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Info Medicus

April-June 2012

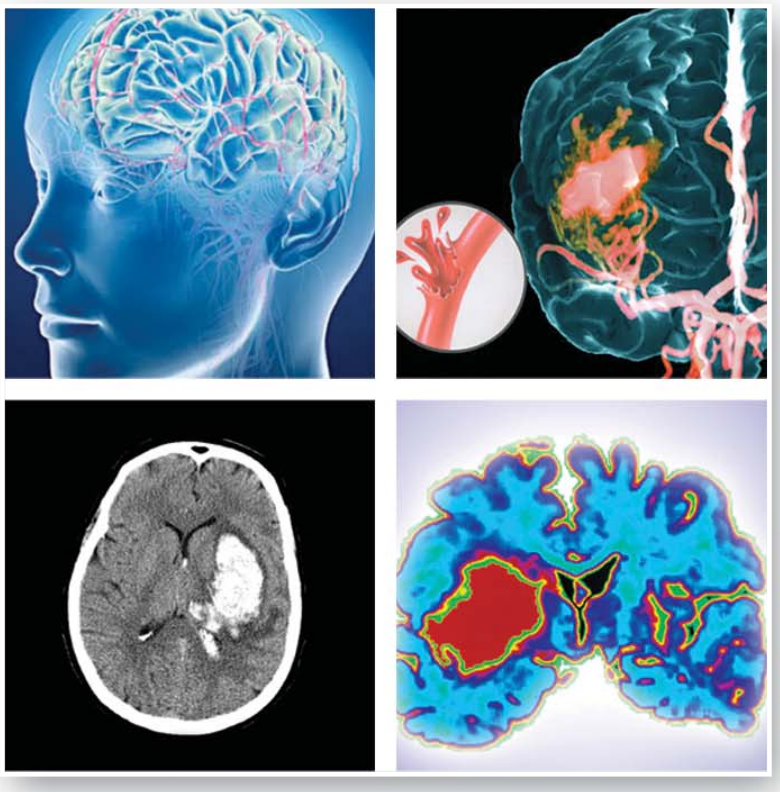
ISSN 2222-5188

info MEDICUS

The essence of medical practice

Volume 9 Issue 2

Evaluation of Hemorrhagic Stroke



April-June, 2012

Published by

Medical Services Department
ACI Pharmaceuticals
Novo Tower, 9th Floor
270 Tejgaon Industrial Area
Dhaka-1208

Designed by

Creative Communication Ltd.
Road # 123, House # 18A
Gulshan 1, Dhaka 1212

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EDITORIAL

Dear Doctor

We thank you for your remarkable support and appreciations for our earlier issue of Info Medicus. We assure you our best commitment to bring the most recent developments in the health segment around the globe at your desk. Moreover we would like to be your trusted partner working together towards adding value to life. Our team has been working effortlessly to accomplish your academic quest at all times.

In this issue we have introduced two new sections - Clinical Review and Clinical Focus. We anticipate you would like these new additions and wait for your earnest feedback if any on them.

Hemorrhagic Stroke is a leading cause of death and disability, and its diagnosis can be challenging. Hence, we are highlighting the Evaluation of Hemorrhagic Stroke as the topic of "Review Article". In this review our main focus is on the presentation, diagnosis, and management of intracerebral hemorrhage and subarachnoid hemorrhage.

We have our other topics like, pregnancy in Pott's disease in "Case Review" and examination of the larynx and pharynx under the banner of "Clinical Method" and Rhabdomyolysis in "Clinician's Corner". We hope you will enjoy this essence of medical practices.

Thank you for being with us all the way through our journey.

Sincerely yours,

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

(Dr. Rumana Dowla)
Manager, Medical Information & Research

Evaluation of Hemorrhagic Stroke

Introduction

A stroke occurs when brain tissue is damaged due to lacking of enough blood flow or oxygen delivery to the brain's cells. Therefore stroke can result either from ischemia (in which occlusion of a blood vessel and the resulting lack of blood flow causes insult) or from a hemorrhage (results from a weakened blood vessel that ruptures and bleeds) within the brain. Hemorrhagic strokes are less common than ischemic strokes but cause a significant number of deaths worldwide with severe, nonfatal damage to brain tissue and it accounts form about 13% of stroke cases. Stroke is the third most common cause of death after coronary heart disease and all cancer deaths. According to the World Health Organization (WHO), 15 million people suffer stroke worldwide each year. Of these, 5 million die and another 5 million are permanently disabled. There is no doubt that stroke is not only the leading cause of long-term disability in Bangladesh though sufficient data are not available as no large study is done yet in, but also it generates an enormous economic burden for individuals, families and communities. Generally, Hemorrhagic stroke occurs when a weakened blood vessel rupture. Two types of weakened blood vessels usually occurs cause hemorrhagic stroke: aneurysms and arteriovenous malformation (AVMs).

Types of hemorrhagic stroke

The two main categories of hemorrhagic stroke are intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH).

Intracerebral hemorrhage (ICH) occurs when an artery suddenly burst and releases blood within brain tissue. This blood can damage the brain tissues, causing a stroke, and can cause sudden increase in the pressure inside the skull.

Subarachnoid hemorrhage (SAH) most commonly occurs when a cerebral aneurysm ruptures, causing blood into the subarachnoid space outside of the brain, between the skull and the brain itself. This blood can also cause a sudden increase in pressure inside the skull.

In either type of stroke, death or certain symptoms ranging from severe to mild can result, depending on the account of pressure.

Risk factors

- Hypertension is the most important risk factor for hemorrhagic stroke
- Anticoagulant medication make bleeding into the brain more likely, especially if taken improperly or in large doses
- Cerebral aneurysms enlargement of blood vessels
- Substance abuse
- Family history of strokes
- Smoking, diabetes, high cholesterol, obesity and a sedentary life style are risk factors for all types of stroke

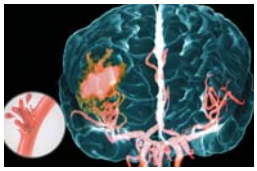
Intracerebral hemorrhage

Epidemiology

Demographics of those affected by ICH are variable. The annual incidence rate of ICH is 12 to 15 per 100,000.ICH accounts for 10% to 15% of all strokes on an annual basis. The mortality rates for ICH at 7 days, 30 days, and 1 year are 34.6%, 50.3%, and 59% respectively, with an overall 10 year survival rate of approximately 24%. According to a study by the American, the average age of a patient presenting with ICH is 73 years, with an equal distribution between males and females.

Pathogenesis

Upto 70% of the patients with primary ICH develop some measureable amount of lesion expansion over the initial few hours. Hematoma growth is an independent determinant of both mortality and functional outcome after ICH. The mass effect of primary bleeding may cause lesions to migrate and dissect through less dense white matter with the patches of intact brain tissue surrounding a hematoma. Although continued bleeding from the primary source is one mechanism for expansion, another could be the mechanism disruption of local vessel by which multiple adjacent micro bleeds develop, accumulate and contribute to overall lesion volume.



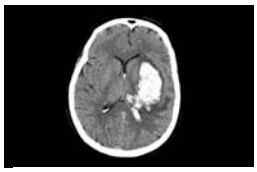
CTA showing rupture of cerebral artery leading to ICH

Causes

- Arteriovenous malformation
- Intracranial aneurysm
- Cavernous angioma
- Venous angioma
- Venous sinus thrombosis
- Intracranial neoplasm
- Coagulopathy
- Vasculaitis
- Drug use (e.g, cocaine, alcohol)

Presentation

Altered mental status and decreased Glasgow Coma Scale (GCS) score are common in patients with ICH. Between the time of initial prehospital emergency medical services and examination in the emergency department (ED), more than 20% of patients with ICH will have a decline of at least 2 points in their GCS score. In the typical presentation of ICH, there is a sudden onset of focal neurologic deficit that progresses during a period of minutes to hours. Headache occurs more often with ICH than with ischemic stroke but is less likely in ICH than in SAH. Vomiting is seen more often with ICH than with either ischemic stroke or SAH. However, it is not possible to differentiate among ischemic stroke, SAH, or ICH based on clinical grounds alone.



CT scan showing ICH

Diagnosis

While CT and MRI are equally sensitive for identifying acute hemorrhage, MRI is more sensitive in identifying prior hemorrhages. However, given the time involved to obtain an MRI and the limited availability of MRI, CT is the first line test in the ED. ICH expansion is associated with lower GCS score and elevated NIH Stroke Scale score and worsening outcomes. In addition, CT angiography (CTA), contrast-enhanced CT, CT venography, contrast-enhanced MRI, MR angiography (MRA), or MR venography are useful for identifying structural lesions that may be the underlying cause of an ICH. The suggestion of an underlying structural cause may be seen on the initial CT and the decision to pursue additional studies can be made at that time.

Subarachnoid hemorrhage

Epidemiology

Every year 2% of all patients who visit the ED have a chief complaint of headache, and approximately 1 of every 100 of these patients has an SAH. 85% of SAHs are caused by a ruptured cerebral aneurysm. Other etiologies include inflammatory lesions of the cerebral arteries, arterial dissection, vascular lesions of the spinal cord, coagulopathies, tumors, or illicit drug use. Cerebral aneurysms are found in approximately 2% of the population. Most aneurysms do not cause any problems. The presence of aneurysm does increase the likelihood of rupture leading to SAH. The risk of aneurysm rupture increases proportionally with the size of the aneurysm.

