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The essence of medical practice

*Management of
hypertension in pregnancy*

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Editorial

Dear Doctor,

We are delighted to submit the new issue of Info Medicus in your hand. In this issue, we have collected some interesting medical information from different renowned medical journals; we believe which will be very much pleasurable for you.

Any kind of medical disorders during pregnancy can lead to serious consequence. Hypertensive disorder in pregnancy is the most common medical disorder in pregnancy. It complicates all pregnancies and is an important cause of maternal and foetal morbidity and mortality. This review article is done with the aim to update knowledge regarding types, causes, risk factors and management of hypertensive disorders during pregnancy.

Retina is the most important and vital part of the eye. In the human body, only the retina allows the examiner to achieve direct visualization of the central nervous system and the vasculature. That's why we have discussed "Examination of the retina" in the Clinical Method section.

Zika virus is most perilous health news in latest time. Its most alarming complication is baby born with microcephaly whose mother is infected with Zika virus. Several areas of the world are affected by Zika virus. That's why in the View Point section, we bring in "Zika virus infection".

And in Clinical Image section, we set some clinical pictures with their description which will be interesting for you.

Finally we are wishing you a healthy and peaceful life.

Thanks and best regards,



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Medical Services Manager



(Dr. Rumana Dowla)
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Management of hypertension in pregnancy

Hypertensive disorders of pregnancy remain a major health issue for women and their infants. Appropriate prenatal care, with observation of women for signs of hypertensive disorders and then delivery to terminate the disorder, has reduced the number and extent of poor outcomes, serious maternal fetal morbidity and mortality still occur. Some of these adverse outcomes are avoidable, whereas others can be ameliorated. Although, some of the problems that face neonates are related directly to hypertension in pregnancy, a large proportion are secondary to prematurity that results from the appropriate induced delivery of the fetuses of women who are ill. Optimal management requires close observation for signs and premonitory findings and after establishing the diagnosis, delivery at the optimal time for both maternal and fetal well being. More recent clinical evidence to guide this timing is now available. Chronic hypertension is associated with fetal morbidity in the form of growth restriction and maternal morbidity manifested as severely increased blood pressure (BP). However, maternal and fetal morbidity increase dramatically with the hypertension in pregnancy. One of the major challenges in the care of women with chronic hypertension is deciphering whether chronic hypertension has developed. In this issue, we have discussed about various types, causes, risk factors and management of hypertensive disorders in pregnancy.



Classification

Hypertensive disorders in pregnancy are comprised of a spectrum of disorders typically classified into categories and stratified according to severity:

- Chronic hypertension
- Gestational hypertension
- Preeclampsia (PE)
- Chronic hypertension with superimposed preeclampsia

Chronic hypertension: It complicates 3-5% of all pregnancies, might be higher in women who become pregnant at 30s or 40s. The diagnosis is based on a known history of hypertension pre pregnancy or an elevated pressure $\geq 140/90$ mm Hg before 20 weeks gestation. The presence of even mild pre existing hypertension almost doubles the risk of preeclampsia (PE).

Gestational hypertension: This hypertension occurring in the second half of pregnancy in previously normotensive women, without significant proteinuria. It complicates 6-7% of all pregnancies and resolves by six weeks postpartum. In most cases there is mild to moderate elevation of blood pressure. The risk of superimposed preeclampsia is 15-26%; risk is influenced by the gestational age when hypertension develops.

Preeclampsia: It is a multi system disorder, defined as gestational hypertension associated with significant proteinuria (>300 mg/L or >500 mg/24 hours urine), occurs usually after 20 weeks of gestation. In most cases it resolves within six weeks postpartum. PE

complicates 5-6% of all pregnancies, the figure may rise up to 25% in women with pre existing hypertension. PE is considered severe if there is sustained elevation of BP $>160/110$ mm Hg on 2 occasions at least 6 hours apart, proteinuria of at least 5 gm/24 hours or multi organ involvement e.g., pulmonary oedema, seizures, oliguria, thrombocytopenia, abnormal liver enzymes and persistent severe CNS symptoms like altered maternal status, headache, blurred vision or blindness.

Causes

There is no definitive known cause found in hypertension during pregnancy, though it is likely related to a number of factors. Some of these factors include:

- Abnormal placentation (formation and development of the placenta)
- Immunologic factors
- Prior or existing maternal pathology - preeclampsia is seen more at a higher incidence in individuals with preexisting hypertension, obesity, antiphospholipid antibody syndrome
- Dietary factors, e.g., calcium supplementation in areas where dietary calcium intake is low has been shown to reduce the risk of preeclampsia
- Environmental factors, e.g., air pollution

Those with long term high blood pressure have a risk 7 to 8 times higher than those without.

Risk factors

There are several risk factors which can elevate hypertension during pregnancy. For early diagnosis of the disease, these risk factors

must be excluded. Table 1 shows the risk factors of hypertension in pregnancy.

Table 1: Risk factor of hypertension during pregnancy

Maternal medical risk factors	Maternal personal risk factors	Placental or fetal risk factors
<p>The following are maternal medical risk factors:</p> <ul style="list-style-type: none"> Chronic hypertension Preexisting diabetes (Type 1 or Type 2), especially with microvascular disease Renal disease Systemic lupus erythematosus Obesity Thrombophilia History of migraine Use of selective serotonin reuptake inhibitor or antidepressants beyond the first trimester 	<p>The following are maternal personal risk factors:</p> <ul style="list-style-type: none"> First pregnancy New partner or paternity Age younger than 18 years or older than 35 years History of preeclampsia Family history of preeclampsia in a first degree relative Race: Black Obesity (BMI ≥ 30) Inter pregnancy interval less than 2 years or longer than 10 years 	<p>The following are placental or fetal risk factors:</p> <ul style="list-style-type: none"> Multiple gestations Hydrops fetalis Gestational trophoblastic disease Triploidy

Diagnosis

It is essential to diagnosis hypertension during pregnancy as early as possible. Because more time to find out hypertension, the more

complication will arise. However, diagnosis is based on physical and laboratory investigations which are given in Table 2.

