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# MEDICUS

The essence of medical practice

***Iron deficiency anemia***

The background of the lower half of the cover is a detailed, 3D-rendered illustration of numerous red blood cells. The cells are depicted as biconcave discs in various sizes and orientations, set against a warm, glowing orange and red background that suggests a microscopic or cellular environment. The lighting creates highlights and shadows on the cells, giving them a realistic, textured appearance.

## Contents

<b>Review Article</b>	<b>3</b>
<b>Clinical Method</b>	<b>6</b>
<b>Case Review</b>	<b>8</b>
<b>Health News</b>	<b>9</b>
<b>Clinical Image</b>	<b>10</b>
<b>View Point</b>	<b>11</b>
<b>Practice</b>	<b>13</b>
<b>Info Quiz</b>	<b>15</b>

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## Editorial

Dear Doctor,

At first we elicit our earnest gratitude for your inspiring advice about our Info Medicus. We always try to provide you the new information of medical science from the reliable sources. We are trying to make this issue interesting as well as enjoyable to you; we hope you will be benefited from all the information of this issue.

Anemia is a very common problem throughout the world and iron deficiency anemia is the major one. In the Review Article section, we have presented "Iron deficiency anemia" with its causes, symptoms, risk factors, complications and treatment.

To control against the infections and infectious diseases, it is important to take proper precaution. The routes of infection transmission include direct contact with an affected person's body fluids and indirect contact by means of contaminated instruments or supplies. Personal protective equipment is used when there is a risk of exposure to infectious material. For this reason, in the Clinical Method we have discussed "Putting on and removing personal protective equipment".

*Clostridium difficile* infection is a leading cause of gastrointestinal illness and places a high burden on health care system. Patients with *Clostridium difficile* infection typically have extended lengths of stay in hospitals and are a frequent cause of large hospital outbreaks of disease. This is why we provides guideline recommendations for the diagnosis and management of "*Clostridium difficile* associated diarrhea and colitis" in the View Point.

Menopause is a normal physiological event in women, occurring at median age where they face many hormonal imbalance and from that many physical and psychological problems arise. So, in Practice section we have inflated "Hormone replacement therapy".

Beside these, we are introducing new section Clinical Image where you can find interesting picture regarding various diseases.

At last we are wishing all of you a healthy and peaceful life.

Thanks and best regards,



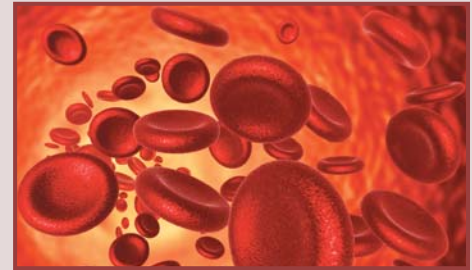
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## Iron deficiency anemia

**I**ron deficiency and iron deficiency anemia are global health problems and common medical conditions seen in everyday clinical practice. Although the prevalence of iron deficiency anemia has recently declined somewhat, iron deficiency continues to be the top ranking cause of anemia worldwide and iron deficiency anemia has a substantial effect on the lives of young children and premenopausal women in both low income and developed countries. The diagnosis and treatment of this condition could clearly be improved. Iron is crucial to biologic functions, including respiration, energy production, DNA synthesis, and cell proliferation. The human body has evolved to conserve iron in several ways, including the recycling of iron after the breakdown of red cells and the retention of iron in the absence of an excretion mechanism. However, since excess levels of iron can be toxic, its absorption is limited to 1 to 2 mg daily and most of the iron needed daily is about 25 mg per day. Iron deficiency refers to the reduction of iron stores that precedes overt iron deficiency anemia or persists without progression. Iron deficiency anemia is a more severe condition in which low levels of iron are associated with anemia and the presence of microcytic hypochromic red cells. In this review iron deficiency anemia with its causes, symptoms, risk factors, complications and treatment are discussed.



### Cause

Iron deficiency anemia occurs when body doesn't have enough iron to produce hemoglobin. Hemoglobin is the part of red blood cells that gives blood its red color and enables the red blood cells to carry oxygenated blood throughout body. If people aren't consuming

enough iron, or losing too much iron, body can't produce enough hemoglobin and iron deficiency anemia will eventually develop. Causes of iron deficiency anemia are listed in table 1.

**Table 1: Causes of iron deficiency anemia**

Causes	Example
<b>Physiologic</b>	
Increased demand	Infancy, rapid growth, menstrual blood loss, pregnancy (second and third trimesters), blood donation
<b>Environmental</b>	Insufficient intake, resulting from poverty, malnutrition, diet (e.g., vegetarian)
<b>Pathologic</b>	
Decreased absorption	Gastrectomy, duodenal bypass, bariatric surgery, <i>Helicobacter pylori</i> infection, celiac sprue, atrophic gastritis, inflammatory bowel diseases
Chronic blood loss	Gastrointestinal tract, including esophagitis, erosive gastritis, peptic ulcer, diverticulitis, benign tumors, intestinal cancer, inflammatory bowel diseases, angiodysplasia, hemorrhoids, hookworm infestation Genitourinary system, including heavy menstruation, menorrhagia, intravascular hemolysis (e.g., paroxysmal nocturnal hemoglobinuria, autoimmune hemolytic anemia with cold antibodies, march hemoglobinuria, damaged heart valves, microangiopathic hemolysis) Systemic bleeding, including hemorrhagic telangiectasia, chronic schistosomiasis, munchausen's syndrome
<b>Drug related</b>	Glucocorticoids, salicylates, NSAIDs, proton pump inhibitors
<b>Genetic</b>	Iron refractory iron deficiency anemia
<b>Iron restricted erythropoietic</b>	Treatment with erythropoiesis stimulating agents, anemia of chronic disease, chronic kidney disease

## Risk factor

These groups of people may have an increased risk of iron deficiency anemia:

- **Women:** Because women lose blood during menstruation, women in general are at greater risk of iron deficiency anemia
- **Infants and children:** Infants, especially those who were low birth weight or born prematurely, who don't get enough iron from breast milk or formula may be at risk of iron deficiency. Children need extra iron during growth. If child isn't eating a healthy, varied diet, he or she may be at risk of anemia
- **Vegetarians:** People who don't eat meat may have a greater risk of iron deficiency anemia if they don't eat other iron rich foods
- **Frequent blood donors:** People who routinely donate blood may have an increased risk of iron deficiency anemia since blood donation can deplete iron stores. Low hemoglobin related to blood donation may be a temporary problem remedied by eating more iron rich foods.

