may be important in certain sleep disorders such as narcolepsy, RLS, OSA and partial arousal disorders. History must be followed by careful physical examination to document evidence of various medical disorders such as respiratory, cardiovascular, endocrinological or neurological disorders, especially those that affect the brain stem region or the neuromuscular system.

Examination may also uncover upper airway anatomical abnormalities, which are noted in many cases with OSA. There are also several scales available to assess subjective degree of sleepiness, such as Stanford Sleepiness Scale, Visual Analogue Scale and Epworth Sleepiness Scale.

Laboratory studies

Laboratory assessment must be considered an extension of the history and physical examination and is described in Table-1.

Table-1: Laboratory tests to assess sleep disorder

- Diagnostic workup for the primary or co-morbid condition causing sleep disturbance
- Laboratory tests for the diagnosis and monitoring of sleep disorders
- Overnight polysomnography (PSG)
- Multiple sleep latency tests (MSLT)
- Maintenance of wakefulness test
- Actigraphy
- Video-PSG
- Standard electroencephalography (EEG) and video-EEG monitoring for suspected seizure disorders
- Imaging studies
- Upper airway imaging for obstructive sleep apnea syndrome
- Neuroimaging studies (e.g., computed tomography, magnetic resonance imaging) and cerebral angiography in cases of suspected neurological illness causing sleep disorder
- Positron emission tomography and single photon emission computed tomography in special situations
- Miscellaneous tests
- Pulmonary function tests in cases of suspected bronchopulmonary and neuromuscular disorders causing sleep disordered breathing
- Histocompatibility leukocyte antigen for suspected narcolepsy
- Cerebrospinal fluid hypocreatin 1 levels in suspected narcolepsy
- Serum iron and ferritin levels for patients with restless legs syndrome
- Electromyography (EMG) and nerve conduction studies to exclude co-morbid or secondary restless legs syndrome

Treatment

Treatment of hypersomnia

Obstructive sleep apnea (OSA): Obstructive sleep apnea causes hypertension so treatment with continuous positive airway pressure (CPAP) decreases blood pressure in patients with obstructive sleep apnea, especially those with severe obstructive sleep apnea and daytime sleepiness. The most effective treatment for obstructive sleep apnea is continuous positive airway pressure, which serves as a pneumatic splint to the upper airway. Autotitrating continuous positive airway pressure is another option that automatically adjusts the pressure within a set range in response to apneas, hypopneas, snoring or flow limitation. Patients who cannot tolerate continuous positive airway pressure may be treated with bi-level positive airway pressure. Compliance with continuous positive airway pressure therapy is challenging for many patients. Other treatment options include weight loss, positional therapy, surgical approaches, oral appliances and provent therapy (a nasal device that has an expiratory valve to create positive end expiratory pressure to keep the upper airway open). Choosing one of these therapies depends on obstructive sleep apnea severity, patient preference and tolerance.

Narcolepsy: Cataplexy, sleep paralysis and hypnagogic hallucinations can be treated with REM suppressing antidepressants, such as venlafaxine or other selective serotonin reuptake inhibitors. Sleepiness may be managed with adequate sleep hygiene and scheduled daytime naps. Otherwise, modafinil 200-800 mg daily or stimulants such as methylphenidate 10-100 mg daily or dextroamphetamine 5-60 mg daily can be used. Besides gamma hydroxybutyric acid (sodium oxybate) can be used in patients with narcolepsy. Sodium oxybate is usually administered twice per night because of its short half life, and is effective for both daytime sleepiness and cataplexy.

Treatment of insomnia

The choice of treatment of insomnia depends on the specific insomnia symptoms, their severity and expected duration, coexisting disorders, the willingness of the patient to engage in behavioral therapies, and the vulnerability of the patient to the adverse effects of medications. Patients with an acute onset of insomnia of short duration often have an identifiable precipitant (e.g., a medical illness or the loss of a loved one). In patients with chronic insomnia, appropriate treatment of coexisting medical, psychiatric and sleep disorders that contribute to insomnia is essential for improving sleep. Nevertheless, insomnia is often persistent even with proper treatment of these coexisting disorders. Treatment for chronic insomnia includes two complementary approaches: cognitive behavioral therapy (CBT) and pharmacologic treatments.