Causes

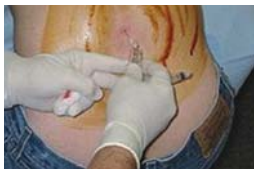
- Traumatic brain injury
- Cerebral aneurysm
- Arteriovenous malformation even in spinal cord
- Bleeding from various tumor
- Cocaine abuse
- Sickle cell anaemia in case of children
- Anticoagulant therapy
- Bleeding disorder
- Pituitary apoplexy

Presentation

It can be difficult to differentiate between SAH and ICH based on clinical presentation alone. However patients with SAH are typically awake and neurologically intact on presentation. Headache is much more common in patients with SAH than in those with ICH, and it is more often the main complaint in SAH than in ICH. The classic presentation of SAH is a headache that is rapid in onset, like a "thunder clap." Patients often describe this headache as the "worst headache of my life." Certain characteristics of the patient's headache may raise clinical suspicion for SAH and prompt further investigation. These characteristics include but are not limited to sudden onset of headache, large qualitative difference in headache compared with previous headaches, and nausea, vomiting, or neck pain. When these features are present, a high level of clinical suspicion for SAH is warranted, even with seemingly benign presentations.

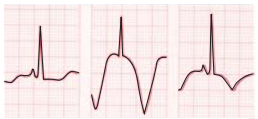
Diagnosis

Non contrast enhanced head CT is the first appropriate test to order when a diagnosis of SAH is possible. MRI can also be used, but due to time constraints and limited availability, it is not considered a first line test. Initial sensitivity is greater but diminishes as time passes. After a negative head CT, the next diagnostic step is lumbar puncture (LP). Sentinel bleeds are smaller events



A lumbar puncture in progress. A large area on the back has been washed with an iodine-based disinfectant leaving brown coloration

that may occur prior to a large SAH. Even small amounts of blood within the CSF can be detected by LP. While no defined CSF red blood cell (RBC) count value has been determined as specific for SAH, an elevated RBC count that remains elevated in consecutive studies can be indicative of SAH. While an RBC count that decreases in subsequent tubes may be suggestive of a traumatic LP, this cannot be relied upon to rule out SAH. The strategy is to do subsequent LP if a negative head CT comes. While no defined CSF red blood cell (RBC) count value has been determined as specific for SAH, an elevated RBC count that remains elevated in consecutive studies can be indicative of SAH. While an RBC count that decreases in subsequent tubes may be suggestive of a traumatic LP, this cannot be relied upon to rule out SAH. The strategy of negative head CT with subsequent LP for diagnosis of SAH has recently been validated. In a 3 year, large prospective cohort study conducted at two EDs, the sensitivity of CT and subsequent LP for diagnosis of SAH was 100%.



ECG changes in Stroke

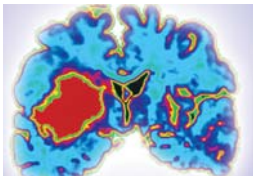
Xanthochromia is a pink to yellow coloring of the CSF that is caused by degradation products of lysed RBCs. Xanthochromic CSF can be highly suggestive of SAH. However, other causes of xanthochromia do exist and may lead to false positive results in the evaluation of CSF for SAH. These causes include systemic jaundice, elevated CSF protein concentration, Rifampin therapy, and dietary hypercarotenemia. After SAH is diagnosed, it is appropriate to further search for the etiology of the hemorrhage. The current gold standard for this purpose is cerebral angiography, which provides the best information for documenting the presence and features of aneurysms that may be corrected with surgical intervention. However, angiography may not be 100% sensitive for detecting aneurysms 5 mm or larger in diameter and 64% to 83% sensitive for aneurysms with a diameter less than 5 mm. The information provided by CTA may be sufficient to proceed directly to intervention. With selected patients, a decision for intervention can be made on the results of CTA alone. MRA can also be used in evaluation. However, the availability of MRA may be limited in many areas. MRA is 85% to 100% sensitive for detecting aneurysms 5 mm or greater in diameter, and approximately 56% sensitive for aneurysms with a diameter less than 5 mm.MRA does not require iodinated contrast or ionizing radiation and may be useful in patients with renal insufficiency or in pregnant women. If CTA or MRA is negative, the next step is cerebral angiography, neurosurgical consultation, or both. Depending on the clinical condition of the patient, the consultant may choose either to proceed with cerebral angiography immediately or to observe for 24 to 48 hours before reimaging.

After a subarachnoid hemorrhage is confirmed, its origin needs to be determined. If the bleeding is likely to have originated from an aneurysm (as determined by the CT scan appearance), the choice is between cerebral angiography (injecting radiocontrast through a catheter to the brain arteries) and CT angiography (visualizing blood vessels with radio contrast on a CT scan) to identify aneurysms. Catheter angiography also offers the possibility of coiling an aneurysm.

Treatment

Intracerebral hemorrhage

The ABCs (airway, breathing, and circulation) are obvious concerns for any patient with hemorrhagic stroke. Neurologic decline and depressed level of consciousness may result in inability to maintain an airway. Failure to appropriately manage the airway with endotracheal intubation may lead to aspiration, hypoxemia, or hypercapnea. Using medications that do not raise intracerebral pressure (ICP) in patients with hemorrhagic stroke may prevent further neurologic damage and yield maximum benefit. Patients with ICH and a known factor deficiency should undergo transfusion with appropriate factor replacement. Patients taking oral anticoagulants who are diagnosed with ICH should stop taking the anticoagulant for the short term. Warfarin causes depletion of vitamin K dependent factors II, VII, IX, and X as well as proteins C and S. These factors should be replaced and the international normalized ratio (INR) should be corrected. Vitamin K should be given intravenously, but because this takes hours to correct the INR, it is not suitable as a sole agent. INR can be corrected with fresh frozen plasma (FFP) or with prothrombin complex concentrates (PCC). PCC has several advantages over FFP, one being that it is more concentrated and requires less volume when transfused, constituted in a shorter period of time than FFP, does not need a type and screen, and can reverse an elevated INR faster than FFP. Forty eight hours after initial transfusion of PCC, INR remained at 1.3 or less, suggesting a sustained effect. New oral anticoagulants have been approved and are currently or will soon be available. Among them are Apixaban,



3D CT guieded angiography

Dabigatran, and Rivaroxaban. There is no reversal strategy available for a patient with ICH who is receiving these new oral anticoagulants.

Recombinant factor VIIa (rFVIIa) is the activated form of factor VII in the clotting cascade and interacts with tissue factor and can also activate factor IX and factor X to promote clot formation. rFVIIa has been used extensively in uncontrolled bleeding in hemophilia patients. Hypertension is seen in all forms of stroke. Systolic blood pressure (SBP) of 140 mm Hg or higher is seen in 67% of ischemic stroke cases, 75% of ICH cases, and 100% of SAH cases. The recommendations for blood pressure management is that if SBP is greater than 200 mm Hg or mean arterial pressure (MAP) is greater than 150 mm Hg, aggressive management that is reduction of elevated pressure with an IV antihypertensive infusion is necessary, with blood pressure checks every 5 minutes and infusion rates titrated as needed. If SBP is greater than 180 mm Hg or MAP is greater than 130 mm Hg and there is evidence of elevated intracranial pressure (ICP), invasive monitoring of ICP should be considered. Once an ICP monitor has been placed, cerebral perfusion pressures should be maintained at 60 mm Hg or higher with IV infusions or intermittent medications. If SBP is greater than 180 mm Hg or MAP is greater than 130 mm Hg and there is no evidence of elevated ICP, then reduction of MAP to 110 mm Hg using infusion or intermittent IV medications with reexamination every 15 minutes is needed and considered safe.

Strict glucose control, with target glucose levels near 100 mg/dL, may cause adverse hypoglycemic events and be detrimental. It has been suggested previously that suitable glucose levels may be 140 to 185 mg/dL. Patients with glucose levels greater than 185 mg/dL may benefit from insulin. Currently, only ICH patients who have seizures documented either by electroencephalography (EEG) or clinical observation should be treated with antiepileptics. The role of surgical treatment in the majority of ICH cases is unclear. However patients treated surgically had markedly better outcome. Currently, surgical treatment in the form of craniotomy and evacuation is recommended for cerebellar ICH larger than 3 cm in diameter and for patients with brain stem compression or hydrocephalus.

Subarachnoid hemorrhage

Subarachnoid hemorrhage usually present with increased episodes of rebleeding which is found to occur with elevated SBP, especially with SBP greater than 150 mm Hg. It is reasonable to attempt blood pressure control in this setting, using short acting IV infusion medications such as Nicardipine, Labetalol, or Esmolol. Management of SAH patients taking oral anticoagulants is similar to that described for ICH patients. Regarding morbidity and the mortality in case of the SAH, vasospasm plays a significant role.

Hunt and Hess Grading Scale for Subarachnoid Hemorrhage

Grade	Clinical Description
1	Asymptomatic or low grade headache and minimal nuchal rigidity
2	Moderate/severe headache, nuchal rigidity, possible cranial nerve palsy, but no other focal neurologic deficit
3	Somnolence, mildly altered mental status, mild focal neurologic deficit
4	Stupor, moderate/severe hemiparesis, decerebrate rigidity, vegetative disturbances
5	Profound coma, decerebrate rigidity, death-like appearance

Adapted from Brisman et al47; Hunt and Hess.

Vasospasm typically occurs in the days following SAH and gradually resolves within 2 to 4 weeks. In SAH patients surviving to treatment, vasospasm accounts for approximately 50% of deaths, with rebleeding and complications from surgery making up the remaining 50%. Oral Nimodipine has been shown to improve outcomes related to vasospasm.