Table 2: Diagonosis of hypertension during pregnancy

Physical examination	Laboratory investigations
<ul style="list-style-type: none"> Symptoms <ul style="list-style-type: none"> Swelling of the foot (early) Gradually swelling may extend to face, abdominal wall, vulva and even the whole body Headache Disturbance of sleep Diminished urinary output (<500 ml in 24 hours) Epigastric pain Blurring of vision Signs <ul style="list-style-type: none"> Rise of blood pressure Oedema Abnormal weight gain 	<ul style="list-style-type: none"> Urine exam <ul style="list-style-type: none"> Heat coagulation test to detect proteinuria 24 hour urinary protein Urine R/M/E and C/S Blood exam <ul style="list-style-type: none"> Serum uric acid Blood urea Serum creatinine Coagulation factors Ultrasonogram X-ray Liver function test CT Scan of brain and liver

Differential diagnosis

In pregnancy there are many factors which can increase the both fetal and maternal mortality. Hypertension is one of the factors. This

hypertension during pregnancy can be confused with many other diseases, which are given in Table 3.

Table 3: Differential diagnosis

<ul style="list-style-type: none"> ● Antiphospholipid antibody syndrome ● Antithrombin deficiency ● Aortic coarctation ● Autoimmune thyroid disease ● Cardiomyopathy ● Cushing syndrome ● Diabetes mellitus ● Disseminated intravascular coagulation ● Hypertensive encephalopathy ● Systemic lupus erythematosus ● Protein C and protein S deficiency 	<ul style="list-style-type: none"> ● Gastrointestinal disease ● Glomerulonephritis ● Graves' disease ● Hashimoto's thyroiditis ● Hematologic disease ● Hemolytic uremic syndrome ● Hydatiform mole ● Primary hyperaldosteronism ● Hyperparathyroidism ● Hypothyroidism ● Nephrotic syndrom
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Treatment during pregnancy

Antihypertensives are agents that lower blood pressure. Antihypertensive therapy decreases the incidence of stroke and cardiovascular complications among pregnant women with diastolic blood pressure above 110 mm Hg. There is general agreement that pregnant women with severe hypertension should receive pharmacological treatment, but the value of treating mild essential hypertension is controversial. There seems to be less risk of developing severe hypertension (risk ratio 0.50) but no difference was found in the outcome of PE, neonatal death, preterm birth and small for gestational age with treatment.

Usually treatment is started when SBP >140 mm Hg or DBP >90 mm Hg. International guidelines for the treatment of hypertension in pregnancy vary with respect to thresholds for starting treatment and targeted BP goal. Therapy is recommended at > 140/90 mm Hg targeting to 80 to 90 mm Hg.

Opinions differ as to which is the best agent for treatment of hypertension during pregnancy. The choice of drugs will differ between acute and more chronic clinical presentation. Suitable oral agents in less acute situations include methyldopa, β blockers including labetalol and calcium channel blockers (Nifedipine, Nicardipine). In more acute situations intravenous agents may be required and options include β blockers (Labetolol), sublingual nifedipine and hydralazine.

First line therapy

Alpha methyldopa and labetalol as appropriate first line antihypertensive therapies for women with severe hypertension.

Methyldopa is a centrally acting agent (β adrenergic receptor blockers) and remains the drug of first choice for treating

hypertension in pregnancy. It has been the most frequently assessed antihypertensive in randomized trial and has the longest safety track record. Treatment does not seem to have adverse effects on utero placental or on foetal haemodynamics. Dose of methyldopa is 250mg (thrice or four times daily), not exceeding 3 gm/day. Methyldopa may take a few days for the onset of hypotensive effect, so rapid change of dose during the first 2 or 3 days should not be undertaken. Higher dose may cause sodium and fluid retention and may need diuretic therapy to maintain the hypotensive effect.

Labetalol is an adrenergic receptor blocking agent possessing both α_1 (post synaptic) and β receptor blocking activity. It lowers blood pressure by partially blocking β adrenoceptors in the peripheral arterioles, thus causing vasodilatation and resulting reduction of peripheral resistance. At the same time, blocking of β adrenoceptors in the myocardium prevents reflex tachycardia and subsequent elevation of blood pressure. Recommended initial dose 100mg twice daily. The dose should be adjusted semi weekly or weekly according to response. Total maximal daily dose is 1200mg.

Second line therapy

These agents should be used when monotherapy is insufficient or when women cannot tolerate it. Calcium channel blockers and direct vasodilator are the second line drugs for hypertension during pregnancy.

Nifedipine is the most widely used calcium channel blocker and is safe at any gestation. It reduces vascular resistance by inhibiting transmembrane calcium influx into vascular smooth muscle.

Nifedipine does not seem to cause a detectable decrease in uterine blood flow. Oral administration lowers BP within 10-15 minutes, slow release tablet has slower onset of action (60 min); long acting nifedipine given once daily is usually preferred. Use of sublingual form should be avoided to minimize the risk of sudden hypotension and foetal distress.