Cognitive behavioral therapy (CBT): Cognitive behavioral therapy addresses dysfunctional behaviors and beliefs about sleep

that contribute to the perpetuation of insomnia and it is considered the first line therapy for all patients with insomnia, including those with coexisting conditions that is described in Table-2.

Pharmacologic therapy: Several medications, with differing mechanisms of action, are used to treat insomnia, reflecting the multiple neural systems that regulate sleep. Roughly 20% of adults use a medication for insomnia in a given month, and many others use alcohol for this purpose. Nearly 60% of medication use is with nonprescription sleep aids, primarily antihistamines. However, diphenhydramine was a best benefit for either mild intermittent insomnia or insomnia in the elderly and caused daytime sedation and anticholinergic side effects (e.g., constipation and dry mouth) that are particularly problematic in older persons.

Benzodiazepine receptor agonists: They vary predominantly in their half life, the specific choice of drug from this class is usually based on the insomnia symptom. Medications is for bedtime use, with the exception of specifically formulated sublingual zolpidem at a dose of 1.75 mg for women and 3.5 mg for men. Short acting agents e.g., zolpidem at a dose of 2.5 mg, and zaleplon at a dose of 5 mg can also be used effectively to promote a return to sleep as long as 4 hours remain before the user plans to get up in the morning. The use of very long acting benzodiazepines e.g., clonazepam, which has a half life of 40 hours is for uncomplicated insomnia

Sedating antidepressants: The use of sedating antidepressants to treat insomnia takes advantage of the antihistaminergic, anticholinergic and serotonergic and adrenergic antagonistic activity of these agents. At the low doses commonly used for insomnia, most have little antidepressant or anxiolytic effect. Trazodone is used as a hypnotic agent by roughly 1% of adults, generally at doses of 25-100 mg. Doxepin, a tricyclic antidepressant, is used for the treatment of insomnia at doses of 3-6 mg. It has shown significant effects on sleep maintenance (time awake after sleep onset and total sleep time) but no significant benefit for sleep onset latency beyond 2 days of treatment. Mirtazapine has antidepressant and anxiolytic efficacy at doses used for insomnia and is a reasonable first option if patients have insomnia coexisting with those disorders, but it may cause substantial weight gain.

Others: Suvorexant is and orexin antagonist which was used for the treatment of insomnia, showed decreased time to sleep onset, decreased time awake after sleep onset and increased total sleep time. At higher doses (30-40 mg), suvorexant showed persistent efficacy for these measures after 1 year of nightly use; lower doses have not been studied for more than 12 weeks. Its major side effect at lower doses is morning sleepiness. Gabapentin is occasionally used for insomnia, predominantly in patients who have had an inadequate response to other agents, who have a contraindication to benzodiazepine receptor agonists (e.g., a history of drug or alcohol abuse) or who have neuropathic pain or the restless legs syndrome.

Restless legs syndrome: Pharmacologic treatment of restless legs syndrome depends on the frequency of symptoms which is given in Table-3. Dopaminergic agonists are first line therapy for patients with nightly, persistent symptoms. Common adverse effects of dopaminergic agonists include insomnia, nasal congestion, swelling of the extremities and daytime sleepiness. There have also been reports of increased tendency toward compulsive behaviors, such as gambling, in patients taking these medications. In patients with iron deficiency, iron supplementation may improve or resolve symptoms of restless legs syndrome.