## Symptom

There may have no symptoms if the anemia is mild. Most of the time, symptoms are mild at first and develop slowly. Symptoms may include:

- Feeling grumpy
- Feeling weak or tired more often than usual, or with exercise
- Headache
- Problem concentrating or thinking

As the anemia gets worse, symptoms may include:

- Blue color to the whites of the eyes
- Brittle nails
- Desire to eat ice or other non food things (pica)
- Pale skin color
- Shortness of breath
- Sore tongue

Symptoms of the conditions that cause iron deficiency anemia include:

- Dark, tar colored stools or blood
- Heavy menstrual bleeding (women)
- Pain in the upper abdomen (from ulcers)
- Weight loss (in people with cancer).

## Determination of iron status

The traditional laboratory measures and results used to determine iron status and iron deficiency and iron deficiency anemia which are well established (Table 2). Serum ferritin level is the most sensitive and specific test used for the identification of iron deficiency. Levels are lower in patients with iron deficiency anemia. A transferrin saturation level of less than 16% indicates an iron supply that is insufficient to support normal erythropoiesis. However, in determining iron status, it is important to consider the whole picture rather than relying on single test results. Guidelines for the differential diagnosis of microcytic anemia have recently been reviewed elsewhere. The diagnosis of iron deficiency anemia in the context of inflammation is challenging and cannot be determined on the basis of the results of a single test significantly higher cutoff levels for ferritin are used to define iron deficiency anemia accompanied by inflammation, with the best predictor being a ferritin level of less than 100 µg per liter. Higher cutoff levels for ferritin are used in the diagnosis of iron deficiency in other conditions (e.g., <300 µg per liter for heart failure and for chronic kidney disease in the presence of a transferrin saturation level of less than 30%). The assessment of iron stores through iron staining of bone marrow specimens obtained by means of biopsy is an option that is not used frequently.

**Table 2: Laboratory tests for the measurement of iron status in adults**

Test	Normal value	Iron deficiency anemia
Iron (µmol/liter)	10 - 30	Low
Transferrin saturation (%)	>16 to <45	<16
Ferritin (µg/liter)		<10
Men	40 - 300	
Women	20 - 200	
Hemoglobin (g/dl)		Low
Men	>13	
Women	>12	
Mean corpuscular volume (fl:femtoliters)	80 - 95	<80
Mean corpuscular hemoglobin (pg:picogram)	27 - 34	<27

## Examination and test

To diagnose anemia, following blood tests is helpful:

- Hematocrit and hemoglobin (red blood cell measures)
- RBC indices

To check iron levels in blood following test is done:

- Serum iron level
- Serum ferritin
- Total iron binding capacity (TIBC) in the blood
- Bone marrow examination (rare)

Tests that may be done to look for the cause of iron deficiency:

- Colonoscopy
- Fecal occult blood test
- Upper GIT endoscopy.

## Treatment

### Treatment of underlying cause

Patients with an underlying condition that causes iron deficiency anemia should be treated or referred to a subspecialist (e.g., gynecologist, gastroenterologist) for definitive treatment.

### Oral iron therapy

The dosage of elemental iron required to treat iron deficiency anemia in adults is 120 mg per day for three months. The dosage for children is 3 mg per kg per day, up to 60 mg per day. An increase in hemoglobin of 1 g per dl after one month of treatment shows an adequate response to treatment and confirms the diagnosis. In adults, therapy should be continued for three months after the anemia is corrected to allow iron stores to become replenished. Adherence to oral iron therapy can be a barrier to treatment because of GI adverse effects such as epigastric discomfort, nausea, diarrhea, and constipation. These effects may be reduced when iron is taken with meals, but absorption may decrease by 40 percent. Medications such as proton pump inhibitors and factors that induce gastric acid hyposecretion (e.g., chronic atrophic gastritis, recent gastrectomy or vagotomy) are associated with reduced absorption of dietary iron and iron tablets.

### Parenteral iron therapy

Parenteral therapy may be used in patients who cannot tolerate or absorb oral preparations, such as those who have undergone gastrectomy, gastrojejunostomy, bariatric surgery, or other small bowel surgeries. The most common indications for intravenous therapy include GI effects, worsening symptoms of inflammatory bowel disease, unresolved bleeding, renal failure induced anemia treated with erythropoietin and insufficient absorption in patients with celiac disease.

## Blood transfusion

There is no universally accepted threshold for transfusing packed red blood cells in patients with iron deficiency anemia. Guidelines often specify certain hemoglobin values as indications to transfuse, but the patient's clinical condition and symptoms are an essential part of deciding whether to transfuse. Transfusion is recommended in pregnant women with hemoglobin levels of less than 6 g per dl because of potentially abnormal fetal oxygenation resulting in non reassuring fetal heart tracings, low amniotic fluid volumes, fetal cerebral vasodilation and fetal death. If transfusion is performed, two units of packed red blood cells should be given, then the clinical situation should be reassessed to guide further treatment.

## Complication

Mild iron deficiency anemia usually doesn't cause complications. However, left untreated, iron deficiency anemia can become severe and lead to health problems, including the following:

- **Heart problems:** Iron deficiency anemia may lead to a rapid or irregular heartbeat. Heart must pump more blood to compensate for the lack of oxygen carried in blood when anyone is anemic. This can lead to an enlarged heart or heart failure
- **Problems during pregnancy:** In pregnant women, severe iron deficiency anemia has been linked to premature births and low birth weight babies. But the condition is preventable in pregnant women who receive iron supplements as part of their prenatal care
- **Growth problems:** In infants and children, severe iron deficiency can lead to anemia as well as delayed growth and development. Additionally, iron deficiency anemia is associated with an increased susceptibility to infections.