Hydralazine selectively relaxes arteriolar smooth muscle by an as yet unknown mechanism. Its greatest use is in the urgent control of severe hypertension or as a third line agent for multi drug control of refractory hypertension. It is effective orally, intravenously or intramuscularly. Oral hydralazine is safe throughout pregnancy although occurrence of maternal and neonatal lupus like syndromes have been reported following chronic use. Taken orally as monotherapy hydralazine is not tolerated well because of adverse effects e.g., palpitation, headaches and dizziness. It is therefore combined with methyldopa or labetalol.

Third line therapy

β adrenergic blockers are the group of drugs act by competitive inhibition of catecholamines at β_1 and β_2 adrenoceptors. In the past β adrenergic blocker have been highlighted as a class of antihypertensives associated with an increased risk of intrauterine growth retardation (IUGR), in particular atenolol have been signed out. Use of β blockers should be limited to women with chronic hypertension, in whom methyldopa and nifedipine have unsatisfactory control. Lipid soluble oxprenolol, metoprolol, propynolol have short half life compared to atenolol. The safety and efficacy of parazocine have also been demonstrated.

Although not a teratogenic drug but it is used infrequently in pregnancy because it interferes with plasma volume expansion associated with pregnancy. Many women with chronic hypertension are treated with diuretics, whether therapy should be continued during pregnancy is controversial. Diuretic therapy is particularly useful in pregnant women with salt sensitive hypertension or with left ventricular diastolic dysfunction, however it should be discontinued if the women develops superimposed preeclampsia or there is evidence of reduced fetal growth.

Treatment during postpartum period and breast feeding

Immediately after delivery BP falls but rises typically over the first five days, perhaps reflecting vasomotor instability. Antihypertensive drugs should be given if the BP exceeds 150 mm Hg systolic or 100 mm Hg diastolic in the first 4 days of the

puerperium. Choice of antihypertensive agent in the postpartum period is often influenced by breast feeding. Most antihypertensive drugs are present in very low concentration in the breast milk exceptatenolol and metoprolol whose concentration is similar to that of maternal plasma, possibly to levels that could affect the infant; by contrast, exposure to labetalol and propranolol seems low.

Methyldopa should be avoided during postpartum period because of the risk of postnatal depression. Diuretics should also be avoided as it may reduce milk volume by suppressing lactation. Therefore β blocker plus nifedipine may be used if another agent is required. Women with gestational hypertension or preeclampsia are usually able to stop all antihypertensives within six weeks postpartum. Those with chronic hypertension can resume their pre pregnancy drugs. Angiotensin converting enzyme (ACE) inhibitor and ARBs should be avoided because of their side effect on neonatal renal function.

Conclusion

Hypertensive disorders are an important cause of maternal and perinatal mortality and morbidity worldwide. Pre pregnancy counseling is essential in women with chronic hypertension as well as those with history of preeclampsia. Opinions differ as to which is the best antihypertensive during pregnancy. It is important to balance the risk to the fetus associated with treating the illness against risk to both the mother and the fetus in failing to treat the mother. Maternal and neonatal outcomes are generally good in women who have mild chronic hypertension or gestational hypertension. Antihypertensive therapy may permit these women to continue their pregnancies to term. Close medical supervision and timely delivery are the keys to the treatment of hypertension during pregnancy. Both ACE inhibitors and Angiotensin receptor blockers (ARBs) are fetotoxic, therefore all women of childbearing age treated with these drugs must be informed of the need for drug discontinuation, should they become pregnant. Used in the first trimester, the babies are 4 times likely to develop cardiovascular problem and 5 times likely to develop CNS malformation. ACE inhibitors are also contraindicated in the second and third trimester because of risk of ACE inhibitor fetopathy including IUGR, pulmonary hypoplasia, foetal renal tubular dysplasia, neonatal renal failure and death.

References:

1. *The American College of Obs. & Gyn.*; November, 2013; Vol. 122, No. 5:1122-1131
2. *Bangladesh J Obstet Gynaecol*, 2008; Vol. 23, No (2):65-72
3. www.wikipedia.org
4. www.emedicine.medscape.com

Examination of the retina

In the human body, only the retina allows the examiner to achieve direct visualization of the central nervous system and the vasculature. Therefore, the fundoscopic examination is important in the detection of certain systemic diseases and diseases that primarily affect the eye. For non ophthalmologists, the direct ophthalmoscope is the preferred instrument for examination of the retina.



Indications

The retinal examination is part of a complete physical examination. It is particularly important in patients with a history of such systemic diseases as diabetes, hypertension, and atherosclerosis. Patients with the human immunodeficiency virus (HIV) or the acquired immunodeficiency syndrome (AIDS) are also at increased risk for retinal diseases. Evaluation of the retina may reveal the initial signs of diabetic retinopathy, hypertensive retinopathy, macular edema, glaucoma, or macular degeneration. Indications for urgent direct ophthalmoscopy include a clinical suspicion of increased intracranial pressure, occluded retinal vessels, and retinal detachment. Any of these conditions, or the sudden loss of vision or a change in vision, constitutes an ophthalmic emergency. The patient should be seen by an ophthalmologist immediately or should be sent to the emergency department.

Anatomy

The inner structures of the eye can be visualized through the pupil, the central opening in the iris. The light rays from the ophthalmoscope pass through the cornea, pupil, and lens to focus on the retina, producing an upright, magnified image. The retina is located on the inner surface of the globe, opposite the pupillary opening. The color should appear red, orange, or brown and varies from person to person.