Table-2: Components of cognitive behavioral therapy for insomnia

Component	Intended effect	Specific directions for patients
Sleep restriction	Increase sleep drive and stabilize circadian rhythm	Reduce time in bed to perceived total sleep time (not less than 5–6 hours), choose specific hours on the basis of personal preference and circadian timing, increase time in bed gradually as sleep efficiency improves
Stimulus control	Reduce arousal in sleep environment and promote the association of bed and sleep	Attempt to sleep when sleepy, get out of bed when awake and anxious at night, use the bed only for sleep or sexual activity (e.g., no watching TV in bed)
Cognitive therapy	Restructure maladaptive beliefs regarding daytime and health consequences of insomnia	Maintain reasonable expectations about sleep; review previous insomnia experiences, challenging perceived catastrophic consequences
Relaxation therapy	Reduce physical and psychological arousal in sleep environment	Practice progressive muscle relaxation, breathing exercises, or meditation
Sleep hygiene	Reduce behaviors that interfere with sleep drive or increase arousal	Limit caffeine and alcohol, keep bedroom dark and quiet, avoid daytime or evening napping, increase exercise (not close to bedtime), remove bedroom clock from sight

Table-3: Medications for restless legs syndrome		
Symptoms	**First choice**	**Alternative choice**
Occasional	Carbidopa or levodopa 10-25 mg/100 mg at bedtime, as needed	Opiates such as oxycodone, 5-10 mg at bedtime, as needed
Frequent	Dopaminergic agonist such as pramipexole, 0.125 mg, or ropinirole, 0.25 mg, at bedtime; increase dose every third night to a maximum of four tablets or until symptoms are controlled	Opiates such as oxycodone, 5-10 mg at bedtime, as needed
Nightly	Dopaminergic agonist such as pramipexole, 0.125 mg, or ropinirole, 0.25 mg, at bedtime; increase dose every third night to a maximum of four tablets or until symptoms are controlled rotigotine transdermal patch, 1 mg per 24 hours; increase dosage once weekly to a maximum of 3 mg per 24 hours (for moderate to severe symptoms)	Gabapentin and pregabalin Gabapentin, 300 mg at bedtime; increase dose every three or four nights to a maximum of 1,800 mg Pregabalin, 25 mg at bedtime, increase dose every four nights to a maximum of 100 mg Opiates
Painful	Gabapentin and pregabalin Gabapentin, 300 mg at bedtime; increase dose every three or four nights to a maximum of 1,800 mg pregabalin, 25 mg at bedtime; increase dose every four nights to a maximum of 100 mg Opiates	Dopaminergic agonists pramipexole, 0.125 mg, or ropinirole, 0.25 mg, at bedtime; increase dose every third night to a maximum of four tablets or until symptoms are controlled Rotigotine transdermal patch, 1 mg per 24 hours; increase dosage once weekly to a maximum of 3 mg per 24 hours

Treatment of circadian rhythm disorder

Treatment options vary based on the type of disorder and how severely it is affecting the quality of life. Options included are:

- Behavior therapy: This includes standardizing sleep times, getting regular exercise, and avoiding caffeine and stimulating activities before bedtime
- Bright light therapy: 30-60 minute treatments to reset the circadian clock
- Medications: Medications such as such as melatonin, wake-promoting agents and short term sleep aids can help
- Chronotherapy: Adjusting sleep times by 1-2 hours per day to shift the sleep cycle will be useful

Treatment of parasomnia

Parasomnic attacks in healthy children and adolescents normally require no treatment. Some cases respond to a psychological approach. Parents should be taught to avoid waking the children, instead, they should gently accompany them to bed. Several conditions or substances that increase stage 3, NREM sleep may trigger arousal parasomnias. Avoiding or treating these conditions is usually sufficient, with pharmacotherapy considered only when the episodes are frequent or dangerous to the patient or others. In the cases of nocturnal wandering or violent parasomnias, parents should make the environment as safe as possible (securing windows, removing obstacles, installing alarms) to avoid serious injuries. Clinicians should consider therapy if the episodes cause undesirable secondary consequences, such as excessive daytime sleepiness or cause distress to the patient or family. The most widely prescribed therapies in adults with arousal disorders are clonazepam (0.5-2 mg at bedtime) and imipramine. The effectiveness of clonazepam for suppressing these disorders relates to inhibition of arousals or of locomotor activity, rather than to pharmacologic suppression of stage 3 NREM sleep. The treatment of REM behavior disorder comprises primarily the prevention of potentially dangerous situations that can expose the patient to injuries. The first line pharmacologic treatment is clonazepam at low doses at bedtime. This is effective in most patients, but the motor behavior often relapses after it is stopped. Melatonin 3-12 mg at bedtime, pramipexole 0.18-0.72 mg, or levodopa are also effective.