Some patients with SAH are candidates for surgical intervention. The Hunt and Hess grading scale are useful to determine the severity of SAH in the clinical setting and to determine if surgical intervention may be helpful. Patients with Hunt and Hess grades 1 to 4 are generally treated early with surgical intervention. In grade 5, the most severe grade, the benefit from surgical intervention is less clear. Prognosis with or without surgical intervention is grim in these patients. For this reason, early surgical intervention has typically been withheld. However, if clinical improvement occurs, delayed surgical intervention may be appropriate.

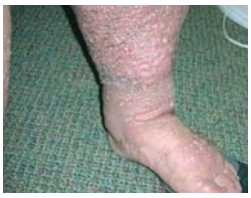
Two basic types of surgical intervention are available: craniotomy with microsurgical clipping and endovascular occlusion with detachable coils. Endovascular occlusion is a procedure performed with an interventionalist and does not involve an open cranial procedure. Availability of this procedure varies. Ultimately, the decision to treat the aneurysm is best made in consultation with the specialist whether going with craniotomy with microsurgical clipping or endovascular occlusion with detachable coils.

However hydrocephalus is more commonly seen in patients with a poor clinical grade developed within 72 hours. Many patients with hydrocephalus are asymptomatic and may not require any intervention. Moreover when the patient has a change in level of consciousness or mental status or worsening findings on neurologic exam, ventriculostomy is recommended. Long term or permanent shunting may also be required and has been reported in 18% to 26% of patients surviving SAH.

References:
1. www.emedmag.com
2. Emergency medicine, December 2011
3. American College of Physicians Foundation, 2011
4. JAMA, 9 June 2010, Vol. 303, No. 22
5. Clinical Publishing by Oxford, 2010

DERM DILEMMA

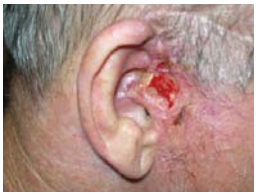
What is your diagnosis?



CASE 1

A 64 year old woman presents with swelling and pain in both lower extremities. She states that these symptoms have persisted for several months. She is very obese and has been diagnosed with chronic lymphedema. Examination reveals that both legs are significantly swollen with cobblestoning. The skin has a hyperkeratotic verrucous surface with fibrosis. The patient is referred to a vascular specialist for evaluation.

What is your diagnosis?



CASE 2

A 74 year old man has a rapidly growing, bleeding tumor near his right ear. He reports burning and pruritus surrounding the nodule. He has a history of substantial sun exposure and has had previous skin cancers. On physical examination, he demonstrates a 1.5 cm erythematous nodule involving the right preauricular surface. A head and neck surgical consult is ordered.

Reference: Emergency Medicine November 2011, Vol. 43, No. 11: 17-18

Answers 13

Gene therapy used in a bid to save a man's sight

A rare genetic disorder known as Choroideraemia where patients start off life with normal vision and it's not until their late childhood that they notice that they cannot see anything at night and usually the diagnosis is made during middle to late childhood. The disease is caused by an inherited faulty gene, called REP1. Without a functioning copy of the gene, the light detecting cells in the eye die. Researchers in Oxford have treated a man with an advanced gene therapy technique to prevent him from losing his sight. It is the first time that anyone has tried to correct a genetic defect in the light-sensing cells that line the back of the eye. The idea behind the gene therapy is simple: stop the cells from dying by injecting working copies of the gene into them. Specialist believes that if this gene therapy works it could be used to treat a wide variety of eye disorders, including the most common form of blindness in the elderly, macular degeneration.

Cannabis drivers 'twice as likely to cause car crash'

Cannabis can impair a driver's ability to respond to potential dangers, research shows. Cannabis impairs brain and motor functions needed for safe driving, the researchers suggest. Study reveals collisions between one or more moving vehicles on a public road involved in the consumption of cannabis. Study shows a near doubling of risk of a driver being involved in a motor vehicle collision resulting in serious injury or death if cannabis had been consumed less than three hours before. Blood sample studies tested for tetrahydrocannabinol, or THC, the active chemical in cannabis, by analyzing blood samples or using direct reports of cannabis use from those involved. Most studies used one nanogram per milliliter of cannabis or any amount greater than zero as the cut off for a positive test result, with one study using a 2ng/ml cut off. This new research strengthens the evidence that driving under the influence of cannabis increases the likelihood of being seriously injured or killed in a collision. This adds to the argument that a system needs to be put in place to monitor the number of serious and fatal accidents where impairment from illegal drugs was a contributory factor, so that appropriate action can be taken to prevent them. The researchers conclude that despite the increased risk posed by cannabis to car drivers, alcohol remains the substance most often present in crashes. The observed association between alcohol and crash risk is more significant than that for cannabis, the study says.

Alzheimer's: Diet 'can stop brain shrinking'

Diet affected tests of memory and thinking skills. A diet rich in vitamins and fish may protect the brain from ageing research suggests. Elderly people with high blood levels of vitamins and omega 3 fatty acids had less brain shrinkage and better mental performance. The research help analyzed blood samples from 104 healthy people with an average age of 87 who had few known risk factors for Alzheimer's. They found those who had more vitamin B, C, D and E in their blood performed better in tests of memory and thinking skills. They found individuals with high levels of vitamins and omega 3 in their blood was more likely to have a large brain volume. These results are very exciting to think that people could potentially stop their brains from shrinking and keep them sharp by adjusting their diet. It's important to note that this study looked at a small group of people with few risk factors for Alzheimer's disease, and did not investigate whether they went on to develop Alzheimer's at a later stage. There is a clear need for conclusive evidence about the effect of diet on our risk of Alzheimer's, which can only come from large scale, long term studies.

Reference: bbc.co.uk

Evaluation and management of Rhabdomyolysis

Rhabdomyolysis is a clinical syndrome caused by insults to myocytes and muscle membranes that lead to the destruction of skeletal muscle and release of muscle fiber contents into the bloodstream. Although a broad range of conditions can result in Rhabdomyolysis, the final common pathway of myocyte necrosis involves a rapid increase in intracytoplasmic calcium. This leads to the release of myocyte constituents into the circulation, which can produce life threatening complications including acute hyperkalaemia and acute renal failure (ARF). The most sensitive indicator of Rhabdomyolysis is an elevated serum creatine kinase (CK) level. In the absence of brain or cardiac issues, a CK concentration of 5,000 U/L or greater (with 50 to 250 U/L considered the normal range) is indicative of significant muscle injury.

Pathophysiology

Despite the diversity of conditions leading to Rhabdomyolysis, the final common pathway leading to myocyte necrosis is consistent. Damage to the myocyte causes an influx of sodium into the cell and an accumulation of cytosolic calcium due to a combination of direct injury to the cell and to increased activity of the Na^{+}/Ca^{2+} exchange mechanism that attempts to extrude sodium from the cell in exchange for calcium. The high intracytoplasmic calcium concentration has a number of deleterious effects, including activation of phospholipase A2, which results in the production of toxic metabolites and cell death.

Etiology and risk factors

Several investigators have attempted to categorize the many diverse causes and risk factors for Rhabdomyolysis. The most common causes are alcohol abuse, muscle overexertion, muscle compression and the use of certain medications or illicit drugs. Other significant causes of Rhabdomyolysis include electrical shock injury and crush injury. In crush injury, Rhabdomyolysis occurs because of the release of necrotic muscle material into the circulation after compression is relieved in, for example, persons trapped in crashed cars or collapsed buildings. Heatstroke and sporting activities, especially in previously untrained persons, are also common causes of the syndrome.

Heat dissipation impairment from wearing heavy sports equipment or exercising in humid, warm weather increases the risk of Rhabdomyolysis. Traumatic, heat-related, ischemic and exertional causes of Rhabdomyolysis. Numerous infectious and inflammatory processes can lead to Rhabdomyolysis. Certain metabolic and endocrinologic disorders can also increase the risk of developing the syndrome. The cause of Rhabdomyolysis can be obscure. In this situation, genetic etiologies should be considered. A genetic disorder should be suspected in patients who have recurrent Rhabdomyolysis after minimal to moderate exertion or after viral infections starting in childhood.

Medications and toxic substances that increase the risk of Rhabdomyolysis

Direct Myotoxicity

- HMG-CoA reductase inhibitors, especially in combination with fibrate-derived lipid lowering agents such as niacin
- Cyclosporine
- Itraconazole
- Erythromycin
- Colchicine
- Zidovudine
- Corticosteroids

Indirect muscle damage

- Alcohol
- Central nervous system depressants
- Cocaine
- Amphetamine
- Ecstasy (MDMA)
- LSD
- Neuromuscular blocking agents

HMG-CoA = 3-hydroxy-3-methylglutaryl coenzyme A;
LSD = lysergic acid diethylamide;

MDMA = 3,4-methylene dioxymethamphetamine

Traumatic, heat-related, ischemic and exertional causes of Rhabdomyolysis

Traumatic causes

- Lightning strike
- Immobilization
- Extensive third degree burn
- Crush injury

Heat-related causes

- Heatstroke
- Malignant hyperthermia
- Neuroleptic malignant syndrome

Ischemic causes

- Ischemic limb injury

Exertional causes

- Marathon running
- Physical overexertion in untrained athletes
- Pathologic muscle exertion
- Heat dissipation impairment
- Physical overexertion in persons with sickle cell disease

Infectious, inflammatory, metabolic and endocrinologic causes of Rhabdomyolysis

Infectious causes

- Virus: influenza virus B, parainfluenza virus, adenovirus, coxsackievirus, echovirus, herpes simplex virus, cytomegalovirus, Epstein-Barr virus, Human Immunodeficiency Virus (HIV)
- Bacteria: *Streptococcus, Salmonella, Legionella, Staphyloccus and Listeria species*

Inflammatory causes

- Polymyositis
- Dermatomyositis
- Capillary leak syndrome
- Snake bites (mostly in South America, Asia and Africa)

Metabolic and endocrinologic causes

- Electrolyte imbalances: hyponatremia, hypernatremia, hypokalemia, hypophosphatemia, hypocalcemia
- Hypothyroidism
- Thyrotoxicosis
- Diabetic ketoacidosis
- Nonketotic hyperosmolar syndrome

Genetic causes of Rhabdomyolysis

Lipid metabolism

- Carnitine palmitoyltransferase deficiency
- Carnitine deficiency
- Short-chain and long-chain acyl-coenzyme A dehydrogenase deficiency

Carbohydrate metabolism

- Myophosphorylase deficiency (McArdle's disease)
- Phosphorylase kinase deficiency
- Phosphofructokinase deficiency
- Phosphoglycerate mutase deficiency
- Lactate dehydrogenase deficiency

Purine metabolism

- Myoadenylate deaminase deficiency
- Duchenne's muscular dystrophy

Clinical presentation

Depending on the aetiology, the presentation of Rhabdomyolysis can range from an asymptomatic elevation in creatinine kinase through to life threatening electrolyte imbalance, hypovolemic shock and ARF. Muscle pain and weakness are common manifestations, often accompanied by generalized malaise, fever and tachycardia. The appearance of discolored urine may be the first indication of muscle injury.