Direct ophthalmoscopic settings

The direct ophthalmoscope (Figure 1) consists of a handle, which contains the power supply and a light source, and a head, which contains the viewing window and lenses. The on-off switch adjusts the brightness of the light. The apertures include a large circle, a medium circle, a small circle, and a slit beam. To reduce the patient's pupillary constriction it is best to use the ophthalmoscope at a brightness level of 80 to 90%, with the aperture set to the small or medium circle.



Figure 1: Direct ophthalmoscope

The ophthalmoscope contains a range of lenses with positive and negative diopters that compensate for refractive error on the part of the examiner and the patient. If the patient has hyperopia, the retina will be closer to the pupil than normal. If the patient has myopia, the retina will be farther away from the pupil than normal. The lenses are adjusted by turning the dial. Negative numbers focus on objects that are farther away and positive numbers focus on objects that are closer.

Patient preparation

Explain the procedure and tell the patient that direct ophthalmoscopy has virtually no risks, although there may be some discomfort caused by the bright light shining into the patient's eyes. Ask the patient to sit, with legs uncrossed. Have the patient remove eyeglasses, if present. Contact lenses will not affect the examination and may be left in place.

Procedure

Darken the room to maximize pupillary dilatation. Designate a point for the patient to look at that is at least one (1) meter away from the patient. It is easier to fixate on an image or object than a blank wall. Switch on the ophthalmoscope light, and set the diopters to zero (0). Always use right eye to examine the patient's right eye and left eye to examine the patient's left eye to avoid being nose to nose with the patient.

CLINICAL METHOD

Start by locating the red reflex, which is the reflection of light from the retina. Hold the viewing window of the ophthalmoscope directly in front of eye. Position the ophthalmoscope about 30 cm from the patient's eye, slightly temporal to the center, and shine light into the pupil. A diminished red reflex or the absence of a red reflex could indicate an obstruction (e.g., cataracts).

Follow the red reflex as gradually move closer to the patient. Turn the dial clockwise to decrease the diopters until focus on the retina. Hold the ophthalmoscope as close to the patient's eye as possible, since this will optimize your view. Tilt the ophthalmoscope as needed to visualize different areas. Find and follow a vessel as it increases in caliber, tracing it back to its origin at the optic disk. The optic disk is located approximately 15 degrees nasal to the center of the retina and should appear to be yellowish orange (Figure 2). The optic cup is a pale central depression in the optic disk. The axons of the retinal ganglion cells exit the retina at the optic disk to form the optic nerve. In the retinal vasculature, veins are thicker and darker than arteries. The fovea is the area responsible for the highest visual acuity. It is temporal and slightly inferior to the optic disk and is surrounded by a more darkly pigmented region called the macula.

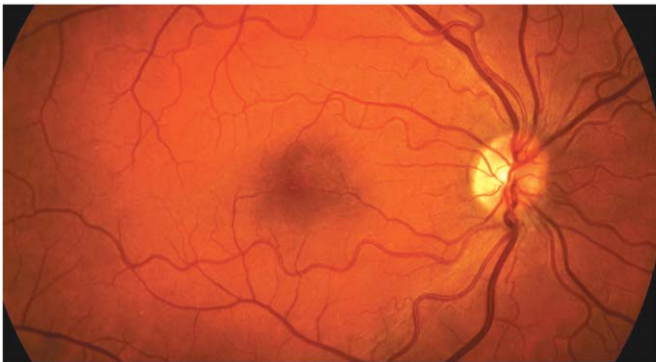


Figure 2: Normal retina

The cup to disk ratio, or the ratio of the diameter of the optic cup to the diameter of the optic disk, is normally 0.3. A higher cup to disk ratio, particularly a ratio above 0.5, may indicate glaucoma. Swelling of the optic disk can have multiple causes, including papilledema, optic neuritis, and anterior ischemic optic neuropathy. Any of the conditions associated with a swollen optic disk requires an emergency workup and an evaluation by an ophthalmologist.

Next, examine each quadrant of the retina, tracing vessels away from and back toward the optic disk. Ask the patient to look in a particular direction to facilitate visualization of the corresponding part of the retina.

Non proliferative diabetic retinopathy may cause microaneurysms, exudates, dot blot hemorrhages, and flame hemorrhages. The proliferative form of diabetic retinopathy features neovascularization. Hypertension can result in changes in the color and caliber of blood vessels, giving them the appearance of copper

wire or silver wire. "Arteriovenous nicking" refers to the narrowing or disappearance of the vein on each side of an arteriole. Cotton wool spots result from axons that were damaged by infarction and local ischemia. The occlusion of retinal arteries is usually caused by atherosclerosis or emboli and requires an emergency workup for systemic stroke. The appearance of a cherry red spot in the fovea is a sign of occlusion of the central retinal artery. Occlusion of the central retinal vein may result in retinal hemorrhages.

Limitations

Since direct ophthalmoscopy is performed without dilatation of the pupil, it provides only a limited view of the retina and is best used for screening rather than diagnostic purposes. If there is clinical suspicion of ocular disease, the patient should be referred to an ophthalmologist for a dilated fundus examination that will be performed with the use of specialized equipment.

Patients with cataracts may have a diminished or missing red reflex. To obtain the best visualization of the fundus, the size of the aperture may be reduced in order to minimize light scattering. It may not be possible to visualize the fundus in patients with dense cataracts. Patients with dense cataracts should be evaluated by an ophthalmologist.