## Prevention

People can reduce the risk of iron deficiency anemia by choosing iron rich foods. Foods which are rich in iron include red meat, poultry, seafood, beans, dark green leafy vegetables such as spinach, dried fruit such as raisins and apricots, iron fortified cereals, breads and pastas, peas. Body absorbs more iron from meat than it does from other sources. If anyone choose to not eat meat, he or she may need to increase intake of iron rich, plant based foods to absorb the same amount of iron as someone who eats meat. People also can enhance body's absorption of iron by drinking citrus juice or eating other foods rich in vitamin C at the same time that they eat high iron foods. Vitamin C in citrus juices, like orange juice, helps body to better absorb dietary iron. Vitamin C is also found in broccoli, grapefruit, leafy greens, melons, oranges, peppers, strawberries, tangerines, tomatoes.

- References:**
1. *N. Engl. J. Med.*, 7 May, 2015; Vol. 372, N (19)
  2. *Am. Fam. Physician*, 15 January, 2013; Vol. 87, N (2)
  3. [www.medlineplus.com](http://www.medlineplus.com)
  4. [www.myoclinic.com](http://www.myoclinic.com)

# CLINICAL METHOD

## Putting on and removing personal protective equipment

**I**n light of the threat of infectious disease, it is important to emphasize the use of proper precautions for infection control in health care settings. The routes of infection transmission include direct contact with an affected person's body fluids and indirect contact by means of contaminated instruments or supplies. Personal protective equipment (PPE) is used when there is a risk of exposure to infectious material. PPE is designed to protect the skin and mucous membranes from exposure to pathogens. This review demonstrates one procedure that will minimize the risk of exposure to infectious material when putting on and removing PPE.



### Equipment

The PPE used to prevent exposure includes gloves, boot coverings, gowns or coveralls, respirators (N95 masks or powered air purifying respirators [PAPR]), hoods, aprons, and full face shields.

Disposable medical gloves with extended cuffs should be used. Two pairs of gloves should be worn to provide an additional layer of protection. Boot coverings should also be disposable and should cover the leg up to the midcalf. Gowns or coveralls should be fluid resistant or impermeable, depending on the patient and circumstances presented. Gowns should cover the body at least from the neck to the midcalf. Gowns with integrated thumb hooks may help to secure the sleeves over the inner pair of gloves. A disposable, fluid resistant apron that covers the torso and extends to the midcalf should also be worn for additional protection in case a patient has diarrhea or vomiting.

Although the some virus has not been shown to be airborne, precautions should be taken in case aerosol generating procedures (e.g., cardiopulmonary resuscitation and endotracheal intubation) are performed. If disposable N95 respirators are worn, they must be certified by the National Institute for Occupational Safety and Health (NIOSH) and fit tested by occupational health officials. The respirator should be used along with a disposable surgical hood and full face shield that protect the head and neck. Alternatively, a NIOSH certified PAPR can be used. The PAPR should include a full face shield, helmet, or headpiece and a hood that extends to the shoulders to fully cover the neck. An integrated PAPR with a self contained filter unit inside the helmet is preferred.

### Putting on PPE

Before putting on PPE, bear in mind that equipment should be wear in a warm environment for an extended period of time. To minimize discomfort during patient care, use the restroom before putting on PPE. In case of wearing prescription eye glasses, make sure they are secure on face.

PPE should be put on near the patient's room, in a clean room or a marked area in the hallway. Clean PPE should also be stored in this area. Before entering the area where PPE is put on, change into scrubs and ensure that a trained observer is available. Change into washable shoes, secure long hair or bangs, and ensure that all personal items (e.g., jewelry, pagers, and cell phones) have been removed. Enter the PPE donning area and visually check the integrity of the equipment. The trained observer will use a checklist to review the correct sequence of events and read aloud a description of the procedure for putting on PPE. Before handling any PPE, clean hands with an alcohol based hand rub. When hands are dry, put on the first pair of gloves. Next, sit down and put on boot coverings over washable shoes.



**Figure 1:** Health care worker wearing an N95 respirator.

Insert the arms through the sleeves of the gown, ensuring that the cuff of each inner glove remains under the sleeve. Place the head through the opening at the neck, if the gown has such an opening. Overlap the left and right sides of the gown at the back and secure the ties. The observer may assist in securing the ties. Bring the and N95 respirator to face (Figure 1). Secure the lower strap around the back of the neck and then secure the upper strap behind the head. Mold the pliable nasal strip around the bridge of the nose. Perform a

seal check. Begin by covering the respirator with the hands and inhaling deeply and quickly several times. The respirator should collapse slightly against face. Next, place the hands around the edges of the respirator and exhale to determine whether there are any air leaks. If the respirator fails to collapse or if air leaks from the sides, remold the nasal strip and adjust the positioning of the respirator on face. If there are still unable to obtain a complete seal, consider using a PAPR.

Place the hood over the head, ensuring that it overlaps the gown, covers the head and neck fully and extends to the shoulders. In case of using an apron, place the head through the opening at the neck. Have the observer secure the ties in the back. Put on the second pair of gloves. Extend this set of gloves over the sleeves of the gown.

Place the face shield over the hood, letting the cushion rest on forehead and securing the strap on the back of the head. If hair is tied in a bun, make sure the strap is positioned in a manner that ensures that the strap will not slide up or down. Adjust the elastic strap if necessary to ensure a snug fit. If case of wearing eyeglasses, adjust all PPE that covers the head to make sure the comfort, thereby minimizing the need to readjust the PPE during patient care. Disinfect the outer gloves with an alcohol based hand rub.

## Removing PPE

The proper removal and disposal of contaminated PPE is the most difficult challenge in preventing exposure to pathogens, careful attention is required and persons who wear prescription eye glasses should make sure their glasses are not contaminated when they remove PPE. Removal of PPE should take place in an anteroom that is separate from the patient's room. The following equipment should be available in the anteroom: clean gloves, an alcohol based hand rub, one chair clearly identified as "dirty" for the removal of shoe coverings, a second chair designated as "clean" to be used for the disinfection of washable shoes, disinfectant wipes registered by the Environmental Protection Agency (EPA) for use in health care and a leak proof container designated for the disposal of biohazardous waste for disposable equipment. If any reusable equipment is used, a second biohazardous waste container should be available to hold such equipment.