Laboratory evaluation

Laboratory investigation is important in the diagnosis of Rhabdomyolysis. Leukocytosis and myoglobinuria may be seen in affected patients. Destruction of myocytes leads to leakage of intracellular contents, including CK and potassium, into the circulatory system. The most sensitive marker for significant muscle injury is a CK level five times above normal in the absence of cardiac or brain injury. However, the rise in serum myoglobin precedes the rise in CK. Grossly visible myoglobinuria does not manifest until approximately 100g or more of muscle is destroyed; therefore, measurement of serum and urine myoglobin is essential for the early diagnosis of Rhabdomyolysis. Urinalysis results will be positive for hemoglobin, and yet no red blood cells will be found on microscopic examination. Additional laboratory findings in Rhabdomyolysis include elevated serum potassium concentrations (potassium levels may rise with progression of the process), either hypocalcemia or hypercalcemia, hyperphosphatemia,

and elevated liver enzyme levels (which occur in 25% of patients with Rhabdomyolysis). Typically, through the course of the process, serum potassium and phosphate levels increase as myocytes are destroyed, and later decrease due to excretion by the kidneys. The mechanism of severe hyperkalemia is two fold. Hyperkalemia may be caused by leakage from damaged myocytes as well as the reduction in glomerular filtration rate secondary to acute renal failure. The acute rise in serum potassium may potentiate cardiac arrhythmias and subsequent cardiac arrest. Calcium levels may initially decrease due to cell membrane destruction and calcium intrusion into cells, and then gradually increase due to re-equilibration. Later findings (occurring 12 to 72 hours after the initial process) may include thrombocytopenia, elevated creatinine concentrations, and evidence of DIC.

Management

Foremost in the treatment of this condition is resuscitation of the patient. Airway, breathing, and circulation must be promptly evaluated and the patient stabilized. In addition, consideration must be given to the preservation of renal function. Aggressive fluid replacement is key in preserving renal function, and the greater the delay in rehydration, the greater the possibility of renal failure. There are no specific data on how much fluid should be used in volume loading, but an initial 10 to 20 mL/kg IV bolus should be considered. This should be repeated as needed. In all patients, the initial bolus should be followed by maintenance fluids to maintain a urine output of 1 to 2 mL/kg/h. Forced diuresis initiated within 6 hours of admission may reduce the risk of acute renal failure. Mannitol has also been used to prevent renal damage. However, there is minimal evidence of the superiority of this agent over aggressive fluid resuscitation. Some studies have indicated that saline alone prevents progression to renal failure, with no benefit at all from mannitol and sodium bicarbonate. Furthermore, mannitol infusion has been associated with complications due to hypernatremia, hyperosmolarity, and extracelluar fluid shifts, especially in the brain. At large doses (especially in patients who have not had adequate fluid replacement), mannitol may actually worsen renal failure.

Urinary alkalinization (achieving a urinary pH >6.5 by the infusion of sodium bicarbonate alone or with saline) theoretically reduces urinary cast formation in animal models and prevents oxidative injury to the kidneys. Unfortunately, many of the same studies refuting mannitol as a reasonable treatment option have also failed to demonstrate any benefit from urinary alkalinization in the prevention of acute renal failure. However, alkalinizing the urine has not been shown to cause harm. Caution should be exercised if urinary pH is above 7.5 or the initial urinary sodium bicarbonate level is above 30 mEq/L. Furthermore, sodium bicarbonate should be administered only after the patient has undergone appropriate volume loading and demonstrated adequate urine output (1 to 2 mL/kg/h). If renal failure has developed, especially with the onset of severe acidosis and hyperkalemia, hemodialysis may be required. Initially, daily hemodialysis or continuous hemofiltration may be necessary to remove the byproducts of myocyte necrosis, allowing for correction of fluid overload and the removal of solutes. It is critical to normalize potassium levels due to the potential of early hyperkalemia to promote cardiac arrhythmias and possibly cardiac arrest.

Since hypercalcemia occurs during recovery in approximately 25% of patients with renal failure resulting from Rhabdomyolysis, it is imperative to avoid the administration of calcium during the renal failure phase, except for symptomatic hypocalcemia or severe hyperkalemia.

Conclusion

Rhabdomyolysis can be a limb and potentially life threatening condition that must be evaluated in patients with a history of muscle injury. This muscle injury can arise from numerous causes. Common findings include muscle pain, tenderness, and weakness, along with a darkening of urine color. In addition, laboratory testing often reveals elevated serum CK levels, and urinalysis demonstrates hemoglobin without evidence of red blood cells. Aggressive fluid resuscitation is the standard of care, with initial boluses to maintain hemodynamic status and a urine output of 1 to 2 mL/kg/h. Sodium bicarbonate and mannitol, although used traditionally, have been shown to offer limited benefit. Hemodialysis is necessary if renal failure has occurred.

References:

1. Emergency Medicine, January 2012:11-16

2. Ame. Fam. Phy., Mar. 1, 2002, Vol. 65, No. 5: 907-912

3. Cont. Edu. in Anaes., Crit. Care & Pain 2006, Vol. 6, 4: 141-43

Pregnancy in Pott's Disease

Spinal tuberculosis (Pott's Disease) during pregnancy reported to be rare and can be associated with destruction of the intervertebral disc and adjacent vertebra that can lead to cord compression and thereby paraplegia or quadriplegia. Delay in diagnosis is common and most cases are diagnosed when paraplegia has already been occurred. This serious complication requires special attention during pregnancy and delivery. Here we reported a case of term pregnancy with Pott's paraplegia. As the patient had complete motor and sensory loss from D7 level, (above the level of umbilicus to the lower limb) LUCS was done without anesthesia and a healthy female baby was delivered. She did not require any analgesia postoperatively.

Introduction

A 22 years old lady admitted in RMCH, Rajshahi at 35 weeks pregnancy with the complaint of unable to walk, loss of sensation of both lower limbs and incontinence for two weeks. She was relatively well upto 22 weeks of her pregnancy, thereafter she noticed mid back pain which was localized and aggravated by movement. She was treated by local doctor but the pain was not improved. One and half months later she developed weakness and numbness of both limbs and finally patient became completely bed retained. She also developed urinary incontinence which required an in dwelling catheter. In this period she had low grade fever with marked weight loss but had no cough or heamoptysis. She had no family history or personal history of pulmonary TB. The patient did not have any regular antenatal care but she was immunized against tetanus.

On admission, the patient was anaemic, normotensive and had no lymphadenopathy or organomegaly. Higher psychic functions including speech are normal, all cranial nerves were intact and upper limbs revealed no abnormality. A gibbous was present at D7-8 level and tenderness was present at and around the level of D7-8. Motor power was grade 0 within minimum muscle wasting. All reflexes were brisk with bilateral clonuses and up going planter reflexes. There was pan sensory loss up to the level of T9 (above the level of umbilicus). Investigations showed hypochromic anaemia and increased ESR. Chest radiography was normal but MRI of the spine confirmed the localized destruction and collapse of the vertebral body and disc between D7-8. there was also para-spinal soft tissue swelling causing significant cord compression. Treatment was started according to advice of neurologist consisting of Isoniazide 300mg, Rifampicin 450mg. Ethambutol 800mg, Pyrizinamide 1500mg and Pyridoxin 50mg daily along with short course of steroid (40mg/kg/day) for 4 weeks and then gradually tapered within 2 weeks. Neurosurgeon gave opinion for surgical decompression but patient's attendant refuse operation. The pregnancy was monitored constantly. Careful attention was paid to the skin to prevent decubitus ulcer. Urinary tract was also monitored for any infection nutritional and haematological status of the patient was assessed. As the presentation of the fetus was breech, a decision was made for elective caesarean section at 37 weeks of gestation. As there was complete motor and sensory loss from D7 level to the lower limbs, LUCS was done without anesthesia under close observation of anesthesiologist. A healthy female baby was delivered and the patient discharged on 10th postoperative day with the baby.

During discharge, the patient advised to continue the anti TB drug therapy and to come for follow up after 6 weeks.

After 6 weeks there was no significant sensory improvement, only deep pinprick sensation was present. Muscle power was grade 2 (can move the both limbs side to side with difficult but can not move against gravity).

Discussion

Lower back pain in pregnant women is not always benign and delayed diagnosis can lead to serious complication. The sub clinical course of spinal TB in early pregnancy can progress to aggravation or worsening of the disease leading to spinal injury in late pregnancy. The most difficult part was being performing spinal nursing in presence of gravid uterus in the third trimester.

