MINISTRY OF HEALTH OF UKRAINE
ODESSA NATIONAL MEDICAL UNIVERSITY

Faculty : International

Department of Surgery №3

CONFIRMED by

Acting vice-rector for scientific and pedagogical work
Svitlana KOTIUZHYNSKA

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Recommendations *for LECTURES:*

Faculty : International , Year **5**

Discipline **"Surgery with pediatric surgery"**

Lecture is approved at the meeting of the Department of Surgery No. 3
Minutes No. 1 dated August 28, 2022.

The head of the department, professor

V. G. Bondar

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Lecture №__1

Theme: " Surgical pathology of respiratory system. ".

1. Introduction.

The cause of traumatic injury to the chest varies greatly in different parts of the world. Currently, in large American cities and parts of South Africa, black males have a 1 in 20 chance of being fatally shot or stabbed before the age of 30. Although terrorism and civilian violence are on the increase throughout Europe, the absolute numbers of victims remains small in comparison. In England and Wales, the annual death rate from stabbing and gunshot wounds is less than 200. Britain and Europe, nevertheless, have increasing figures for road casualties. Road traffic accidents in England and Wales account for 60000 hospital admissions per year, and London and south-east England have 57 fatal or serious road traffic accidents per 100 km of road. Blunt thoracic injury is almost exclusively caused by rapid deceleration in motor vehicle collisions. A small number of injuries follow crushing industrial accidents. Although less than 15 per cent of patients with chest trauma require surgical intervention, many needless deaths occur through inadequate or delayed treatment of an easily remediable injury. The majority of chest injuries are confined to the thoracic cage. These consist of rib fractures with underlying pulmonary contusion, haemothorax, or pneumothorax, which can usually be dealt with simply and effectively by chest drain insertion and fluid restriction. When ignored, underestimated, or inadequately treated, chest injuries may cause the death of a patient during surgical intervention for seemingly more pressing intracranial or abdominal haemorrhage. The basis for successful management of thoracic trauma is effective cardiopulmonary resuscitation followed by early detection and treatment of life-threatening injuries. The former is based on the ABC principle. A. Establish a reliable airway. B. Restore the mechanics of breathing. C. Stabilize the cardiovascular system. The most serious intrathoracic injuries often occur in the absence of significant chest wall damage. Recognition must depend upon exclusion rather than direct manifestation of injury. The latter depends upon prediction of likely lesions according to the mechanism of injury. Important injuries to rule out are aortic transection or dissection, major airways disruption, ruptured diaphragm, and severe cardiac contusion or valvular regurgitation. Although all are relatively rare, they may coexist after major trauma. A high index of suspicion is the key to early diagnosis.

2. Aims of the Lecture:

- **Educational:**

To know:
- definition of the pathology;
- contemporary general data about trauma of the chest;
- classification of the chest trauma ;
- general symptoms and clinical course of the chest trauma ;
- methods of examination of the patient;
- first aid ;
- indications to surgery;
- types of surgical treatment;
- working capacity.

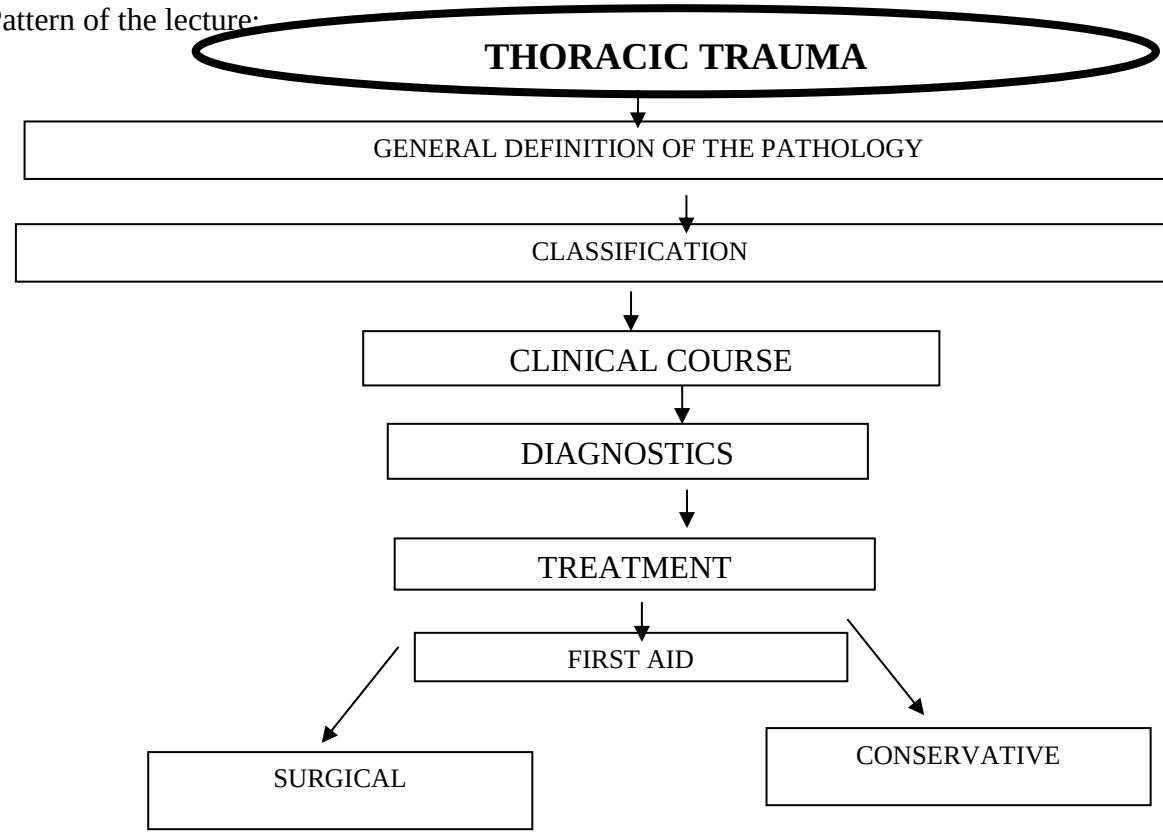
Basic concepts: *Altered mechanics of breathing. Blunt injury to the major airways. Diagnostic techniques. Treatment.*

3.**Plan and structure of the lecture.**

#	Contents and units of the lecture.	Tasks in abstract levels.	Equipment of the lecture.	Time.
1	2	3	4	5
	Preliminary part			
1.	Determination of educational aims	I-10	Topic	3%
2.	Positive motivation	-"-	lecture.	2%
	Main part			
3.	Exposition of the lecture's matter Plan:		Tables, schemes,	90%
	1. Definition of the pathology.	-"-	codograms,	
	2. General information about hest trauma in Ukraine.	-"-	slides. Films.	
	3. Classification.	-"-		
	4. Methods of the patient's examination and diagnostics of the chest trauma.	-"-		
	5. Clinical course.	-"-		
	6. Organization of the surgical aid.	-"-		
	8. Working capacity. Rehabilitation.	-"-		
	Final part			5%
4.	Lecture summary			
5.	Lecturer's answers to possible questions		Literature	
6.	Tasks for self-control		Questions. Tasks.	

4. Contents of the lecture.

Pattern of the lecture:



Contents of the lecture:

MECHANISM OF MAJOR VISCERAL INJURY IN THORACIC TRAUMA. The existence of serious visceral injury can usually be predicted with knowledge of the type of accident or assault and should be confirmed or excluded by appropriate investigation such as chest radiographs and CT scan. There are three broad categories for the mechanism of injury associated with blunt thoracic trauma. The patterns of injuries sustained are different in each case.

High velocity impact. Sudden profound deceleration produces the so called intrathoracic "bell clanger" effect. The chest wall suffers direct impact. The aorta, a heavy column of blood with inertia, swings like the clanger of a bell within the thorax, producing severe shear forces. These forces may tear the vessel at its fixed points above the aortic valve or, more frequently, at the posterior chest wall, causing transection. The main bronchi situated beneath the aortic arch are subject to similar forces and may rupture. Impact of the neck may transect the trachea, and compression of the abdominal viscera may rupture the diaphragm, the spleen, or the liver. There may be little or no injury to the bony chest wall, though bilateral clavicular fractures or a fractured sternum must arouse suspicion. Anterior chest wall contusion is an indicator of underlying myocardial injury. *Low velocity impact*. Low velocity impact causes direct damage to the bony thorax, with or without contusion of the underlying lungs or myocardium. This type of injury does not usually create stress or compression forces sufficient to damage the aorta, bronchi, or diaphragm, although the liver or spleen may be ruptured by a direct blow over the lower part of the thoracic cage.

Crush injury. Following compression, multiple bilateral rib fractures are likely. However, in the young the sternum may be forced backwards to touch the spine without fracture. Such low velocity forces seldom damage the aorta or myocardium, but may rupture the diaphragm or lacerate the bronchi by a different mechanism from that above. When sudden forceful compression of the thoracic cage decreases the anteroposterior diameter and produces a widening of the transverse diameter, the negative intrapleural pressure ensures that the lungs remain in contact with the chest wall. Lateral motion pulls the two lungs apart thus producing traction on the trachea at the carina. Rupture occurs when the elasticity of the tracheobronchial tree is exceeded. If the glottis is closed at the moment of impact, intrabronchial pressure may rise suddenly. The greatest tension develops in the larger bronchi and increases the tendency to rupture.

Penetrating chest wounds. Knife and gunshot wounds are now more commonplace in British accident departments and in some North American cities they are responsible for up to 40 per cent of trauma admissions. The extent of damage inflicted by a penetrating agent depends on the size, shape, stability, and above all, the velocity of the missile. The vast majority of civilian gunshot wounds and accidental industrial or road traffic penetrating injuries occur with low velocity. Such missiles core out a hole through the body and damage only those tissues with which they are in direct contact. They cause death by damage to vital structures or exsanguinating haemorrhage. Because of their low kinetic energy, the path taken by a hand gun bullet through the body is unpredictable, deflection being caused by bone or even parenchymal organs such as the liver or spleen. Chest wounds may be accompanied by abdominal injury, and vice versa. The greater the mass of the penetrating object the greater the damage inflicted. In contrast, high velocity rifle bullets and fragments from explosive devices over a short range have a large amount of energy which causes damage remote from the path of the missile itself. High velocity bullets cause extensive tissue damage by cavitation and shock waves. Energy from the bullet is dissipated into the surrounding tissues, which are violently accelerated forwards and outwards. This creates a large temporary cavity 30 to 40 times the diameter of the missile. The greatest extent of cavitation occurs only after the missile has passed through the tissues. This has subatmospheric pressures and is open at both entrance and exit holes. The cavity then collapses in a pulsatile fashion sucking air, debris, and bacteria into the wound and producing a large amount of dead or devitalized contaminated tissue. .Damage is directly proportional to the density of the tissue: homogeneous structures such as brain, liver, spleen, or muscle are very sensitive, whereas light tissues like lung, which mainly consists of air, are resistant. The destruction is also inversely proportional to the proportion of elastic fibres present: skin and lung are resistant whereas bone is shattered. The external appearance of a bullet wound in the chest is therefore deceptive. The elasticity of the skin produces tiny entry and exit holes that disguise extensive internal destruction.

PATHOPHYSIOLOGY OF TRAUMA TO THE LUNGS AND CHEST WALL. Chest injuries adversely affect pulmonary function by three separate mechanisms: altered mechanics of breathing, ventilation/perfusion imbalance, and impairment of gas transfer.

Altered mechanics of breathing. The great majority of blunt injuries to the thoracic cage and those penetrating injuries that cause haemothorax or pneumothorax impair ventilation Even relatively minor trauma with fractured ribs but no underlying pathology may cause pain sufficiently to lead to hypoventilation, atelectasis, failure to clear secretions, pneumonia, septicaemia, respiratory failure, and even death in an elderly or bronchitic patient. More serious problems which cause severe impairment of the mechanics of breathing include pneumothorax (particularly tension pneumothorax), haemothorax, ruptured diaphragm, multiple rib fractures with unstable segments, and injuries to the major airways The most extensive disruption of the chest wall tends to occur with crush injuries where multiple bilateral rib fractures, ruptured diaphragm, or fractures of the spine or sternum coexist. A single rib fracture is associated with a blood loss of 150 ml. Multiple fractures may cause substantial blood loss into the chest wall and pleural cavity; this may be increased by laceration of the underlying lung by sharp edges. There are two main types of chest wall derangement, a functionally important traumatic defect (sucking chest wound) or a flail segment. The latter may be unilateral with double fractures of three or more ribs, or anterior with fractures of three or more ribs on both sides of the sternum. Some fractures may occur through the costochondral junctions, and are therefore invisible on plain chest radiographs. The unstable segment moves inwards on inspiration (paradoxical movement) and consequently compromises ventilation by reducing tidal volume. Following diaphragmatic rupture, the abdominal contents are similarly sucked into the chest on inspiration. If the pleural cavity is filled with air or blood, ventilation of partially collapsed lung is similarly compromised. Injuries to the major airways or inhalation of foreign material including teeth, windscreen glass, or stomach contents may physically occlude the large or small airways, thereby obstructing air entry.

Ventilation/perfusion imbalance. Effective oxygenation of the blood and elimination of CO_2 depends on a balance between ventilation of the lung and its blood supply. Thoracic injuries compromise ventilation perfusion balance by a number of different mechanisms. Mechanical obstruction of the airway is an obvious cause of impaired ventilation, but in practice other mechanisms predominate. Distribution of ventilation in the lung is influenced by regional variations in airways resistance and compliance. The latter is governed by gravity-dependent intrapleural pressure gradients, and gas distribution in the lung is therefore uneven during normal resting tidal ventilation. In the lower or more dependent pleural space the pressure is closest to atmospheric (least negative). It becomes increasingly negative towards the apex or non-dependent region of the lung. When a normal inspiration is taken from end-expiration (functional residual capacity) expansion of the initially smaller dependent alveoli is governed by the steep portion of the compliance curve. Consequently, they expand more for each unit of pressure change than do those at the apices which are influenced
by the upper, flatter portion of the curve. These differences result in preferential distribution of inspired gases to the areas of greater expansion in the dependent portions of the lungs. However, if terminal air spaces have collapsed due to haemopneumothorax or adult respiratory distress syndrome, inspiration results in preferential distribution to already expanded areas because of the influence of the compliance curve. The maldistribution of ventilation is worsened by airflow obstruction in terminal airways due to external compression, elevated intrapleural pressure, or interstitial oedema fluid. When a whole lobe or lung eventually collapses, there is perfusion of non-ventilated lung and a serious veno-arterial shunt effect. Ineffective oxygenation of the venous blood is reflected by widening of the alveolar-arterial oxygen tension difference and systemic hypoxia.

Movement of blood through the lungs is also influenced by gravity and the pressure gradient between the pulmonary arteries and left atrium. Blood flow is normally directed preferentially to the dependent parts of normal lung where ventilation is also most efficient. However, perfusion is often impaired by thrombosis of vessels in contused lung or widespread pulmonary microembolism by fat from bone marrow or platelet /neutrophil microemboli in patients with disseminated intravascular coagulation or adult respiratory distress syndrome. In many patients after even minor thoracic trauma, the effects of ventilation/perfusion mismatch may lead to unsuspectedly severe hypoxia which is seldom recognized

without blood gas analysis. Pulmonary contusion, intrapulmonary haemorrhage, and haemothorax or pneumothorax is invariably associated with serious deterioration in pulmonary function.
Impairment of gas transfer. Passive diffusion of gas across the alveolar capillary barrier is dependent on the surface area available, the width of the membrane, certain plasma and erythrocyte enzymic factors, and the partial pressure gradient between the alveolar and vascular spaces. Following thoracic trauma a number of factors, including injury to the pulmonary parenchyma by contusion, damage to the alveolar capillary barrier by inhalation of gastric contents or smoke, impaired cardiac output, and interstitial pulmonary oedema due to overtransfusion of crystalloid, colloid, or blood (elevated left atrial pressure) may adversely affect gas exchange. However, the most sinister process involved is that which begins with the pathophysiological effects of shock and, if uninterrupted by prompt resuscitation, may progress to adult respiratory distress syndrome. It is not appropriate to discuss the detailed humoral and cytological changes that culminate in this syndrome. Nevertheless, they are important, are probably triggered by activation and interaction of the complement, coagulation, kallikrein, and plasminogen cascades, and result in trapping of "activated", neutrophils in the pulmonary microvasculature. Here they release protease enzymes and generate oxygen free radicals with the potential to damage the alveolar capillary membrane. When full-blown adult respiratory distress syndrome occurs in a patient with thoracic trauma, particularly following multiple injuries, the chances of survival decrease markedly. Gas exchange is impaired by extension of the diffusion pathway by the presence of hyaline membrane and oedema fluid in the alveoli; accumulation of interstitial fluid within the septum and of proliterated type II cells along its alveolar border; reduction in the surface for diffusion because of terminal air space collapse and closure of capillary channels; and the detrimental influence of consequent hypoxaemia, hypercapnia, and acid-base shifts in erythrocyte enzyme kinetics. Some of the consequences of this process precipitate further deterioration in pulmonary dysfunction. Pulmonary arterial hypertension develops because of hypoxic arteriolar vasoconstriction. Higher flow resistance in small vessels can be made worse by increased interstitial fluid pressure. Intravascular coagulation may exacerbate these problems and contribute to ventilation/perfusion mismatch. Hypoxaemia is the first objective sign of the onset of adult respiratory distress syndrome, and is the cardinal index of its progressive severity. At a later stage CO_2 retention develops, with its consequent disturbances of acid-base balance. Unless blood gases are monitored continuously in patients with thoracic trauma the primary effects in the lung may be misinterpreted. The manifestations of respiratory insufficiency are reflected principally in deterioration of cardiovascular and central nervous system dysfunction.
PRACTICAL ASPECTS OF RESUSCITATION IN MAJOR THORACIC TRAUMA. Advances in pre-hospital transportation have provided an opportunity to sustain life in patients who would previously have died. In the United States, Europe, and Japan helicopter retrieval with resuscitation en route by positive pressure ventilation, external cardiac massage, and blood volume replacement are employed routinely for patients with major trauma. Relief of cardiac tamponade, control of exsanguinating haemorrhage, stabilization of respiratory dynamics, and the use of mechanical circulatory assistance should therefore be integral steps in accident department resuscitation rather than sequels to resuscitation. The decision to employ such procedures must be undertaken on clinical judgement and without recourse to radiology or special investigations. More than 80 per cent of all patients with ruptured aorta, trachea or bronchus die rapidly at the site of injury. Those who reach hospital alive are a self-selected group who should survive with appropriate treatment. Once in hospital, resuscitative manoeuvres are best carried out with caution and in an unhurried way, since most survivors have reached an impaired but balanced respiratory and haemodynamic status compatible with life. More drastic measures, such as thoracotomy in the accident department, are reserved strictly for those with penetrating injuries or severe chest wall disruption who arrive moribund and in circulatory arrest. The admitting department should have an area set aside for patients with severe injuries. This should contain a trolley that can be tipped, and that has adequate space around it on all sides for manoeuvre. An anaesthetic trolley should be readily at hand with chest drains, peritoneal lavage cannulas, and a variety of intravenous and central venous cannulas for use in the large veins. An overhead radiograph machine and CT scanner should be available and an

autotransfusion system is desirable. Once in the accident department, the airways, breathing, and cardiovascular status are reviewed and take priority over other procedures as appropriate (Table 1).

Table 1 The ABC principle of cardiopulmonary resuscitation

A. Establish a reliable airway
Oropharyngeal airway
Endotracheal tube
Bronchoscope
Tracheostomy
B. Restore the mechanics of breathing
Artificial respiration
Evacuation of haemopneumothorax
Stabilization of unstable chest wall
Mechanical ventilation
C. Resuscitate the cardiovascular system
Intravenous infusion of crystalloid colloid or blood
Restore acid–base status and electrolytes
Inotropic support
External or internal cardiac massage
Immediate surgery to stem haemorrhage

A brief but thorough history is obtained from the patient, witnesses, or police officers. The time and mechanism of injury, type of weapon, and condition of the victim during transport are noted. Nursing and medical staff remove all the patient's clothes but, in the case of penetrating wounds, must preserve them carefully for future forensic or medicolegal investigation. Orientation of the garment on the patient, traces of gunpowder, or missile fragments may constitute important evidence, and even tissue debrided from wound edges should be retained. The vital signs, pulse and respiratory rate, blood pressure, and central venous pressure are measured, and the haemodynamic state and volume of overt or concealed haemorrhage assessed. A central venous catheter and one or more large bore peripheral cannulae are inserted.In the collapsed patient a Ryle's nasogastric tube, quickly inserted by cutting down into an antecubital vein and passing into the superior vena cava, is excellent for rapid blood transfusion, venous pressure measurement, and repeated venous sampling. An arterial line facilitates blood pressure recording and blood gas analysis. Blood volume replacement is initially carried out using crystalloid or colloid substitutes, but after massive blood loss or continued rapid bleeding, oxygen carrying capacity and coagulation must be preserved with group O Rhesus
negative blood or the bleeding stopped by immediate surgical intervention. No attempt should be made to attain normal blood pressure at this stage: this may precipitate fatal haemorrhage from lacerated major vessels, intracranial bleeding, or cardiac tamponade. Controlled hypotension is desirable until the extent of injury is determined or surgical access to damaged structures is obtained. Whenever feasible, initial evaluation (including radiology) and resuscitation should be completed within 5 to 10 min. A patient whose vital signs cease or continue to deteriorate should undergo rapid endotracheal intubation and should be removed immediately to an area where operative resuscitation and repair can begin. For some moribund patients operation is a co-ordinated part of resuscitation .External cardiac massage is seldom successful in restoring cardiac activity in patients who have suffered penetrating trauma. Immediate thoracotomy for control of haemorrhage, cardiac compression, preservation of available blood volume, and direct repair of critical injuries can be life saving in patients who present in extremis with injuries that preclude transportation to the operating theatre, and in those whose condition deteriorates during the first few minutes following arrival, suggesting impending death despite resuscitation. “Do not meddle with an obviously dead patient”is an important dictum: patients with detectable vital signs can usually be sustained as far as the operating theatre. However, within these constraints there have been encouraging results from the use of immediate anterolateral thoracotomy for release of cardiac tamponade, suture repair of great vessels and cardiac wounds, internal cardiac massage, and cross-

clamping of the descending thoracic aorta. This last manoeuvre improves perfusion of the coronary and cerebral circulation in patients with profound hypovolaemia and stems exsanguinating haemorrhage in the abdomen. In one group of patients with no immediately discernible vital signs or with systolic blood pressure less than 60 mmHg, and with preterminal respiratory pattern and cerebral activity, who did not respond to volume replacement and ventilatory support, there was a 66 per cent survival rate following immediate thoracotomy when the injuries were limited to intrathoracic organs. This contrasted strongly with only 20 per cent survival when thoracotomy was performed for cardiac resuscitation in patients whose injuries were totally extrathoracic. The blood pressure level at 60 mmHg is important: young and fit individuals compensate for blood loss by vasoconstriction and pressure is maintained until critical hypovolaemia and acidosis occur. The extent of blood loss is disclosed by insertion of a central venous pressure line, though false elevation of venous pressure occurs with cardiac tamponade, shivering, straining, or poor position of the catheter. Measurement of base deficit is a sensitive index of the efficacy of resuscitation. Typing and cross-matching for at least six units of blood is performed at the same time. In victims of assault or attempted homicide, the entire body should be examined for signs of penetration, each site being marked with a radio-opaque marker so that the track of the missile can be established. Decreased or absent breath sounds, subcutaneous emphysema, tracheal displacement, and neck vein distension are sought. The girth of the abdomen is measured and the presence of abdominal distension, localized and rebound tenderness, guarding, rigidity, frank dullness on percussion, and hyperaesthesia over the shoulder (Kehr's sign indicative of subdiaphragmatic irritation by blood) are sought. When the patient is unconscious it is easy to miss serious injuries such as paraplegia. A catheter is inserted into the bladder to monitor urine flow. A nasogastric tube is used to empty the stomach.

Procuring the airway. After basic steps, including clearance of blood and mucus from the pharynx, conventional endotracheal intubation can usually be used to secure an airway. This may prove impossible or undesirable in patients with direct injury to the major airways or severe facio-maxillary trauma. Clues to disruption of the larynx, trachea, or major bronchi include aphonia, stridor, haemoptysis, and free air in the subcutaneous tissues or thorax (radiologically, pneumothorax, pneumomediastinum, or pneumopericardium). The severity of such injuries may be deceptive .Direct negotiation of the airway by rigid bronchoscopy or flexible intubating fibrescope is safer than blind intubation, which may completely obliterate a critical narrowing. If a patient with stridor is breathing spontaneously a helium-oxygen mixture may alleviate asphyxia until the bronchoscope is passed. Severe laryngeal injuries usually require tracheostomy. In patients with tracheal trauma tracheostomy adds a second tracheal injury and may fail to secure an airway when the lesion is intrathoracic. In those with tracheal transection an endotracheal tube can be passed distal to the injury over a guide bougie inserted at bronchoscopy. Alternatively, high frequency jet ventilation can be used via a narrow catheter inserted into the distal segment pending direct surgical exposure. In desperate circumstances, immediate exploration of the neck is required. The distal trachea is located by a finger passed into the superior mediastinum, grasped in forceps, delivered, and intubated directly.