Before leaving the patient's room, use an EPA registered disinfectant wipe to disinfect any visible contamination on PPE. Disinfect outer gloves with an alcohol based hand rub and allow gloves to dry. An EPA registered disinfectant spray can be used on heavy contamination if permitted by institution. Disinfect outer gloves with an alcohol based hand rub. If wearing an apron, break the strap behind back and then break the strap that secures the apron around neck. Pull the apron away from body, and then roll it inside out. Discard the apron in the biohazardous waste container.

Inspect the PPE again for visible contamination or tears. If visual contamination remains, wipe the area again with a disinfectant wipe. Sit down on the chair designated as "dirty" to remove boot covers. Grasp the heel of one cover and slowly pull it off leg and foot. Avoid touching scrubs and shoes. Dispose of the boot covering

in the biohazardous waste container. Repeat with the other boot covering. Afterward, stand up, step away from the dirty chair and disinfect the outer gloves.

Remove the outer gloves by grasping the glove on one hand with the other hand (Figure 2). Grasping the exterior of the glove at the wrist, pull the glove off of hand, with the contaminated exterior folded inside. Hold the removed glove in the double gloved hand. Slide a single gloved finger under the wristband of the remaining outer glove. Gently pull off the glove so that it is now inside out, forming a bag for the other glove and discard. Disinfect the inner pair of gloves. Remove the face shield. It is particularly important to avoid contamination of the eyes and mucous membranes when removing facial PPE. Tilt the head forward and lift the shield by the strap. Lift it above and away from the head without touching the shield itself and discard it in the biohazardous waste container.



Figure 2: Removal of gloves.

Leaning forward, grasp the hood near the top and carefully pull it off and away from the head. Discard it in the biohazardous waste container and disinfect the gloves. Remove the gown by first undoing the fastening at the waist. Grasp the shoulder area and peel the gown away from the body, turning the gown inside out and wrapping it into a bundle. Only the interior of the gown should remain visible. Discard the gown and then disinfect the gloves. Remove the inner pair of gloves as described for the outer pair, taking precaution to avoid contaminating the bare hands. Use an alcohol based hand rub for disinfection after taking off the gloves. Put on a new pair of gloves once the hands have dried.

Remove the N95 respirator. To minimize the possibility of contamination, avoid contact with the respirator itself, touching only the straps. Discard the respirator, then disinfect gloves. Sit down on the designated clean chair and use disinfectant wipes to clean all external surfaces of shoes. Disinfect the gloves. Remove the last set of gloves as described previously. Disinfect the hands with an alcohol based hand rub.

## Summary

PPE is available to minimize the potential harm from exposure to pathogens. When PPE is worn, removed and discarded properly, it is effective in protecting the person wearing it and the patients and health care workers with whom that person comes into contact.

Reference: *N. Engl. J. Med.*, 19 March 2015; Vol. 372, N (12)

# CASE REVIEW

## An old woman with pressure ulcer, rigidity and opisthotonus: never forget tetanus!

**A** 77 year old woman with advanced Alzheimer's disease and type 2 diabetes was admitted to hospital with fever. She lived at home with a carer and had been bedridden for 2 months. She had a stage 4 sacral pressure ulcer that had recently been debrided and treated with amoxicillin and clavulanic acid because of *Enterococcus faecalis* infection. On admission, chest radiograph showed left lung opacity consistent with pneumonia and she was started on piperacillin, tazobactam and vancomycin. A week after admission she developed intermittent generalised rigidity, opisthotonus (hyperextension of the neck and trunk), flexion of the upper limbs, extension of the lower limbs, trismus (lockjaw), and risus sardonicus (smile like retraction of the lips). She would suddenly adopt these abnormal postures, often after sensory stimulation such as noise, light or touch.

The old woman was not taking neuroleptics or other drugs that can cause parkinsonism. Head CT scan showed no acute lesions, cerebrospinal fluid and serum calcium were normal. In view of the characteristic findings on neurological examination and history of infected skin ulcer we diagnosed tetanus and her son confirmed that she had not received a tetanus vaccine booster for 30 years. We gave a dose of intramuscular tetanus and diphtheria toxoid, intramuscular human tetanus immune globulin 500 IU, intravenous metronidazole 500 mg four times daily and clonazepam 0.7 mg three times daily via nasogastric tube and she had a repeat surgical debridement of the sacral ulcer. 1 week later her rigidity and spasms had reduced in severity and frequency. However, unfortunately she developed sepsis and died 3 weeks later. Blood cultures grew acinetobacter and enterococcus.



**Figure 1:** *Clostridium tetani*

Tetanus is caused by the toxin of the anaerobic bacterium *Clostridium tetani* (Figure 1). The spores enter the host through

breaks in the skin, particularly necrotic wounds and those made by penetrating foreign bodies. The toxin blocks central inhibitory GABAergic neurotransmission, causing excessive tonic muscle contraction with superimposed spasms. Cognition is characteristically spared. Tetanus can be found on PCR and bacterial culture but the diagnosis is essentially clinical. Although several pathological conditions can lead to subacute generalized stiffness and spasms (appendix) the pattern of muscle rigidity is unique in tetanus, consisting of opisthotonus, trismus, and risus sardonicus. Tetanus is now rare in industrialised countries, but incidence is higher among the elderly because of inadequate immunisation. Diabetes is a predisposing factor. 594 cases were reported in Italy between 2001 and 2010 and older women were at higher risk, probably because of fewer opportunities for vaccination. There is little evidence supporting specific treatment and few randomised trials have been done.

In case of this patient, the entry was a pressure ulcer. Clostridia can proliferate in such lesions even if there is only a small border of necrotic tissue. Some confounding factors hindered early diagnosis. Her mental state was impaired by dementia, hypoxaemia secondary to pneumonia and sepsis, so her intermittent abnormal posturing in the context of disorientation and drowsiness suggested the more common diagnosis of meningitis. The rigidity might have been interpreted as a terminal manifestation of dementia, but its extensor character, sudden exacerbations in response to stimuli and subacute onset pointed towards the diagnosis of tetanus, further supported by the improvement following immunoglobulin treatment.