The regions of the spine which are of interest to us for their relation to the gravid uterus are,the lower dorsal, the lumber and the sacral vertebrae. Kyphosis due to disease process lead to diminished vertical diameter of the abdominal cavity.

In kyphotic pelvis, only the voluntary forces of labour are much affected and delay usually occur in second stage of labour. However, histories of these cases reported a considerable number of labour in paraplegic women, which prove that the assistance of abdominal muscles is not absolutely necessary to the accomplishment of parturition in the absence of deformity of the pelvis or from resistant soft tissue at the outlet. The essential involuntary muscles likely not much affected by the disease of the spine and the uterus may be excited to contraction by the most varied peripheral and the central influences.

The onset and detection of labour process a problem in paraplegic woman. When the lesion is above the 11^{th} thoracic spinal level, painless labour occurs and premature labour tends to be more common. Paraplegia is not contraindicated to vaginal delivery. Episiotomy in paraplegic woman should be repaired with non absorbable suture like silk or nylon or delayed absorbable suture like vicryl or dexon. Catgut sutures are poorly absorbed and often cause abscess formation. In this patient, caesarean section without anesthesia and no analgesia used postoperatively.

According to the recommendations issued in 2003 by the US centres for disease control and prevention, the infectious disease society of America and American thoracic society, a 4 drug regime should be used empirically to treat Pott's disease. Isoniazide and Rifampicin should be administered during the whole course of therapy. The duration of treatment is somewhat controversial. It should be individualized and based on the resolution of active symptoms and the clinical stability of the patient. The anti tubercular drugs should be associated with the steroid (20-60mg/day for 6-8 weeks). As our patient was pregnant, we used anti TB drugs safe for the fetus.

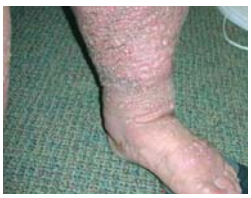
Conclusion

Tuberculosis can causes significant morbidity in the pregnant women, fetus and members of the community. The first line agents suggested by the Centers for Disease Control (CDC) during pregnancy seem to have minimal risk of induced congenital anomalies. Education of patient concerning the potential side effects may decrease the maternal morbidity. Therapy should be started as soon as diagnosis of TB is confirmed. Worsening of the neurological condition necessitates early surgical intervention and in some cases, termination of pregnancy. Management by a healthy care team attentive to the special problems that may complicate pregnancy offers the best chance for a successful pregnancy outcome.

Reference: Bang. J. Obs. & Gynae., Mar. 2010; Vol. 25(1); 37-40

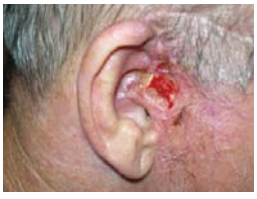
DERM DILEMMA

Answers



CASE 1

The patient has elephantiasis nostras verrucosa complicating chronic lymphedema. Patients with this condition usually are morbidly obese and have chronic swelling of the legs. The skin develops a thick, hyperkeratotic, verrucous texture. Management goals include arresting the progression of lymphedema, reducing swelling, preventing infection, and weight loss. Manual lymphatic drainage, complex wrapping with low stretch bandages, and use of compression garments may help.



CASE 2

Biopsy demonstrates an invasive squamous cell cancer. Squamous cell carcinoma represents the second most common form of skin cancer. The metastatic potential of squamous cell cancers is low, except in high risk sites, which include the lips and ears. This patient has no evidence of metastatic disease, but there is neuroinvasion of malignant cells causing the burning and pruritus. Treatment is wide excision or Mohs micrographic surgery. Any palpable lymph nodes should be biopsied.

Examination of the larynx and pharynx

Visualization of the larynx and pharynx is an essential part of a complete head and neck examination. Although the location of these structures often precludes direct visualization, simple techniques can be used to evaluate them in the clinical setting. Indirect laryngoscopy can be performed with either a simple dental mirror or a flexible fiber optic endoscope. The procedure can be performed when patients are awake, and it is usually well tolerated. Laryngoscopy can identify a wide variety of disorders acute or chronic, benign or malignant.

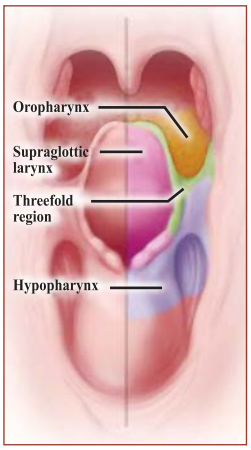
Indications

Common indications for laryngoscopy include chronic cough, laryngotracheal dyspnea, dysphonia, voice changes, chronic throat pain, persistent otalgia, swallowing problems, dysphagia, and symptoms of aspiration. Laryngoscopy can be used to elucidate the anatomic location of the problem and, in some cases, the cause. Patients who are at high risk for head and neck cancer benefit from screening examinations with indirect mirror laryngoscopy or flexible endoscopic laryngoscopy. Any adult patient with ear pain, hoarseness, or a sore throat that lasts longer than 2 weeks should have a complete laryngopharyngeal examination because of the possibility of cancer. Patients with a history of long term tobacco and alcohol use merit special attention and require careful examination. Laryngoscopy is also important for evaluating patients with a difficult airway. This examination can be performed in emergency departments when timely airway control is imperative. Patients presenting with angioedema, uncontrolled epistaxis, cervicofacial trauma, stridor, or suspected ingestion of a foreign body should be examined by laryngoscopy to evaluate the presenting problem and to rule out an airway compromise. Finally, laryngoscopy may also be useful in the diagnosis of various diseases, such as gastroesophageal reflux, tuberculosis, sarcoidosis, allergy, or neurologic diseases.

Indication	
Therapeutic	**Diagnostic**
■ Carcinoma of larynx and pharynx	■ Gastroesophageal reflux
■ Chronic throat pain	■ Tuberculosis
■ Persistant otalgia	■ Sarcoidosis
■ Dysphagia	■ Allergy
■ Cevicofascial Trauma	■ Neurological disease
■ Angioedema	
■ Uncontrolled epistaxis	
■ Foreign body ingestion	

Equipment

For mirror laryngoscopy, a curved dental mirror, an external light, a 4 by 4 in. gauze pad, and antifogging solution are needed. For a flexible laryngoscopic examination, it will need a standard flexible nasolaryngoscope, a nasal speculum, surgical lubricant, antifogging solution, decongestant spray, anesthetic spray, and a wall suction setup with a Frazier tip suction catheter. It is also useful to have tissues available. Decongestants, such as 0.05% oxymetazoline or 0.1% to 1.0% phenylephrine, are used to elicit mucosal vasoconstriction of the nasal passages, so that the endoscope can pass more comfortably. Lidocaine (4.0%) is used to anesthetize the pharynx and larynx. The flexible endoscope has a thumb dial control that allows the examiner to deflect the tip up or down. When rotated 90 degrees, the thumb dial lets the examiner turn corners and maneuver from side to side, as well as up and down.



The division between the larynx and pharynx The oropharynx, supraglottic larynx, and hypopharynx converge on the threefold region (pink, center). Thevocal cords are found below the supraglottic larynx and are not shown

Equipment

For mirror laryngoscopy

- Curved dental mirror
- An external light
- 4 by 4 inch gauze pad
- Antifogging solution

For flexible laryngoscopic examination

- Standard flexible nasolaryngoscope
- Gloves
- Nasal speculum
- Surgical lubricant
- Antifogging solution
- Decongestant spray
- Anesthetic spray
- Wall suction setup with a Frazier tip suction catheter

Mirror laryngoscopy

During mirror laryngoscopy, the patient should sit opposite and slightly elevated relative to the examiner. The patient's legs should be uncrossed, and the patient should lean forward slightly, with mouth wide open and tongue protruding. To prevent fogging of the mirror, warm it to just above body temperature or coat it with an antifogging solution. Gently grasp the anterior portion of the patient's tongue with a sterile, 4 by 4 in. cotton gauze pad and hold it just outside the mouth. Ask the patient to take slow, deep breaths through the mouth. Keep the light source focused on the patient's oropharynx while performing the exam. To avoid a gag reflex, pass the mirror into the patient's oropharynx without touching the mucosa of the oral cavity, soft palate, or posterior oropharyngeal wall. Gently angle the mirror downward until see the mucosal surfaces of the larynx and hypopharynx. Note that in mirror laryngoscopy, the image is inverted: the right vocal cord appears on the left side of the mirror and the left cord appears on the right side of the mirror. Ask the patient to say "e" (as in "eel") and observe the dynamic motion of the true vocal cords and arytenoids cartilages. The vocal cords will lengthen and adduct along the midline. The anterior aspect of the larynx can be seen by asking the patient to say "e" in a higher register. This maneuver fully exposes the anterior commissure, permitting complete visualization. To increase visualization, ask the patient to stand when the examiners are seated and vice versa while performing the examination. The oropharyngeal vallecula and base of the tongue, as well as the hypopharynx (pyriform sinuses and posterior pharyngeal wall), can also be seen with the mirror. Inspect these structures for symmetry and any potential mucosal abnormalities.

Flexible laryngoscopy

Preparation and Positioning: Setup for this exam is quick and easy. Before you begin, explain the procedure to the patient and obtain consent. At the very least, the patient should provide verbal consent, but increasingly, the use of written informed consent is recommended. Ascertain whether the patient has any allergies to medication or medical contraindications before performing the procedure. Prepare the patient's nose by applying a decongestant and an anesthetic agent to the nasal mucosa. Any delivery method, whether by an atomized spray device or a plain syringe, is acceptable. Administer the medication by opening the patient's nose with a nasal speculum. Ask the patient to hold his or her breath during spraying to avoid inhalation of the agents. Once the nose is adequately prepared, position the chair so that the patient's face is at eye level with yours. Then have the patient lean slightly forward, with hands placed on the knees.