The mechanics of breathing. Arterial blood gases should be analysed in all patients with chest injury since apparently minor chest wall injuries may cause major degrees of hypoxaemia. In those with uncomplicated chest wall injuries pain and anxiety are usually the biggest barrier to adequate respiratory excursion; once these are relieved ventilation improves substantially. It is imperative to restore both gas exchange and acid-base balance as soon as possible, by whatever means, since these abnormalities seriously compromise cardiovascular function. The mechanics of breathing may be compromised by disruption of the bony chest wall or diaphragm, accumulation of blood or air in the pleural cavities, or haemorrhage and oedema in the lung itself, which reduces compliance. A neurological injury may alter the respiratory drive and pattern of breathing. Early resuscitative measures include stabilization of a flail segment or covering a chest wall defect (sucking chest wound), intercostal drainage of a haemopneumothorax, and, sometimes, positive pressure ventilation from the outset. A large plastic adhesive membrane such as “Opsite” is useful for covering or stabilizing the chest wall; this can be supported by dressings and strapping until surgical debridement. A tension pneumothorax is always readily apparent on clinical examination and should never wait for radiological confirmation. A needle inserted through the chest wall will confirm the diagnosis but is useless therapeutically. A scalpel incision will relieve tension and restore both ventilation and venous return; an intercostal drain can then

be inserted with aseptic technique. At this point remember that by lowering intrathoracic pressure venous return will increase, as will bleeding from damaged structures. Ventilatory support is initiated promptly when respiratory efforts are inadequate or obstructed. If a bronchial or pulmonary air leak coexists, it is important to allow air to escape continuously, otherwise tension pneumothorax results. A large volume suction pump (Tubbs-Barrett) should be applied to chest drains inserted for haemopneumothorax. Negative pressures of -15 to 20 cmH_2O are applied unless a large bronchial air leak results in extraction of a significant proportion of the tidal volume. Low volume (Roberts) pumps should never be used in trauma patients because they may obstruct air flow.

Cardiovascular system. Assessment of external or concealed blood loss is particularly difficult in patients with chest trauma accompanied by multiple long bone fractures or abdominal injury. Physical signs and measurement of systemic and central venous pressure may be deceptive for the following reasons. First, cardiac contusion (predominantly of the right ventricle) or cardiac tamponade produces spuriously elevated right atrial pressure. After substantial haemorrhage this may fall within normal limits even in the presence of severe tamponade. Second, major vascular injuries such as aortic transection separate the baroreceptors from the vessel lumen and reflexly produce systemic hypertension. After serious blood loss the systolic blood pressure can still be normal. Lastly, fit young adults compensate for blood loss remarkably well. For these reasons it is imperative to measure and continue to monitor central venous pressure in every patient who is thought to require volume replacement. Peripheral pulses are checked and the presence of bruits sought in the neck. The possibility of injury to the heart or great vessels must be considered, however unlikely, since it is the unexpected rather than the obvious which most often leads to disaster. When there is no exit wound in the chest an abdominal injury may coexist. In patients surviving with either cardiac tamponade or a ruptured aorta, a balance is established between systemic hypotension and occlusion of the traumatic defect by blood clot or haematoma, which can create pressure beneath the surrounding tissues. Over-aggressive blood volume replacement raises intravascular pressures, upsets this equilibrium, and may cause fatal bleeding or tamponade. In these circumstances, controlled hypotension is maintained until surgical repair. A systolic pressure of 80 to 100 mmHg should not be exceeded, especially in the presence of satisfactory acid-base balance and urine flow. Needle pericardiocentesis is usually a waste of valuable time in trauma patients: cardiac tamponade is diagnosed clinically and should be relieved surgically. Except in the moribund patient, this procedure should be performed in the operating theatre to enable control of the source of haemorrhage. In patients with severe myocardial contusion or unexplained haemodynamic deterioration, a Swan-Ganz catheter is used both to measure the right ventricular, pulmonary arterial, and left atrial (wedge) pressures, and to monitor the need for, and efficacy of, inotropic support. Contused lungs are very sensitive to volume overload and often contain fat emboli. The goal of fluid and blood replacement in such cases is to restore the intravascular volume, tissue perfusion, and oxygen carrying capacity as rapidly as possible, without causing pulmonary dysfunction or reactionary haemorrhage. The debate regarding composition of such an infusion is self-perpetuating. There is general agreement that acute massive blood loss requires resuscitation, at least in part, with whole blood and/or blood components. When packed cell volume falls below a critical value, oxygen delivery to the tissues is severely impaired as a result of insufficient circulating red cells. In healthy adults, compensatory cardiac and pulmonary mechanisms are effective when packed cell volume falls below 0.20 but generally if this falls below 0.30 red cells should be infused. Thus, in acute loss of 1 to 1.5litres, whole blood is not essential and blood volume can safely be restored with a plasma substitute. If the volume of haemorrhage is larger than this, whole blood should be available early in order that fluid volume and oxygen carrying capacity can be simultaneously replaced.

Radiology. When the patient is haemodynamically stable an upright chest and abdominal radiograph (preferably posteroanterior) is obtained in full inspiration. The patient may require physical support and care must be taken not to disconnect catheters, since air embolism may occur on inspiration in the presence of low venous pressure. Supine radiographs are of limited value for assessment of intrapleural haemorrhage or intra-abdominal injury but may be the only alternative in the patient with multiple injuries. Sometimes there is surprisingly little abnormality, especially when direct injury to the mediastinum leaves the pleural cavities unscathed. Heart size may prove deceptively normal despite cardiac laceration and tamponade, and this should not cast doubt on a clinical diagnosis based on

circulatory collapse with raised venous pressure. Widening of the mediastinum occurs after damage to the major vessels, and if ruptured aorta is suspected an aortogram (not CT scan) must follow. Mediastinal air, subcutaneous emphysema, pneumothorax, and pneumopericardium are good evidence for injury to the bronchial tree or lung parenchyma. Haemopneumothorax is the most common finding after penetration of the pleural cavity. The CT scan provides little information that cannot be derived from plain chest radiographs but is excellent for identifying associated head and abdominal injuries.

DECISION MAKING AND EARLY INTERVENTION. Penetrating injuriesIn practice, insertion of an intercostal drain (size 28-36 F) is the only intervention required in up to 85 per cent of patients with penetrating thoracic wounds. This allows evaluation of blood loss and re-expansion of the lung. The usual approach is via the sixth or seventh interspace in the mid-axillary line. The tube is directed towards the apex of the chest posteriorly, and is immediately placed on suction. The initial blood loss and presence of an air leak are noted so that ongoing drainage can be assessed. Subsequent management is based upon the results of chest drainage. When the wound is several hours old the blood is dark in colour. Initial drainage may be large in volume, due to reactive pleural effusion stimulated by blood in the pleural cavity. Continued bleeding and the increasing or decreasing hourly trend is more important than the initial value and determines what further intervention must be undertaken. A persistent air leak associated with bleeding and haemopneumothorax indicates major pulmonary laceration, though in a stable patient this may not require surgical treatment. Damage to a large bronchus usually produces a massive air leak with surgical emphysema; this does require early intervention. With blood transfusion and intercostal drainage, most pulmonary lacerations resolve. When the chest tube drainage yields less than 250 ml/h without a large or continuous air leak, and if diagnostic studies show no major structural damage to the trachea, bronchial tree, oesophagus or cardiovascular system, chest drainage and supportive measures are sufficient. If the patient's haemodynamics are stable and an arterial bruit, absent pulse, widened mediastinum, or a wound track passing across the mediastinum is observed an aortogram should be performed to assess major vessel injury, bleeding from which may be deceptively controlled by a haematoma under tension. Signs of cardiac tamponade or failure to stabilize the haemodynamics mitigate against this course and prompt early surgical exploration (Table 2)

Table 2. Criteria for thoracotomy in open or closed chest injury

1.	When the initial chest drain insertion yields more than 1250 ml of blood immediately or more than 1000 ml plus 250 ml in the first hour, or if 500 ml is drained in three consecutive hours with no decreasing trend
2.	When cardiac tamponade is present even if pericardiocentesis is negative or relieves symptoms
3.	For massive air leak where pneumothorax persists despite adequate drainage, suggesting major bronchial or tracheal injury. Bronchoscopy is performed first to confirm the diagnosis and clear blood and secretions
4.	In all transmediastinal wounds
5.	For chest wall defects and diaphragmatic lacerations
6.	For removal of clotted haemothorax in order to expand the underlying lung and prevent empyema or fibrothorax. This should be considered after 48–72 h of drainage. Enzymic clot lysis is seldom successful
7.	For combined thoracic and abdominal wounds before laparotomy except where entry and exit wounds preclude heart or great vessel injury or when the source of major haemorrhage is abdominal

When a missile path is known to traverse the mediastinum and the patient remains stable bronchoscopy and oesophagoscopy are useful before exploration, particularly if mediastinal emphysema is seen on the chest radiograph or subcutaneous emphysema is felt in the neck. Well-defined protocols exist for thoracotomy either on an urgent or delayed basis (Table 2) .

The most frequent indications for emergency surgery are exsanguinating haemorrhage via the intercostal drain from pulmonary hilar wounds, or tamponade from cardiac laceration. Unless the patient is moribund and thoracotomy is required for resuscitation, it is preferable to maintain a state of controlled hypotension, insert the appropriate lines for transfusion, correct acid-base deficit and move quickly towards the appropriate facilities in the operating theatre.

Penetrating cardiac wounds. Approximately 80 per cent of patients with penetrating cardiac wounds are dead on arrival in the accident department or are taken directly to the coroner. Major intracardiac injuries such as valve disruption, coronary artery transection, or septal defects are therefore rare in patients but more frequent in autopsy series. Autopsy series have a preponderance of gunshot wounds

whilst, with few exceptions, clinical papers discuss predominantly stab wounds. This reflects the relative severity of these modes of injury. The triad of a mediastinal entrance wound, clinical evidence of cardiac tamponade, and a pulseless patient with profound systemic hypotension are pathognomonic of important cardiac injury. Though a posterior, subxiphoid, or subcostal penetrating wound may also produce cardiac injury, a mediastinal site of penetration is responsible for 57 to 85 per cent of cases. The diagnosis must be made rapidly from the clinical condition and will seldom await elective diagnostic studies other than the plain chest radiograph or two-dimensional echocardiography in a few stable and equivocal cases with tamponade. Many patients appear lifeless but have not sustained irreversible brain damage. The first question, therefore, is whether the patient is dead or alive. Those patients who reach hospital alive are a self-selected group who survive through arrest of haemorrhage by cardiac tamponade, or who are conveyed rapidly with bleeding from potentially fatal injuries. Cardiac wounds consequently present with one or two distinct syndromes-pericardial tamponade or haemorrhagic shock. The key to successful management of penetrating cardiac injuries is prompt diagnosis and immediate resuscitation and repair.

Haemorrhagic shock Haemorrhagic shock follows cardiac wounding when the pericardial laceration is large enough to allow free exit of blood so that tamponade cannot occur. Those patients who arrive moribund with haemorrhagic shock should undergo immediate thoracotomy on the side of injury, with the objective of controlling haemorrhage from the cardiac laceration and restoring blood volume and acid-base status. Thoracotomy is performed in the accident department only when the patient arrives warm with reactive pupils but with circulatory arrest, or when acute deterioration, uncontrolled haemorrhage, or cardiac arrest occurs in a patient whose injuries suggest cardiac involvement. In this situation, transfer to an operating theatre is not feasible, since a 5- to 10-min delay is not compatible with survival. The patient is rapidly intubated before thoracotomy and infused with a crystalloid solution such as Ringer's lactate. Unmatched type-specific or non-specific universal donor blood is given as soon as possible. Arterial pH and blood gas measurements are taken early and bicarbonate administered to correct profound acidosis. Anaesthesia is not required for the incision in a moribund patient: survivors will not recall the events. An anterolateral thoracotomy through the 5th intercostal space is used most frequently. The incision can be taken across the sternum for access to the right atrium and venae cavae or through the costal cartilages on the left side superiorly for involvement of the great vessels. This approach is also useful for patients with blunt trauma or flail or crushed chest who have suffered cardiopulmonary arrest and cannot undergo external cardiac compression safely. Moribund or profoundly hypotensive patients who have suffered blunt or penetrating abdominal trauma can be stabilized by resuscitative thoracotomy and cross-clamping of the descending thoracic aorta. This arrests intra-abdominal haemorrhage, facilitates internal cardiac massage, and allows perfusion of the brain and myocardium in preference to other organs. Patients with ruptured abdominal aortic aneurysms can be revived in the same way. Median sternotomy gives a better access to all cardiac chambers but sternal saws are not readily available in most United Kingdom accident departments. Surgical management of cardiac laceration depends on the location. Control of haemorrhage can usually be obtained by digital or manual compression, and the wound can be sutured directly or over felt pledgets. A small number of patients who survive laceration of a major coronary artery or valvular or septal disruption may require cardiopulmonary bypass after urgent thoracotomy. Left or right atrial lacerations may be controlled by inserting a Foley catheter and inflating the balloon. This facilitates direct suture repair of the defect. Autotransfusion is a valuable adjunct in patients with a major cardiac laceration, though few of these patients survive to reach hospital. Frequently, the lacerated heart has already arrested or is fibrillating. Control of the penetrating wound must then be carried out in association with cardiac massage and defibrillation. All patients who respond to treatment are transferred to an operating theatre for formal exploration, and more secure cardiorrhaphy if necessary. Cleansing and closure of the chest are then undertaken in sterile surroundings. Intravenous antibiotics, such as gentamicin, flucloxacillin, and penicillin, are administered postoperatively for 5 days or more. Treatment with steroids, mannitol, calcium channel blockers, or hypothermia may be considered for patients with signs of cerebral hypoxia. Complications of the procedure often relate to the uncontrolled operative circumstances and the need for rapid intervention. Iatrogenic lacerations of the heart, coronary arteries, and lung may contribute to failure. Considerable

experience is essential in deciding which patient should be explored in the accident department. The heart is relatively easy to resuscitate. The outcome depends more on the cerebral status. Reviews of large series of patients undergoing immediate thoracotomy in the United States demonstrate two groups with clear prognostic differences. Patients who suffer circulatory arrest more than 4 min prior to admission to the accident department and who are virtually dead on arrival rarely survive. Those patients who are admitted with some
minimal signs of life have a better prognosis. Survival correlates well with neurological status immediately after resuscitation. Those patients who show prompt improvement in neurological status with resuscitation usually have a satisfactory outcome. Young age, a brief period of cerebral hypoxia, and lack of major intracardiac structural injury are good prognostic features. Factors associated with high mortality in penetrating cardiac injuries include shotgun wounds (100 per cent mortality), left ventricular injury (47 per cent mortality), unconsciousness at the time of arrival (86 per cent mortality), and the absence of measurable blood pressure on arrival (66 per cent mortality). The mortality associated with knife wounds is usually lower than that associated with gunshot wounds.
Cardiac Tamponade. Tamponade occurs when the pericardial laceration is small so that blood accumulates within the sac and clots, thus arresting haemorrhage. Patients presenting with cardiac tamponade are easily recognized by the combination of an appropriate entrance wound, systemic hypotension and tachycardia, and distended neck veins despite haemorrhage. The majority of these patients remain conscious but are extremely anxious, cold, clammy, and cerebrally obtunded. The cardiac wound is usually small, and bleeding stops when intracardiac pressures fall and intrapericardial pressure and blood clot in the wounds arrests haemorrhage. The distended pericardium usually contains blood clot equivalent to between 500 to 1500 ml of blood. Bleeding of this degree may not lower the systemic pressure and the patient's overall condition may not suggest a cardiac wound. On arrival in the accident department, large bore central and the peripheral venous cannulae are inserted, though it is important at this stage to avoid transfusion, which may elevate the intracardiac and systemic pressures beyond 100 mmHg. This upsets the homeostatic mechanisms of cardiac tamponade and may cause fatal reactive haemorrhage. Full volume replacement and administration of a muscle relaxant must wait until the tamponaded patient is prepared and draped on the operating table with sternotomy or thoracotomy underway.For patients whose circulatory status remains good and where there is doubt as to whether the heart has been damaged, plain chest radiographs or two-dimensional echocardiography can be carried out once venous lines have been inserted. In tamponade patients the cardiac shadow is typically globular shaped. Two-dimensional echocardiography shows a pericardial effusion with compression of the cardiac chambers and abnormal ventricular filling. Patients with tamponade who survive a prolonged journey to hospital can usually survive the further short transfer to an operating theatre. Most centres who treat large numbers of penetrating cardiac wounds have abandoned pericardiocentesis in favour of early thoracotomy since the pericardial blood has usually clotted. Some advocate surgical transdiaphragmatic pericardotomy through a small subxiphoid incision for diagnosis and relief of suspected tamponade. This may produce temporary clinical improvement until median sternotomy or thoracotomy can be carried out. However, it may also disturb the blood clot in the cardiac wound and precipitate fatal haemorrhage before adequate surgical access is possible. If the knife or wounding implement is still in place it is important not to withdraw this until exposure of the damaged structures has been obtained.
Surgical intervention. Median sternotomy is the incision of choice for cardiac wounds. This provides access to all aspects of the heart and both pleural cavities, and the pulmonary hila, mediastinal trachea, and upper oesophagus area are also accessible. Penetrating wounds involving the heart can be approached via lateral thoracotomy, the position of which depends upon the site of penetration and predicted track of the weapon. Wounds above the nipple line require an incision through the fifth interspace. Those below, with possible diaphragmatic and abdominal damage, should be approached through the seventh interspace. Opening of the sternum and evacuation of blood clot is usually followed by fresh bleeding from the site of penetration. Most bleeding areas in the ventricles or great vessels can be controlled with finger pressure followed by suture. It is important to inspect the rest of the heart carefully for an exit wound. Only rarely is cardiopulmonary bypass required at this stage. Excessive bleeding from the lung can be arrested by a clamp across the hilum. In the profoundly

hypotensive patient, bleeding is minimal; once haemorrhage is stopped, blood or crystalloid infusion can be used to restore the intravascular volume and blood pressure. If ventricular fibrillation occurs during thoracotomy, cross-clamping of the descending aorta allows perfusion of the cerebral and coronary
vessels while blood volume is restored. Severe pulmonary laceration or contusion may require debridement or resection, whereas cardiac, bronchial, or oesophageal lacerations can usually be repaired by direct suture. Suture of cardiac lacerations should avoid the coronary arteries. If a major coronary artery is divided proximally, a saphenous vein or internal mammary arterial graft may be required. Damage to intracardiac structures such as the interventricular septum or valves may require open repair at a later stage but cardiopulmonary bypass is rarely required in the acute phase. In difficult situations such as inaccessible hole in the left atrium, balloon tamponade with a Foley catheter can allow time to organize appropriate equipment and personnel. Gunshot or stab wounds below the nipple line may produce combined thoracoabdominal injuries. The abdominal component may be recognized by preoperative peritoneal lavage or examination of the diaphragm during thoracotomy. Diaphragmatic injury must be repaired carefully since the morbidity associated with strangulated diaphragmatic herniation is considerable.

Blunt injury to the major airways. All levels of the trachea or main bronchi may be involved. More than 80 per cent of injuries occur within 2.5 cm of the carina, equally distributed between right and left sides. Mainstem bronchi are injured in 80 per cent of patients and the distal bronchi in only 9 per cent. The type of lesion varies from simple linear mucosal lacerations to extensive full thickness tears involving the trachea, main bronchi, and branch bronchi. Following complete transverse rupture and separation of the trachea, some continuity is usually maintained by the intact elastic mucosa or loose peribronchial tissue. In some patients the bronchial cartilage and muscle fractures, leaving an unsupported mucosal tube with a “flap valve” effect. Pathogenic features of airways injury are free air in the soft tissues, signs of airways obstruction, and haemoptysis (Table 3).

Table 3 Physical signs suggesting the presence of major airways injury.

High index of suspicion from mechanism of injury
Free air
Subcutaneous or deep cervical emphysema
Pneumothorax
Pneumomediastinum
Pneumopericardium
Haemoptysis
Airways obstruction
Stridor
Aphonia
Difficult intubation
Presence of common associated injuries:
Sternal or first rib fracture
Rupture aorta

When the chest is crushed, petechial haemorrhage of the upper chest and face may develop. This traumatic asphyxia syndrome is caused by retrograde venous flow from the right side of the heart. Patients with intrathoracic tracheal or bronchial disruption show distinct clinical patterns, depending on whether or not there is free communication between the site of disruption and the pleural cavity In the first group (70 per cent) the damaged bronchus opens into the pleural cavity causing a large (often tension) pneumothorax which continues to leak air after insertion of an intercostal drain. As a rule the lung fails to re-expand. The usual signs of injury are dyspnoea, haemoptysis, subcutaneous and mediastinal emphysema, and, in severe cases, cyanosis. Pericardial laceration in proximity to a bronchial rupture causes pneumopericardium. In the second group rupture occurs proximal to the pleural sheath and there is little or no communication between the site of injury and the pleural cavity, even when disruption is complete. There is usually no pneumothorax; if one is present it is small and does not recur after chest drainage. Small pleural lacerations become sealed by fibrin or blood clot, allowing the lung to re-expand providing bronchial continuity is not immediately lost. Air generally escapes into the mediastinum and

tracks under the deep cervical fascia. Mediastinal emphysema may be insufficient to be clinically detectable, or may be massive. Positive pressure ventilation worsens the subcutaneous emphysema or pneumothorax, and complete respiratory obstruction may occur.

Diagnostic techniques. Chest and neck radiographs are essential since they may disclose free air not detectable on physical examination. Pneumomediastinum is an early diagnostic sign but may easily be overlooked because of the technical quality of the film. The deep cervical fascia is in direct continuity with the mediastinum and air almost invariably tracks into the cervical region. Since this area is easily penetrated by X-rays and is not obscured by overlying soft tissue structures, deep cervical emphysema is easily recognized on lateral radiographs of the neck. Other important radiological signs include hyoid bone elevation (indicating tracheal transection), pneumothorax, subcutaneous air, pneumopericardium, fractures limited to the upper rib cage or sternum, air surrounding the bronchus, and obstruction in the course of an air-filled bronchus. Air trapping distal to a "flap valve" causes over-distension of the ipsilateral lung with mediastinal shift to the opposite side or herniation of the hyperinflated lung across the anterior mediastinum. When a main bronchus is transected within its pleural sheath, the characteristic radiographic appearance is of the affected lung dropped down onto the diaphragm. This picture contrasts with the findings in patients with pneumothorax without transection, in whom the lung collapses towards the mediastinum. Definitive diagnosis depends on bronchoscopy. This is best performed in a thoracic surgical unit with experienced anaesthetic support and facilities for complex intubation, thoracotomy, and respiratory support. However, it is often better for a thoracic surgeon to take his equipment to a referring hospital rather than risk interhospital transfer for bronchoscopy in circumstances where complete respiratory obstruction may occur en route. Bronchoscopy is performed only when initial resuscitative measures such as restoration of circulatory blood volume correction of acid-base balance and stabilization of the mechanics of breathing (e.g. insertion of an intercostal drain) have been carried out. An exception to this rule occurs when bronchoscopy is required to establish an airway after intrathoracic tracheal transection. A rigid Negus or Stortz instrument is preferable since bronchoscopy must also be used to remove blood clot, broken teeth, and secretions.

Treatment. The site, nature, and extent of injury must be carefully defined. The airways may be full of blood clot and mucus. Torn bronchial mucosa and oedema may obscure the true extent of the injury. Care must be taken not to displace the ends of a transected trachea or bronchus if a satisfactory airway exists. Details of surgical techniques are beyond the scope of this chapter. A successful outcome depends on prompt diagnosis, procurement of a reliable airway, stabilization of the cardiovascular status and the mechanics of breathing, correction of acid-base balance, and early primary repair. Conservative treatment is permissible only in certain well-defined circumstances. The first is when a longitudinal tear involves only a short length of posterior tracheal membrane, following thoracic compression against a closed glottis. This "bursting" injury self-seals when the intratracheal pressure is normal. "Minitracheostomy" can be used to maintain a low intratracheal pressure and discourage air leakage into the mediastinum whilst the mucosal laceration heals spontaneously. The second is when bronchoscopy shows the tear to be less than one-third the circumference of the bronchus and chest tube drainage re-expands the lung completely with early cessation of air leak. Repair is then usually unnecessary. When the acute injury is undiagnosed, and the patient survives, symptoms of respiratory distress usually follow in 7 to 10 days. These are caused by an ingrowth of granulation tissue, displacement of the injured segment, oedema, and surrounding haematoma. Untreated partial rupture of a
mainstem bronchus leads to bronchopulmonary suppuration, atelectasis, and fibrosis. Reconstructive surgery with excision of the granulation tissue is indicated at this stage, otherwise stenosis will develop at the site. In complete bronchial rupture the separated lung is atelectatic and uninfected, and is often capable of circulatory and ventilatory function after being re-expanded. Normal pulmonary function has been observed following re-anastomosis 2 months after the initial injury. However, the chances of performing successful delayed primary repair for the missed bronchial injury complicated by infection, are poor and pneumonectomy is often required. Bronchial stenosis has a similarly poor outlook unless the segment is short and resection with reconstruction can be performed.