*Reference: The Lancet, 20/27 December, 2014; Vol. 384*

## Info Quiz Answers (July-September 2015)

1. b      2. a      3. d      4. d      5. b      6. a      7. b, e      8. d      9. a      10. c



## Treating clubfoot one step at a time

Clubfoot affects around 200,000 babies every year. It results from the abnormal development of muscles, tendons and bones in the foot during pregnancy which makes the foot twist downwards and inwards, making it difficult to walk. The main way of treating the



condition across the world is the non surgical Ponseti method, it involves correcting the feet by gently stretching the tendons and ligaments in the foot so they assume the right position with a series of braces and plaster casts and the treatment ideally starts in the first few weeks of life. Once a child has received the initial treatment, they must wear a foot brace for between 16 and 23 hours a day for four to five years, to prevent the feet from turning back in.

The miraclefeet brace is a low cost foot abduction brace designed to treat clubfoot using the non surgical Ponseti method. This brace was designed specifically for low resource settings with children and their parents in mind. The brace was designed to be tamper proof and easy to use, simplifying the daily bracing struggle that caregivers endure so as to improve compliance rates in the 5 year treatment process. The Miraclefeet brace is made of canvas, rather than leather, so is lighter to wear in hot climates.

*Reference: [www.bbc.com/health](http://www.bbc.com/health)*

## Doctors graft hand to man's leg

Surgeons in China have restored the use of a hand severed in an industrial accident by grafting it onto a man's ankle for a month



before re attaching it to his arm. The groundbreaking surgery was carried at Changsha, the capital of Hunan Province in central China. The patient lost his left hand when it was completely severed by a spinning blade machine at the factory where he worked. The injuries to his arm were so severe that the surgical team, headed by Dr. Tang Juyu of Xiangya Hospital, believed time had to be allowed for nerves and tendons to heal, but the delay would have meant the patient would have lost the use of the hand. Instead the team attached to his ankle, where it was "kept alive" for more than a month. Then, in another operation lasting 10 hours, the hand was re attached to his arm. The patient can already move his fingers slightly, but more rehabilitation will be needed before he regains full use of his hand.

*Reference: [www.telegraph.co.uk/health](http://www.telegraph.co.uk/health)*

## Pill on a string can detect throat cancer

A pill on a string has been developed by the University of Cambridge to detect the early signs of throat cancer without the



need for a biopsy. The pill is swallowed and when the outer case dissolves it reveals a sponge which can then be pulled up the throat lining, collecting cells. Researchers say the tiny sponge is more effective at picking up cancer because it takes a swab of the whole throat and not just a small area that a biopsy would examine. Oesophageal cancer is often preceded by Barrett's oesophagus, a condition in which cells within the lining of the oesophagus begin to change shape and can grow abnormally. The new test can pick up the earlier condition which means treatment can start sooner.

*Reference: [www.telegraph.co.uk/health](http://www.telegraph.co.uk/health)*

# CLINICAL IMAGE

## Acro-osteolysis



A 71 year old man hospitalised with tracheobronchitis, complained of hand discolouration. His hands showed the three phases of skin colour changes (white, blue and red) and a diagnosis of Raynaud's syndrome was established. When questioned about the first time he

had these symptoms, the patient noted that they had been recurrent for about 20 years. He had relatively short fingers, particularly of the thumbs and no bone was palpable in most of the distal phalanges. Radiography of his hands showed bone resorption of almost all terminal phalanges of both hands, so called acro-osteolysis. Immunological investigations and clinical features excluded several diseases commonly associated with Raynaud's syndrome. Nailfold capillaroscopy was done and showed no changes, supporting the diagnosis of primary Raynaud's syndrome. The most common causes of acro-osteolysis include scleroderma, psoriatic arthritis, occupational causes, injury (e.g., thermal burn) and hereditary syndromes. In patients with long standing primary Raynaud's syndrome, chronic vascular deficiency may lead to acro-osteolysis.

*Reference: The Lancet, 8 September, 2012; Vol. 380*

## Cutaneous larva migrans



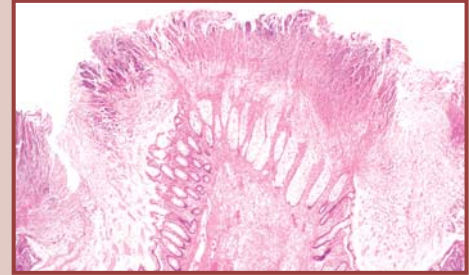
A 38 year old man presented with an itchy serpiginous eruption on the plantar aspect of his right foot that had developed after a trip to Mexico. He reported walking barefoot in the sand where cats and cat faeces were present. Physical examination showed an erythematous serpiginous eruption on the sole of his right foot. A clinical diagnosis of cutaneous larva migrans was made. Cutaneous larva migrans is most often caused by the larvae of the animal hookworm *Ancylostoma braziliense*, which is able to penetrate

and migrate through the epidermis of a host by releasing degradative enzymes. Usually, a clinical diagnosis is made on the basis of typical clinical features, and empirical treatment with topical (thiabendazole) or oral (thiobenzadole, albendazole, ivermectin) anthelmintics are initiated. Histopathological confirmation and removal of the larvae are not usually attempted because the migrating larvae are difficult to locate. We used a high resolution bed side instrument, a reflectance confocal microscope employed in experimental and clinical dermatology, to effectively locate the larvae. Imaging showed honeycomb pattern of the epidermis corresponding to the larval burrow and a highly refractile oval larva. Identification of the larvae is done and a 4 mm punch biopsy extraction was done. The intact hookworm larva was successfully revealed within the epidermis. Patient's symptoms resolved after removal of the larvae. However, he also requested treatment with thiobenzadole.