Troubleshooting

Although the fundoscopic examination is challenging for beginners, it becomes easier with practice. Familiarize with the ophthalmoscope before examining patients. When examining patients, dim the room lights to maximize the dilatation of the pupils and improve the visual contrast of the fundus. First elicit the red reflex, since the red reflex indicates successful illumination of the retina. To locate the optic disk, approach the patient at an angle of about 15 degrees temporal to center; if the retina is not visualized, make small adjustments in the angle relative to the patient's visual axis. Technological advances include the development of instruments that facilitate examination of the retina by non ophthalmologists. Some of these devices contain cameras. However, these new devices are not yet widely available.

Conclusion

Direct ophthalmoscopy is an important technique for examination of the retina that can be mastered with practice. It can be performed in minutes during the general medical examination and poses virtually no risks to the patient. Ophthalmoscopy allows the general practitioner to evaluate the retina for pathologic changes, particularly in patients with common systemic diseases such as diabetes, hypertension, or atherosclerosis. Ophthalmoscopy can also help to identify ophthalmic emergencies that require immediate attention.

Reference: N. Engl. J. Med., August 20, 2015; 373:e9

Disseminated blastomycosis with cutaneous involvement

A 42 year old man presented to a hospital in June, 2014, with a 7 month history of progressive verrucous plaques on his chin (Figure 1). The patient reported living in Kenora, Ontario, a region of Canada that is hyperendemic for *B dermatitidis* 17 years earlier, where he had worked repairing railroad tracks. *B dermatitidis* is a dimorphic fungus endemic to the St Lawrence Great Lakes and Mississippi river systems in North America. Cases have also been reported in Africa and the Middle East. He had seen many different doctors and been given topical corticosteroid, antifungal, and antibacterial treatment without improvement. He also reported an intermittent cough productive of white sputum and mild dyspnoea on exertion for the past 2 months.

His physical examination was normal apart from the skin lesions. Chest radiograph and CT (Figure 2) showed multiple large cavitations in the upper lobes (arrows) and tree in bud opacities. A biopsy sample of the skin lesions showed broad based budding yeast with Gomori methenamine silver stain in the dermis consistent with blastomycosis. Fungal culture from a bronchoalveolar lavage grew *Blastomyces dermatitidis*.

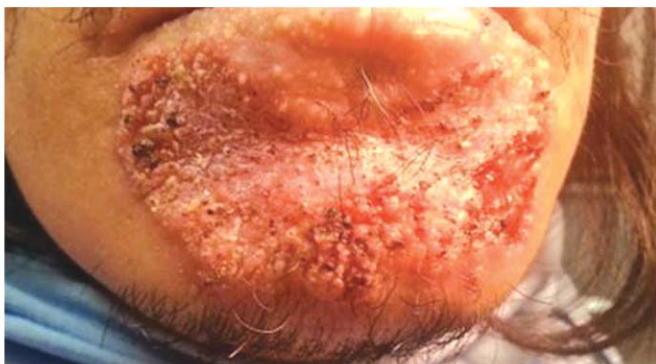


Figure 1: Verrucous lesion of the skin

The fungus is generally acquired through exposure to soil or moist organic debris and primarily affects the lower respiratory tract causing acute or chronic pneumonia. After seeding the respiratory tract *B dermatitidis* disseminates haematogenously to extrapulmonary sites in 20-50% of cases, most often to the skin, bones, and joints. Primary cutaneous inoculation can also occur.

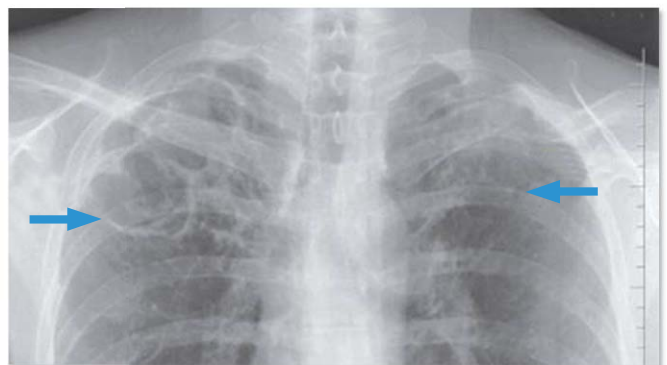


Figure 2: Chest radiograph showing upper lobe cavities

Reactivation of latent disease has been described and might explain our patient's presentation.

Cutaneous blastomycosis is characteristically a verrucous "wart like" lesion with irregular borders. Ulcerative lesions with raised borders are also common. Any patient with cutaneous blastomycosis should be investigated for pulmonary involvement and other sites of dissemination. We started our patient on 6 months of 200 mg itraconazole twice daily. At 5 month follow up in November, 2014, the patient is doing well, with no respiratory symptoms and improvement in the skin lesions.

Reference: The lancet, March 7, 2015, Vol. 385(9971):883

Info Quiz Answers

January-March 2016

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



Youngest ever conjoined twins successfully separated

A medical team in Switzerland has separated eight day old conjoined sisters, believed to be the youngest babies to be successfully parted. The twins, born in December 2015, were fused at the liver and chest. Doctors had originally planned to separate them when they were several months old but brought the operation forward when they each suffered a life threatening condition. The operation reportedly carried a 1% chance of