Treatment of chest wall injuries. In most patients with thoracic trauma injuries are limited to the thoracic cage, with or without underlying pulmonary contusion, pneumothorax, or haemothorax. The extent of chest wall derangement varies considerably. The most extensive disruption occurs in patients with severe crush injuries, in whom multiple bilateral rib fractures and fractures of the spine and sternum coexist. A flail segment moves inwards on inspiration (paradoxical movement) and consequently compromises ventilation by reducing tidal flow. Physical examination is more valuable than radiology in defining the nature and extent of such an injury. Both pleural cavities act as single bellows. If the bellows are damaged and cannot produce sufficient negative pressure in the presence of a large flail segment, then to and fro movement of the segment may equal the attempted tidal volume of that side of the chest and ventilation is seriously compromised. It is important to restore full expansion of the lungs as soon as possible by drainage of a haemopneumothorax.
The two almost always coexist to some extent after trauma, and the size and position of the intercostal drain is important. This must be sufficiently large to drain blood and some fresh blood clot. A size 32 to 36 F Argyle tube is appropriate and is usually inserted laterally between the anterior and mid-axillary lines. The intercostal space and precise site chosen depends upon the site of injury and the location of blood or air. It is important not to enter the bony thorax too low or penetration of the diaphragm and abdominal viscera may occur: the fifth to seventh interspaces laterally at the anterior axillary line are usually safe. It is unnecessary for the drain to be in the "basal" position to drain blood, or in the apical position for air. A safe insertion is the first consideration, especially when radiological landmarks are obscured by a haemothorax and the chest wall itself is bruised or deformed. Liquid, blood, and air will "find" the drain as the lung expands. Established blood clots will not drain and an extensive clotted haemothorax requires surgical evacuation. It is important to incise the chest wall through to the pleura with a scalpel and to complete the entry with scissors or an artery forcep. Blood or air will then drain through the entry wound and the large drain can be inserted and directed to its required position without difficulty. Blood loss is measured carefully, since the need for thoracotomy is determined on the basis of the initial volume lost and the continued rate of bleeding. . There is no contradiction against insertion of the drain through the area of injury. Three commonly performed manoeuvres are inadvisable. These are, first, insertion of a chest drain "prophylactically" after injury on the pretext of preventing pneumothorax during positive pressure ventilation. If there is no pneumo- or haemothorax the underlying lung may be damaged by the procedure, thus creating an air leak or bleeding. This applies particularly to the 15 per cent of patients whose pleural cavity has been obliterated by fibrous adhesions from previous "pleurisy". In the presence of a pneumothorax, a drain should always be inserted prior to positive pressure ventilation. Second, insertion of a chest drain anteriorly in the second intercostal space. This causes pain and transfixes the principal accessory respiratory muscle, the pectoralis major. If an apical drain is specifically required then the posterior suprascapular route to the second interspace can be used.. Third, clamping of a chest drain at any time in the presence of an airleak. This produces serious risk of tension pneumothorax. The alternative, without clamping, is disconnection of the drain from its underwater seal. This merely produces a simple pneumothorax which is rapidly resolved by reconnection. When the chest drain has served its purpose, it should be removed directly. It will otherwise act as a conduit for bacterial infection and hamper chest wall movement and mobility during physiotherapy. Further management is aimed not at the chest wall itself but at preservation of respiratory function. Two or three simple fractures may lead to the death of a patient with chronic bronchitis: pain causes decreased respiratory excursion and failure to ventilate the basal segments. Atelectasis supervenes. Pain may also inhibit cough, so that secretions are not cleared from the bronchial tree. Pneumonia follows and profuse retained secretions cause respiratory obstruction. The patient then rapidly deteriorates into acute respiratory failure. A flail segment in itself is not an indication for mechanical ventilation: it is the functional rather than the anatomical consequence of injury which determine the necessity for ventilatory support.
Surgical treatment of chest wall injury.
This is only rarely undertaken for fracture fixation and stabilization of the bony chest wall, or correction of serious deformity with functional sequelae. Chest wall fixation may also be performed during evacuation of an extensive clotted haemothorax or for haemostasis in a severely lacerated lung. The vogue for nail or clip fixation of fractured ribs in flail chest waned with widespread use of positive

pressure ventilation for these patients. However, it has recently been resurrected, particularly in the United States, with the trend towards “conservative”, non-ventilatory management. Provided that rib fractures are not too comminuted, internal fixation may eliminate the need for artificial ventilation in a few patients and lessen the risks of pulmonary infection. When a clotted haemothorax is left in situ the long-term complications are debilitating. The haematoma deposits fibrin on the chest wall and lung and fibrotic contraction eventually causes crowding of the ribs, with severe restriction of lung compliance and expansion. There is also a significant risk of infection and emphysema. Thoracotomy should therefore be performed early when intercostal drainage fails to evacuate a substantial haemothorax. Respiratory function and recovery rate are improved by this procedure. Surgical morbidity and mortality are negligible when the patient is haemodynamically stable beforehand.

5. Materials for activating students during lectures (questions, problems, problem situations, etc.).

Case scenarios.

1. An 18-year-old man is brought to the emergency department with a stab wound just to the right of the sternum in the sixth intercostal space. His blood pressure is 80 mmHg. Faint heart sounds and pulsus paradoxus are noted. Auscultation of the right chest reveals decreased breath sounds. The illitial management of this patient should be which of the following?
(A) aspiration of the right chest cavity
(B) aspiration of the pericardium
(C) echocardiogram
(D) pericardia I window
(E) insertion of central venous access line

2. A 60-year-old woman runs her car off the road and it hits a telephone pole. She presents to the emergency department with severe anterior chest pain and a blood pressure of 110/80. A chest x-ray shows a questionably widened mediastinum. The next step in management should be which of the following?
(A) transthoracic echocardiogram
(B) pericardiocentesis
(C) aortogram
(D) central venous access line
(E) computed tomography (CT) of chest

3. An 18-year-old man presents to the emergency department with a gunshot wound to the left chest in the anterior axillary line in the seventh intercostal Sp'lCC. A rushing sound is audible during inspiration. Immediate management is which of the following?
(A) exploratory laparotomy
(B) exploratory thoracotomy
(C) pleurocentesis
(D) closure of the hole with sterile dressing
(E) insertion of chest tube

4. A 25-year-old man is shot in the left lateral chest. I n the emergency department, his blood pressure is 120/90, his pulse rate is 104 bpm, and his respiration rate is 36 breaths per minute. Chest x-ray shows air and fluid in the left pleural cavity. Nasogastric aspiration revels blood-stained fluid. What is the best step to rule out esophageal injury?
(A) insertion of chest tube
(B) insertion of nasogastric tube
(C) Esophagogram with gastrografin
(D) esophagoscopy

(E) peritoneallavage

5. A 32-year-old female falls from the 10th floor of her apartment building in an apparent suicide attempt. Upon presentation, the patient has obvious head and extremity injuries. Primary survey reveals that the patient is totally apneic. By which method is the immediate need for a definitive airway in this patient best provided?
(A) orotracheal intubation
(B) nasotraCheal intubation
(C) percutaneous cricothyroidotomy
(D) intubation over a bronchoscope
(E) needle cricothyroidotomy

6. **Methodological lecture support**:
- classrooms №1;
- Equipment - Multymedia;
- illustrative material - slides.

7. **Questions for self-control:**
1. Classification of thoracic trauma.
2. Pathological and anatomical features of thorax.
3. Methods of inspection of the patients with thoracic trauma.
4. Tool methods of inspection of the injured with thoracic trauma.
5. Tactics in the patient with thoracic trauma.
6. Tactics in the patient with associated trauma
7. Clinical presentations of thoracic organs damage.
8. Clinical presentations of thoracic trauma complications. The indications, terms and types of treatment.

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Lecture №__2

Theme: " Oesophageal diseases and trauma of the oesophagus. ".

1. Introduction.

Traumatic lesions of the cervical esophagus were identified in ancient times, and survival was observed when a cervical esophageal fistula formed that allowed the wound to heal gradually by secondary intention. Benign as well as neoplastic strictures of the esophagus were treated by dilatation at this time. Anatomic dissections performed during the Renaissance provided a systematic way to study the consequences of esophageal injury and stricture, so by the middle of the 18th century, techniques had been developed to remove foreign bodies and to dilate strictures of the cervical esophagus. By the middle of the 19th century, strictures were being approached by internal as well as external myotomies with some success but with a prohibitive leak and death rate. Major advances in esophageal surgery awaited the imaging potential of radiography and endoscopy, which occurred in the early part of the 20th century. Successful transthoracic operations on the thoracic esophagus were enhanced by the development of endotracheal anesthesia, antibiotics, and blood transfusions during World War II. More recently, video-assisted thoracoscopic techniques gained popularity.

2. Aims of the Lecture:

- **educational**

to know:

- definition of the pathology;
- contemporary general data about diseases of the oesophagus;
- classification of the diseases of the oesophagus;
- general symptoms and clinical course of the diseases of the oesophagus;
- methods of examination of the patient;
- indications for surgical methods of treatment;
- surgical treatment;
- working capacity.

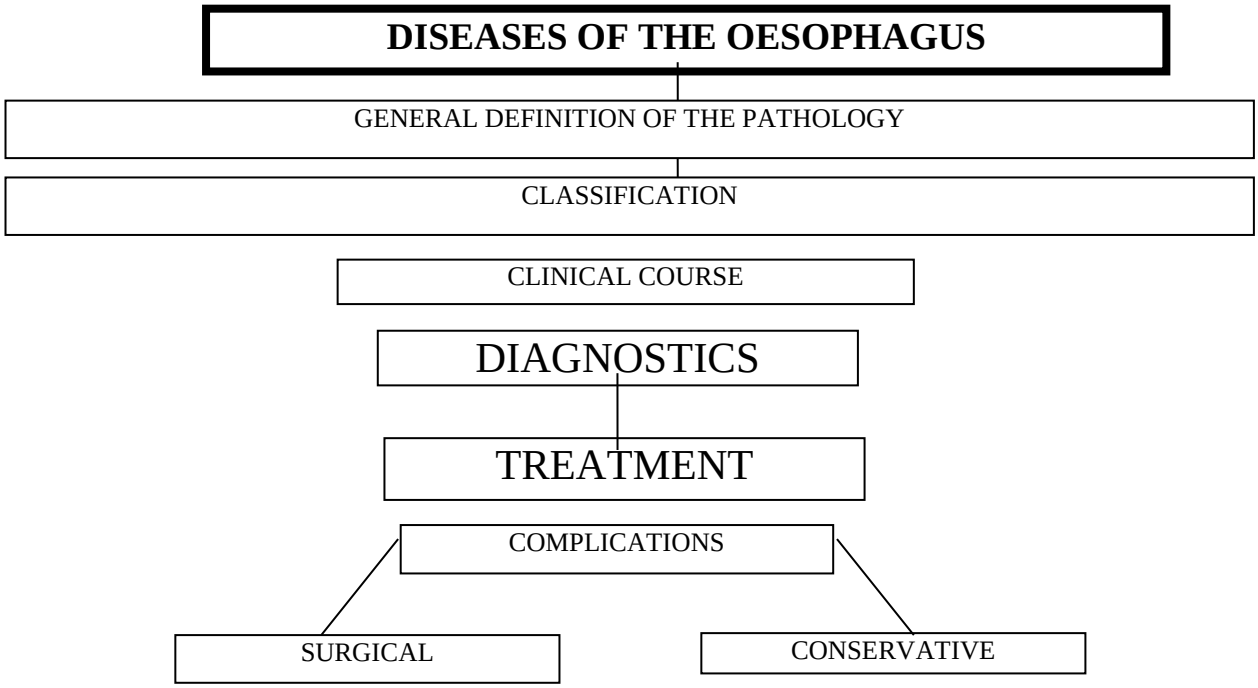
Basic concepts: esophageal diverticulum, achalasia, caustic ingestion.

3. **Plan and structure of the lecture.**

#	Contents and units of the lecture.	Tasks in abstract levels.	Equipment of the lecture.	Time.
	Preliminary part			
1.	Determination of educational aims		Recom.	3%
2.	Positive motivation		lecture.	2%
	Main part			
3.	Exposition of the lecture's matter Plan: 1. Definition of the pathology. 2. General information about the diseases of the oesophagus in Ukraine. 3. Classification. 4. Methods of the patient's examination and diagnostic of the diseases of the oesophagus. 5. Clinical course. 6. Organization of the surgical aid. 8.Working capacity . 9.Rehabilitation.	1-10 -"- -"- -"- -"- -"-	Tables, schemes, codograms, slides. Films.	90%
	Final part			5%
4.	Summary			
5.	Lecturer's answers to possible questions		Literature	
6.	Tasks for self-control		Questions. Tasks.	

4. Contents of the lecture

Structure of the lecture:



Text of the lecture:

DIVERTICULA

An esophageal diverticulum is an epithelium-lined mucosal pouch that protrudes from the esophageal lumen. Most esophageal diverticula are acquired, and they occur predominantly in adults. Esophageal diverticula may be classified according to their location, the wall layers that they contain, or their presumed mechanism of formation (124). Pharyngoesophageal (Zenker's) diverticula occur at the junction of the pharynx and esophagus; parabronchial (midesophageal) diverticula develop close to the tracheal bifurcation; and epiphrenic (supradiaphragmatic) diverticula occur in the distal 10 cm of the esophagus. Diverticula containing all layers of the normal esophageal wall (mucosa, submucosa, and muscle) are termed true diverticula, whereas those consisting only of mucosa and submucosa are false diverticula. Most esophageal diverticula arise when elevated intraluminal pressure cause the mucosa and submucosa to herniate through the esophageal musculature; these are false diverticula. On the other hand, traction diverticula result from an external inflammatory reaction in which adjacent mediastinal lymph nodes adhere to the esophagus and then pull the wall toward them as they heal and contract; these are true diverticula. Pharyngoesophageal and epiphrenic diverticula are pulsion diverticula that are generally associated with abnormal esophageal motility. Parabronchial diverticula are usually but not always of the traction variety and include all layers of the esophageal wall.

Pharyngoesophageal Diverticulum

The pharyngoesophageal (Zenker's) diverticulum is the most common esophageal diverticulum and typically occurs in patients between 30 and 50 years of age. The diverticulum consistently arises within the inferior pharyngeal constrictor muscle, between the oblique fibers of the thyropharyngeus muscle and the more horizontal fibers of the cricopharyngeus muscle, the upper esophageal sphincter (Fig. 1). The point of transition in the direction of these muscles (Killian's triangle) represents an area of potential weakness in the posterior pharynx and is the site of formation of the diverticulum. Manometric measurement of upper esophageal sphincter function is difficult with existing standard recording equipment, which may not document rapid movements of swallowing in an asymmetric sphincter that changes position with laryngeal excursions. Some degree of incoordination in the swallowing mechanism, however, is thought to be the basis for the formation of Zenker's diverticula. Inappropriate pharyngeal contraction after cricopharyngeal closure has been demonstrated in these patients. Regardless of the precise motor dysfunction, a pulsion diverticulum would not occur without some cause of unusually elevated esophageal pressures. As the swallowed bolus exerts pressure within the pharynx, mucosa and submucosa herniate through the anatomically weak area above the cricopharyngeus muscle. The diverticulum may gradually enlarge with time, extending over the cricopharyngeus muscle, and dissect downward in the prevertebral space posterior to the esophagus and occasionally into the superior mediastinum.

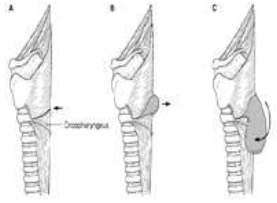


Figure 1. Formation of pharyngoesophageal (Zenker's) diverticulum. (A) Herniation of the pharyngeal mucosa and submucosa occurs at the point of potential weakness (Killian's triangle) (arrow) between the oblique fibers of the thyropharyngeus muscle and the more horizontal fibers of the cricopharyngeus muscle. (B,C) As the diverticulum enlarges, it drapes over the cricopharyngeus sphincter and descends into the superior mediastinum in the prevertebral space.

Patients with pharyngoesophageal diverticula characteristically present with cervical dysphagia, effortless regurgitation of undigested food or pills, a gurgling sensation in the neck on swallowing, periodic choking, and aspiration (Fig. 2). Marked weight loss and dysphagia in an elderly patient may be misdiagnosed as an esophageal malignancy (Fig. 3). The diagnosis of a Zenker's diverticulum is established with a barium esophagogram. In evaluating the patient with a Zenker's diverticulum, it must be realized that it is the degree of upper esophageal sphincter muscle dysfunction, not the absolute size of the pouch, that determines the severity of symptoms. In other words, a patient with a 5-mm Zenker's diverticulum may have as many or more symptoms than a patient with a 3-cm pouch. In most patients with symptoms, surgical treatment is indicated regardless of the size of the pouch to prevent additional complications (aspiration and nutritional impairment). As is the case with every

pulsion diverticulum, the proper surgical treatment of a Zenker's diverticulum must be directed at relieving the underlying neuromotor functional obstruction responsible for the increased pharyngeal pressure.

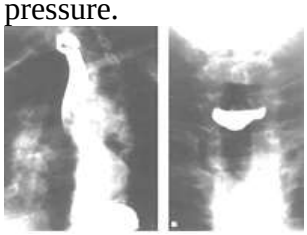


Fig. 2. Small Zenker's diverticulum. (A) The 2.5-cm pouch and the esophageal narrowing distal to it representing the tight cricopharyngeus sphincter. (B) Detail of pouch showing retained barium.

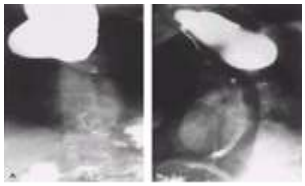


Fig. 3. Posteroanterior (A) and oblique (B) views from barium esophagogram in an elderly woman presenting with cervical dysphagia and a 40-lb weight loss that were initially thought to be secondary to an esophageal malignancy. This 15-cm pharyngoesophageal diverticulum was treated successfully with diverticulectomy and cervical esophagomyotomy.

The first surgical approaches to Zenker's diverticula involved simply excising the pouch and suturing the pharyngeal defect. The underlying upper esophageal sphincter dysfunction and resulting functional obstruction were not appreciated, and the incidence of suture line disruption with resulting cervical and mediastinal infection was high. Currently, a cricopharyngeal myotomy, which relieves the relative obstruction distal to the pouch, is regarded as the most important aspect of surgical treatment in these patients (Fig. 4). This operation is performed through a left cervical incision that parallels the anterior border of the sternocleidomastoid muscle. The sternocleidomastoid muscle and carotid sheath and its contents are retracted laterally, and the thyroid and trachea medially. The inferior thyroid artery is an important anatomic landmark in this operation. Once it is divided, the diverticulum is consistently found beneath it. The diverticulum is identified and dissected to its base, and an extramucosal esophagomyotomy is performed in either vertical direction for several centimeters from the base of the pouch to ensure that all cricopharyngeal muscle fibers are divided. Pouches of up to 2 cm in size simply are incorporated with the mucosa and submucosa, which bulge through the divided muscle at the site of the esophagomyotomy, and no resection of the pouch is needed. Larger pouches are excised with use of the surgical stapler. The results of treatment are excellent, and recurrence is rare if the relative obstruction distal to the pouch has been relieved by complete division of the upper esophageal sphincter. An alternative approach is diverticulopexy, which involves mobilizing the pouch, inverting it, and suspending it from adjacent tissues so that the mouth is dependent. This operation is successful only if combined with a cervical esophagomyotomy. Endoscopic division of the common wall between the diverticulum (internal pharyngoesophagomyotomy, or the Dohlman procedure) for treatment of Zenker's diverticulum has been used with success, particularly by European surgeons.

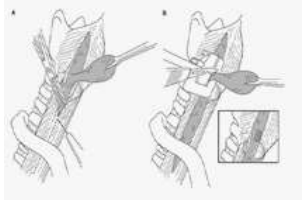


Fig. 4. Cervical esophagomyotomy and concomitant resection of a pharyngoesophageal diverticulum. (A) An esophagomyotomy is performed for several centimeters in either vertical direction from the base of the mobilized diverticulum. (B) After completion of the esophagomyotomy, the base of the pouch is crossed with a TA-30 stapler and amputated.

Midesophageal *Traction Diverticulum*

Mediastinal granulomatous disease (e.g., tuberculosis or histoplasmosis) is the common cause of midesophageal traction diverticula. This type of diverticulum is much smaller than the pulsion diverticulum and has a characteristic blunt tapered tip that points toward the adjacent subcarinal and parabronchial lymph nodes to which it adheres (Fig. 5). It is typically diagnosed as an incidental finding on a barium esophagogram and almost always is asymptomatic. No specific treatment is indicated. At times, however, inflammatory necrosis of the granulomatous reaction may produce a fistula between the esophagus and the tracheobronchial tree requiring division of the fistula and interposition of normal tissues. Midesophageal traction diverticula must be differentiated from pulsion

diverticula, which may also develop in this location and are associated with neuromotor esophageal dysfunction, as are epiphrenic diverticula.

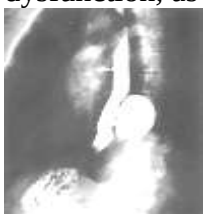


Fig. 5. Barium esophagogram showing an epiphrenic diverticulum and a small traction diverticulum (arrow) of the middle esophagus.

Epiphrenic Diverticulum

An epiphrenic or supradiaphragmatic diverticulum occurs within the distal 10 cm of the thoracic esophagus. It is a pulsion diverticulum that arises because of abnormally elevated intraluminal esophageal pressure (Fig. 5). Although many patients have no symptoms at the time of diagnosis on barium esophagogram, others do have symptoms resulting from the frequently associated esophageal conditions: hiatal hernia, diffuse esophageal spasm, and reflux esophagitis. Dysphagia and regurgitation are the common symptoms of an epiphrenic diverticulum, and retrosternal pain may be caused by associated diffuse esophageal spasm. Esophageal manometry and acid reflux testing should be performed to define the associated motor abnormality and assess the competence of the lower esophageal sphincter mechanism. Pouches smaller than 3 cm and causing little or no symptoms require no treatment. Severe dysphagia, chest pain, or an anatomically dependent or enlarging pouch are indications for repair. Unless an associated distal esophageal stricture or tumor is present, it must be inferred that the patient with an epiphrenic diverticulum has an abnormally elevated intraesophageal pressure that has caused the pouch to form and is the result of neuromotor dysfunction. This can often, but not always, be documented manometrically.

The surgical approach to epiphrenic diverticula is through a left sixth or seventh interspace posterolateral thoracotomy. This is the case even for diverticula that present to the right of the esophagus. A long, extramucosal thoracic esophagomyotomy is performed from the level of the aortic arch to the esophagogastric junction (Fig. 6). If an associated hiatal hernia or incompetent lower esophageal sphincter is found, an antireflux operation should be carried out at the same operation. If an adequate esophagomyotomy is performed and the abnormally elevated intraesophageal pressure is thus relieved, suture line disruption and recurrence of the diverticulum are rare. Just as in the surgical treatment of achalasia, controversy exists regarding the distal extent of the muscle incision and the requirement for a concomitant antireflux operation. One school argues that the lower esophageal sphincter should not be disturbed if preoperative esophageal manometry and reflux testing show that it is normal. Others argue that to relieve the distal esophageal functional obstruction completely, which must be present regardless of normal manometry values, the esophagomyotomy must be carried distally through the lower esophageal sphincter and onto the stomach for 1.5 cm. The resulting incompetent lower esophageal sphincter necessitates the routine addition of an antireflux operation. Because the myotomized esophagus does not have normal propulsive force, when an antireflux procedure is added, a partial, 240-degree Belsey fundoplication, rather than a 360-degree Nissen fundoplication, is preferred so that functional obstruction is avoided. A Mayo Clinic report citing a 9% operative mortality rate associated with diverticulectomy and esophagomyotomy underscores the fact that patients with minimally symptomatic diverticula should not be subjected to surgery.