*Reference: The Lancet, 4 June, 2011; Vol. 377*

## *Clostridium difficile* associated diarrhea and colitis

**C**lostridium *difficile* is a gram positive, spore forming rod that is responsible for 15 to 20 percent of antibiotic related cases of diarrhea and nearly all cases of pseudomembranous colitis. The species was named "difficile" because initially it was hard to culture. Early studies showed that *C. difficile* could be isolated from the gastrointestinal tracts of most neonates. Thus, it was believed to be a commensal organism. However, *C. difficile* was found to be the primary cause of pseudomembranous colitis. Because of the frequent use of broad spectrum antibiotics, the incidence of *C. difficile* diarrhea has risen dramatically in recent decades. *C. difficile* associated diarrhea of ten is perceived to be an occasional and easily treated side effect of antibiotic therapy. In severe cases, flexible sigmoidoscopy can provide an immediate diagnosis. Treatment of *C. difficile* associated diarrhea includes discontinuation of the precipitating antibiotic (if possible) and the administration of metronidazole or vancomycin. Preventive measures include the judicious use of antibiotics, thorough hand washing between patient contacts, use of precautions when handling an infected patient or items in the patient's immediate environment, proper disinfection of objects, education of staff members and isolation of the patient. The condition is a common cause of significant morbidity and even death in elderly or debilitated patients.



### Pathophysiology

The precipitating event for *C. difficile* colitis is disruption of the normal colonic microflora. This disruption usually is caused by broad spectrum antibiotics, with clindamycin and broad spectrum penicillins and cephalosporins most commonly implicated. Antibiotics with a reduced propensity to induce infection include aminoglycosides, metronidazole, antipseudomonals and vancomycin. The risk of developing antibiotic associated diarrhea more than doubles with longer than three days of antibiotic therapy. After disruption of the colonic microflora, colonization of *C. difficile* generally occurs through the ingestion of heat resistant spores, which convert to vegetative forms in the colon. Depending on host factors, an asymptomatic carrier state or clinical manifestations of *C. difficile* colitis develop. Manifestations of the disease range from mild diarrhea to life threatening *C. difficile* colitis. *C. difficile* associated diarrhea can occur up to eight weeks after the discontinuation of antibiotics. The major host factors predisposing patients to the development of symptomatic *C. difficile* associated diarrhea include antibiotic therapy, advanced age, number and severity of underlying diseases and faulty immune response to *C. difficile* toxins.

### Risk factor

Although *C. difficile* occasionally causes problems in healthy people, it is most likely to affect patients in hospitals or long term care facilities. Most have conditions that require long term treatment with antibiotics, which kill off other intestinal bacteria that keep *C. difficile* in check. While use of any antibiotic can potentially lead to *C. difficile* overgrowth, it most commonly occurs with the use of an antibiotic that is broad spectrum, or able to kill a wide variety of bacteria. It also happens more often when multiple antibiotics are

needed to fight infection and when the antibiotics need to be taken for a long period of time.

Other risk factors for *C. difficile* infection include:

- Surgery of the gastrointestinal (GI) tract
- Diseases of the colon such as inflammatory bowel disease or colorectal cancer
- A weakened immune system
- Use of chemotherapy drugs
- Previous *C. difficile* infection
- Advanced age - 65 or older
- Kidney disease
- Use of drugs called proton pump inhibitors, which lessen stomach acid.

### Clinical feature

Patients with *C. difficile* associated disease have profuse watery diarrhea, with 5 to 20 watery bowel movements per day, malaise, anorexia and nausea. Other features that may be seen include dehydration, fever (30% - 50% of patients), leukocytosis (50% - 60%) and abdominal pain or cramping (20% - 33%). The pain and cramps are relieved by the passage of stools. The mean peripheral white blood cell count of patients with *C. difficile* associated diarrhea is typically 15,000 to 16,000/ $\mu$ L. *C. difficile* colitis should be considered in all hospitalized patients with unexplained leukocytosis. Toxic megacolon is a serious complication of *C. difficile* associated disease. It is characterized by the development of an enlarged dilated colon (>7 cm in its greatest

diameter) and may be accompanied by severe systemic toxicity. Pseudomembranous colitis is characterized by the presence of an inflammatory pseudomembrane overlying the intestinal mucosa. The pseudomembrane is made of cellular and inflammatory debris and forms visible patches of yellow or gray exudate. Unusual manifestations of *C. difficile* associated disease include protein losing enteropathy with ascites, ileus with minimal or no diarrhea and extraintestinal manifestations such as bacteremia, splenic abscess, cellulitis, and osteomyelitis. Recurrent *C. difficile* associated diarrhea complicates the course in approximately 20% of patients.

### Treatment

The first and most important step in treating *C. difficile* associated disease is to discontinue the implicated antibiotic agent or agents. Specific antimicrobial therapy to treat the infection should be administered orally for 10 days. The drug of choice is metronidazole 500 mg orally 3 times daily for 10 days. Vancomycin at a dose of 125 to 250 mg orally every 6 hours for 10 days is as effective as metronidazole, but it is more expensive. The potential emergence of vancomycin resistant staphylococci and enterococci is concerning but does not obviate the need to use vancomycin for severely ill or rapidly deteriorating patients at high risk for *C. difficile* associated disease in the hospital setting. Vancomycin is also used in patients who are intolerant of metronidazole, pregnant women and children. Metronidazole crosses the placenta and should be avoided during the first trimester since there are no adequate studies demonstrating safety in pregnant women. For patients with severe disease who do not respond rapidly to metronidazole, therapy should be switched to vancomycin.

For patients who lack oral access, intravenous metronidazole (500 mg every 6-8 hr), vancomycin retention enemas (500 mg every 4-8 hours), or vancomycin via colonic catheter should be considered. Intravenous vancomycin should not be used to treat *C. difficile* colitis because the antibiotic is not excreted into the colon. Colonoscopic decompression with vancomycin instillation has been

used successfully in toxic megacolon. For patients who have a first recurrence of diarrhea following treatment of *C. difficile* associated disease, treatment in the same manner as the initial episode (metronidazole or vancomycin) is recommended. Indications for surgery include severe peritoneal disease, bacteremia, unresponsiveness to antibiotics, unremitting fever and computed tomography evidence of significant pericolonic inflammation with increasing bowel wall edema.