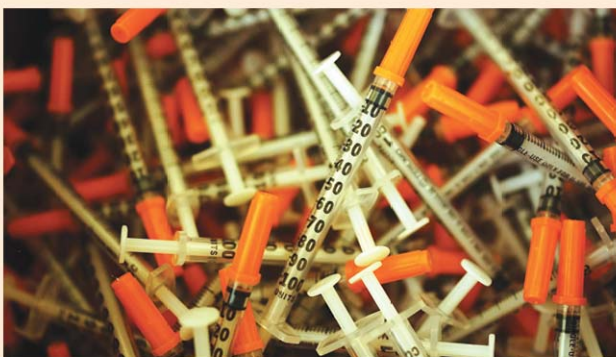


success. The twins, named Lydia and Maya, were born eight weeks premature at the Inselspital hospital in Bern, along with a triplet who was fully separate and healthy. According to the medical team, the twins were extensively conjoined on the liver, but had all vital organs. The conjoined twins were initially stable and doctors had planned to allow them to settle after birth and separate them after a few months. But after a week, their situation deteriorated dramatically: one suffering from hypertension and the other suffering from the opposite condition, known as hypotension. Both conditions were life threatening to the frail twins, who weighed just 2.4lb (1.1kg) each, and the doctors decided their only chance was attempting surgery never before performed on such young infants. A medical team includes five surgeons, assisted by two nurses and six anesthesiologists, carried out the successful, five hours operation to separate the tiny identical twins. The girls underwent further surgery to close their abdominal walls and are now recovering in a paediatric intensive care ward.

Reference: www.bbc.com

World first needle phobic pancreas transplant

A British woman has become the first person in the world to have a pancreas transplant because of a severe needle phobia. She had Type 1 diabetes since she was seven. She would shake uncontrollably and vomit when injecting her with insulin. Her phobia had reached a critical point in 2012, when the DVLA (Driver & Vehicle Licensing Agency) had changed its



regulations in relation to diabetic drivers, insisting they checked blood glucose levels, requiring her to prick her skin before driving and once every two hours behind the wheel. She had tried hypnotherapy and cognitive behavioral therapy in an attempt to cure her phobia, but without success. And injecting herself with insulin would frequently take 20 minutes. It took more than two years for her to be placed on a waiting list for the transplant, during which time she appeared in front of a panel three times to discuss her eligibility. Questions had been raised over her need for the transplant, given that she did not have any kidney complications and over whether her phobia was a strong enough reason to undergo major surgery. But a phobia of needles was common among long term diabetics and her story could give hope to others.

Reference: www.bbc.com

Aquagenic keratoderma



A 44 year old otherwise healthy man presented with thickening of his palms after their immersion in water, accompanied by burning pain, pruritus and edema. Onset was at 37 years of age. The patient had no family history of similar skin findings and said that he did not have a history of hyperhidrosis, thyroid disease, or medication use. Physical examination after the

patient held a piece of gauze soaked in water for 2 minutes revealed hypopigmented, translucent papules and plaques in both palms. The lesions became more evident when examined with a Wood's lamp. A skin biopsy specimen showed orthohyperkeratosis of the stratum corneum, dilatation of intraepidermal eccrine ducts, and hyperplasia of the eccrine sweat glands. A sweat chloride test was normal. The patient received a diagnosis of aquagenic keratoderma, an unusual condition characterized by transitory, flat topped papules and plaques, with hyperwrinkling and eccrine duct prominence on the palms and fingers and in rare cases, the soles, induced by exposure to water. Aquagenic keratoderma is more frequent in women than in men and has been associated with a heterozygous mutation in the cystic fibrosis gene. The patient was treated with subcutaneous injections of botulinum toxin, with prompt improvement of his symptoms.

Reference: N. Engl. J. Med., September 4, 2014; 371;10:952

Squamous cell carcinoma resembling pyoderma gangrenosum



A 53 year old woman presented with a nonhealing wound on her right hand. The wound was a slowly progressing ulceration that had occurred after the patient had what was believed to be a wart removed by means of laser therapy approximately 1 year before presentation. The patient had no notable medical history,

including no history of chronic inflammatory conditions. For the previous 6 months, she had received treatment with topical and systemic immunosuppressive medications, including oral glucocorticoids, for a clinical diagnosis of pyoderma gangrenosum, with no improvement. Examination of two punch biopsy specimens from the edge of the ulcer revealed squamous cell carcinoma. This common cancer is associated with risk factors including increasing age, light skin color, exposure to ultraviolet light, chronic immunosuppression, and exposure to ionizing radiation. The patient reported that she had worked for several years as a technical assistant performing mammography and that she had followed standard radiation precautions. The tumor was excised surgically but relapsed locally after 6 months; the relapse was followed by reexcision and radiation therapy.

Reference: N. Engl. J. Med., July 30, 2015; 373;5:e5

Acral lentiginous melanoma



A 68 year old man presented with a 2 year history of a nonhealing ulceration involving the lateral aspect of the left heel. The physical examination revealed an ulcerated black plaque measuring 5.5 cm by 6.5 cm. An excisional biopsy

showed an acral lentiginous melanoma with a Breslow depth of 2.0 mm. The patient underwent a wide local excision with 2 cm margins. A sentinel lymph node biopsy of the left inguinal nodes was negative. After 2 years of follow up, there was no evidence of recurrence. Acral lentiginous melanoma is an uncommon variant of melanoma that typically occurs on the palms and soles. It is the most common histologic subtype of melanoma among black patients. Despite the higher incidence of melanoma among non Hispanic white patients, black patients with melanoma (regardless of histologic subtype) are more likely to present with advanced stage disease and are more likely to have lower survival rates than their white counterparts. The reasons for advanced disease at presentation are not entirely clear but are thought to be due in part to delays in diagnosis.