Procedure: Place the tip of the laryngoscope into the nostril and slowly advance it lateral to the septum and medial to the inferior turbinate. Visualize the inferior meatus and follow along the inferior turbinate. Advance the scope posteriorly into the nose beyond the middle turbinate along the nasal floor. Visualize the eustachian tube orifice ("the torus tubarius") lateral to the entrance of the nasopharynx. Visualize the adenoid or the central lymphoid tissue of Waldeyer's ring. Immediately posterior to the Eustachian tube opening is a shallow depression called Rosenmüller's fossa. Because nasopharyngeal carcinoma may arise from these recesses, this part of the exam merits especially careful evaluation. Any bleeding when the mucosa is touched with the tip of the laryngoscope should alert the possibility of nasopharyngeal carcinoma.

Examine the posterior nasal septum and the nasopharyngeal aspect of the soft palate. Ask the patient

to breathe through the nose; this will separate the palate from the posterior nasal wall and allow passage of the scope into the oropharynx. From this location, the scope shows a panoramic view of the oropharynx below.

Continue to pass the scope inferiorly until the examine can easily visualize the larynx. The true vocal cords should appear clean, white, and taut. Note any changes in the color of the mucosa or any superficial irregularities. When the patient is breathing deeply, the glottis remains wide open, with the vocal cords abducted. Some portion of the subglottic larynx can usually be seen. The anterior ring of the cricoid cartilage is often visible just below the true vocal cords. However, the laryngoscope should not be passed through the true vocal cords, since contact can elicit laryngospasm. Ask the patient to sniff or to inspire deeply through the nose. This causes maximal vocal cord abduction, permitting optimal assessment of the larynx. Then, ask the patient to say "e" or "ah" to assess the function and movement of the vocal cords and arytenoid cartilages. Examine the epiglottis, arytenoids, aryepiglottic folds, false vocal folds, true vocal cords, and subglottic region, or cricoid shelf. Videostroboscopy can be performed to evaluate the patient's speech. During human speech, a vibratory wave is formed as the vocal cords produce sound. Stroboscopic illumination of the larynx can reveal subtle alterations of vocal fold vibration that are not visible with standard laryngoscopy. The hypopharyngeal anatomy should be distinguished from both the larynx and the oropharynx, using the boundaries of the aryepiglottic and pharyngoepiglottic folds, respectively. For all portions of this examination, advance the endoscope as close to the tissue being examined as possible without making contact. Touching the mucosa may elicit a gag reflex. The paired pyriform sinuses are visible on either side of the larynx. Ask the patient to puff out the cheeks and hold them; this will push out the walls of the hypopharynx, allowing for an easier and more complete view. Rotate the head from one side to the other to maximize visualization of lateral structures'.

Tips and troubleshooting

Occasionally, patients may not tolerate the mirror laryngoscopic examination because of a prominent gag reflex, apprehension, or discomfort. In these circumstances, apply a mild topical anesthetic to the throat and allow sufficient time for the medication to take effect before reattempting the examination. Sometimes the procedure simply cannot be performed; flexible laryngoscopy should be attempted in such cases.

Aftercare and complications

Since laryngoscopy is generally painless, no post procedure analgesia is necessary. Patients should be advised to avoid eating and drinking for 1 hour after the application of Lidocaine. Until mucosal anesthesia resolves, reduced laryngopharyngeal sensation might predispose the patient to aspiration. Otherwise, there are few complications associated with laryngoscopy. Epistaxis and hemoptysis are uncommon.

Contraindications

There are few, if any, contraindications to performing laryngoscopy with the fiberoptic nasal laryngoscope. However, it should be exercised with great care when performing laryngoscopy in a patient with impending airway compromise (e.g., epiglottitis). Only a skilled operator should perform a laryngoscopic examination in this clinical scenario. Inadvertent trauma to the laryngopharynx may exacerbate swelling and precipitate respiratory arrest. Laryngoscopy can usually be performed in young children, although the patient's tolerance and compliance may limit the extent of the examination.

Conclusions

Evaluation of the larynx and pharynx is an important part of a complete physical examination. Laryngoscopy by mirror or by flexible fiberoptic exam can be safely performed in adults and children for benign or malignant conditions. With the advent of multidisciplinary care for head and neck cancer, knowledge of laryngoscopy and laryngopharyngeal anatomy is important in an increasing number of medical specialties.

References: N Engl. J Med. January 17, 2008; 358:e2

Purtscher-like retinopathy caused by acute pancreatitis

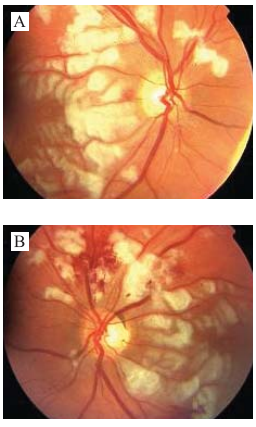


Figure: Fundoscopy
Cotton-wool spots and intraretinal haemorrhages.
(A) right eye; (B) left eye

A 30 year old woman with acute pancreatitis was referred to our eye clinic because of sudden blindness. Visual acuity was reduced to counting fingers in both eyes. Fundoscopy showed cotton-wool spots and intraretinal haemorrhages surrounding a normal optic disc bilaterally (figure A, B). At 3 month follow up, the patient's retinal findings had much improved spontaneously. However, her visual acuity did not recover completely (right, 20/40, left, 20/25), although the underlying pancreatitis had been treated successfully. Purtscher retinopathy is caused by microembolisation of retinal and choroidal arterioles by fat emboli after severe trauma and is characterized by retinal ischaemia and haemorrhages. Purtscher-like retinopathy shows the same clinical findings but is associated with other diseases, including acute pancreatitis, systemic collagen vascular diseases, chronic renal failure, and thrombotic thrombocytopenic purpura. Enzymes from an inflamed pancreas seem to lead to complement activation, resulting in granulocyte aggregation and subsequent retinal microembolisation. There is no evidence-based treatment for this retinopathy.

Reference: The Lancet, November 5, 2011, Vol. 378: 1653

Sturge-Weber angiomatosis

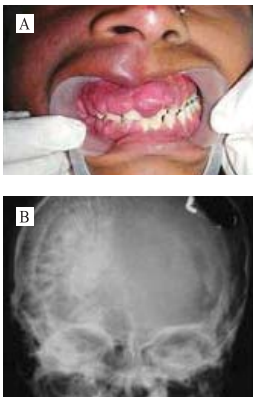


Figure: Sturge-Weber angiomatosis
(A) Gingival enlargement
(B) Radiographs showing tram-line calcifi cation

A 20 year old woman presented with a 1 month history of swollen gums. Her medical history included seizures for the past 19 years and a macular patch on the right side of her face since birth. She was taking phenytoin for her seizures. Intraoral examination showed extension of the macular patch on the right side of the oral cavity and generalised gingival enlargement. On the basis of her history and clinical presentation she was diagnosed with Sturge-Weber angiomatosis and drug-induced gingival enlargement. Extraoral skull radiographs showed tramline calcification because of angiomas affecting the leptomeninges. The patient was given meticulous oral treatment and her antiepileptic medication was changed. The angiomas present in our patient are malformations of blood vessels in the pia mater causing the calcification and loss of nerve cells in the cerebral cortex. These sequelae of the malformations give rise to the clinical symptom of seizures and radiological sign of tramline calcifi cation.

Reference: The Lancet, October 29, 2011, Vol. 378: 1580

Info Quiz Participants

- Have you selected the correct answer (s) You still have time to put your entry submission together for Info Quiz Prize
- The closing date for entries is 15 May 2012
- We look forward to receiving your winning entry

Info Quiz Answers
January-March 2012

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

Managing motion sickness

Motion sickness is a common and potentially disabling problem, thought to be due to sensory conflict or “mismatch” involving the vestibular system Management using behavioural methods such as habituation can be effective and has few adverse effects, but can be unpleasant and time consuming Hyoscine is an effective preventive medication for which oral preparations and transdermal patches are established in clinical practice, and emerging evidence suggests that hyoscine nasal spray is effective in preventing motion sickness Evidence to support the use of other drugs, taking into account the trade off between efficacy and adverse effects, is weaker. Management of motion sickness with traditional remedies such as ginger and acupressure bands has not been shown to be effective.

Motion sickness is a syndrome of nausea and vomiting, pallor, sweating, headache, dizziness, malaise, increased salivation, apathy, drowsiness, belching, hyperventilation, and stomach awareness. Symptoms can be provoked by externally imposed motion, or implied self motion from a moving visual field, such as in a cinema. The condition has been recognised from the early days of sea travel and the word for sickness, "nausea," derives from the Greek word *ναυζ*, meaning "ship." Travel by car, train, or other transport is part of everyday life for most people, and motion sickness is a common problem.

Estimating its prevalence is complex because reported symptoms depend on variables such as previous avoidance and exposure, as well as presumed inherent susceptibility. Some estimates are presented table 1. Motion sickness may have an important effect on occupational activity for some people, such as airline pilots, those in the armed forces, and emergency services staff. General practitioners may frequently encounter patients who report difficulties in work or daily life related to motion sickness, or those seeking advice about prevention before a forthcoming journey. We review the management of patients with motion sickness for the generalist. This article is based on evidence obtained largely from controlled studies in patients and in healthy volunteers.