Fig. 6. Technique of resection of epiphrenic diverticulum and concomitant esophagomyotomy. (A) The diverticulum is mobilized to its base and amputated with a TA-30 surgical stapler. (B) The staple suture line is oversewn. (C) A long esophagomyotomy is performed from the esophagogastric junction to the aortic arch 180 degrees on the opposite wall of the esophagus. (D) Air is insufflated through an intraesophageal nasogastric tube with the esophagus submerged under saline solution to be certain that the integrity of the mucosa has been maintained.

ACHALASIA

The term achalasia is of Greek derivation and literally means "failure or lack of relaxation." The name achalasia focuses on the LES, but the condition involves the entire esophageal body. Achalasia is usually a disease of middle age, with equal incidence for either sex. The classic triad of presenting symptoms includes dysphagia, regurgitation, and weight loss. In the early stages of achalasia, the

patient notes a sticking sensation, usually at the level of the xiphoid, after ingestion of liquids, especially cold liquids, and later after ingestion of solids. Patients with achalasia eat slowly, use large volumes of water to wash food into the stomach, and may twist the upper torso, to elevate the chin and extend the neck, or they walk about the room in an effort to force down food. As more water is swallowed, the weight of the fluid column in the esophagus increases, along with the sensation of retrosternal fullness, until the LES is forced open, with sudden relief as the esophagus empties. Dysphagia progresses slowly and is well tolerated for many years. As a consequence, patients with achalasia often do not seek medical attention until progressive dysphagia interferes with their lifestyle. Regurgitation of undigested food is common as the disease progresses, and aspiration becomes life-threatening. Effortless regurgitation after eating, particularly on bending forward or reclining, is usually not associated with the sour taste of undigested food experienced in patients with acid regurgitation from gastroesophageal reflux. As the esophagus dilates, regurgitation of foul-smelling, stagnant intraesophageal contents occurs. Achalasia often results in recurrent respiratory symptoms related to aspiration, which may cause pneumonia, lung abscess, bronchiectasis, hemoptysis, or bronchospasm. Marked distention of the dilated esophagus may produce dyspnea from compression of the main stem bronchi and hilum. Weight loss is common and may be significant enough to suggest malignancy.

The origin of achalasia is unknown, but the characteristic clinical, radiographic, and manometric findings have resulted from various situations, including severe emotional stress, major physical trauma, drastic weight reduction, and Chagas' disease in South America. Chagas' disease, a parasitic infection by the leishmanial forms of Trypanosoma cruzi, is characterized by destruction of the smooth muscle ganglion cells of the Auerbach myenteric plexus, with resulting motor dysfunction and progressive dilation not only of the esophagus but also of the colon, ureters, and other viscera. In achalasia, the parasympathetic ganglion cells within the myenteric plexus, between the longitudinal and circular muscle layers of the esophagus, are markedly reduced in number. At autopsy, a decrease in the dorsal motor nucleus of the vagus has been found. Likewise, injury to the esophageal myenteric plexus by cold, heat, chemicals, or excision also leads to the characteristic manometric signs of the disease.

Achalasia is a premalignant esophageal lesion, with carcinoma developing as a late complication in 1 to 10% of patients who have this condition for an average of 15 to 25 years. Long-standing mucosal irritation from retention esophagitis appears to induce the metaplasia. Esophageal carcinoma in achalasia tends to arise in the middle third of the esophagus, below the air-fluid level, where the mucosal irritation is most pronounced.

DIAGNOSIS

The radiographic appearance of achalasia varies with progression of the disease. The characteristic appearance on a standard chest x-ray is a double mediastinal stripe throughout the length of the chest and a retrocardiac air-fluid level in a patient with typical symptoms. The barium esophagogram shows mild dilatation in the early stages and massive dilatation, tortuosity, and a sigmoid shape in the later stages. Retained intraesophageal food contents are typically seen. The roentgenographic hallmark of achalasia on barium swallow examination is the distal bird-beak taper of the esophagogastric junction (Fig. 7) .

The manometric criteria of achalasia are failure of the LES to relax reflexively with swallowing and lack of progressive peristalsis throughout the length of the esophagus. In the early stages of achalasia, contractions after swallowing may be of normal amplitude, but they are synchronous and simultaneous. Later, contractions are either totally absent or weak. The distal esophageal HPZ pressure is generally normal or elevated, but the marked hypertonicity of DES is not seen. Administration of a mild vagomimetic agent (i.e., bethanechol [Urecholine]) produces marked elevation of intraesophageal pressure and increased amplitude and frequency of simultaneous esophageal contractions that correspond with the patient's complaint of chest pain.

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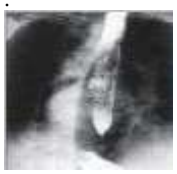

Fig. 7. Barium swallow in a patient with achalasia. (a) Retained food, moderate oesophageal dilatation, and bird's beak deformity of distal oesophagus.

This response does not occur in scleroderma, but it is common both in DES and achalasia. However, the patient with intermittent DES, unlike someone with achalasia, usually has some degree of progressive peristalsis on standard manometric evaluation, and the LES shows reflex relaxation with swallowing.

In achalasia, esophagoscopy is indicated to evaluate the severity of esophagitis, the possibility of associated carcinoma, a distal esophageal stricture from reflux esophagitis, or a tumor of the cardia mimicking achalasia (pseudoachalasia). Retention esophagitis in advanced achalasia is different endoscopically from reflux esophagitis. When the patient has prolonged retention esophagitis from achalasia, the irritating effects of putrefying food on the esophageal mucosa may induce severe edema, with reddish purple discoloration and marked friability. When one performs esophagoscopy in the evaluation of achalasia, the presence of retained fluid and food in the dilated esophagus, even after an overnight fast, may complicate the procedure, and cricoid pressure to protect the airway is indicated. Secondary achalasia or pseudoachalasia, caused by a tumor at or near the gastroesophageal junction, is also best detected by endoscopy and biopsy. The precise imaging of endoscopic ultrasound can be used when endoscopic examination alone fails to confirm the diagnosis of secondary or primary achalasia. Endoscopic ultrasound may identify subepithelial tumor infiltration in secondary achalasia when results of biopsies of the cardia or gastroesophageal junction are negative. Furthermore, high-frequency ultrasound probes (20 MHz) allow more precise imaging of the various muscle layers that make up the muscularis propria and allow identification of patients with primary achalasia. The EUS can then be used to direct injection of botulinum toxin as therapy for achalasia. The high-frequency probes also can assess the response of the esophageal wall to therapy (pneumatic balloon versus botulinum toxin injection).

TREATMENT

Because the derangement in esophageal motor function does not return to normal, the treatment of achalasia is purely palliative. Both nonsurgical and surgical treatments of achalasia are directed toward relieving the obstruction caused by the nonrelaxing LES. In the early stages of the disease, before the esophagus dilates, use of sublingual nitroglycerin before or during meals, long-acting nitrates, and calcium-channel blocking agents may improve swallowing. Passage of mercury-weighted bougies, 48 to 54 French, may relieve the dysphagia for several days or weeks, but it is seldom a satisfactory long-term solution.

The definitive treatment of achalasia requires disruption of the circular layer of smooth muscle within the LES area. The two most widely used and analyzed methods of therapy for achalasia are forceful dilatation, either pneumatic or hydrostatic, and esophagomyotomy. Results were considered excellent or good in 65% of patients with dilatation and 85% of those after esophagomyotomy. The perforation (4% versus 1%) and mortality rates (0.5 versus 0.2%) were reported to be higher with dilatation than with esophagomyotomy. However, the advent of volume-limited pressure-controlled balloons (Gruntzig-type) has decreased the perforation rate and mortality of balloon dilatation. A Gruntzig-type balloon is positioned under fluoroscopic control within the LES. The balloon is rapidly inflated to a pressure of 300 torr for 15 seconds. Results from dilatation show that approximately 60% of patients receive complete relief of symptoms after one treatment, and an additional 10% respond to a second treatment. Most patients referred for myotomy have had at least one failed balloon dilatation.

A novel pharmacologic treatment of achalasia is intrasphincteric botulinum toxin injected into the LES through the flexible esophagoscope. This potent neurotoxin inhibits the release of acetylcholine from nerve endings and has been used with good results in a number of diseases characterized by muscle spasm (e.g., strabismus and various dystonias). Encouraging early results have been reported, but

longer follow-up in patients with achalasia has been disappointing. The efficacy of botulinum toxin has yet to be established.

Surgical treatment, either open or video-assisted, with division of the circular muscle of the lower end of the esophagus, offers precise and less traumatic division of the circular muscle layer of the lower esophagus than that achieved through forceful dilatation with surgery. Results appear superior to those of balloon dilatation, and mortality is low. Major disadvantages include the need for hospitalization, thoracic access, and a low but finite incidence of reflux esophagitis. Excellent early results with laparoscopic esophagomyotomy in the treatment of achalasia have been reported, and this approach is clearly superior to the transthoracic video-assisted esophagomyotomy.

The traditional transthoracic distal esophagomyotomy for achalasia is performed through a left thoracotomy in the sixth or seventh intercostal space. The pleural reflection is incised and the distal esophagus is mobilized, with careful preservation of the vagus nerve. In addition, the esophagogastric junction is mobilized from the esophageal hiatus to allow visualization of 1 to 2 cm of stomach. A linear incision (7 to 10 cm) is made through the longitudinal and circular muscle layer, from the level of the inferior pulmonary vein superiorly down and across the lower sphincter inferiorly, to bring the incision onto the stomach 3 to 5 mm to divide all circular muscle fibers (Fig. 8) . Separation of the muscularis from the submucosa at the margin of the incision is important to ensure that the divided layers do not reapproximate as healing occurs.

Unresolved technical questions concern the distal extent of the esophagomyotomy and the need for a concomitant antireflux procedure. Some surgeons advocate a short esophagomyotomy carried onto the stomach only far enough to ensure complete division of the distal esophageal musculature, but not far enough to induce incompetence of the LES mechanism. With this approach, several surgeons reported a late incidence of postoperative gastroesophageal reflux of about 8%. Many surgeons believe that complete relief of the obstruction caused by the uncoordinated LES can be achieved only by rendering the LES incompetent, by carrying the esophagomyotomy onto the stomach for 1 to 2 cm. Most esophageal surgeons now carry out a complete esophagocardiomyotomy for achalasia with some type of fundoplication to prevent the subsequent development of gastroesophageal reflux. A 360-degree loose fundoplasty, in which the stomach is wrapped around the lower esophagus, has the potential disadvantage of offering too much resistance to the passage of food. Excellent long-term results suggest that a distal esophagomyotomy combined with a partial fundoplication may be the surgical approach of choice in achalasia. Even with this approach, however, gradual deterioration of esophageal function over time and the late development of gastroesophageal reflux and esophagitis jeopardize the long-term outcome.

Minimally invasive video-assisted techniques to accomplish an esophagomyotomy, both laparoscopically and thoracoscopically, have yielded comparable results to the open approach with less postoperative pain and a shorter hospital stay. Some surgeons prefer a laparoscopic (transabdominal) approach with a partial fundoplication to avoid postoperative reflux.

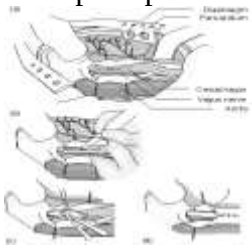

Fig. 8 Oesophagomyotomy via left thoracotomy. (a) Operative exposure. Dotted line indicates extent of myotomy. (b) Incision of the muscularis. (c) Separation of mucosa and muscularis over half the oesophageal circumference. (d) Suture narrowing of the hiatus in the presence of a hernia.

The laparoscopic myotomy has advantages over the thoracoscopic technique. First, anesthesia is easier to administer because a double-lumen tube is not needed. Second, the myotomy can be performed more easily through the abdomen. Last, the absence of a chest tube may decrease postoperative pain. Patti and colleagues reported on 168 patients undergoing minimally invasive esophagomyotomy over an 8-year period. Good or excellent relief of dysphagia was noted in 90% of patients. Even those with a dilated, end-stage esophagus had excellent relief of dysphagia, and none required esophagectomy.

They originally performed the myotomy through a thoracoscopic approach but now prefer the laparoscopic approach combined with a partial fundoplication. Based on these excellent results and long-term follow-up (median 28 months), laparoscopic Heller myotomy and partial fundoplication probably should be considered the primary treatment for achalasia. Laparoscopic Heller myotomy is a safe and effective procedure even after unsuccessful treatment with botulinum toxin.

Patients with recurrent esophageal obstruction after esophagomyotomy or a reflux-induced peptic stricture after either esophagomyotomy or forceful dilatation pose a difficult dilemma for the surgeon. Only two thirds of patients undergoing a repeat esophagomyotomy benefit from the operation, and fundoplication for reflux symptoms has even poorer results. A more reliable approach may be esophageal resection and esophageal substitution, preferably with stomach. Esophageal resection provides definitive treatment of the esophageal abnormality, eliminates the late risk of carcinoma, and can be accomplished transhiatally without opening the thorax. This approach is being used with increased frequency in patients with failed prior operations for achalasia or in those with a megaesophagus that may fail to empty adequately even after an esophagomyotomy. Esophagectomy for end-stage achalasia should be strongly considered in symptomatic patients with end-stage disease in whom lesser approaches offer little relief. Banbury and associates reported that 32 patients underwent esophagectomy with gastric transposition during a 10-year period with excellent functional results. Eighty-three percent had no or only mild dysphagia, and most had no dietary restrictions.

CAUSTIC INJURY

Caustic ingestion is most common in two broad categories of patients—children younger than 5 years of age who accidentally swallow these agents and adults who attempt suicide. More than 5,000 cases of caustic ingestion occur annually in the United States. The agents most frequently responsible for caustic esophageal injuries are alkalis, acids, bleach, and detergents containing sodium tripolyphosphate. Ingestion of detergents and bleach virtually always causes only mild esophageal irritation that heals without significant adverse sequelae. Acids and alkalis, on the other hand, may have devastating effects that range from acute multiple-organ necrosis and perforation to chronic esophageal and gastric strictures. Alkalis are more destructive, producing liquefaction necrosis, which almost ensures deep penetration, whereas acids usually cause coagulation necrosis, which in part limits the depth of the injury.

In 1967, the introduction in the United States of concentrated liquid alkali preparations (e.g., Drano, Liquid Plumber) dramatically altered the nature and extent of caustic esophageal injuries. Before that time, alkali (lye) was typically available only in solid form, and lye crystals tend to adhere to the mucosa of the oropharynx and upper esophagus, producing burns in patches or linear streaks. Thus, solid alkali rarely reached the stomach in sufficient quantity to damage it. In contrast, the high viscosity of the newer liquid alkali preparations prolongs the contact between these substances and the mucous membranes and also facilitates their rapid transit into the stomach, so that severe damage to the esophagus and stomach, and also adjacent organs such as the trachea, colon, small bowel, pancreas, and aorta, is common. Ingested acids typically pass through the esophagus, quickly producing major gastric injury with relative sparing of the esophagus, although significant esophageal damage can occur.

In response to the ingestion of either acid or alkali, reflex pyloric spasm develops, with resultant pooling of these agents in the gastric antrum. Antral stenosis then produces a typical hourglass-like deformity (Fig. 9). Laboratory studies in a canine model have shown that cricopharyngeal and pyloric spasm occurs when concentrated lye enters the esophagus and stomach. The esophagus contracts vigorously, propelling the caustic agent into the stomach. Pyloric and gastric contraction follows and propels the caustic agent back up into the esophagus. This seesaw movement of the caustic agent between the esophagus and stomach continues for several minutes until gastric and esophageal atony develops as the result of extensive damage to both organs.

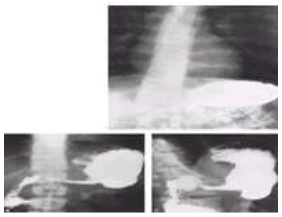

Fig. 9. (A) Caustic stricture of the esophagus and stomach. (B,C) Detail of the stomach showing the typical hourglass deformity resulting from severe antral stenosis with sparing of the body of the stomach and duodenum.

Clinical Features

The clinical manifestations of caustic ingestion are directly related to the amount and character of the agent ingested (98). Virtually no symptoms may be caused by mild pharyngeal, esophageal, or gastric burns (99). Solid alkali typically burns the mouth, pharynx, and upper esophagus. The resulting severe pain usually causes immediate expectoration, so that relatively little of the caustic agent is swallowed. These burns usually induce excessive salivation. On examination, the mucosa of the mouth and oropharynx shows patchy areas of white to gray-black pseudomembranes. Patients may also present with hoarseness, stridor, aphonia, and dyspnea from laryngotracheal edema or destruction. At the other end of the spectrum is liquid alkali ingestion. This form of alkali is usually swallowed quickly and produces less injury to the mouth and pharynx but more damage to the esophagus and stomach than its solid counterpart. Patients may present with dysphagia, odynophagia, and aspiration. Severe retrosternal, back, or abdominal pain and signs of peritoneal irritation suggest that mediastinitis or peritonitis resulting from esophageal or gastric perforation has developed. With acid ingestion, gastric injury is more common; therefore, signs and symptoms are frequently localized to the abdomen. When esophageal or gastric perforation results from caustic ingestion, patients demonstrate progressively severe sepsis and hypovolemic shock until appropriate resuscitative measures are instituted. In the absence of gastric or esophageal perforation, the acute clinical manifestations typically resolve within several days, with clinical improvement lasting for several weeks. After this, symptoms of either esophageal or gastric stricture begin. Although strictures develop in only 10% to 25% of adult patients who ingest solid alkali, most patients who ingest liquid alkali sustain severe esophageal and usually gastric injury that often results in stricture formation. Children with limited exposure from accidental ingestion are less likely to have severe injuries. Acid ingestion most often results in stricture or contracture of the antrum or pylorus.

Immediate Diagnosis and Treatment

Acute caustic ingestion is an indication for hospitalization. Initial management centers on stabilizing the patient and assessing the severity of the injury. Vomiting should not be induced. Because caustic injuries produce almost instantaneous tissue damage, attempts to dilute the agent by having the patient drink water are futile. In fact, this may only aggravate the problem by causing an increase in gastric distention and vomiting. Oral intake should be withheld and hypovolemia corrected with intravenous fluids. Careful observation for evidence of airway obstruction is mandatory. Endotracheal intubation or tracheostomy may be required in cases of significant laryngeal edema or actual laryngeal destruction. Broad-spectrum antibiotics are indicated once the diagnosis of substantial esophageal injury has been established to diminish the risk for pulmonary infection resulting from aspiration and bacterial invasion through the damaged esophageal wall. Although corticosteroids have been advocated in the acute phase of caustic ingestion to minimize subsequent stricture formation, their efficacy has not been established. Because corticosteroids may mask signs of sepsis and visceral perforation and impair healing, their use in caustic esophageal injury is potentially deleterious and is therefore not recommended.

A relatively urgent contrast examination of the esophagus may provide important information in the patient with a caustic injury. Radiographically, acute mucosal esophageal injuries are seen as blurred, irregular margins with linear streaking of contrast in deeper ulcers. Submucosal edema may be manifested by scalloped or straightened esophagogastric junction margins. Dilation of the esophagus and stomach, gastric ulcerations, air in the gastric wall, and frank extravasation of contrast material from the esophagus or stomach are common. A contrast esophagogram is the best way to make the diagnosis of esophageal perforation and should be performed if the diagnosis is suspected either at the time of admission or in subsequent follow-up. Identification of the site of perforation is vitally

important in the planning of subsequent intervention. The initial esophagogram in these patients can be performed with a water-soluble agent (e.g., Gastrografin), but dilute barium provides much better mucosal detail and should be used if the diagnosis of perforation is suspected.

Management

Esophagogastroscopy should be performed soon after admission to establish whether significant esophageal injury has occurred and to permit grading of the severity of the injury. Endoscopic evaluation alone, however, cannot determine with certainty the actual depth of the injury. The risk for perforation can be minimized by using a small-caliber, flexible pediatric endoscope and adequate sedation to prevent retching and movement by the patient. Although in the past it was taught that the endoscope should not be advanced beyond the first burned area, more recently, complete examination of the esophagus and stomach has been recommended, especially if severe burns are not detected proximally. This can be accomplished safely.

After the initial resuscitative and diagnostic measures have been performed, patients with caustic injuries must be observed carefully. Those with no more than first-degree burns require no other specific therapy for 24 to 48 hours. The incidence of subsequent esophageal stricture is low in patients with such injuries. Those who have second- or third-degree burns require careful and more prolonged observation for evidence of esophageal or gastric necrosis during the acute phase of the injury. Full-thickness necrosis of the esophagus, stomach, or other organs requires emergent resection. It is extremely difficult to determine on the basis of clinical, endoscopic, and radiographic information whether full-thickness necrosis has occurred. Patients with free intraperitoneal air, mediastinal air, extravasation of contrast material from the stomach or esophagus, peritonitis, or abdominal or mediastinal sepsis require immediate surgical exploration. Similarly, exploration is indicated in patients with severe persistent back or retrosternal pain, suggestive of mediastinitis, and in those with metabolic acidosis, suggestive of visceral necrosis. A gastric pH of more than 7 has been suggested as an indicator of severe gastric damage and the need for exploration. Unfortunately, this is not a reliable finding, particularly in the presence of gastric blood. Clinical evidence of peritonitis remains a much more sound indication for abdominal exploration in these patients.

Patients who have ingested caustic liquid and require operative intervention are generally best explored through the abdomen. This approach permits the assessment of injury to the intraabdominal organs and resection of areas of full-thickness gastric necrosis. Although only the lower portion of the esophagus is well visualized through the diaphragmatic hiatus, if an esophageal resection is required, transhiatal esophagectomy without thoracotomy is readily performed by the addition of a cervical incision. Before the abdominal exploration is begun, therefore, the operative field should be prepared and draped to include the area from the mandible to the pubis and anteriorly to both midaxillary lines. In patients who have sustained an acute caustic esophageal injury necessitating a resection, the surrounding periesophageal edema resulting from the caustic burn often facilitates transhiatal dissection.

When esophageal or gastric resection for acute caustic injury is required, restoration of alimentary continuity should be deferred until the patient has recovered from the acute insult and the development of chronic stricture in retained organs can be evaluated. As a rule, when the injury resulting from acid or alkali ingestion is severe enough to warrant gastric resection, esophageal resection is usually also required. Even if the esophagus has been spared, it is generally unwise simply to close off the distal esophagus and leave it as a blind pouch within the mediastinum. It is safer to perform a transhiatal dissection of the esophagus at the time of the gastrectomy. The mobilized thoracic esophagus is then delivered out of the cervical incision, and only the necrotic portion is resected, with as much potentially viable esophagus spared as possible. The remaining esophageal stump is then tunneled subcutaneously for construction of an esophagostomy on the lower neck or, preferably, on the anterior chest wall (described later).

Estrera and associates have advocated a much more aggressive protocol than the approach just described, in which all patients with second- or third-degree caustic injuries identified at endoscopy undergo immediate exploratory laparotomy. Those who are found to have full-thickness injuries are treated by resection, typically esophagogastrectomy. A silicone stent is placed in those without full-

thickness injuries, which is left in the esophagus for 3 weeks to prevent stricture formation. Further experience with this approach is needed before it can be advocated routinely.

Esophageal stricture formation after second- and third-degree burns is the rule, and dilation has been the traditional therapy for chronic caustic esophageal strictures. Dilation therapy should not be instituted until at least 6 to 8 weeks after the injury, when reepithelialization is complete, to minimize the risk for esophageal perforation (Fig. 10). If a caustic esophageal stricture is perforated during dilation, esophagectomy and visceral esophageal substitution are the best approach because repair of a perforation proximal to a stricture is rarely successful. Strictures that cannot be adequately dilated (with a 46F dilator or larger for adults) and those that remain refractory to dilation after 6 to 12 months require esophageal substitution, usually with colon. The stomach is the preferred esophageal substitute, but its use in these patients may be precluded by gastric scarring and contracture secondary to the original injury.

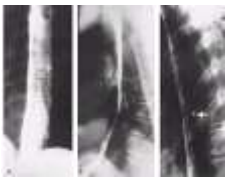

Fig. 10. Posteroanterior (A) and lateral (B) views of a patient undergoing a Gastrografin swallow. The patient complained of chest pain after his caustic esophageal stricture was incorrectly and prematurely dilated within 10 days after his having ingested Drano, before reepithelialization of the esophagus was complete. No perforation was seen on this study. (C) Barium esophagogram demonstrates a perforation (arrow) in the middle third of the thoracic esophagus

Severe esophageal strictures resulting from caustic ingestion were managed in the past by retrosternal colonic interposition, with the native, destroyed esophagus left in situ in the posterior mediastinum. Recent data, however, favor resection of the damaged esophagus in virtually every case, for several reasons: First, the retained obstructed esophagus can develop into a posterior mediastinal retention cyst or abscess. Second, after caustic injuries, the lower esophageal sphincter may be destroyed by fibrosis of the esophagogastric junction, and reflux esophagitis can then develop in the retained esophagus if it is still in continuity with the stomach. Finally, the risk for the development of esophageal carcinoma after a caustic injury is about 1,000 times greater than the usual risk; the incidence is 0.8% to 4%, with carcinoma typically appearing after a latent period of 20 to 40 years. Therefore, a young patient whose caustic esophageal stricture is simply bypassed must be followed indefinitely for the development of carcinoma in the native esophagus, contrast studies of which are virtually impossible to obtain. Resection of the strictured esophagus also permits placement of the esophageal substitute in the posterior mediastinum in the original bed. This is the shortest and most direct route between the neck and abdominal cavity, and resection of the clavicle and adjacent sternum to enlarge the superior opening into the anterior mediastinum is not required, as it is when a retrosternal esophageal substitution is carried out.