Reference: N. Engl. J. Med., November 5, 2015; 373:19:1864

Bullous pemphigoid



A healthy 73 year old woman reported severe itching and intense blisters on her forearms, lower back, and legs within the previous 2 weeks. Clinical examination was notable for tenderness, erythema, and blistering, as seen on the back of her

hands. Laboratory findings included eosinophilia and autoantibodies to bullous pemphigoid antigen 230 (BP230). Subepidermal blistering and eosinophil accumulation in the histologic analysis and linear fluorescence of IgG and complement C3 at the dermoepidermal junction on a direct immune fluorescence assay confirmed the diagnosis of bullous pemphigoid. The age at onset of bullous pemphigoid is commonly 70 years or older. Its pathogenesis is typically defined by autoantibodies against basement membrane structures, including BP180 and BP230. The patient was given a short course of high dose systemic glucocorticoids, and treatment with dapsone was started. Blisters were punctured and treated locally with an eosin solution to dry them out. The patient was symptom free 2 weeks after therapy was initiated, and her condition was stable on dapsone therapy 5 months later.

Reference: N. Engl. J. Med., October 22, 2015; 373:17:1659

Zika virus infection

The explosive pandemic of Zika virus infection occurring throughout South America, Central America, and the Caribbean and potentially threatening the United States is the most recent of four unexpected arrivals of important arthropod borne viral diseases in the Western Hemisphere over the past 20 years. It follows dengue, which entered this hemisphere stealthily over decades and then more aggressively in the 1990s; West Nile virus, which emerged in 1999; and chikungunya, which emerged in 2013. Zika, had until now remained an obscure virus confined to a narrow equatorial belt running across Africa and into Asia.



Introduction

Zika virus is spread by mosquitoes, which can cause fever, rash, joint pain, and conjunctivitis. Most people infected with Zika virus do not even get sick. It can also be transmitted from a pregnant mother who has been bitten by an infected mosquito to her baby during pregnancy or around the time of birth.

- Genre: Flavivirus
- Vector: Aedes mosquitoes
- Reservoir: Unknown
- Incubation period: Incubation period of Zika virus disease is not known, but is likely to be a few days to a week

History

In 1947, scientists researching yellow fever placed a rhesus macaque in a cage in the Zika Forest (zika meaning "overgrown" in the Luganda language), near the East African Virus Research Institute in Entebbe, Uganda. The monkey developed a fever, and researchers isolated from its serum a transmissible agent that was first described as Zika virus in 1952. It was subsequently isolated from a human in Nigeria in 1954. From its discovery until 2007, confirmed cases of Zika virus infection from Africa and Southeast Asia were rare.

In April 2007, the first outbreak outside of Africa and Asia occurred on the island of Yap in the Federated States of Micronesia, characterized by rash, conjunctivitis, and arthralgia, which was initially thought to be dengue, chikungunya or Ross River disease. However, serum samples from patients in the acute phase of illness contained RNA of Zika virus. There were 49 confirmed cases, 59 unconfirmed cases, no hospitalizations, and no deaths. More recently, epidemics have occurred in Polynesia, Easter Island, the Cook Islands and New Caledonia. Since April 2015, a large,

ongoing outbreak of Zika virus that began in Brazil has spread to much of South and Central America, and the Caribbean.

As of early 2016, the most widespread outbreak of Zika virus disease, has been ongoing mostly in the Americas. In January 2016, the World Health Organization (WHO) said that the virus was likely to spread throughout the majority of the Americas by the end of the year. Subsequently, in February 2016, the WHO declared that microcephaly and Guillain Barre syndrome, believed to be associated with the virus outbreak, were a public health emergency of international concern. In January 2016, the center for disease control and prevention (CDC) issued a level 2 travel alert for people traveling to regions and certain countries where Zika virus transmission is ongoing. The agency also suggested that women thinking about becoming pregnant should consult with their physicians before traveling. Governments or health agencies of the United Kingdom, Ireland, New Zealand, Canada, and the European Union soon issued similar travel warnings. In Colombia, Minister of Health and Social Protection Alejandro Gaviria Uribe recommended to avoid pregnancy for eight months, while the countries of Ecuador, El Salvador, and Jamaica have issued similar warnings.

Areas with evidence of Zika virus

Figure 1 shows the countries affected by Zika virus:

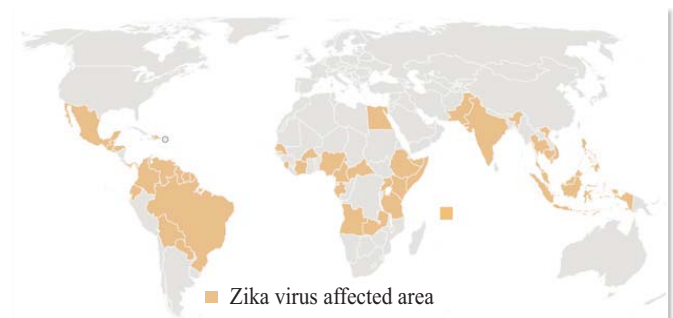


Figure 1: Zika virus affected area

Transmission

Mosquito bites

Zika virus is transmitted to people primarily through the bite of an infected *Aedes* species mosquito. These are the same mosquitoes that spread dengue and chikungunya viruses.

- These mosquitoes typically lay eggs in and near standing water in things like buckets, bowls, animal dishes, flower pots and vases. They prefer to bite people, and live indoors and outdoors near people. Mosquitoes that spread chikungunya, dengue, and Zika are aggressive daytime biters. They can also bite at night
- Mosquitoes become infected when they feed on a person already infected with the virus. Infected mosquitoes can then spread the virus to other people through bites

Mother to child

A mother already infected with Zika virus near the time of delivery can pass on the virus to her newborn around the time of birth, but this is rare.