Evidence to support the efficacy of probiotic agents in *C. difficile* associated disease is lacking and in fact, numerous reports show that they may be harmful. Fungemia due to *Saccharomyces boulardii* and bacteremia due to *Lactobacillus* species after administration to both immunocompetent and immunocompromised hosts have been reported. Anti motility agents such as diphenoxylate and loperamide should be avoided in *C. difficile* associated disease. Several case reports have linked the use of anti motility agents in patients with *C. difficile* associated disease with the development of toxic megacolon because they probably delay excretion of the toxin.

### Prevention and control

Important preventive measures include hand washing, glove use, isolation of patients in a single room, barrier precautions and cleaning of the physical environment throughout the duration of symptomatic disease. Hand washing with soap and water after glove removal is recommended during outbreaks. Because alcohol is ineffective in killing *C. difficile* spores, health care workers should wash their hands with soap and water rather than with alcohol based waterless hand sanitizers when dealing with outbreak. Implementation of contact precautions combined with the use of private rooms has been successful in limiting transmission of *C. difficile* in hospital and long term care settings. Thorough cleaning of surfaces and disinfection with agents that eradicate *C. difficile* and its spores (e.g., 10% sodium hypochlorite solution) are also recommended. Reusable rectal thermometers can spread the infection and should be replaced by disposable ones.

### Key Points

- Judicious use of antibiotics is extremely important in reducing the incidence of *Clostridium difficile* associated disease
- *C. difficile* colitis should be considered in all hospitalized patients with unexplained leukocytosis
- Strictly following infection control guidelines is vital to prevent spread of the disease
- When *C. difficile* associated disease is suspected, the implicated antimicrobial agent should be discontinued or substituted, if possible
- Antimotility agents should be avoided
- Symptom free carriers should not be treated
- Health care workers should wash their hands with soap and water rather than with alcohol based hand sanitizing agents when dealing with outbreaks because alcohol is ineffective in killing *C. difficile* spores
- Reusable rectal thermometers can spread the infection and should be replaced by disposable ones.

**References:** 1. *Am. Fam. Physician*, 1 March 2005; Vol. 71 N (5)  
 2. *Hospital Physician*, July 2007  
 3. [www.webmd.com](http://www.webmd.com)

## Hormone replacement therapy

**H**ormone replacement therapy (HRT) or menopause hormone therapy (MHT), is medication containing hormones that a woman's body stops producing after menopause. HRT is used to treat menopausal symptoms. While HRT reduces the likelihood of some debilitating diseases such as osteoporosis, colorectal (bowel) cancer and heart disease, it may increase the chances of developing a blood clot (when given in tablet form) or breast cancer (when some types are used long term). For women who experience menopause before the age of 45 (early or premature menopause), HRT is strongly recommended until the average age of menopause onset (around 51 years), unless there is a particular reason for a woman not to take it.



### What is hormone replacement therapy

Menopause is a normal physiological event in women, occurring at a median age of 51 years. Hormone replacement therapy (HRT) contains oestrogen for relieving menopausal symptoms; for women who still have their uterus it is combined with a progestogen for endometrial protection. The oestrogen can be oral, intravaginal, or transdermal. The progestogen can be oral, transdermal, or delivered via an intrauterine device.

### Types of HRT

Hormone therapy can be either systemic or local. These two terms describe where and how the hormones act in the body.

#### Systemic therapy

With systemic therapy, the hormones are released into bloodstream and travel to the organs and tissues where they are needed. Systemic form of estrogen include pills, skin patches, gel and spray. If progestin is applied, it can be given separately or combined with estrogen in the same pill or in a patch. For women taking estrogen only therapy, estrogen may be taken every day or every few days, depending on the way the estrogen is given. For women taking combined therapy, there are two types of regimens:

- Cyclic therapy: Estrogen is taken every day and progestin is added for several days each month or several days every 3 or 4 months
- Continuous therapy: Estrogen and progestin taken every day.

#### Local therapy

Women who only have vaginal dryness may be prescribed local estrogen therapy in the form of vaginal ring, tablet or cream. These forms release small doses of estrogen into the vaginal tissue. The estrogen helps restore the thickness and elasticity to the vaginal lining while relieving dryness and irritation.

### Indication of HRT

Current evidence based guidelines advise consideration of HRT for troublesome vasomotor symptoms in perimenopausal and early postmenopausal women without contraindications and after

individualised discussion of likely risks and benefits. Starting HRT in women over age 60 years is generally not recommended. For women with premature (age <40 years) or early (<45 years) menopause, current guidelines recommend HRT until aged 50 for the treatment of vasomotor symptoms and bone preservation. HRT reduces fracture risk, but increased risk of osteoporosis alone is not an indication for HRT. Similarly, although HRT may also improve mood and libido, these are not primary indications for treatment. Vaginal symptoms alone do not require systemic HRT and can be managed with local oestrogens.

Menopause symptoms that may be relieved by HRT include:

- Hot flushes and night sweats
- Thinning of vaginal walls and vaginal dryness
- Vaginal and bladder infections
- Mild urinary incontinence
- Aches and pains
- Insomnia and sleep disturbance
- Cognitive changes, such as memory loss
- Mood disturbance and reduced sex drive
- Abnormal sensations, such as 'crawling' under the skin
- Palpitations
- Hair loss or abnormal hair growth
- Dry and itching eyes
- Tooth loss and gingivitis

HRT reduces the risk of various chronic conditions that can affect postmenopausal women, including:

- Diabetes
- Osteoporosis
- Bowel cancer.

## HRT related health risks

While HRT reduces the risk of some debilitating diseases, it may increase the risk of others. These small risks must be balanced against the benefits of HRT for the individual woman.

### Cardiovascular disease

Women over 60 have a small increased risk of developing both heart disease and stroke on combined oral HRT. Although the increase in risk is small, it needs to be considered when starting HRT, as the risk occurs early in treatment and persists with time. Oestrogen used on its own increases the risk of stroke further if taken in tablet form, but not if using a skin patch. Women who commence HRT around the typical time of menopause have lower risks of cardiovascular disease than women aged 60 or more, and may have no increase in risk if treated with low doses by mouth or through the skin. It is not recommended to commence HRT in women over 60.