5. Materials for activating students during lectures (questions, problems, problem situations, etc.).

Case scenarios.

DIRECTIONS: Each item below contains a question or incomplete statement followed by suggested responses. Select the one best response to each question.

1.

An 18-year-old female presents complaining of severe retrosternal chest pain that is aggravated by swallowing and deep breathing. She admits to extensive episodes of recurrent binge eating followed by self-induced vomiting. Which of the following is the most probable cause of her pain?

A. Gastroesophageal reflux
B. Boerhaave's syndrome
C. Tension pneumothorax
D. Gastric ulcer disease
E. Esophageal cancer

Explanation

Boerhaave's syndrome refers to a full thickness rupture of the distal thoracic esophagus or stomach and is associated with vomiting or retching. In most cases, this syndrome is associated with alcoholics who have forceful vomiting or retching. However, it is also the most serious complication of bulimia, an eating disorder associated with binging on excessive amounts of food and self-induced vomiting.

Gastroesophageal reflux (choice **A**), tension pneumothorax (choice **C**), gastric ulcer disease (choice **D**), and esophageal cancer (choice **E**) are not associated with bulimia or Boerhaave's syndrome.

2.

A 60-year-old man who is an alcoholic complains of difficulty swallowing solids. In addition, he has progressive weight loss and weakness. Which of the following is the most likely diagnosis?

A. Diffuse esophageal spasm
B. Zenker's diverticulum
C. Achalasia
D. Esophageal carcinoma
E. Plummer-Vinson syndrome

Explanation

The patient has an esophageal carcinoma. Squamous cell carcinoma accounts for 95% of esophageal cancers. Predisposing factors include smoking, alcohol, lye strictures, Plummer-Vinson syndrome, diverticular diseases, nitrosamines, and achalasia. Esophageal cancers are most commonly located in the mid-esophagus (50%). Dysphagia for solids, weakness, and weight loss are the usual presenting complaints. These cancers initially spread locally by lymphatics and drain into surrounding lymph nodes. Distant metastasis is to the liver (70%), lungs (60%), and adrenal glands (35%). Approximately 50% of esophageal carcinomas are resectable at the time of presentation. An esophagectomy is usually performed followed by radiation and chemotherapy. The 5-year survival rate is 5%.

3.

A 65-year-old Asian American man comes to the clinic for a follow-up appointment for symptoms of dysphagia. He has had difficulty swallowing solid food off and on for the past year. He has no difficulty swallowing liquids or pills. He has no significant medical problems and his only medication is an occasional aspirin for arthritis pain in his knees. He denies cigarette smoking, but he does drink 1-2 glasses of wine each week. An outpatient esophagram was performed 3 days ago and the x-ray shown is one of the films obtained during the study. Based on the findings of the esophagram, this patient is at increased risk for developing

A. Barrett's esophagus
B. esophageal cancer
C. gastric ulcers
D. gastroesophageal reflux
E. Zencker's diverticulum

.

Explanation:

The correct answer is E. The esophagram demonstrates an indentation on the posterior cervical esophagus, which is due to a hypertrophied cricopharyngeus muscle. A Zencker's diverticulum is a pharyngoesophageal pulsion diverticulum that occurs at the point of transition between the oblique fibers of the thyropharyngeus muscle and the horizontal fibers of the cricopharyngeus muscle. A hypertrophied cricopharyngeus muscle is thought to predispose the development of the diverticulum at this transition point. This can be an incidental finding or in some patients, as in this case, it can cause symptoms of dysphagia.

Barrett's esophagus (choice A) is a complication of gastroesophageal reflux disease. There is metaplasia of the normal cells in the esophagus to what is called "specialized columnar epithelium". Chronic damage from the acidic gastric contents is believed to promote the replacement of the normal esophageal epithelium with the metaplastic columnar cells. This is a predisposing condition for adenocarcinoma of the esophagus. There is no association with hypertrophy of the cricopharyngeus muscle.

There is no relationship between a hypertrophied cricopharyngeus muscle and esophageal cancer (choice B).

There is no relationship between a hypertrophied cricopharyngeus muscle and gastric ulcers (choice C).

There is no relationship between a hypertrophied cricopharyngeus muscle and gastroesophageal reflux (choice D). Reflux can occur due to a hiatal hernia or a dysfunctional lower esophageal sphincter.

4.

A 37-year-old woman comes to the office because of a "burning sensation" in the chest for the past 3 months. The "burning" typically begins in the "upper stomach and travels up to the neck." The symptoms worsen when she lies down to go to sleep. She is a chef at a local American restaurant, has 3 children, and has been married for 12 years. She "tries" to eat a healthy diet, but it is difficult because she is around food all day and night. She has no chronic medical conditions, takes no medications, and does not drink alcohol or caffeine-containing beverages. She recently quit smoking. Her temperature is 37.0 C (98.6 F), blood pressure is 120/80 mm Hg, pulse is 65/min, and respirations are 14/min. Physical examination is unremarkable. An electrocardiogram is unremarkable. A complete blood count and metabolic profile are normal. Serologic testing for H. pylori is negative. The most appropriate next step is to

A. order ambulatory esophageal pH testing
B. order an upper gastrointestinal barium radiograph
C. recommend elevation of the head of bed and avoidance of food before bedtime
D. schedule an upper endoscopy
E. schedule esophageal manometry

Explanation:

The correct answer is C. This patient complains of the classic symptoms of gastroesophageal reflux disease (GERD). Reflux disease is usually worse at night because the recumbent position allows gastric acid contents to go up into the esophagus. Since all of the tests ordered in the case were normal, you should first recommend non-pharmacologic therapy before continuing with further diagnostic studies. Elevation of the head of bed, avoiding eating before bed, and avoiding alcohol, tobacco, chocolate, and caffeine should all be recommended. Alcohol, tobacco, chocolate, and caffeine all lower the lower esophageal sphincter pressure leading to gastric reflux. If these measures are ineffective, pharmacologic therapy with a H2 blocker such as cimetidine, famotidine, or ranitidine is indicated. For more severe symptoms, a proton pump inhibitor, such as omeprazole or lansoprazole, is indicated.

Ambulatory esophageal pH testing (choice A) is usually reserved for patients who fail nonpharmacologic and pharmacologic management.

An upper gastrointestinal barium radiograph (choice B) is useful in detecting esophageal rings or strictures, which typically present with dysphagia. This patient complains of heartburn, not dysphagia.

An upper endoscopy (choice D) is usually indicated only after the failure of nonpharmacologic and pharmacologic management for GERD and when a patient has GERD for >5 years, and upper endocsopy is recommended to screen for Barrett's metaplasia. However, it is not indicated at this time.

Esophageal manometry (choice E) is typically reserved for cases of GERD when surgical therapy is being considered.

5.

A 73-year-old man with emphysema comes to the clinic with complaints of food getting stuck when he swallows, which has been getting progressively worse over the last 8 months. He denies problems swallowing liquids and thinks he has lost about 5 pounds. He used alcohol heavily for many years but quit drinking 10 years ago. He still smokes 1 pack of cigarettes per day and has done so since age 20. He uses albuterol, steroid inhalers and theophylline. His blood pressure is 123/73 mm Hg, pulse is 87/min, and respirations are 20/min. Physical examination reveals bilateral scattered wheezes in the lungs. A chest x-ray shows hyperexpansion and no nodules. The most appropriate next step in management is to

A. order a barium esophagram
B. order an esophageal manometry
C. order an esophageal pH probe
D. treat with omeprazole and follow up in 3 months
E. treat with ranitidine and follow up in 3 months

Explanation:

The correct answer is A. This patient most likely has an esophageal squamous cell carcinoma (the most common type of esophageal malignancy). In any patient with dysphagia that is progressive for only solids, it suggests a growing and obstructive lesion. The history of tobacco and alcohol use, puts this person at a much higher risk of carcinoma. The two ways to diagnose this are a barium swallow study, which will show the mucosal mass, or an upper endoscopy study to directly visualize and biopsy the lesion.

Esophageal manometry (choice B) is used to evaluate dysphagia caused by motility disorders. These typically present with dysphagia for solids and liquids and may or may not be progressive.

A pH probe (choice C) is used to evaluate esophageal reflux disease, which does not in itself typically cause dysphagia, but over long periods of time will

increase the risk of esophageal adenocarcinoma.

Both omeprazole (choice D) and ranitidine (choice E) are used to treat symptoms of gastroesophageal reflux disease and would not address his dysphagia. Furthermore, waiting 3 months to see the patient again would be inappropriate.

6. A 75-year-old African-American man reports progressive dysphagia that started two months ago with difficulty swallowing. He has lost over 20 lbs. during that time. He has a history of heavy smoking and drinking. After examination the diagnosis of cancer of the oesophagus established. Choose the most rational management in this case.

A. Cardiodilatation by Shtark's rigid dilatator
B. Operation of extramucosal oesophagocardiomyotomy with plasty by the gastric fundus.
C. Cardiodilatation with balloon dilatator.
D. Barium swallow first, then endoscopy and biopsies, eventually CT scan to determine operability.
E. Cardioresection with oesophagogastroanastomosis.

Explanation

Management:

• Barium swallow first, then endoscopy and biopsies, eventually CT scan to determine operability. Treatment will probably be palliative only.
• Although endoscopy and biopsy provides the diagnosis, the fear of perforation prevents their use without a previous “road map” (provided by the barium swallow).
• Other esophageal tests, and when to do them:
o Questionable symptoms of reflux: pH monitoring
o Long standing clear picture of reflux: endoscopy and biopsies
o Dysphagia that is worse for liquids: manometry studies
o Hematemesis after prolonged vomiting: endoscopy

7. Instrumental dilatation of the post-burn and peptic strictures of the oesophagus carries danger of perforation with purulent mediastinitis and empyema of pleura development. Which of the least dangerous methods should be applied during the first dilatation of stricture for avoidance of perforation?

A. Dilatation of stricture by balloon dilatator with stable diameter of the cylinder.
B. Bougieunage under oesophagoscope control.
C. Bougieunage alone a wire conductor
D. Bougieunage under local anesthesia blindly.
E. Bougieunage under roentgenoscopy control

8. A 38-year-old woman complains of difficulty of food passage through the oesophagus, vomiting with unchanged food, night regurgitations ("wet pillow” sign) and weight loss. She is ill about 10 years. Roentgenoscopy reveals the IVth stage cardiac achalasia with "S” - shaped deformity of the oesophagus. What optimal treatment will you administer?

A. Cardiodilatation by Shtark's rigid dilatator
B. Operation of extramucosal oesophagocardiomyotomy with plasty by the gastric fundus.
C. Cardiodilatation with balloon dilatator.
D. Operation of oesophagofundoanastomosis by Gairovskiy.
E. Cardioresection with oesophagogastroanastomosis.

9. A 52-year-old man has been admitted to the hospital with complaints to full obstruction of the oesophagus, salivation, a general weakness and body temperature to $38,7^0$C. Dysphagia has been being marked for 8 days. It appeared when she had swallowed a piece of meat with a bone. During

roentgenoscopy the barium meal is being delayed at the level of the middle third of the oesophagus. Fibrooesophagoscopy reveals the bone wedged in the oesophageal wall, hyperaemia and oedema of mucosa covered by fibrin. What is the optimal medical tactics in this case?

A. Surgical treatment: thoracotomy, oesophagotomy, removal of the foreign body (bone), suturing of the wound in the oesophagus + gastrostomy.
B. Endoscopic removal of the foreign body through the rigid oesophagoscope.
C. Pushing the foreign body into the stomach by bougie.
D. Removal of the foreign body with Fogarty's probe
E. Removal of the foreign body with fibroendoscope

10. A 14-year-old girl complains of heartburn sensation that is being aggravated after fat and fried food intake and air eructation. Fibrogastroscopy reveals a hyperaemia of the distal parts of the oesophagus. Initial diagnosis is:

A. Peptic ulcer
B. Chronic cholecystitis
C. Reflux - esophagitis
D. Chronic viral hepatitis
E. Chronic pancreatitis

6. **Methodological lecture support**:

- classrooms №1;
- Equipment - Multymedia;
- illustrative material - slides.

7. **Questions for self-control:**

9. Classification of oesophageal diverticulae.
10. Pathological and anatomical features of oesophageal diverticulae.
11. Methods of inspection of the patients with of oesophageal diverticulae.
12. Tool methods of inspection of oesophageal diverticulae.
13. Tactics in the patient with of oesophageal diverticulae.
14. Classification of oesophageal achalasia
15. Clinical presentations of oesophageal achalasia.
16. Clinical presentations of oesophageal caustic injury.

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Lecture №_3

Theme: " Euthyroid and toxic goitre. Diseases of parathyroid glands. ".

1.Introduction.

The name thyroid is derived from the Greek description of a shield-shaped gland in the anterior neck ("thyreoides"). Classical anatomic descriptions of the thyroid were available in the 16th and 17th centuries, but the function of the gland was not well understood. By the 19th century, pathologic enlargement of the thyroid, or goiter, was described. Medical treatment of this condition was described, using what was most likely iodine-rich seaweed. However, direct surgical approach of thyroid masses had frighteningly high complication and mortality rates.

In the late 19th century, two surgeon-physiologists revolutionized treatment of thyroid diseases. Theodor Billroth and Emil Theodor Kocher established large clinics in Europe and, through development of skilled surgical techniques combined with newer anesthetic and antiseptic principles, provided surgical results that proved the safety and efficacy of thyroid surgery for benign and malignant problems. As a result of his pioneering developments in the understanding of thyroid physiology, Kocher received the Nobel Prize in 1909.

The 20th century started with the contributions of Kocher and Billroth. In rapid succession, the understanding of altered physiology, including hypothyroidism and hyperthyroidism, thyroid cancer, advances in imaging, epidemiology, and most recently, minimally invasive diagnostic and surgical techniques have taken place. These advances have allowed the diagnosis and treatment of thyroid diseases to become rapid, cost-effective, low-morbidity procedures.

2. Aims of the Lecture:

- **educational**

to know:

- anatomical and functional specifications of the thyroid gland;
- general data about morbidity in Ukraine;
- classification of diseases of the thyroid gland;
- general symptoms and clinical course of diseases of the thyroid gland;

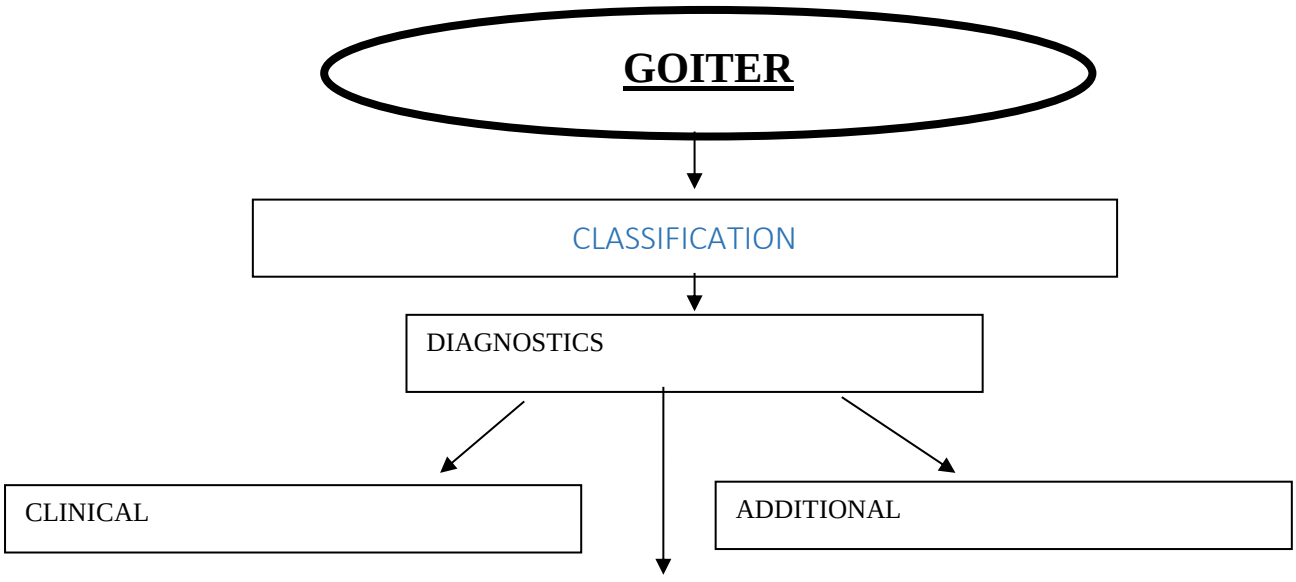
- methods of patient's examination ;
- indications for conservative and surgical methods of treatment ;
- general methods of treatment of diseases of the thyroid gland;
- methods of surgical treatment;
- working capacity.

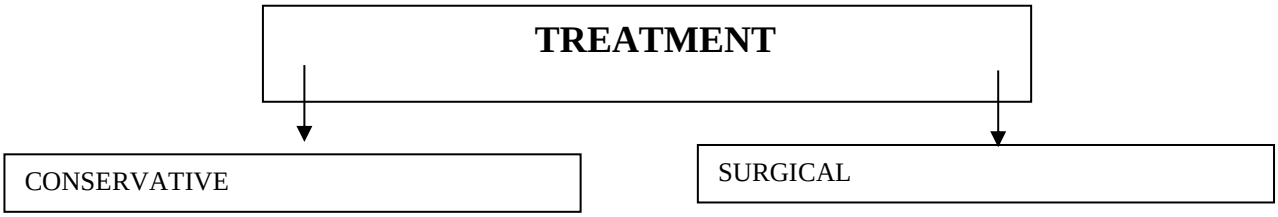
Basic concepts: Goiter. Hypothyroidism. Thyrotoxicosis. Graves' disease.Thyroiditis. *Treatment. Diseases of parathyroids.*

3. **Plan and structure of the lecture.**

	Contents and units of the lecture.	Tasks in abstract levels.	Equipment of lecture.	Time.
	Preliminary part			
1.	Determination of educational tasks		Topic	3%
2.	Positive motivation		lecture.	2%
	Main part			
3	Exposition of the lecture's matter		Tables,	90%
	Plan:		schemes,	
	1. Anatomical and functional specifications of the thyroid gland.		codograms,	
	2. General information about morbidity in Ukraine.	-"-	slides. Films.	
	3. Classification of the diseases of thyroid gland.	-"-		
	4. Methods of the patient's examination and diagnostics of diseases of the thyroid gland.	-"-		
	5. Clinical course of different diseases of TG.	-"-		
	6. Conservative and surgical treatment.	-"-		
	8. Working capacity.	-"-		
	Final part			5%
4.	Summary			
5.	Lecturer's answers to possible questions		Literature list	
6.	Tasks for self-control		Questions. Tasks.	

4. **Structure of the lecture**





Text of the lecture:

The thyroid gland produces two related hormones, thyroxine (T_4) and triiodothyronine (T_3) (Fig. 1). Acting through nuclear receptors, these hormones play a critical role in cell differentiation during development and help maintain thermogenic and metabolic homeostasis in the adult. Disorders of the thyroid gland result primarily from autoimmune processes that either stimulate the overproduction of thyroid hormones (thyrotoxicosis) or cause glandular destruction and hormone deficiency (hypothyroidism). In addition, benign nodules and various forms of thyroid cancer are relatively common and amenable to detection by physical examination.

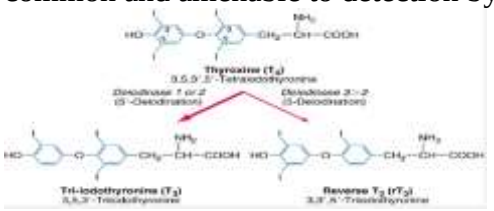


FIG. -1 Structures of thyroid hormones. Thyroxine (T_4) contains four iodine atoms. Deiodination leads to production of the potent hormone, triiodothyronine (T_3), or the inactive hormone, reverse T_3.

PHYSICAL EXAMINATION

In addition to the examination of the thyroid itself, the physical examination should include a search for signs of abnormal thyroid function and the extrathyroidal features of ophthalmopathy and dermopathy (see below). Examination of the neck begins by inspecting the seated patient from the front and side, and noting any surgical scars, obvious masses, or distended veins. The thyroid can be palpated with both hands from behind or while facing the patient, using the thumbs to palpate each lobe. It is best to use a combination of these methods, especially when the nodules are small. The patient's neck should be slightly flexed to relax the neck muscles. After locating the cricoid cartilage, the isthmus can be identified and followed laterally to locate either lobe (normally the right lobe is slightly larger than the left). By asking the patient to swallow sips of water, thyroid consistency can be better appreciated as the gland moves beneath the examiner's fingers.

Features to be noted include thyroid size, consistency, nodularity, and any tenderness or fixation. An estimate of thyroid size (normally 12 to 20 g) should be made, and a drawing is often the best way to record findings. However, ultrasound is the method of choice when it is important to determine thyroid size accurately. The size, location, and consistency of any nodules should also be defined. A bruit over the gland indicates increased vascularity, as occurs in hyperthyroidism. If the lower borders of the thyroid lobes are not clearly felt, a goiter may be retrosternal. Large retrosternal goiters can cause venous distention over the neck and difficulty breathing, especially when the arms are raised (Pemberton's sign). With any central mass above the thyroid, the tongue should be extended, as thyroglossal cysts then move upward. The thyroid examination is not complete without assessment for lymphadenopathy in the supraclavicular and cervical regions of the neck.

LABORATORY EVALUATION

MEASUREMENT OF THYROID HORMONES

The enhanced sensitivity and specificity of TSH assays have greatly improved laboratory assessment of thyroid function. Because TSH levels change dynamically in response to alterations of T_4 and T_3, a logical approach to thyroid testing is to first determine whether TSH is suppressed, normal, or elevated. With rare exceptions (see below), a normal TSH level excludes a primary abnormality of thyroid function. This strategy depends on the use of immunoradiometric assays (IRMAs) for TSH that are sensitive enough to discriminate between the lower limit of the reference range and the suppressed values that occur with thyrotoxicosis. Extremely sensitive (fourth generation) assays can

detect TSH levels ≤0.004 mU/L, but for practical purposes assays sensitive to ≤0.1 mU/L are sufficient. The widespread availability of the TSH IRMA has rendered the TRH stimulation test obsolete, as the failure of TSH to rise after an intravenous bolus of 200 to 400 μg TRH has the same implications as a suppressed basal TSH measured by IRMA.

The finding of an abnormal TSH level must be followed by measurements of circulating thyroid hormone levels to confirm the diagnosis of hyperthyroidism (suppressed TSH) or hypothyroidism (elevated TSH). Radioimmunoassays are widely available for serum total T_4 and total T_3 . T_4 and T_3 are highly protein-bound, and numerous factors (illness, medications, genetic factors) can influence protein binding. It is useful, therefore, to measure the free, or unbound, hormone levels, which correspond to the biologically available hormone pool. Two direct methods are used to measure unbound thyroid hormones: (1) unbound thyroid hormone competition with radiolabeled T_4 (or an analogue) for binding to a solid-phase antibody, and (2) physical separation of the unbound hormone fraction by ultracentrifugation or equilibrium dialysis. Though early unbound hormone immunoassays suffered from artifacts, newer assays correlate well with the results of the more technically demanding and expensive physical separation methods. An indirect method to estimate unbound thyroid hormone levels is to calculate the free T_3 or free T_4 index from the total T_4 or T_3 concentration and the thyroid hormone binding ratio (THBR). The latter is derived from the T_3-resin uptake test, which determines the distribution of radiolabeled T_3 between an absorbent resin and the unoccupied thyroid hormone binding proteins in the sample. The binding of the labeled T_3 to the resin is increased when there is reduced unoccupied protein binding sites (e.g., TBG deficiency) or increased total thyroid hormone in the sample; it is decreased under the opposite circumstances. The product of THBR and total T_3 or T_4 provides the free T_3 or T_4 index. In effect, the index corrects for anomalous total hormone values caused by abnormalities in hormone-protein binding.