Table 1 | Estimates of motion sickness by mode of transport

	Prevalence of vomiting	Prevalence of other symptoms
Air	0.5%	25%
Sea	7%	29%
Road (bus or coach)	2%	41%

Why do people get motion sickness?

There is no universally accepted explanation about why people get motion sickness. One commonly held view is that motion sickness originates from a mismatch between sensory inputs, especially between the visual and vestibular systems. For example, when travelling in a vehicle with limited outside visibility, the vestibular system reports motion to the central nervous system, but information from the visual system suggests the individual is not moving. Other forms of mismatch, such as visual motion without actual motion-for example, in a large cinema-can have the same effect. Motion sickness itself could have evolved from a system designed to protect from potential ingestion of neurotoxins by inducing vomiting when unexpected central nervous system inputs are detected (the "toxin detector" hypothesis). This system would then be activated by modern methods of transport that cause mismatch. Less popular alternatives to the toxin detector hypothesis propose that motion sickness could be the result of aberrant activation of vestibular-cardiovascular reflexes1; or that it might originate from a warning system that evolved to discourage development of perceptual motor programmes that are inefficient or cause spatial disorientation or that motion sickness is a unfortunate consequence of the physical proximity of the motion detector (vestibular) and vomiting circuitry in the brainstem.

Who is most susceptible to motion sickness?

Experimental evidence supports the theory that, with varying thresholds of susceptibility, almost all healthy unmedicated individuals can get motion sickness in the right conditions. Some people may be more troubled by the condition than others, and reports of motion sickness depend on lifestyles and situations. For example, a professional pilot will be more troubled by new symptoms of air sickness than someone who never needs or wants to travel by aeroplane. Bearing these difficulties in mind, various large prospective surveys have estimated the frequency of symptoms of motion sickness (table 1). Babies and young children under 2 do not usually get motion sickness. However, motion sickness is more common in children under 15 than in adults, perhaps because of habituation-that is, reduction in symptom severity with repeated exposure. It is also more commonly reported in women than in men, although a number of potentially confounding variables related to social roles may account for this observation.

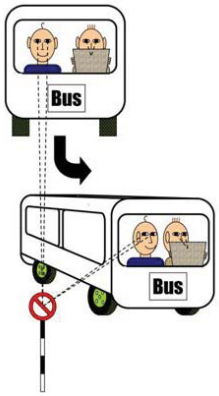


Fig 1 - Visual-vestibular conflict. As the bus turns, the passenger on the left has a fixed external visual reference and has no visual-vestibular conflict. The passenger on the right, who is reading the paper, experiences a conflict because the visual input is still but the vestibular system is sensing motion (modified from Bronstein and Lempert)

Evidence from twin studies has shown that a large proportion of individual variation in susceptibility is due to genetic factors, with heritability estimates in the range 55-70%. Some groups of patients are particularly susceptible. Self reported motion sickness is higher in people who have migraines than in those who have other types of headache. Furthermore, migraineurs characteristically report heightened sensitivity of all senses for example, phonophobia and photophobia-including vestibular and visual-vestibular inputs. Many symptoms of motion sickness are reminiscent of a migraine attack. One large observational study of female yacht racers found that those individuals with migraine are more susceptible to motion sickness, and are prone to develop migraine headaches during provocative motion exposure. Patients with vestibular migraine, in which vestibular symptoms and migraine are strongly associated, report greater susceptibility than those with other forms of migraine. Many patients with vestibular disorders also report symptoms during external motion. By contrast, patients with absent vestibular function do not normally become motion sick, although they are still partially susceptible to visually induced motion sickness.

How should the patient with motion sickness be assessed?

The diagnosis of motion sickness is made on the basis of reported symptoms in externally imposed motion. It is rare for motion sickness to be the presenting symptom of serious disease. Vestibular disease (peripheral or central) can present with motion sickness, but dizziness or vertigo will usually exist between exposures. Unilateral vestibular disease can be suggested by a positive head thrust test or positional manoeuvre. Central vestibular disease can present with cerebellar symptoms and signs, so an eye movement and gait examination is essential. Mal de debarquement is a distinct presentation, which is discussed later in this article.

How can motion sickness be treated?

Behavioural counter measures

Simple behavioural counter measures can be effective treatments for patients who experience motion sickness. A within person comparison showed that sickness was reduced when a stable visual reference point, such as the horizon, was provided, minimising visual-vestibular conflict during sea travel (fig 1). Forward visibility is particularly helpful in coach or bus travel. Alternatively, laboratory based observations showed that lying supine, where practical, reduces symptoms of motion sickness and is preferable to an upright seated posture. Controlled studies have shown that deliberate restriction of head movements is helpful, as is avoidance of tasks that enhance visual-vestibular conflict, such as reading when travelling. Prospective controlled studies have shown that repeated exposure to the nauseogenic stimulus (habituation) is an effective treatment for motion sickness. Habituation programmes pioneered by the military are effective but time consuming. For maximum efficacy, the exposure to the stimuli needs to be frequent and graded. The exposure is initially gentle, and is then increased by gradual increments to maximize acceptability and speed up recovery between sessions, and to avoid the undesirable effect of sensitisation to the stimulus.

Habituation is specific to a particular stimulus, Tolerance to car travel may have no effect on susceptibility to seasickness. A prospective controlled study of healthy volunteers has shown that coping strategies such as controlled regular breathing or listening to music are more effective than placebo in reducing nausea. However the effect size was small, with provocative stimuli tolerated for around 10% longer. A small but well designed prospective placebo controlled study showed no benefit of acupressure bands over control, although a small trial showed Korean hand pressure to be more effective than sham pressure in reducing subjective nausea for emergency patients transported in ambulances. Motion sickness is increasingly reported in the context of virtual environments, with head mounted or large field of view displays, when it is known as cybersickness or visually induced motion sickness. These devices are potentially useful tools for various research, health, training, and leisure activities. Cybersickness can be treated with habituation.

Antiemetic drugs

Most drugs in common use for motion sickness have been used for more than 30 years. Consider drug treatment carefully in patients who could benefit from using habituation methods to overcome motion sickness, and discuss this disadvantage of using drugs with them before embarking on treatment. Gastric stasis occurs with motion sickness before the vomiting phase, so non-oral routes of administration such as transdermal patches are advantageous.

Table 2| Common anti-motion sickness drugs

Drug	Route	Adult dose	Time to onset	Duration of action (h)
Hyoscine	Oral	0.3-0.6 mg	30 min	4
Hyoscine	Injection	0.1-0.2 mg	15 min	4
Hyoscine	Transdermal patch		6-8 h	72
Promethazine	Oral	25-50 mg	2 h	15
Promethazine	Injection	25 mg	15 min	15
Promethazine	Suppository	25 mg	1 h	15
Dimenhydrinate	Oral	50-100 mg	2 h	8
Dimenhydrinate	Injection	50 mg	15 min	8
Cyclizine	Oral	50 mg	2 h	6
Cyclizine	Injection	50 mg	15 min	6
Meclizine	Oral	25-50 mg	2 h	8
Buclizine	Oral	50 mg	1 h	6
Cinnarizine	Oral	15-30 mg	4 h	8

Medication is most effective when taken before exposure rather than after the onset of symptoms. Drugs are useful in situations where habituation is impractical, such as solitary or infrequent journeys.

Antimuscarinics

Hyoscine is available as tablets or liquid for oral ingestion, intravenous and subcutaneous injection, and transdermal patches. Patches are applied to the mastoid area 6-8 hours before exposure. Selective M3 or M5 muscarinic receptor antagonists may also be effective against motion sickness.

Antihistamines

Antihistamines-including cinnarizine, meclozine, dimenhydrinate, cyclizine, chlorphenamine, and promethazine-are the other main group of drugs frequently used to treat motion sickness.

Central nervous system stimulants

Sympathomimetics such as dextroamphetamine have been documented to have efficacy in the prevention of motion sickness, either alone or in combination with other drugs, but their usefulness is limited by the potential for abuse and legal problems. Amphetamine has been discontinued as an anti-motion sickness treatment. Modafinil, an alternative central nervous system stimulant, was recently evaluated as a potential treatment for motion sickness.

Ondansetron

Individuals with a history of motion sickness are at higher risk for postoperative and chemotherapy induced nausea and vomiting. Because 5-HT3 receptor antagonists such as ondansetron have revolutionised the management of nausea and vomiting, experts hoped they would be efficacious in the management of motion sickness.

Non drug remedies

Ginger is a popular traditional remedy for nausea. Supplemental oxygen may reduce motion sickness in patients being transported by ambulance, but does not alleviate the problem in individuals who are otherwise healthy.

Combination treatments

Combinations of agents have also been selected with the aim of increasing efficacy and others to increase tolerability. One small study examined the combination of chlorpheniramine with ephedrine to combat the drowsiness which is so frequently a problem in managing motion sickness.