References: 1. J. of Obe. And Eat. Dis., 2015, Vol. 1, N. 2:2
2. Ame. Aca. Of Neuro., 2012
3. Prog. In Neuro. And Psych., September/October 2013
4. The Ind. J. of Ches. Dis. And Alli. Sci., 2008, Vol. 50
5. Ind. J. Med. Res., February 2010, Vol. 131
6. Am. Fam. Phy., 15 August 2013, Vol. 88, N.4:231-238
7. N. Eng. J. Med., 8 October 2015, Vol. 373, N. 15:1437-1444
8. Epilepsia, 53, 2012, Suppl. 7
9. Understand sleep disorders, Cleaveland clinic

Bioactive signaling in next generation pharmacotherapies for heart failure

Importance: The standard pharmacotherapy for heart failure (HF), particularly HF with reduced ejection fraction (HFrEF), is primarily through the use of receptor antagonists, notably inhibition of the renin angiotensin system by either angiotensin converting enzyme inhibition or angiotensin II receptor blockade (ARB). However, the completed prospective comparison of angiotensin receptor neprilysin inhibitor (ARNI) with an ACE inhibitor to determine impact on global mortality and morbidity in heart failure (PARADIGM-HF) trial identified that the use of a single molecule (sacubitril or valsartan), which is an ARB and the neutral endopeptidase inhibitor (NEPi) neprilysin, yielded improved clinical outcomes in HFrEF compared with angiotensin converting enzyme inhibition alone.

Observations: This review examined specific bioactive signaling pathways that would be potentiated by NEPi and how these would affect key cardiovascular processes relevant to HFrEF. It also addressed potential additive or synergistic effects of ARB. A number of biological signaling pathways that may be potentiated by sacubitril or valsartan were identified, including some novel candidate molecules, which will act in a synergistic manner to favorably alter the natural history of HFrEF.

Conclusions and relevance: This review identified that activation rather than inhibition of specific receptor pathways provided favorable cardiovascular effects that cannot be achieved by renin angiotensin system inhibition alone. Thus, an entirely new avenue of translational and clinical research lies ahead in which HF pharmacotherapies will move beyond receptor antagonist strategies.

Reference: JAMA Cardiol., 28 November 2018

Benefits of improved air quality on aging lungs - impacts of genetics and obesity

Introduction: The beneficial effect of improving air quality on lung function in the elderly remains unclear. We examined associations between decline in air pollutants and lung function and effect modifications by genetics and body mass index (BMI) in elderly German women.

Methods: Data were analysed from the prospective study on the influence of air pollution on lung function, inflammation and aging (SALIA; N=601). Spirometry was conducted at baseline (1985-1994; 55 years), in 2007-2010 and in 2012-2013. Air pollution concentrations at home addresses were determined for each time point using land use regression models. Global lung initiative 2012 *z*-scores were calculated. Weighted genetic risk scores (GRS) were determined from lung function related risk alleles and used to investigate interactions with improved air quality. Multiple linear mixed models were fitted.

Results: Air pollution levels decreased substantially during the study period. Reduction of air pollution was associated with an increase in *z*-scores for the forced expiratory volume in 1 s (FEV_1) and the ratio between FEV_1 and forced vital capacity (FVC). For a decrease of 10 $\mu g \cdot m^{-3}$ in nitrogen dioxide (NO_2), the *z*-score for FEV_1 increased by 0.14 (95% confidence interval [CI]: 0.01; 0.26). However, with an increasing number of lung function related risk alleles, the benefit from improved air quality decreased ($GRS \times NO_2$ interaction: p=0.029). Interactions with BMI were not significant.

Conclusions: Reduction of air pollution is associated with a relative improvement of lung function in elderly women, but also depends on their genetic make up.

Reference: European Respiratory Journal, 2019

Gynecologic cancer in HIV positive women: a systematic review and meta analysis

Objective: While there is a significant body of literature on cervical cancer in HIV positive women, little is known about other gynecologic cancers in this population. The objective of this systematic review and meta analysis is to describe the incidence, presentation, treatment and outcomes for HIV positive women with non AIDS defining gynecologic cancers.