Total thyroid hormone levels are elevated when TBG is increased due to estrogens (pregnancy, oral contraceptives, hormone replacement therapy, tamoxifen), and decreased when TBG binding is reduced (androgens, the nephrotic syndrome). Genetic disorders and acute illness can also cause abnormalities in thyroid hormone binding proteins, and various drugs (phenytoin, carbamazepine, salicylates, and nonsteroidal anti-inflammatory drugs) can interfere with thyroid hormone binding. Because unbound thyroid hormone levels are normal and the patient is euthyroid in all of these circumstances, assays that measure unbound hormone are preferable to those for total thyroid hormones.

For most purposes, the unbound T_4 level is sufficient to confirm thyrotoxicosis, but 2 to 5% of patients have only an elevated T_3 level (T_3 toxicosis). Thus, unbound T_3 levels should be measured in patients with a suppressed TSH but normal unbound T_4 levels.

There are several clinical conditions in which the use of TSH as a screening test may be misleading, particularly without simultaneous unbound T_4 determinations. Any severe nonthyroidal illness can cause abnormal TSH levels (see below). Although hypothyroidism is the most common cause of an elevated TSH level, rare causes include a TSH-secreting pituitary tumor, thyroid hormone resistance, and assay artifact. Conversely, a suppressed TSH level, particularly <0.1 mU/L, usually indicates thyrotoxicosis but may also be seen during the first trimester of pregnancy (due to hCG secretion), after treatment of hyperthyroidism (because TSH remains suppressed for several weeks), and in response to certain medications (e.g., high doses of glucocorticoids or dopamine). Importantly, secondary hypothyroidism, caused by hypothalamic-pituitary disease, is associated with a variable (low to high-normal) TSH level, which is inappropriate for the low T_4 level. Thus, TSH should not be used to assess thyroid function in patients with suspected or known pituitary disease.

Tests for the end-organ effects of thyroid hormone excess or depletion, such as estimation of basal metabolic rate, tendon reflex relaxation rates, or serum cholesterol, are not useful as clinical determinants of thyroid function.

TESTS TO DETERMINE THE ETIOLOGY OF THYROID DYSFUNCTION

Autoimmune thyroid disease is detected most easily by measuring circulating antibodies against TPO and Tg. As antibodies to Tg alone are uncommon, it is reasonable to measure only TPO antibodies. About 5 to 15% of euthyroid women and up to 2% of euthyroid men have thyroid antibodies; such individuals are at increased risk of developing thyroid dysfunction. Almost all patients with

autoimmune hypothyroidism, and up to 80% of those with Graves' disease, have TPO antibodies, usually at high levels.

TSI are antibodies that stimulate the TSH-R in Graves' disease. They can be measured in bioassays or indirectly in assays that detect antibody binding to the receptor. The main use of these assays is to predict neonatal thyrotoxicosis caused by high maternal levels of TSI in the last trimester of pregnancy.

Serum Tg levels are increased in all types of thyrotoxicosis except thyrotoxicosis factitia caused by self-administration of thyroid hormone. The main role for Tg measurement, however, is in the follow-up of thyroid cancer patients. After total thyroidectomy and radioablation, Tg levels should be undetectable; measurable levels (>1 to 2 ng/mL) suggest incomplete ablation or recurrent cancer.

RADIOIODINE UPTAKE AND THYROID SCANNING

The thyroid gland selectively transports radioisotopes of iodine (^{123}I, ^{125}I, ^{131}I) and ^{99m}Tc pertechnetate, allowing thyroid imaging and quantitation of radioactive tracer fractional uptake. Nuclear imaging of Graves' disease is characterized by an enlarged gland and increased tracer uptake that is distributed homogeneously. Toxic adenomas appear as focal areas of increased uptake, with suppressed tracer uptake in the remainder of the gland. In toxic multinodular goiter, the gland is enlarged—often with distorted architecture—and there are multiple areas of relatively increased or decreased tracer uptake. Subacute thyroiditis is associated with very low uptake because of follicular cell damage and TSH suppression. Thyrotoxicosis factitia is also associated with low uptake.

Although the use of fine-needle aspiration (FNA) biopsy has diminished the use of thyroid scans in the evaluation of solitary thyroid nodules, the functional features of thyroid nodules have some prognostic significance. So-called cold nodules, which have diminished tracer uptake, are usually benign. However, these nodules are more likely to be malignant (~5 to 10%) than so-called hot nodules, which are almost never malignant.

Thyroid scanning is also used in the follow-up of thyroid cancer. After thyroidectomy and ablation using ^{131}I, there is diminished radioiodine uptake in the thyroid bed, allowing the detection of metastatic thyroid cancer deposits that retain the ability to transport iodine. Whole-body scans using 111 to 185 MBq (3 to 5 mCi) ^{131}I are typically performed after thyroid hormone withdrawal to raise the TSH level or after the administration of recombinant human TSH.

THYROID ULTRASOUND

Ultrasonography is used increasingly to assist in the diagnosis of nodular thyroid disease, a reflection of the limitations of the physical examination and improvements in ultrasound technology. Using 10-MHz instruments, spatial resolution and image quality are excellent, allowing the detection of nodules and cysts >3 mm. In addition to detecting thyroid nodules, ultrasound is useful for monitoring nodule size, for guiding FNA biopsies, and for the aspiration of cystic lesions. Ultrasound is also used in the evaluation of recurrent thyroid cancer, including possible spread to cervical lymph nodes.

HYPOTHYROIDISM

Iodine deficiency remains the most common cause of hypothyroidism worldwide. In areas of iodine sufficiency, autoimmune disease (Hashimoto's thyroiditis) and iatrogenic causes (treatment of hyperthyroidism) are most common (Table 1).

TABLE 1 Causes of Hypothyroidism

Primary
Autoimmune hypothyroidism: Hashimoto's thyroiditis, atrophic thyroiditis
Iatrogenic: 131I treatment, subtotal or total thyroidectomy, external irradiation of neck for lymphoma or cancer
Drugs: iodine excess (including iodine-containing contrast media and amiodarone), lithium, antithyroid drugs, p-aminosalicyclic acid, interferon-α and other cytokines, aminoglutethimide
Congenital hypothyroidism: absent or ectopic thyroid gland, dyshormonogenesis, TSH-R mutation
Iodine deficiency
Infiltrative disorders: amyloidosis, sarcoidosis, hemochromatosis, scleroderma, cystinosis, Riedel's thyroiditis
Overexpression of type 3 deoiodinase in infantile hemangioma
Transient
Silent thyroiditis, including postpartum thyroiditis
Subacute thyroiditis
Withdrawal of thyroxine treatment in individuals with an intact thyroid

After 131I treatment or subtotal thyroidectomy for Graves' disease
Secondary
Hypopituitarism: tumors, pituitary surgery or irradiation, infiltrative disorders, Sheehan's syndrome, trauma, genetic forms of combined pituitary hormone deficiencies
Isolated TSH deficiency or inactivity
Bexarotene treatment
Hypothalamic disease: tumors, trauma, infiltrative disorders, idiopathic
Note: TSH, thyroid-stimulating hormone; TSH-R, TSH receptor.

CONGENITAL HYPOTHYROIDISM

Prevalence

Hypothyroidism occurs in about 1 in 4000 newborns. It may be transient, especially if the mother has TSH-R blocking antibodies or has received antithyroid drugs, but permanent hypothyroidism occurs in the majority. Neonatal hypothyroidism is due to thyroid gland dysgenesis in 80 to 85%, inborn errors of thyroid hormone synthesis in 10 to 15%, and is TSH-R antibody-mediated in 5% of affected newborns. The developmental abnormalities are twice as common in girls. Mutations that cause congenital hypothyroidism are being increasingly recognized, but the vast majority remain idiopathic.

Clinical Manifestations

The majority of infants appear normal at birth, and <10% are diagnosed based on clinical features, which include prolonged jaundice, feeding problems, hypotonia, enlarged tongue, delayed bone maturation, and umbilical hernia. Importantly, permanent neurologic damage results if treatment is delayed. Typical features of adult hypothyroidism may also be present (Table 2). Other congenital malformations, especially cardiac, are four times more common in congenital hypothyroidism.

TABLE 2 Signs and Symptoms of Hypothyroidism (Descending Order of Frequency)

Symptoms
Tiredness, weakness
Dry skin
Feeling cold
Hair loss
Difficulty concentrating and poor memory
Constipation
Weight gain with poor appetite
Dyspnea
Hoarse voice
Menorrhagia (later oligomenorrhea or amenorrhea)
Paresthesia
Impaired hearing
Signs
Dry coarse skin; cool peripheral extremities
Puffy face, hands, and feet (myxedema)
Diffuse alopecia
Bradycardia
Peripheral edema
Delayed tendon reflex relaxation
Carpal tunnel syndrome
Serous cavity effusions

Diagnosis and Treatment

Because of the severe neurologic consequences of untreated congenital hypothyroidism, neonatal screening programs have been established in developed countries. These are generally based on measurement of TSH or T_4 levels in heel-prick blood specimens. When the diagnosis is confirmed, T_4 is instituted at a dose of 10 to 15 μg/kg per day and the dosage is adjusted by close monitoring of TSH levels. T_4 requirements are relatively great during the first year of life, and a high circulating T_4 level is usually needed to normalize TSH. Early treatment with T_4 results in normal IQ levels, but subtle neurodevelopmental abnormalities may occur in those with the most severe hypothyroidism at diagnosis or when treatment is suboptimal.

AUTOIMMUNE HYPOTHYROIDISM

Classification

Autoimmune hypothyroidism may be associated with a goiter (Hashimoto's, or goitrous thyroiditis) or, at the later stages of the disease, minimal residual thyroid tissue (atrophic thyroiditis). Because the autoimmune process gradually reduces thyroid function, there is a phase of compensation when normal thyroid hormone levels are maintained by a rise in TSH. Though some patients may have minor symptoms, this state is called subclinical hypothyroidism or mild hypothyroidism. Later, free T_4 levels fall and TSH levels rise further; symptoms become more readily apparent at this stage (usually TSH > 10 mU/L), which is referred to as clinical hypothyroidism or overt hypothyroidism.

Prevalence

The mean annual incidence rate of autoimmune hypothyroidism is up to 4 per 1000 women and 1 per 1000 men. It is more common in certain populations, such as the Japanese, probably because of genetic factors and chronic exposure to a high-iodine diet. The mean age at diagnosis is 60 years, and the prevalence of overt hypothyroidism increases with age. Subclinical hypothyroidism is found in 6 to 8% of women (10% over the age of 60) and 3% of men. The annual risk of developing clinical hypothyroidism is about 4% when subclinical hypothyroidism is associated with positive TPO antibodies.

Pathogenesis

In Hashimoto's thyroiditis, there is a marked lymphocytic infiltration of the thyroid with germinal center formation, atrophy of the thyroid follicles accompanied by oxyphil metaplasia, absence of colloid, and mild to moderate fibrosis. In atrophic thyroiditis, the fibrosis is much more extensive, lymphocyte infiltration is less pronounced, and thyroid follicles are almost completely absent. Atrophic thyroiditis likely represents the end stage of Hashimoto's thyroiditis rather than a distinct disorder.

As with most autoimmune disorders, susceptibility to autoimmune hypothyroidism is determined by a combination of genetic and environmental factors, and the risk of either autoimmune hypothyroidism or Graves' disease is increased among siblings. HLA-DR polymorphisms are the best documented genetic risk factors for autoimmune hypothyroidism, especially HLA-DR3, -DR4, and -DR5 in Caucasians. A weak association also exists between polymorphisms in CTLA-4, a T cell–regulating gene, and autoimmune hypothyroidism. Both of these genetic associations are shared by other autoimmune diseases, which may explain the relationship between autoimmune hypothyroidism and other autoimmune diseases, especially type 1 diabetes mellitus, Addison disease, pernicious anemia, and vitiligo. HLA-DR and CTLA-4 polymorphisms account for approximately half of the genetic susceptibility to autoimmune hypothyroidism. The other contributory loci remain to be identified. A gene on chromosome 21 may be responsible for the association between autoimmune hypothyroidism and Down syndrome. The female preponderance of thyroid autoimmunity is most likely due to the effects of sex steroids on the immune response, but an X chromosome–related genetic factor is also possible, which may account for the high frequency of autoimmune hypothyroidism in Turner syndrome. Environmental susceptibility factors are also poorly defined at present. A high iodine intake may increase the risk of autoimmune hypothyroidism by immunologic effects or direct thyroid toxicity. There is no convincing evidence for a role of infection, except for the congenital rubella syndrome, in which there is a high frequency of autoimmune hypothyroidism. Viral thyroiditis does not induce subsequent autoimmune thyroid disease.

The thyroid lymphocytic infiltrate in autoimmune hypothyroidism is composed of activated CD4+ and CD8+ T cells, as well as B cells. Thyroid cell destruction is believed to be primarily mediated by the CD8+ cytotoxic T cells, which destroy their targets by either perforin-induced cell necrosis or granzyme B–induced apoptosis. In addition, local T cell production of cytokines, such as tumor necrosis factor (TNF), IL-1, and interferon (IFN) γ, may render thyroid cells more susceptible to apoptosis mediated by death receptors, such as Fas, which are activated by their respective ligands on T cells. These cytokines also impair thyroid cell function directly, and induce the expression of other proinflammatory molecules by the thyroid cells themselves, such as cytokines, HLA class I and class II molecules, adhesion molecules, CD40, and nitric oxide. Administration of high concentrations of

cytokines for therapeutic purposes (especially IFN-α) is associated with increased autoimmune thyroid disease, possibly through mechanisms similar to those in sporadic disease.

Antibodies to Tg and TPO are clinically useful markers of thyroid autoimmunity, but any pathogenic effect is restricted to a secondary role in amplifying an ongoing autoimmune response. TPO antibodies fix complement, and complement membrane attack complexes are present in the thyroid in autoimmune hypothyroidism. However, transplacental passage of Tg or TPO antibodies has no effect on the fetal thyroid, which suggests that T cell–mediated injury is required to initiate autoimmune damage to the thyroid. Up to 20% of patients with autoimmune hypothyroidism have antibodies against the TSH-R, which, in contrast to TSI, do not stimulate the receptor but prevent the binding of TSH. These TSH-R-blocking antibodies therefore cause hypothyroidism and, especially in Asian patients, thyroid atrophy. Their transplacental passage may induce transient neonatal hypothyroidism. Rarely, patients have a mixture of TSI- and TSH-R-blocking antibodies, and thyroid function can oscillate between hyperthyroidism and hypothyroidism as one or the other antibody becomes dominant. Predicting the course of disease in such individuals is difficult, and they require close monitoring of thyroid function. Bioassays can be used to document that TSH-R-blocking antibodies reduce the cyclic AMP–inducing effect of TSH on cultured TSH-R-expressing cells, but these assays are difficult to perform. Assays that measure the binding of antibodies to the receptor by competition with radiolabeled TSH [TSH-binding inhibiting immunoglobulins (TBII)] do not distinguish between TSI- and TSH-R-blocking antibodies, but a positive result in a patient with spontaneous hypothyroidism is strong evidence for the presence of blocking antibodies. The use of these assays does not generally alter clinical management, although they may be useful to confirm the cause of transient neonatal hypothyroidism.

Clinical Manifestations

The main clinical features of hypothyroidism are summarized in Table 4. The onset is usually insidious, and the patient may become aware of symptoms only when euthyroidism is restored. Patients with Hashimoto's thyroiditis may present because of goiter rather than symptoms of hypothyroidism. The goiter may not be large but is usually irregular and firm in consistency. It is often possible to palpate a pyramidal lobe, normally a vestigial remnant of the thyroglossal duct. Rarely, uncomplicated Hashimoto's thyroiditis is associated with pain.

Patients with atrophic thyroiditis, or the late stage of Hashimoto's thyroiditis, present with symptoms and signs of hypothyroidism. The skin is dry, and there is decreased sweating, thinning of the epidermis, and hyperkeratosis of the stratum corneum. Increased dermal glycosaminoglycan content traps water, giving rise to skin thickening without pitting (myxedema). Typical features include a puffy face with edematous eyelids and nonpitting pretibial edema (Fig. 2).

FIGURE 2 Facial appearance in hypothyroidism. Note puffy eyes and thickened, pale skin.

There is pallor, often with a yellow tinge to the skin due to carotene accumulation. Nail growth is retarded, and hair is dry, brittle, difficult to manage, and falls out easily. In addition to diffuse alopecia, there is thinning of the outer third of the eyebrows, although this is not a specific sign of hypothyroidism.

Other common features include constipation and weight gain (despite a poor appetite). In contrast to popular perception, the weight gain is usually modest and due mainly to fluid retention in the myxedematous tissues. Libido is decreased in both sexes, and there may be oligomenorrhea or amenorrhea in long-standing disease, but menorrhagia is also common. Fertility is reduced and the incidence of miscarriage is increased. Prolactin levels are often modestly increased and may contribute to alterations in libido and fertility and cause galactorrhea.

Myocardial contractility and pulse rate are reduced, leading to a reduced stroke volume and bradycardia. Increased peripheral resistance may be accompanied by hypertension, particularly diastolic. Blood flow is diverted from the skin, producing the cool extremities. Pericardial effusions occur in up to 30% of patients but rarely compromise cardiac function. Though alterations in myosin heavy chain isoform expression have been documented, cardiomyopathy is unusual. Fluid may also accumulate in other serous cavities and in the middle ear, giving rise to conductive deafness.

Pulmonary function is generally normal, but dyspnea may be caused by pleural effusion, impaired respiratory muscle function, diminished ventilatory drive, or sleep apnea.

Carpal tunnel and other entrapment syndromes are common, as is impairment of muscle function with stiffness, cramps, and pain. On examination, there may be slow relaxation of tendon reflexes and pseudomyotonia. Memory and concentration are impaired. Rare neurologic problems include reversible cerebellar ataxia, dementia, psychosis, and myxedema coma. Hashimoto's encephalopathy is a rare and distinctive syndrome associated with myoclonus and slow-wave activity on electroencephalography, which can progress to confusion, coma, and death. It is steroid-responsive and may occur in the presence of autoimmune thyroiditis, without hypothyroidism. The hoarse voice and occasionally clumsy speech of hypothyroidism reflect fluid accumulation in the vocal cords and tongue.

The features described above are the consequence of thyroid hormone deficiency. However, autoimmune hypothyroidism may be associated with signs or symptoms of other autoimmune diseases, particularly vitiligo, pernicious anemia, Addison disease, alopecia areata, and type 1 diabetes mellitus. Less common associations include celiac disease, dermatitis herpetiformis, chronic active hepatitis, rheumatoid arthritis, systemic lupus erythematosus (SLE), and Sjögren's syndrome. Thyroid-associated ophthalmopathy, which usually occurs in Graves' disease (see below), occurs in about 5% of patients with autoimmune hypothyroidism.

Autoimmune hypothyroidism is uncommon in children and usually presents with slow growth and delayed facial maturation. The appearance of permanent teeth is also delayed. Myopathy, with muscle swelling, is more common in children than in adults. In most cases, puberty is delayed, but precocious puberty sometimes occurs. There may be intellectual impairment if the onset is before 3 years and the hormone deficiency is severe.

Laboratory Evaluation

A summary of the investigations used to determine the existence and cause of hypothyroidism is provided in Fig. 3.

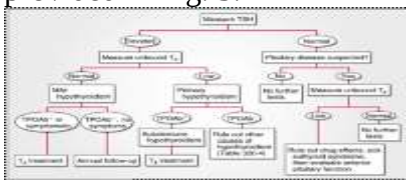


FIG. 3 Evaluation of hypothyroidism. $TPOAb^+$, thyroid peroxidase antibodies present; $TPOAb^-$, thyroid peroxidase antibodies not present. TSH, thyroid-stimulating hormone.

A normal TSH level excludes primary (but not secondary) hypothyroidism. If the TSH is elevated, an unbound T_4 level is needed to confirm the presence of clinical hypothyroidism, but T_4 is inferior to TSH when used as a screening test, as it will not detect subclinical or mild hypothyroidism. Circulating unbound T_3 levels are normal in about 25% of patients, reflecting adaptive responses to hypothyroidism. T_3 measurements are therefore not indicated.

Once clinical or subclinical hypothyroidism is confirmed, the etiology is usually easily established by demonstrating the presence of TPO antibodies, which are present in 90 to 95% of patients with autoimmune hypothyroidism. TBII can be found in 10 to 20% of patients, but these determinations are not needed routinely. If there is any doubt about the cause of a goiter associated with hypothyroidism, FNA biopsy can be used to confirm the presence of autoimmune thyroiditis. Other abnormal laboratory findings in hypothyroidism may include increased creatine phosphokinase, elevated cholesterol and triglycerides, and anemia (usually normocytic or macrocytic). Except when accompanied by iron deficiency, the anemia and other abnormalities gradually resolve with thyroxine replacement.

Differential Diagnosis

An asymmetric goiter in Hashimoto's thyroiditis may be confused with a multinodular goiter or thyroid carcinoma, in which thyroid antibodies may also be present. Ultrasound can be used to show the presence of a solitary lesion or a multinodular goiter, rather than the heterogeneous thyroid enlargement typical of Hashimoto's thyroiditis. FNA biopsy is useful in the investigation of focal nodules. Other causes of hypothyroidism are discussed below but rarely cause diagnostic confusion (Table 1).

TREATMENT

Clinical Hypothyroidism

If there is no residual thyroid function, the daily replacement dose of levothyroxine is usually 1.6 μg/kg body weight (typically 100 to 150 μg). In many patients, however, lower doses suffice until residual thyroid tissue is destroyed. In patients who develop hypothyroidism after the treatment of Graves' disease, there is often underlying autonomous function, necessitating lower replacement doses (typically 75 to 125 μg/d).

Adult patients under 60 without evidence of heart disease may be started on 50 to 100 μg levothyroxine (T_4) daily. The dose is adjusted on the basis of TSH levels, with the goal of treatment being a normal TSH, ideally in the lower half of the reference range. TSH responses are gradual and should be measured about 2 months after instituting treatment or after any subsequent change in levothyroxine dosage. The clinical effects of levothyroxine replacement are often slow to appear. Patients may not experience full relief from symptoms until 3 to 6 months after normal TSH levels are restored. Adjustment of levothyroxine dosage is made in 12.5- or 25-μg increments if the TSH is high; decrements of the same magnitude should be made if the TSH is suppressed. Patients with a suppressed TSH of any cause, including T_4 overtreatment, have an increased risk of atrial fibrillation and reduced bone density.

Although dessicated animal thyroid preparations (thyroid extract USP) are available, they are not recommended as potency and composition vary between batches. Interest in using levothyroxine combined with liothyronine (triiodothyronine, T_3) has been revived, based on studies suggesting that patients feel better when taking the T_4/T_3 combination compared to T_4 alone. However, a long-term benefit from this combination is not established. There is no place for liothyronine alone as long-term replacement, because the short half-life necessitates three or four daily doses and is associated with fluctuating T_3 levels.

Once full replacement is achieved and TSH levels are stable, follow-up measurement of TSH is recommended at annual intervals and may be extended to every 2 to 3 years, if a normal TSH is maintained over several years. It is important to ensure ongoing compliance, however, as patients do not feel any difference after missing a few doses of levothyroxine, this sometimes leads to self-discontinuation.

In patients of normal body weight who are taking ≥200 μg of levothyroxine per day, an elevated TSH level is often a sign of poor compliance. This is also the likely explanation for fluctuating TSH levels, despite a constant levothyroxine dosage. Such patients often have normal or high unbound T_4 levels, despite an elevated TSH, because they remember to take medication for a few days before testing; this is sufficient to normalize T_4, but not TSH, levels. It is important to consider variable compliance, as this pattern of thyroid function tests is otherwise suggestive of disorders associated with inappropriate TSH secretion (Table 2). Because T_4 has a long half-life (7 days), patients who miss doses can be advised to take up to three doses of the skipped tablets at once. Other causes of increased levothyroxine requirements must be excluded, particularly malabsorption (e.g., celiac disease, small-bowel surgery), estrogen therapy, and drugs that interfere with T_4 absorption or clearance such as cholestyramine, ferrous sulfate, calcium supplements, lovastatin, aluminum hydroxide, rifampicin, amiodarone, carbamazepine, and phenytoin.

Mild Hypothyroidism

By definition, subclinical or mild hypothyroidism refers to biochemical evidence of thyroid hormone deficiency in patients who have few or no apparent clinical features of hypothyroidism. There are no universally accepted guidelines for the treatment of mild hypothyroidism. As long as excessive treatment is avoided, there is little risk in correcting a slightly increased TSH, and some patients likely derive modest clinical benefit from treatment. Moreover, there is some risk that patients will progress to overt hypothyroidism, particularly when the TSH level is >6 mU/L and TPO antibodies are present. Treatment is administered by starting with a low dose of levothyroxine (25 to 50 μg/d) with the goal of normalizing TSH. If thyroxine is not given, thyroid function should be evaluated annually.