Reference: BMJ 2011;343:d7430 doi: 10.1136/bmj.d7430

Unstable Angina

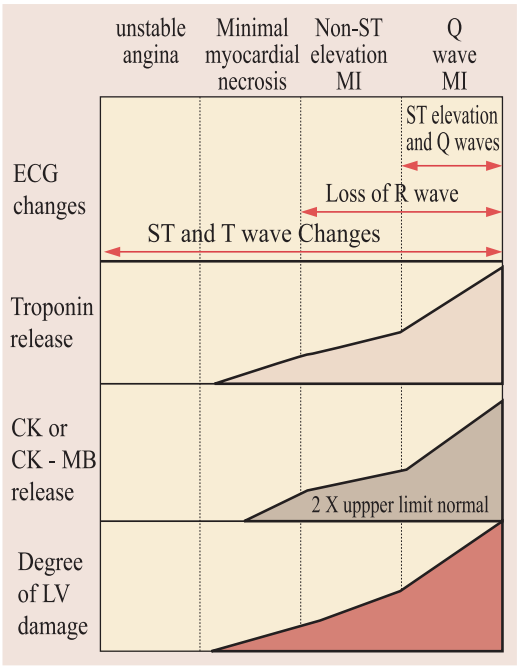
Unstable angina refers to new-onset or rapidly worsening angina (crescendo angina), angina on minimal exertion or angina at rest. It may present de novo or against a background of chronic stable angina. The underlying pathophysiology (fissured atheromatous plaque with adherent thrombus formation) is the same as in acute MI. The term 'acute coronary syndrome' is used to describe these disorders collectively and encompasses ischaemia with no myocardial damage, partial thickness (non-ST elevation) myocardial infarction (NSTEMI), and full-thickness (ST-elevation) myocardial infarction (STEM1).

Investigations

- ECG is the most important investigation in the assessment of acute chest pain and guides initial therapy. In patients with unstable angina or NSTEMI, the ECG may show ST/T-wave changes including ST depression, transient ST elevation and T-wave inversion.
- Serial measurements of biochemical markers of cardiac damage, such as troponins, also assist in diagnosis and risk stratification.
- Unstable angina and NSTEMI carry a high risk of progression to STEMI or death, and risk stratification guides the use of more complex pharmacological and interventional treatment.
- Risk markers indicative of an adverse prognosis include recurrent ischaemia, extensive ECG changes, elevated troponin, arrhythmias and haemodynamic complications (e.g, hypotension) during ischaemic episodes.

Management

- Initial treatment includes combined antiplatelet therapy with aspirin and clopidogrel, low molecular weight heparin and a β-blocker.
- I.V. nitrates may help if pain persists or recurs.
- Most low risk patients stabilise with these measures and can undergo exercise testing prior to or shortly following discharge.
- Coronary angiography, with a view to PCI or surgery, should be considered in all patients at moderate or high risk, those who fail to settle on medical therapy and those with extensive ECG changes or elevated plasma troponin.
- The addition of a glycoprotein IIb/IIIa antagonist may be helpful in these patients.

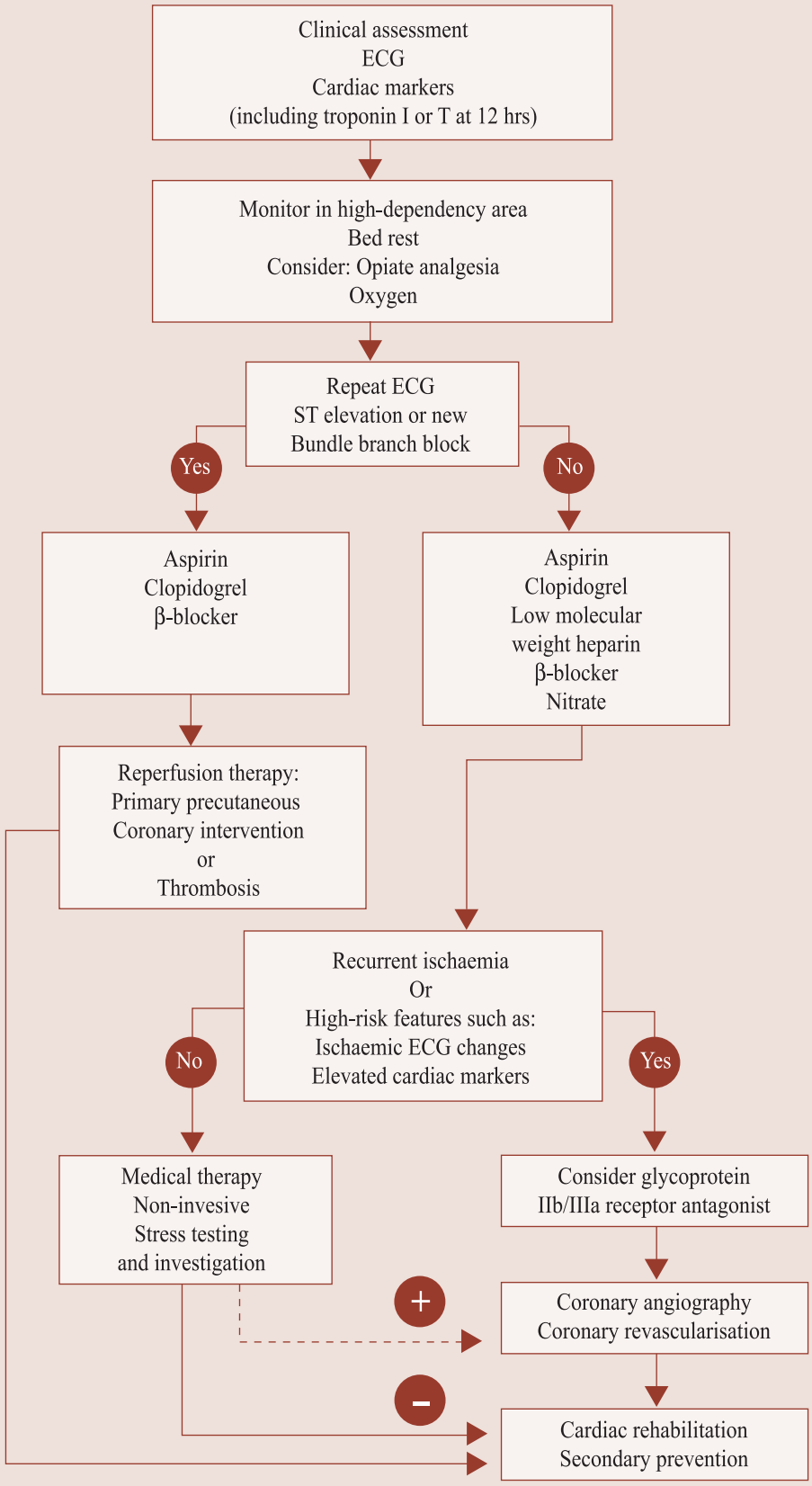


Unstable Angina: Risk Stratification

	High risk	Low risk
Clinical	Post-infarct angina Recurrent pain at rest Heart failure	No history of Ml Rapid resolution of symptoms
ECG	Arrhythmia ST depression Transient ST elevation Persistent deep T-wave inversion	Minor or no ECG changes
Biochemistry	Troponin T >0.1 µg/l	Troponin T <0.1 µg/l

N.B. There is a 5- to 10-fold difference in risk between the lowest and highest risk groups.

Summery of treatment for unstable angina



Ref: Davidson's essentials of Medicine, International edition

Jog your memory

Please select the correct answer by (√) against a, b, c & d of each questions in the Business Reply Card and send it through our colleagues or mail within 15 May 2012; this will ensure eligibility for the Raffle Draw and the lucky winners will get attractive prizes!

1. All of the following statements regarding amoebiasis (*Entamoeba hystolitica* infection) are correct, except

a. The disease is transmitted by the ingestion of cysts

b. Digestive enzymes release trophozoites from the cysts

c. Bacteria of the intestinal flora also contribute to the intestinal damage caused by the trophozoits

d. The intestinal lesions are superficial

2. All of the following statements regarding maple syrup urine disease are correct, except

a. Newborns are symptomless at birth

b. Early symptoms include difficulties of feeding, irregular respiration and a weak Moro reflex

c. Spasms are rarely seen

d. The time of the onset of symptoms is the third to fifth day after birth

3. All of the following statements concerning congenital adrenal hyperplasia are correct, except

a. Cortisol production is elevated in the second week following birth

b. The overproduction of androgens causes masculinization of the external genitals in females

c. The acute sodium deficiency adrenal crisis is due to deficient aldosterone production

d. These infants have a decreased appetite and somatic growth is impaired

4. All of the following statements about the adrenogenital syndrome are correct, except

a. Androgen hypersecretion in the adrenal medulla causes virilization and increased protein anabolism

b. Virilizing adrenal tumors are rarely palpable, but they do dislocate the kidney

c. The urinary 17-KS levels are decreased

d. Virilizing adrenal tumors do not cause excessive cortisol production

5. The most likely cause of goiter in a newborn is

a. The maternal consumption of goitrogenic substances (foods)

b. Congenital hypothyroidism

c. A severe peroxidase defect

d. An abnormality of the thyrolingual duct

6. All of the following statements about heart sounds in children are correct, except

a. A third heart sound is commonly detected during childhood

b. The second heart sound is generated by the closing of the semilunar valves

c. T intensity of the first heart sound decreases if the ejection fraction increases

d. A fourth heart sound can only be heard if ventricular ejection is impeded

7. Rectal prolapse is a possible complication of all of the following conditions, except

a. Severe malnutrition

b. Whooping cough

c. Chronic dysentery

d. Enterobiasis

8. All of the following statements about congenital obstruction of the upper gastrointestinal tract are correct, except

a. Vomiting might become continuous even without feeding

b. The obstruction is frequently associated with polyhydramnios

c. In the initial phases of the obstruction, meconium can pass

d. The vomit is always stained with bile

9. Which of the following symptoms is not characteristic for progeria?

a. Mortality rate is highest at the age of 14

b. The usual causes of death are cardiac and cerebrovascular abnormalities

c. Osteoarthritis and cataract are possible complications

d. The affected child's father is usually old

10. All of the following statements concerning the incidence of the sudden infant death syndrome (SIDS) are correct, except

a. The incidence of the sudden infant death syndrome is the highest at the age of 5-6 months

b. It is more frequent in families with poor social conditions

c. The incidence is higher among the subsequent siblings of SIDS victims

d. The incidence is higher among girls

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