### Venous thrombosis

Venous thromboses are blood clots that form inside veins. Women under 50 years of age and women aged 50 to 60 face an increased risk of venous thrombosis if they take oral HRT. The increase in risk seems to be highest in the first year or two of therapy and in women who already have a high risk of blood clots. This especially applies to women who have a genetic predisposition to developing thrombosis, who would normally not be advised to use HRT. Limited research to date suggests the increased risk of clots is mainly related to combined oestrogen and progestogen in oral form. Some studies suggest a lower risk with non oral therapy (patches, implants or gels).

### Stroke

Overall, HRT increases the risk of stroke. Stroke risk increases with age and is rare in women under 60 years. The risk of stroke may be lower with transdermal HRT at doses of 50 µg or less, but this has not been shown in randomised controlled trials. In older women (>65 years) estrogen increases the risk of stroke. In clinical practice avoid HRT in women at high risk of stroke.

### Breast cancer

Women over 50 years of age who use combined oestrogen and progesterone replacement for less than five years have little or no increased risk of breast cancer. Women who use combined HRT for more than five years have a slightly increased risk. Women on oestrogen alone have no increased risk up to 15 years of usage.

### Endometrial cancer

Use of oestrogen only HRT increases the risk of endometrial cancer, but this risk is not seen with combined continuous oestrogen and progestogen treatment. There is no risk if a woman has had her uterus removed (hysterectomy).

### Ovarian cancer

A recent review of women with ovarian cancer has linked HRT use to an increased risk of two types of ovarian tumours; serous and endometrioid tumours. However, the increased risk was very small.

### Contraception

HRT is not a form of contraception. The treatment does not contain high enough levels of hormones to suppress ovulation, so pregnancy is still possible in women who are ovulating occasionally in perimenopause. It is generally advised that menopausal women should continue to use contraception until their natural periods have ceased for at least one year if they are aged over 50, or after two years without periods if they are younger than 50.

### Cholecystitis

Cholecystitis is a disease where gallstones in the gallbladder block ducts, causing infection and inflammation. On average, there is a slightly higher risk that a woman will develop cholecystitis when using oral (tablet form) oestrogen or oestrogen and progestogen for five years, but patch treatment is associated with a lower risk. Treatment for cholecystitis includes surgery to remove gallstones or the gallbladder.

## Precautions for HRT

No consensus has been reached on absolute contraindications to HRT. However, HRT should be avoided or discontinued in patients with the following:

- A history of breast cancer, as HRT may increase the risk of breast cancer recurrence and of new breast cancers. Exclude breast disease and investigate any abnormalities before starting HRT. Counsel women considering HRT that it may increase their risk of an abnormal mammogram and that combined HRT may increase their risk of breast cancer after four to five years of use
- A personal history or known high risk of venous or arterial thromboembolic disease, including stroke and cardiovascular disease, as HRT may further increase risk
- Uncontrolled hypertension
- HRT should not be started in women with undiagnosed abnormal vaginal bleeding. Combined HRT may often cause unscheduled bleeding in the first six months of use. Persistent or new onset (after six months) unscheduled bleeding on HRT requires investigation to exclude pelvic disease
- In case of abnormal liver function, avoid oral HRT
- Consider using HRT, if anyone has History of endometrial or ovarian cancer.

**References:** 1. *BMJ*, 2012; 344:e763  
2. *American College of Obs. & Gynae. April 2015*  
3. [www.betterhealth.vic.gov.au](http://www.betterhealth.vic.gov.au)

## Refresh your memory

Please select the correct answer by (✓) against a, b, c, d, e of each question in the Business Reply Post Card and sent it through our colleagues or mail within 17 November 2015; this will ensure eligibility for the Raffle Draw and the lucky winners will get attractive prizes!

1. **Which one of the following is the main function of the Golgi apparatus?**
  - a. It packages molecules into vesicles that can be transported out of a cell
  - b. It produces most of the cell's energy requirements
  - c. It is responsible for bacterial phagocytosis
  - d. It regulates cell reproduction
  - e. Protein synthesis
2. **Which one of the following is the definition of 'apoptosis'?**
  - a. Forward movement of the eyeball
  - b. Phagocytosis of nuclear material
  - c. Programmed cell death
  - d. Inflammation of the tendon sheath
  - e. Cell necrosis
3. **What is the mechanism of action of aspirin?**
  - a. Inhibition of lipooxygenase
  - b. Inhibits factor Xa production
  - c. Inhibitor of Cyclooxygenase
  - d. Irreversibly inhibits ADP receptors on platelets
  - e. Antagonists of glycoprotein IIb/IIIa receptors
4. **What investigation should be utilised to confirm an intraventricular thrombus following an Echo?**
  - a. Transthoracic echo
  - b. Cardiac MRI
  - c. Cardiac CT
  - d. Persistent ST elevation on ECG
  - e. Transesophageal echo
5. **A 20 year old has been admitted with chest pain. He admitted to using cocaine and is found to have a STEMI. What do you do next?**
  - a. Aspirin and clopidogrel and LMWH
  - b. Thrombolysis
  - c. IV heparin
  - d. Percutaneous coronary intervention
  - e. Glycoprotein IIb/IIIa inhibitors
6. **Which of the following is strongly linked with Alzheimers?**
  - a. Rett syndrome
  - b. Downs syndrome
  - c. Marfan syndrome
  - d. Lesch Nyhan syndrome
  - e. Fragile X syndrome
7. **Which of the following drugs is not known to be associated with hyperkalaemia?**
  - a. Diclofenac
  - b. Spironolactone
  - c. Ramipril
  - d. Heparin
  - e. Prednisolone
8. **Which of the following ocular signs would you find in acne rosacea?**
  - a. Keratitis
  - b. Uveitis
  - c. Cataract
  - d. Ptosis
  - e. Swollen optic disc
9. **Whilst a patient is on atenolol, which other drug should be avoided?**
  - a. Bendroflumethiazide
  - b. Amlodipine
  - c. Quinine sulphate
  - d. Verapamil
  - e. Isosorbide mononitrate
10. **Which of the following is not a feature of digoxin toxicity?**
  - a. Nausea and vomiting
  - b. Blurred vision
  - c. Yellow discolouration of vision
  - d. Palpitations
  - e. Acute renal failure



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