Special Treatment Considerations

Rarely, levothyroxine replacement is associated with pseudotumor cerebri in children. Presentation appears to be idiosyncratic and occurs months after treatment has begun. Women with a history or high risk of hypothyroidism should ensure that they are euthyroid prior to conception and during early pregnancy as maternal hypothyroidism may adversely affect fetal neural development. Thyroid function should be evaluated once pregnancy is confirmed and at the beginning of the second and third trimesters. The dose of levothyroxine may need to be increased by ≥50% during pregnancy and returned to previous levels after delivery. Elderly patients may require up to 20% less thyroxine than younger patients. In the elderly, especially patients with known coronary artery disease, the starting dose of levothyroxine is 12.5 to 25 μg/d with similar increments every 2 to 3 months until TSH is normalized. In some patients it may be impossible to achieve full replacement, despite optimal antianginal treatment. Emergency surgery is generally safe in patients with untreated hypothyroidism, although routine surgery in a hypothyroid patient should be deferred until euthyroidism is achieved.
Myxedema coma still has a high mortality rate, despite intensive treatment. Clinical manifestations include reduced level of consciousness, sometimes associated with seizures, as well as the other features of hypothyroidism (Table 2). Hypothermia can reach 23°C (74°F). There may be a history of treated hypothyroidism with poor compliance, or the patient may be previously undiagnosed. Myxedema coma almost always occurs in the elderly and is usually precipitated by factors that impair respiration, such as drugs (especially sedatives, anesthetics, antidepressants), pneumonia, congestive heart failure, myocardial infarction, gastrointestinal bleeding, or cerebrovascular accidents. Sepsis should also be suspected. Exposure to cold may also be a risk factor. Hypoventilation, leading to hypoxia and hypercapnia, plays a major role in pathogenesis; hypoglycemia and dilutional hyponatremia also contribute to the development of myxedema coma.
Levothyroxine can initially be administered as a single intravenous bolus of 500 μg, which serves as a loading dose. Although further levothyroxine is not strictly necessary for several days, it is usually continued at a dose of 50 to 100 μg/d. If suitable intravenous preparation is not available, the same initial dose of levothyroxine can be given by nasogastric tube (though absorption may be impaired in myxedema). An alternative is to give liothyronine (T_3) intravenously or via nasogastric tube, in doses ranging from 10 to 25 μg every 8 to 12 h. This treatment has been advocated because $T_4 \rightarrow T_3$ conversion is impaired in myxedema coma. However, excess liothyroxine has the potential to provoke arrhythmias. Another option is to combine levothyroxine (200 μg) and liothyronine (25 μg) as a single, initial intravenous bolus followed by daily treatment with levothyroxine (50 to 100 μg/d) and liothyronine (10 μg every 8 h).
Supportive therapy should be provided to correct any associated metabolic disturbances. External warming is indicated only if the temperature is <30°C, as it can result in cardiovascular collapse. Space blankets should be used to prevent further heat loss. Parenteral hydrocortisone (50 mg every 6 h) should be administered, as there is impaired adrenal reserve in profound hypothyroidism. Any precipitating factors should be treated, including the early use of broad-spectrum antibiotics, pending the exclusion of infection. Ventilatory support with regular blood gas analysis is usually needed during the first 48 h. Hypertonic saline or intravenous glucose may be needed if there is hyponatremia or hypoglycemia; hypotonic intravenous fluids should be avoided because they may exacerbate water retention secondary to reduced renal perfusion and inappropriate vasopressin secretion. The metabolism of most medications is impaired, and sedatives should be avoided if possible or used in reduced doses. Medication blood levels should be monitored, when available, to guide dosage.

THYROTOXICOSIS

Thyrotoxicosis is defined as the state of thyroid hormone excess and is not synonymous with hyperthyroidism, which is the result of excessive thyroid function. However, the major etiologies of thyrotoxicosis are hyperthyroidism caused by Graves' disease, toxic multinodular goiter, and toxic adenomas. Other causes are listed in Table 3.

TABLE 3 Causes of Thyrotoxicosis

Primary hyperthyroidism
- Graves' disease
- Toxic multinodular goiter

Toxic adenoma
Functioning thyroid carcinoma metastases
Activating mutation of the TSH receptor
Activating mutation of Gsα (McCune-Albright syndrome)
Struma ovarii
Drugs: iodine excess (Jod-Basedow phenomenon)
Thyrotoxicosis without hyperthyroidism
Subacute thyroiditis
Silent thyroiditis
Other causes of thyroid destruction: amiodarone, radiation, infarction of adenoma
Ingestion of excess thyroid hormone (thyrotoxicosis factitia) or thyroid tissue
Secondary hyperthyroidism
TSH-secreting pituitary adenoma
Thyroid hormone resistance syndrome: occasional patients may have features of thyrotoxicosis
Chorionic gonadotropin-secreting tumors
Gestational thyrotoxicosis
Circulating TSH levels are low in these forms of secondary hyperthyroidism.
Note: TSH, thyroid-stimulating hormone.

GRAVES' DISEASE

Epidemiology

Graves' disease accounts for 60 to 80% of thyrotoxicosis, but the prevalence varies among populations, depending mainly on iodine intake (high iodine intake is associated with an increased prevalence of Graves' disease). Graves' disease occurs in up to 2% of women but is one-tenth as frequent in men. The disorder rarely begins before adolescence and typically occurs between 20 and 50 years of age, but it also occurs in the elderly.

PATHOGENESIS

AS in autoimmune hypothyroidism, a combination of genetic factors, including HLA-DR and CTLA-4 polymorphisms, and environmental factors contribute to Graves' disease susceptibility. The concordance for Graves' disease in monozygotic twins is 20 to 30%, compared to <5% in dizygotic twins. Indirect evidence suggests that stress is an important environmental factor, presumably operating through neuroendocrine effects on the immune system. Smoking is a minor risk factor for Graves' disease and a major risk factor for the development of ophthalmopathy. Sudden increases in iodine intake may precipitate Graves' disease, and there is a threefold increase in the occurrence of *Graves' disease in the postpartum period.*

The hyperthyroidism of Graves' disease is caused by TSI that are synthesized in the thyroid gland as well as in bone marrow and lymph nodes. Such antibodies can be detected by bioassays or using the more widely available TBII assays. The presence of TBII in a patient with thyrotoxicosis is strong indirect evidence for the existence of TSI, and these assays are useful in monitoring pregnant Graves' patients in whom high levels of TSI can cross the placenta and cause neonatal thyrotoxicosis. Other thyroid autoimmune responses, similar to those in autoimmune hypothyroidism (see above), occur concurrently in patients with Graves' disease. In particular, TPO antibodies occur in up to 80% of cases and serve as a readily measurable marker of autoimmunity. Because T cell–mediated cytotoxicity can also affect thyroid function, there is no direct correlation between the level of TSI and thyroid hormone levels. In the long term, spontaneous autoimmune hypothyroidism may develop in up to 15% of Graves' patients.

Cytokines appear to play a major role in thyroid-associated ophthalmopathy. There is infiltration of the extraocular muscles by activated T cells; the release of cytokines such as IFN-γ, TNF, and IL-1 results in fibroblast activation and increased synthesis of glycosaminoglycans that trap water, thereby leading to characteristic muscle swelling. Late in the disease, there is fibrosis and only then do the muscle cells show evidence of injury. Orbital fibroblasts may be uniquely sensitive to cytokines, perhaps explaining the anatomic localization of the immune response. Though the pathogenesis of thyroid-associated ophthalmopathy remains unclear, there is mounting evidence that expression of the TSH-R may provide an important orbital autoantigen. In support of this idea, injection of TSH-R

into certain strains of mice induces autoimmune hyperthyroidism, as well as features of ophthalmopathy. A variety of autoantibodies against orbital muscle and fibroblast antigens have been detected in patients with ophthalmopathy, but these antibodies most likely arise as a secondary phenomenon, dependent on T cell–mediated autoimmune responses. Similar mechanisms are involved in dermopathy.

Clinical Manifestations

Signs and symptoms include features that are common to any cause of thyrotoxicosis (Table 4) as well as those specific for Graves' disease. The clinical presentation depends on the severity of thyrotoxicosis, the duration of disease, individual susceptibility to excess thyroid hormone, and the patient's age. In the elderly, features of thyrotoxicosis may be subtle or masked, and patients may present mainly with fatigue and weight loss, leading to apathetic hyperthyroidism.

TABLE 4 Signs and Symptoms of Thyrotoxicosis (Descending Order of Frequency)

Symptoms
Hyperactivity, irritability, dysphoria
Heat intolerance and sweating
Palpitations
Fatigue and weakness
Weight loss with increased appetite
Diarrhea
Polyuria
Oligomenorrhea, loss of libido
Signs
Tachycardia; atrial fibrillation in the elderly
Tremor
Goiter
Warm, moist skin
Muscle weakness, proximal myopathy
Lid retraction or lag
Gynecomastia

Excludes the signs of ophthalmopathy and dermopathy specific for Graves' disease.

Thyrotoxicosis may cause unexplained weight loss, despite an enhanced appetite, due to the increased metabolic rate. Weight gain occurs in 5% of patients, however, because of increased food intake.

Other prominent features include hyperactivity, nervousness, and irritability, ultimately leading to a sense of easy fatiguability in some patients. Insomnia and impaired concentration are common; apathetic thyrotoxicosis may be mistaken for depression in the elderly. Fine tremor is a frequent finding, best elicited by having patients stretch out their fingers and feeling the fingertips with the palm. Common neurologic manifestations include hyperreflexia, muscle wasting, and proximal myopathy without fasciculation. Chorea is a rare feature. Thyrotoxicosis is sometimes associated with a form of hypokalemic periodic paralysis; this disorder is particularly common in Asian males with thyrotoxicosis.

The most common cardiovascular manifestation is sinus tachycardia, often associated with palpitations, occasionally caused by supraventricular tachycardia. The high cardiac output produces a bounding pulse, widened pulse pressure, and an aortic systolic murmur and can lead to worsening of angina or heart failure in the elderly or those with preexisting heart disease. Atrial fibrillation is more common in patients >50 years. Treatment of the thyrotoxic state alone reverts atrial fibrillation to normal sinus rhythm in fewer than half of patients, suggesting the existence of an underlying cardiac problem in the remainder.

The skin is usually warm and moist, and the patient may complain of sweating and heat intolerance, particularly during warm weather. Palmar erythema; onycholysis; and, less commonly, pruritus, urticaria, and diffuse hyperpigmentation may be evident. Hair texture may become fine, and a diffuse alopecia occurs in up to 40% of patients, persisting for months after restoration of euthyroidism. Gastrointestinal transit time is decreased, leading to increased stool frequency, often with diarrhea

and occasionally mild steatorrhea. Women frequently experience oligomenorrhea or amenorrhea; in men there may be impaired sexual function and, rarely, gynecomastia. The direct effect of thyroid hormones on bone resorption leads to osteopenia in long-standing thyrotoxicosis; mild hypercalcemia occurs in up to 20% of patients, but hypercalciuria is more common. There is a small increase in fracture rate in patients with a previous history of thyrotoxicosis.

In Graves' disease the thyroid is usually diffusely enlarged to two to three times its normal size. The consistency is firm, but less so than in multinodular goiter. There may be a thrill or bruit due to the increased vascularity of the gland and the hyperdynamic circulation.

Lid retraction, causing a staring appearance, can occur in any form of thyrotoxicosis and is the result of sympathetic overactivity. However, Graves' disease is associated with specific eye signs that comprise Graves' ophthalmopathy (Fig. 4A).

FIGURE 4 Features of Graves' disease. A. Facial appearance in Graves' disease; lid retraction, periorbital edema, and proptosis are marked. B. Thyroid dermopathy over the lateral aspects of the shins. C. Thyroid acropachy.

This condition is also called thyroid-associated ophthalmopathy, as it occurs in the absence of Graves' disease in 10% of patients. Most of these individuals have autoimmune hypothyroidism or thyroid antibodies. The onset of Graves' ophthalmopathy occurs within the year before or after the diagnosis of thyrotoxicosis in 75% of patients but can sometimes precede or follow thyrotoxicosis by several years, accounting for some cases of euthyroid ophthalmopathy.

Many patients with Graves' disease have little clinical evidence of ophthalmopathy. However, the enlarged extraocular muscles typical of the disease, and other subtle features, can be detected in almost all patients when investigated by ultrasound or computed tomography (CT) imaging of the orbits. Unilateral signs are found in up to 10% of patients. The earliest manifestations of ophthalmopathy are usually a sensation of grittiness, eye discomfort, and excess tearing. About a third of patients have proptosis, best detected by visualization of the sclera between the lower border of the iris and the lower eyelid, with the eyes in the primary position. Proptosis can be measured using an exophthalmometer. In severe cases, proptosis may cause corneal exposure and damage, especially if the lids fail to close during sleep. Periorbital edema, scleral injection, and chemosis are also frequent. In 5 to 10% of patients, the muscle swelling is so severe that diplopia results, typically but not exclusively when the patient looks up and laterally. The most serious manifestation is compression of the optic nerve at the apex of the orbit, leading to papilledema, peripheral field defects, and, if left untreated, permanent loss of vision.

Many scoring systems have been used to gauge the extent and activity of the orbital changes in Graves' disease. The “NO SPECS” scheme is an acronym derived from the following classes of eye change:

- 0 = No signs or symptoms
- 1 = Only signs (lid retraction or lag), no symptoms
- 2 = Soft tissue involvement (periorbital edema)
- 3 = Proptosis (>22 mm)
- 4 = Extraocular muscle involvement (diplopia)
- 5 = Corneal involvement
- 6 = Sight loss

Although useful as a mnemonic, the NO SPECS scheme is inadequate to describe the eye disease fully, and patients do not necessarily progress from one class to another. When Graves' eye disease is active and severe, referral to an ophthalmologist is indicated and objective measurements are needed, such as lid fissure width; corneal staining with fluorescein; and evaluation of extraocular muscle function (e.g., Hess chart), intraocular pressure and visual fields, acuity, and color vision.

Thyroid dermopathy occurs in <5% of patients with Graves' disease (Fig. 4B), almost always in the presence of moderate or severe ophthalmopathy. Although most frequent over the anterior and lateral aspects of the lower leg (hence the term pretibial myxedema), skin changes can occur at other sites, particularly after trauma. The typical lesion is a noninflamed, indurated plaque with a deep pink or

purple color and an “orange-skin” appearance. Nodular involvement can occur, and the condition can rarely extend over the whole lower leg and foot, mimicking elephantiasis. Thyroid acropachy refers to a form of clubbing found in <1% of patients with Graves' disease (Fig. 4C). It is so strongly associated with thyroid dermopathy that an alternative cause of clubbing should be sought in a Graves' patient without coincident skin and orbital involvement.

Laboratory Evaluation

Investigations used to determine the existence and cause of thyrotoxicosis are summarized in Fig. 5.

FIG. 5 Evaluation of thyrotoxicosis. [a]Diffuse goiter, positive TPO antibodies, ophthalmopathy, dermopathy; [b]can be confirmed by radionuclide scan. TSH, thyroid-stimulating hormone.

In Graves' disease, the TSH level is suppressed and total and unbound thyroid hormone levels are increased. In 2 to 5% of patients (and more in areas of borderline iodine intake), only T_3 is increased (T_3 toxicosis). The converse state of T_4 toxicosis, with elevated total and unbound T_4 and normal T_3 levels, is occasionally seen when hyperthyroidism is induced by excess iodine, providing surplus substrate for thyroid hormone synthesis. Measurement of TPO antibodies is useful in differential diagnosis. Measurement of TBII or TSI will confirm the diagnosis but is not needed routinely. Associated abnormalities that may cause diagnostic confusion in thyrotoxicosis include elevation of bilirubin, liver enzymes, and ferritin. Microcytic anemia and thrombocytopenia may occur.

Differential Diagnosis

Diagnosis of Graves' disease is straightforward in a patient with biochemically confirmed thyrotoxicosis, diffuse goiter on palpation, ophthalmopathy, positive TPO antibodies, and often a personal or family history of autoimmune disorders. For patients with thyrotoxicosis who lack these features, the most reliable diagnostic method is a radionuclide (^{99m}Tc, ^{123}I, or ^{131}I) scan of the thyroid, which will distinguish the diffuse, high uptake of Graves' disease from nodular thyroid disease, destructive thyroiditis, ectopic thyroid tissue, and factitious thyrotoxicosis. In secondary hyperthyroidism due to a TSH-secreting pituitary tumor, there is also a diffuse goiter. The presence of a nonsuppressed TSH level and the finding of a pituitary tumor on CT or magnetic resonance imaging (MRI) scan readily identify such patients.

Clinical features of thyrotoxicosis can mimic certain aspects of other disorders including panic attacks, mania, pheochromocytoma, and the weight loss associated with malignancy. The diagnosis of thyrotoxicosis can be easily excluded if the TSH and T_3 levels are normal. A normal TSH also excludes Graves' disease as a cause of diffuse goiter.

Clinical Course

Clinical features generally worsen without treatment; mortality was 10 to 30% before the introduction of satisfactory therapy. Some patients with mild Graves' disease experience spontaneous relapses and remissions. Rarely, there may be fluctuation between hypo- and hyperthyroidism due to changes in the functional activity of TSH-R antibodies. About 15% of patients who enter remission after treatment with antithyroid drugs develop hypothyroidism 10 to 15 years later as a result of the destructive autoimmune process. The clinical course of ophthalmopathy does not follow that of the thyroid disease. Ophthalmopathy typically worsens over the initial 3 to 6 months, followed by a plateau phase over the next 12 to 18 months, with spontaneous improvement, particularly in the soft tissue changes. However, the course is more fulminant in up to 5% of patients, requiring intervention in the acute phase if there is optic nerve compression or corneal ulceration. Diplopia may appear late in the disease due to fibrosis of the extraocular muscles. Some studies suggest that radioiodine treatment for hyperthyroidism worsens the eye disease in a small proportion of patients (especially smokers). Antithyroid drugs or surgery have no adverse effects on the clinical course of ophthalmopathy. Thyroid dermopathy, when it occurs, usually appears 1 to 2 years after the development of Graves' hyperthyroidism; it may improve spontaneously.

TREATMENT

The hyperthyroidism of Graves' disease is treated by reducing thyroid hormone synthesis, using antithyroid drugs, or by reducing the amount of thyroid tissue with radioiodine (^{131}I) treatment or by subtotal thyroidectomy. Antithyroid drugs are the predominant therapy in many centers in Europe and Japan, whereas radioiodine is more often the first line of treatment in North America. These differences reflect the fact that no single approach is optimal and that patients may require multiple treatments to achieve remission.

The main antithyroid drugs are the thionamides, such as propylthiouracil, carbimazole, and the active metabolite of the latter, methimazole. All inhibit the function of TPO, reducing oxidation and organification of iodide. These drugs also reduce thyroid antibody levels by mechanisms that remain unclear, and they appear to enhance rates of remission. Propylthiouracil inhibits deiodination of $T_4 \rightarrow T_3$. However, this effect is of minor benefit, except in the most severe thyrotoxicosis, and is offset by the much shorter half-life of this drug (90 min) compared to methimazole (6 h).

There are many variations of antithyroid drug regimens. The initial dose of carbimazole or methimazole is usually 10 to 20 mg every 8 or 12 h, but once-daily dosing is possible after euthyroidism is restored. Propylthiouracil is given at a dose of 100 to 200 mg every 6 to 8 h, and divided doses are usually given throughout the course. Lower doses of each drug may suffice in areas of low iodine intake. The starting dose of antithyroid drugs can be gradually reduced (titration regimen) as thyrotoxicosis improves. Alternatively, high doses may be given combined with levothyroxine supplementation (block-replace regimen) to avoid drug-induced hypothyroidism. Initial reports suggesting superior remission rates with the block-replace regimen have not been reproduced in several other trials. The titration regimen is often preferred to minimize the dose of antithyroid drug and provide an index of treatment response.

Thyroid function tests and clinical manifestations are reviewed 3 to 4 weeks after starting treatment, and the dose is titrated based on unbound T_4 levels. Most patients do not achieve euthyroidism until 6 to 8 weeks after treatment is initiated. TSH levels often remain suppressed for several months and therefore do not provide a sensitive index of treatment response. The usual daily maintenance doses of antithyroid drugs in the titration regimen are 2.5 to 10 mg of carbimazole or methimazole and 50 to 100 mg of propylthiouracil. In the block-replace regimen, the initial dose of antithyroid drug is held constant and the dose of levothyroxine is adjusted to maintain normal unbound T_4 levels. When TSH suppression is alleviated, TSH levels can also be used to monitor therapy.

Maximum remission rates (up to 30 to 50% in some populations) are achieved by 18 to 24 months. For unclear reasons, remission rates appear to vary in different geographic regions. Patients with severe hyperthyroidism and large goiters are most likely to relapse when treatment stops, but outcome is difficult to predict. All patients should be followed closely for relapse during the first year after treatment and at least annually thereafter.

The common side effects of antithyroid drugs are rash, urticaria, fever, and arthralgia (1 to 5% of patients). These may resolve spontaneously or after substituting an alternative antithyroid drug. Rare but major side effects include hepatitis, an SLE-like syndrome, and, most importantly, agranulocytosis (<1%). It is essential that antithyroid drugs are stopped and not restarted if a patient develops major side effects. Written instructions should be provided regarding the symptoms of possible agranulocytosis (e.g., sore throat, fever, mouth ulcers) and the need to stop treatment pending a complete blood count to confirm that agranulocytosis is not present. It is not useful to monitor blood counts prospectively, as the onset of agranulocytosis is idiosyncratic and abrupt.

Propranolol (20 to 40 mg every 6 h) or longer acting beta blockers, such as atenolol, may be helpful to control adrenergic symptoms, especially in the early stages before antithyroid drugs take effect. The need for anticoagulation with warfarin should be considered in all patients with atrial fibrillation. If digoxin is used, increased doses are often needed in the thyrotoxic state.

Radioiodine causes progressive destruction of thyroid cells and can be used as initial treatment or for relapses after a trial of antithyroid drugs. There is a small risk of thyrotoxic crisis (see below) after radioiodine, which can be minimized by pretreatment with antithyroid drugs for at least a month before treatment. Antecedent treatment with antithyroid drugs should be considered for all elderly patients or for those with cardiac problems, to deplete thyroid hormone stores before administration

of radioiodine. Antithyroid drugs must be stopped at least 3 days before radioiodine administration to achieve optimum iodine uptake.

Efforts to calculate an optimal dose of radioiodine that achieves euthyroidism, without a high incidence of relapse or progression to hypothyroidism, have not been successful. Some patients inevitably relapse after a single dose because the biologic effects of radiation vary between individuals, and hypothyroidism cannot be uniformly avoided even using accurate dosimetry. A practical strategy is to give a fixed dose based on clinical features, such as the severity of thyrotoxicosis, the size of the goiter (increases the dose needed), and the level of radioiodine uptake (decreases the dose needed). ^{131}I dosage generally ranges between 185 MBq (5 mCi) to 555 MBq (15 mCi). Incomplete treatment or early relapse is more common in males and in patients <40 years of age. Many authorities favor an approach aimed at thyroid ablation (as opposed to euthyroidism), given that levothyroxine replacement is straightforward and most patients ultimately progress to hypothyroidism over 5 to 10 years, frequently with some delay in the diagnosis of hypothyroidism.

Certain radiation safety precautions are necessary in the first few days after radioiodine treatment, but the exact guidelines vary depending on local protocols. In general, patients need to avoid close, prolonged contact with children and pregnant women for several days because of possible transmission of residual isotope and excessive exposure to radiation emanating from the gland. Rarely there may be mild pain due to radiation thyroiditis 1 to 2 weeks after treatment.

Hyperthyroidism can persist for 2 to 3 months before radioiodine takes full effect. For this reason, β-adrenergic blockers or antithyroid drugs can be used to control symptoms during this interval. Persistent hyperthyroidism can be treated with a second dose of radioiodine, usually 6 months after the first dose. The risk of hypothyroidism after radioiodine depends on the dosage but is at least 10 to 20% in the first year and 5% per year thereafter. Patients should be informed of this possibility before treatment and require close follow-up during the first year and annual thyroid function testing.

Pregnancy and breast feeding are absolute contraindications to radioiodine treatment, but patients can conceive safely 6 months after treatment. The presence of severe ophthalmopathy requires caution, and some authorities advocate the use of prednisone, 40 mg/d, at the time of radioiodine treatment, tapered over 2 to 3 months to prevent exacerbation of ophthalmopathy. The overall risk of cancer after radioiodine treatment in adults is not increased, but many physicians avoid radioiodine in children and adolescents because of the theoretical risks of malignancy.