- It is possible that Zika virus could be passed from mother to fetus during pregnancy. This mode of transmission is being investigated
- To date, there are no reports of infants getting Zika virus through breastfeeding. Because of the benefits of breastfeeding, mothers are encouraged to breastfeed even in areas where Zika virus is found

Infected blood or sexual contact

Spread of the Zika virus through blood transfusion and sexual contact has been reported.

Clinical feature

The incubation period (the time from exposure to symptoms) of Zika virus disease is not clear, but is likely to be a few days. The symptoms are similar to other arbovirus infections such as dengue. The following symptoms may occur with Zika virus:

- About 1 in 5 people infected with Zika virus become ill
- The most common symptoms of Zika are fever, rash, joint pain, or conjunctivitis.
- Other common symptoms include muscle pain and headache.
- The illness is usually mild with symptoms lasting for several days to a week
- Zika virus usually remains in the blood of an infected person for a few days but it can be found longer in some people
- An increase in babies born with microcephaly
- Deaths are rare

Diagnosis

The symptoms of Zika virus are similar to those of dengue and chikungunya, diseases spread through the same mosquitoes that transmit Zika virus. Zika virus is diagnosed through:

- PCR (Polymerase Chain Reaction)
- Virus isolation from blood samples

Diagnosis by serology can be difficult as the virus can cross react with other flaviviruses such as dengue, west Nile and yellow fever.

Treatment

Zika virus disease is usually relatively mild and requires no specific treatment. No vaccine or medications are available to prevent or treat Zika infections. However, the following treatment protocol may be effective against Zika virus:

- Get plenty of rest
- Drink fluids to prevent dehydration
- Take medicine such as acetaminophen to relieve fever and pain
- Aspirin and other non steroidal anti inflammatory drugs (NSAIDs), like ibuprofen and naproxen should not be taken. Aspirin and NSAIDs should be avoided until dengue can be ruled out to reduce the risk of hemorrhage (bleeding).

Prevention

Mosquitoes and their breeding sites pose a significant risk factor for Zika virus infection. Prevention and control relies on reducing mosquitoes through source reduction and reducing contact between mosquitoes and people. This can be done by using insect repellent, wearing clothes that cover as much of the body as possible, using physical barriers such as screens, closed doors and windows and sleeping under mosquito nets. It is also important to empty, clean or cover containers that can hold water such as buckets, flower pots or tyres, so that places where mosquitoes can breed are removed.

Special attention and help should be given to those who may not be able to protect themselves adequately, such as young children, the sick or elderly. During outbreaks, health authorities may advise that spraying of insecticides be carried out. Insecticides recommended by the WHO Pesticide Evaluation Scheme may also be used as larvicides to treat relatively large water containers. Travellers should take the basic precautions described above to protect themselves from mosquito bites.

References:

1. *European Centre for Disease Prevention and Control, January, 2016*
2. *World Health Organization, January, 2016*
3. *N. Engl. J. Med., January 21, 2016*
4. www.cdc.gov/zika
5. en.wikipedia.org

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 May 2016; this will ensure eligibility for the Raffle Draw and the lucky winners will get attractive prizes!

1. **Which drugs have bacteriostatic effect in regular doses?**
 - a. Tetracyclines
 - b. Cephalosporins
 - c. Sulfamethoxazole and trimethoprim (Sumetrolim)
 - d. Erythromycin
 - e. Amoxicillin
2. **What are the possible causes of a 45 year old male reveals episodes of vertigo and loss of consciousness associated with sweating?**
 - a. Hyperventilation
 - b. Hyperglycemia
 - c. Zollinger Ellison syndrome
 - d. Pheochromocytoma
 - e. Paroxysmal tachycardia
3. **Macroglossia is a possible feature of which of the following conditions?**
 - a. Acromegaly
 - b. Marfan's syndrome
 - c. Hurler's syndrome
 - d. Achondroplasia
 - e. Amyloidosis
4. **Which of the following conditions are related to psychosomatic disorders?**
 - a. Systemic lupus erythematosus
 - b. Vasomotor rhinitis
 - c. Peptic ulcer
 - d. Diabetes mellitus
 - e. Bartter's syndrome
5. **Paresthesia associated with pruritus is characteristic for which of the following conditions?**
 - a. Multiple sclerosis
 - b. Temporal lobe epilepsy
 - c. Raynaud's phenomenon
 - d. Acromegaly
 - e. Hypoventilation
6. **In which of the following conditions is polydactyly present?**
 - a. Laurence Moon Biedl syndrome
 - b. Marfan's syndrome
 - c. Turner's syndrome
 - d. Fanconi's congenital aplastic anemia
 - e. Ventricular septal defect
7. **A classic type migraine is characterized by which of the following?**
 - a. It cannot be diagnosed if there are no prodromal symptoms
 - b. It shows a gradual progression
 - c. A homonymous hemianopsia is present
 - d. Edema of the papilla
 - e. Acoustic hallucinations
8. **Which of the following drugs would lower the total serum cholesterol concentration in a patient with atherosclerosis of the coronaries?**
 - a. Saccharin
 - b. Nicotinic acid
 - c. Bezafibrate
 - d. Sulfinpyrazone
 - e. Thyroxine
9. **Which of the following conditions or drugs inhibit uric acid reabsorption?**
 - a. Low dose salicylate
 - b. Hyperlactacidemia
 - c. Phenylbutazone
 - d. Dicoumarol
 - e. Probenecid
10. **In which disease abdominal pain is a clinical feature?**
 - a. Methanol toxicity
 - b. Acute arsenic poisoning
 - c. Acute lead poisoning.
 - d. Acute iron poisoning
 - e. Typhoid fever



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