Study appraisal and synthesis methods: Two authors independently reviewed abstracts and full text articles for inclusion and assessed study quality. Pooled estimates of incidence were calculated using random effects models. Pooled estimates of cancer presentation and outcomes were averaged from case studies.

Results: Of 5,744 abstracts screened, we identified 70 articles on 58 studies on 292,202 women with HIV and 528 women with HIV and gynecologic cancer for inclusion. Most articles (53%) focused on incidence and only 3, 4 and 20 articles focused on treatment and outcomes of endometrial, ovarian and vulvovaginal cancers respectively. The standardized incidence ratios for endometrial, ovarian and vulvovaginal cancers were 4.38 (95% CI 0.26-8.49) for endometrial cancer, 3.21 (95% CI 2.29- 4.13) for ovarian cancer and 21.93 (95% CI 13.50-30.35) for vulvovaginal cancer. 57% of women were diagnosed at an early stage and all received cancer treatment.

Conclusions: In women with HIV, the incidence of ovarian and vulvovaginal cancer were higher than the general population, while incidence of endometrial cancer was similar. However, there was a paucity of data on treatment and outcomes for non AIDS defining gynecologic cancers. Given the increased incidence of gynecologic cancer, specific research on this population is essential to improve treatment and outcomes for HIV positive women.

Reference: American Journal of Obstetrics & Gynecology

Increased mortality of patients with childhood onset inflammatory bowel diseases, compared with the general population

Background and aims: Childhood onset inflammatory bowel disease (IBD) is believed to be a more severe disease than adult onset IBD, but there is little information on all cause and cause specific mortality in patients with childhood onset IBD. We performed a population based cohort study, with 50 years of follow up, to estimate absolute and relative risks for overall and cause specific mortality in patients with childhood onset IBD, during childhood and adulthood.

Methods: We identified children with a diagnosis of IBD (younger than 18 years) in the Swedish nationwide health registers (1964-2014; n = 9442) and individuals from the general population matched for sex, age, calendar year, and place of residence (reference group; n = 93,180). Hazard ratios (HR) for death were estimated using Cox regression separately in patients with ulcerative colitis (n = 4671), Crohn's disease (n = 3780), and IBD unclassified (n = 991). HRs were compared among calendar periods.

Results: During 138,690 person years of follow up, 294 deaths (2.1/1000 person years) occurred among the patients with IBD compared with 940 deaths in the reference group (0.7/1000 person years; adjusted HR, 3.2; 95% CI 2.8-3.7). Mean age at end of follow up was 30 years. HRs were increased for patients with ulcerative colitis 4.0, 95% CI 3.4-4.7; Crohn's disease 2.3, 95% CI 1.8-3.0; and IBD unclassified 2.0, 95% CI 1.2-3.4. Among patients younger than 18 years, there were 27 deaths from IBD 4.9, 95% CI 3.0-7.7. Among young adults with IBD, we found no evidence that HRs for death decreased from 1964 through 2014 (P = .90).

Conclusions: Children with IBD have a 3 fold increase in risk of death when followed through adulthood. The relative risk for death has not decreased with development of new drugs for treatment of IBD.

Reference: Gastroenterology, February 2019; 156(3): 614-622

HISTORY OF WORLD HEALTH DAY

There are many types of diseases in the environment by which many of the people are suffering from many kinds of diseases. It is important for people to get every knowledge of the health to make the health of the people better for lots of work to be accomplished. World Health Day is used to celebrate with lots of people to provide them with awareness about the health. It is important to look after the health of every people to make them more stable and strong to complete any task easily and quickly. World Health Day started in 1948 and is observed on 7th April every year. World assembly of health was started in the year 1948 in the Geneva by World Health Organization (WHO) where the celebration of the World Health Day on the 7th April decided. The day is celebrated by WHO and many other organizations for the people to make them understand and know the importance of health and to build awareness about health.

Advanced Chemical Industries Limited

Medical Services Department, Advanced Chemical Industries Limited
89 Gulshan Avenue, Simpletree Anarkali, Dhaka-1212