Subtotal thyroidectomy is an option for patients who relapse after antithyroid drugs and prefer this treatment to radioiodine. Some experts recommend surgery in young individuals, particularly when the goiter is very large. Careful control of thyrotoxicosis with antithyroid drugs, followed by potassium iodide (3 drops SSKI orally tid), is needed prior to surgery to avoid thyrotoxic crisis and to reduce the vascularity of the gland. The major complications of surgery—i.e., bleeding, laryngeal edema, hypoparathyroidism, and damage to the recurrent laryngeal nerves—are unusual when the procedure is performed by highly experienced surgeons. Recurrence rates in the best series are <2%, but the rate of hypothyroidism is only slightly less than that following radioiodine treatment.

The titration regimen of antithyroid drugs should be used to manage Graves' disease in pregnancy, as blocking doses of these drugs produce fetal hypothyroidism. Propylthiouracil is usually used because of relatively low transplacental transfer and its ability to block $T_4 \rightarrow T_3$ conversion. Also, carbimazole and methimazole have been associated with rare cases of fetal aplasia cutisand other defects, such as choanal atresia. The lowest effective dose of propylthiouracil should be given, and it is often possible to stop treatmentin the last trimester since TSH-R antibodies tend to decline in pregnancy. Nonetheless, the transplacental transfer of these antibodies rarely causes fetal thyrotoxicosis or neonatal thyrotoxicosis. Poor intrauterine growth, afetal heart rate of >160 beats/min, and high levels of maternal TSH-R antibodies in the last trimester may herald this complication. Antithyroid drugs given to the mother can be used to treat the fetus and may be needed for 1 to 3 months after delivery, until the maternal antibodies disappear from the baby's circulation.

The postpartum period is a time of major risk for relapse of Graves' disease. Breast feeding is safe with low doses of antithyroid drugs. Graves' disease in children is best managed with antithyroid drugs, often given as a prolonged course of the titration regimen. Surgery may be indicated for severe

disease. Radioiodine can also be used in children, although most experts defer this treatment until adolescence or later.

Thyrotoxic crisis, or thyroid storm, is rare and presents as a life-threatening exacerbation of hyperthyroidism, accompanied by fever, delirium, seizures, coma, vomiting, diarrhea, and jaundice. The mortality rate due to cardiac failure, arrhythmia, or hyperthermia is as high as 30%, even with treatment. Thyrotoxic crisis is usually precipitated by acute illness (e.g., stroke, infection, trauma, diabetic ketoacidosis), surgery (especially on the thyroid), or radioiodine treatment of a patient with partially treated or untreated hyperthyroidism. Management requires intensive monitoring and supportive care, identification and treatment of the precipitating cause, and measures that reduce thyroid hormone synthesis. Large doses of propylthiouracil (600-mg loading dose and 200 to 300 mg every 6 h) should be given orally or by nasogastric tube or per rectum; the drug's inhibitory action on $T_4 \rightarrow T_3$ conversion makes it the antithyroid drug of choice. One hour after the first dose of propylthiouracil, stable iodide is given to block thyroid hormone synthesis via the Wolff-Chaikoff effect (the delay allows the antithyroid drug to prevent the excess iodine from being incorporated into new hormone). A saturated solution of potassium iodide (5 drops SSKI every 6 h), or ipodate or iopanoic acid (0.5 mg every 12 h), may be given orally. (Sodium iodide, 0.25 g intravenously every 6 h is an alternative but is not generally available.) Propranolol should also be given to reduce tachycardia and other adrenergic manifestations (40 to 60 mg orally every 4 h; or 2 mg intravenously every 4 h). Although other β-adrenergic blockers can be used, high doses of propranolol decrease $T_4 \rightarrow T_3$ conversion, and the doses can be easily adjusted. Caution is needed to avoid acute negative inotropic effects, but controlling the heart rate is important, as some patients develop a form of high-output heart failure. Additional therapeutic measures include glucocorticoids (e.g., dexamethasone, 2 mg every 6 h), antibiotics if infection is present, cooling, oxygen, and intravenous fluids.

Ophthalmopathy requires no active treatment when it is mild or moderate, as there is usually spontaneous improvement. General measures include meticulous control of thyroid hormone levels, advice about cessation of smoking, and an explanation of the natural history of ophthalmopathy. Discomfort can be relieved with artificial tears (e.g., 1% methylcellulose) and the use of dark glasses with side frames. Periorbital edema may respond to a more upright sleeping position or a diuretic. Corneal exposure during sleep can be avoided by taping the eyelids shut. Minor degrees of diplopia improve with prisms fitted to spectacles. Severe ophthalmopathy, with optic nerve involvement or chemosis resulting in corneal damage, is an emergency requiring joint management with an ophthalmologist. Short-term benefit can be gained in about two-thirds of patients by the use of high-dose glucocorticoids (e.g., prednisone, 40 to 80 mg daily), sometimes combined with cyclosporine. Glucocorticoid doses are tapered by 5 mg every 1 to 2 weeks, but the taper often results in reemergence of congestive symptoms. Pulse therapy with intravenous methylprednisolone (1 g of methylprednisolone in 250 mL of saline infused over 2 h daily for 1 week) followed by an oral regimen is also used. Once the eye disease has stabilized, surgery may be indicated for relief of diplopia and correction of the appearance of the eyes. Orbital decompression can be achieved by removing bone from any wall of the orbit, thereby allowing displacement of fat and swollen extraocular muscles. The transantral route is used most often, as it requires no external incision. Proptosis recedes an average of 5 mm, but there may be residual or even worsened diplopia. Alternatively, retrobulbar tissue can be decompressed without the removal of bony tissue. External beam radiotherapy of the orbits has been used for many years, especially for ophthalmopathy of recent onset, but the objective evidence that this therapy is beneficial remains equivocal.

Thyroid dermopathy does not usually require treatment but can cause cosmetic problems or interfere with the fit of shoes. Surgical removal is not indicated. If necessary, treatment consists of topical, high-potency glucocorticoid ointment under an occlusive dressing. Octreotide may be beneficial.

THYROIDITIS

A clinically useful classification of thyroiditis is based on the onset and duration of disease (Table 7).

TABLE 7 Causes of Thyroiditis

Acute

Bacterial infection: especially Staphylcoccus Streptococcus and Enterobacter

Fungal infection: Aspergillus Candida Coccidioides Histoplasma and Pneumocystis

Radiation thyroiditis after 131I treatment
Amiodarone (may also be subacute or chronic)

Subacute

Viral (or granulomatous) thyroiditis
Silent thyroiditis (including postpartum thyroiditis)
Mycobacterial infection

Chronic

Autoimmunity: focal thyroiditis, Hashimoto's thyroiditis, atrophic thyroiditis
Riedel's thyroiditis
Parasitic thyroiditis: echinococcosis, strongyloidiasis, cysticercosis

Traumatic: after palpation

ACUTE THYROIDITIS

Acute thyroiditis is rare and due to suppurative infection of the thyroid. In children and young adults, the most common cause is the presence of a piriform sinus, a remnant of the fourth branchial pouch that connects the oropharynx with the thyroid. Such sinuses are predominantly left sided. A long-standing goiter and degeneration in a thyroid malignancy are risk factors in the elderly. The patient presents with thyroid pain, often referred to the throat or ears, and a small, tender goiter that may be asymmetric. Fever, dysphagia, and erythema over the thyroid are common, as are systemic symptoms of a febrile illness and lymphadenopathy.

The differential diagnosis of thyroid pain includes subacute or, rarely, chronic thyroiditis, hemorrhage into a cyst, malignancy including lymphoma, and, rarely, amiodarone-induced thyroiditis or amyloidosis. However, the abrupt presentation and clinical features of acute thyroiditis rarely cause confusion. The erythrocyte sedimentation rate (ESR) and white cell count are usually increased, but thyroid function is normal. FNA biopsy shows infiltration by polymorphonuclear leukocytes; culture of the sample can identify the organism. Caution is needed in immunocompromised patients as fungal, mycobacterial, or Pneumocystis thyroiditis can occur in this setting. Antibiotic treatment is guided initially by Gram stain and subsequently by cultures of the FNA biopsy. Surgery may be needed to drain an abscess, which can be localized by CT scan or ultrasound. Tracheal obstruction, septicemia, retropharyngeal abscess, mediastinitis, and jugular venous thrombosis may complicate acute thyroiditis but are uncommon with prompt use of antibiotics.

GOITER AND NODULAR THYROID DISEASE

Goiter refers to an enlarged thyroid gland. Biosynthetic defects, iodine deficiency, autoimmune disease, and nodular diseases can each lead to goiter, though by different mechanisms. Biosynthetic defects and iodine deficiency are associated with reduced efficiency of thyroid hormone synthesis, leading to increased TSH, which stimulates thyroid growth as a compensatory mechanism to overcome the block in hormone synthesis. Graves' disease and Hashimoto's thyroiditis are also associated with goiter. In Graves' disease, the goiter results mainly from the TSH-R-mediated effects of TSI. The goitrous form of Hashimoto's thyroiditis occurs because of acquired defects in hormone synthesis, leading to elevated levels of TSH and its consequent growth effects. Lymphocytic infiltration and immune system–induced growth factors also contribute to thyroid enlargement in Hashimoto's thyroiditis. Nodular disease is characterized by the disordered growth of thyroid cells, often combined with the gradual development of fibrosis. Because the management of goiter depends on the etiology, the detection of thyroid enlargement on physical examination should prompt further evaluation to identify its cause.

Nodular thyroid disease is common, occurring in about 3 to 7% of adults when assessed by physical examination. Using more sensitive techniques, such as ultrasound, it is present in >25% of adults. Thyroid nodules may be solitary or multiple, and they may be functional or nonfunctional.

DIFFUSE NONTOXIC (SIMPLE) GOITER

Etiology and Pathogenesis

When diffuse enlargement of the thyroid occurs in the absence of nodules and hyperthyroidism, it is referred to as a diffuse nontoxic goiter. This is sometimes called simple goiter, because of the absence of nodules, or colloid goiter, because of the presence of uniform follicles that are filled with colloid. Worldwide, diffuse goiter is most commonly caused by iodine deficiency and is termed

endemic goiter when it affects >5% of the population. In nonendemic regions, sporadic goiter occurs, and the cause is usually unknown. Thyroid enlargement in teenagers is sometimes referred to as juvenile goiter. In general, goiter is more common in women than men, probably because of the greater prevalence of underlying autoimmune disease and the increased iodine demands associated with pregnancy.

In iodine-deficient areas, thyroid enlargement reflects a compensatory effort to trap iodide and produce sufficient hormone under conditions in which hormone synthesis is relatively inefficient. Somewhat surprisingly, TSH levels are usually normal or only slightly increased, suggesting increased sensitivity to TSH or activation of other pathways that lead to thyroid growth. Iodide appears to have direct actions on thyroid vasculature and may indirectly affect growth through vasoactive substances such as endothelins and nitric oxide. Endemic goiter is also caused by exposure to environmental goitrogens such as cassava root, which contains a thiocyanate, vegetables of the Cruciferae family (e.g., brussels sprouts, cabbage, and cauliflower), and milk from regions where goitrogens are present in grass. Though relatively rare, inherited defects in thyroid hormone synthesis lead to a diffuse nontoxic goiter. Abnormalities at each step in hormone synthesis, including iodide transport (NIS), Tg synthesis, organification and coupling (TPO), and the regeneration of iodide (dehalogenase), have been described.

CLINICAL MANIFESTATIONS AND DIAGNOSIS

If thyroid function is preserved, most goiters are asymptomatic. Spontaneous hemorrhage into a cyst or nodule may cause the sudden onset of localized pain and swelling. Examination of a diffuse goiter reveals a symmetrically enlarged, nontender, generally soft gland without palpable nodules. Goiter is defined, somewhat arbitrarily, as a lateral lobe with a volume greater than the thumb of the individual being examined. If the thyroid is markedly enlarged, it can cause tracheal or esophageal compression. These features are unusual, however, in the absence of nodular disease and fibrosis. Substernal goiter may obstruct the thoracic inlet. Pemberton's sign refers to symptoms of faintness with evidence of facial congestion and external jugular venous obstruction when the arms are raised above the head, a maneuver that draws the thyroid into the thoracic inlet. Respiratory flow measurements and CT or MRI should be used to evaluate substernal goiter in patients with obstructive signs or symptoms.

Thyroid function tests should be performed in all patients with goiter to exclude thyrotoxicosis or hypothyroidism. It is not unusual, particularly in iodine deficiency, to find a low total T_4, with normal T_3 and TSH, reflecting enhanced $T_4 \rightarrow T_3$ conversion. A low TSH, particularly in older patients, suggests the possibility of thyroid autonomy or undiagnosed Graves' disease, causing subclinical thyrotoxicosis. TPO antibodies may be useful to identify patients at increased risk of autoimmune thyroid disease. Low urinary iodine levels (<10 μg/dL) support a diagnosis of iodine deficiency. Thyroid scanning is not generally necessary but will reveal increased uptake in iodine deficiency and most cases of dyshormonogenesis. Ultrasound is not generally indicated in the evaluation of diffuse goiter, unless a nodule is palpable on physical examination.

TREATMENT

Iodine or thyroid hormone replacement induces variable regression of goiter in iodine deficiency, depending on how long it has been present and the degree of fibrosis that has developed. Because of the possibility of underlying thyroid autonomy, caution should be exercised when instituting suppressive thyroxine therapy in other causes of diffuse nontoxic goiter, particularly if the baseline TSH is in the low-normal range. In younger patients, the dose of levothyroxine can be started at 100 μg/d and adjusted to suppress the TSH into the low-normal but detectable range. Treatment of elderly patients should be initiated at 50 μg/d. The efficacy of suppressive treatment is greater in younger patients and for those with soft goiters. Significant regression is usually seen within 3 to 6 months of treatment; after this time it is unlikely to occur. In older patients, and in those with some degree of nodular disease or fibrosis, fewer than one-third demonstrate significant shrinkage of the goiter.

Surgery is rarely indicated for diffuse goiter. Exceptions include documented evidence of tracheal compression or obstruction of the thoracic inlet, which are more likely to be associated with substernal multinodular goiters (see below). Subtotal or near-total thyroidectomy for these or cosmetic reasons should be performed by an experienced surgeon to minimize complication rates, which occur in up to 10% of cases. Surgery should be followed by mild suppressive treatment with

levothyroxine to prevent regrowth of the goiter. Radioiodine reduces goiter size by about 50% in the majority of patients. It is rarely associated with transient acute swelling of the thyroid, which is usually inconsequential unless there is severe tracheal narrowing. If not treated with levothyroxine, patients should be followed after radioiodine treatment for the possible development of hypothyroidism

NONTOXIC MULTINODULAR GOITER

Etiology and Pathogenesis

Depending on the population studied, multinodular goiter (MNG) occurs in up to 12% of adults. MNG is more common in women than men and increases in prevalence with age. It is more common in iodine-deficient regions but also occurs in regions of iodine sufficiency, reflecting multiple genetic, autoimmune, and environmental influences on the pathogenesis.

There is typically wide variation in nodule size. Histology reveals a spectrum of morphologies ranging from hypercellular regions to cystic areas filled with colloid. Fibrosis is often extensive, and areas of hemorrhage or lymphocytic infiltration may be seen. Using molecular techniques, most nodules within a MNG are polyclonal in origin, suggesting a hyperplastic response to locally produced growth factors and cytokines. TSH, which is usually not elevated, may play a permissive or contributory role. Monoclonal lesions also occur within a MNG, reflecting mutations in genes that confer a selective growth advantage to the progenitor cell.

Clinical Manifestations

Most patients with nontoxic MNG are asymptomic and, by definition, euthyroid. MNG typically develops over many years and is detected on routine physical examination or when an individual notices an enlargement in the neck. If the goiter is large enough, it can ultimately lead to compressive symptoms including difficulty swallowing, respiratory distress (tracheal compression), or plethora (venous congestion), but these symptoms are uncommon. Symptomatic MNGs are usually extraordinarily large and/or develop fibrotic areas that cause compression. Sudden pain in a MNG is usually caused by hemorrhage into a nodule but should raise the possibility of invasive malignancy. Hoarseness, reflecting laryngeal nerve involvement, also suggests malignancy.

Diagnosis

On examination, thyroid architecture is distorted and multiple nodules of varying size can be appreciated. Because many nodules are deeply embedded in thyroid tissue or reside in posterior or substernal locations, it is not possible to palpate all nodules. A TSH level should be measured to exclude subclinical hyper- or hypothyroidism, but thyroid function is usually normal. Tracheal deviation is common, but compression must usually exceed 70% of the tracheal diameter before there is significant airway compromise. Pulmonary function testing can be used to assess the functional effects of compression and to detect tracheomalacia, which characteristically causes inspiratory stridor. CT or MRI can be used to evaluate the anatomy of the goiter and the extent of substernal extension, which is often much greater than is apparent on physical examination. A barium swallow may reveal the extent of esophageal compression. MNG does not appear to predispose to thyroid carcinoma or to more aggressive carcinoma. For this reason, and because it is not possible to biopsy all nodular lesions, thyroid biopsies should be performed only if malignancy is suspected because of a dominant or enlarging nodule.

TREATMENT

Most nontoxic MNGs can be managed conservatively. T_4 suppression is rarely effective for reducing goiter size and introduces the risk of thyrotoxicosis, particularly if there is underlying autonomy or if it develops during treatment. If levothyroxine is used, it should be started at low doses (50 μg) and advanced gradually while monitoring the TSH level to avoid excessive suppression. Contrast agents and other iodine-containing substances should be avoided because of the risk of inducing the Jod-Basedow effect, characterized by enhanced thyroid hormone production by autonomous nodules. Radioiodine is being used with increasing frequency because it often decreases goiter size and may selectively ablate regions of autonomy. Dosage of ^{131}I depends on the size of the goiter and radioiodine uptake but is usually about 3.7 MBq (0.1 mCi) per gram of tissue, corrected for uptake [typical dose, 370 to 1070 Mbq (10 to 29 mCi)]. Repeat treatment may be needed. It is possible to achieve a 40 to 50% reduction in goiter size in most patients. Earlier concerns about radiation-

induced thyroid swelling and tracheal compression have diminished as recent studies have shown this complication to be rare. When acute compression occurs, glucocorticoid treatment or surgery may be needed. Radiation-induced hypothyroidism is less common than after treatment for Graves' disease. However, posttreatment autoimmune thyrotoxicosis may occur in up to 5% of patients treated for nontoxic MNG. Surgery remains highly effective but is not without risk, particularly in older patients with underlying cardiopulmonary disease.

TOXIC MULTINODULAR GOITER

The pathogenesis of toxic MNG appears to be similar to that of nontoxic MNG; the major difference is the presence of functional autonomy in toxic MNG. The molecular basis for autonomy in toxic MNG remains unknown. As in nontoxic goiters, many nodules are polyclonal, while others are monoclonal and vary in their clonal origins. Genetic abnormalities known to confer functional autonomy, such as activating TSH-R or $G_{s\alpha}$ mutations (see below), are not usually found in the autonomous regions of toxic MNG goiter.

In addition to features of goiter, the clinical presentation of toxic MNG includes subclinical hyperthyroidism or mild thyrotoxicosis. The patient is usually elderly and may present with atrial fibrillation or palpitations, tachycardia, nervousness, tremor, or weight loss. Recent exposure to iodine, from contrast dyes or other sources, may precipitate or exacerbate thyrotoxicosis. The TSH level is low. The T_4 level may be normal or minimally increased; T_3 is often elevated to a greater degree than T_4. Thyroid scan shows heterogeneous uptake with multiple regions of increased and decreased uptake; 24-h uptake of radioiodine may not be increased

TREATMENT

The management of toxic MNG is challenging. Antithyroid drugs, often in combination with beta blockers, can normalize thyroid function and address clinical features of thyrotoxicosis. This treatment, however, often stimulates the growth of the goiter, and, unlike in Graves' disease, spontaneous remission does not occur. Radioiodine can be used to treat areas of autonomy, as well as to decrease the mass of the goiter. Usually, however, some degree of autonomy remains, presumably because multiple autonomous regions emerge as soon as others are treated. Nonetheless, a trial of radioiodine should be considered before subjecting patients, many of whom are elderly, to surgery. Surgery provides definitive treatment of underlying thyrotoxicosis as well as goiter. Patients should be rendered euthyroid using antithyroid drugs before operation.

Hyperparathyroidism

In this condition, there is overactivity of one or more parathyroid glands with secretion of excessive amounts of PTH. Three subtypes are recognised, as follows.

1)Primary hyperparathyroidism. Without any demonstrable stimulation, the parathyroid gland(s) secrete inappropriately raised amounts of PTH. Serum calcium concentration is raised and negative feedback is abolished, so the level of PTH is inappropriately high for the level of calcium. The cause is most commonly adenomatous change in one parathyroid, but less frequently there may be hyperplasia of all four or a carcinoma of one.

2)Secondary hyperparathyroidism. This occurs in chronic kidney disease (failure of tubular reabsorption); intestinal malabsorption and vitamin D deficiency. There is a reduction in the plasma concentration of calcium, which causes hyperplasia of all four glands. Increased production of PTH is therefore appropriate and, if the cause of hypocalcaemia can be corrected, in most instances the parathyroids return to normal.

3)Tertiary hyperparathyroidism. For patients with chronic kidney disease induced secondary hyperparathyroidism, the situation becomes chronic owing to dialysis. If a patient were then to receive a renal transplant, the implanted kidney retains the ability to activate vitamin D, which, in the presence of continuing parathyroid overactivity, leads to hypercalcaemia.

Primary hyperparathyroidism

Epidemiology.Primary hyperparathyroidism is the commonest subtype to present to the surgeon. The availability of the multichannel autoanalyser, which provides serum calcium concentrations on blood samples sent for other tests, has resulted in an increasing recognition of this disorder. It can occur at

any age but its peak incidence is over 60 years. Women are more commonly affected. It has been reported to occur in 1 in 1000 patients in hospital, but community prevalence is much less.
Aetiology and pathological features. The cause remains obscure.
Eighty per cent of patients have a solitary adenoma. The adenomatous gland is enlarged, and the chief cells are hypertrophied and numerous. The other glands are suppressed, small, their chief cells few, and their stroma contains an abundant amount of fat. In 5% of patients, adenomas are multiple. The remainder (15–20%) have multiple-gland hyperplasia. Patients with hyperplasia may suffer from the multiple endocrine neoplasia (MEN) syndrome.

Clinical features. The symptoms are those of complications of the disorder, often summarised as 'stones, bones, abdominal groans and psychic moans' but more formally listed as:
1)urinary tract stones – mainly renal colic
2)bone decalcification, which may cause bone pain or a pathological fracture
3)abdominal pain – often of obscure cause but occasionally consequent on the presence of a peptic ulcer or recurrent pancreatitis
4)psychological disturbances of altered mood – mainly depression which may remain unrecognised by the patient or the doctor until successful treatment alters the mental state for the better.
Occasionally a rise of serum calcium concentration above 3.5 mmol/L produces a syndrome of vomiting, dehydration, renal failure and coma. The event may be potentially lethal.

Increasingly (up to 80%) patients are without overt symptoms and the possibility of the condition is signalled by an abnormal result on the autoanalyser profile. Most patients admit to fatigue, poor memory and bone and joint pains.
Physical findings. Examination rarely reveals any abnormality. It is most unusual to find a lump in the neck. Features of the complications outlined above may be present.
Investigation. Diagnostic criteria are as follows:
1)Unequivocal hypercalcaemia – blood is taken without applying a tourniquet to the arm, because this may raise serum calcium concentration by provoking regional acidosis. At least three measurements are made on different occasions; since most calcium in serum is bound to albumin, results are adjusted to a standard albumin concentration of 40 g/L.
2)Simultaneous finding of detectable or raised levels of PTH in the blood – excluding other causes of hypercalcaemia.

Other causes of hypercalcaemia to be excluded in the diagnosis of primary hyperparathyroidism

Cause	Method of exclusion
Secondary carcinoma of bone (common sites: breast, bronchus, thyroid, kidney and prostate)	History Typical bone X-rays Bone scan
Multiple myeloma	Typical bone X-rays
	Plasma electrophoresis
	Bence–Jones proteinuria
Vitamin D intoxication	History of intake
Sarcoidosis	
Thyrotoxicosis	
Rare tumours (usually carcinoma of bronchus) which secrete PTH-related peptide	
Familial hypercalcaemic hypocalciuria – diminished renal calcium excretion	Family history Low renal calcium output

Management

Hypercalcaemia. Severe hypercalcaemia (above 3.5 mmol/L) requires rehydration and the administration of bisphosphonates, which inhibit osteoclastic bone resorption. Calcium concentrations are measured at least daily and often need to be followed more frequently. Moderate hypercalcaemia (3.0–3.5 mmol/L) is usually controlled by intravenous rehydration.

Surgical. Surgical removal offers the only cure for primary hyperparathyroidism and should be offered to all symptomatic patients and those asymptomatic patients whose calcium concentration exceeds 2.75 mmol/L. The high success rate and low morbidity of exploration of the neck have led towards a more liberal surgical policy for minimally symptomatic patients with a plasma calcium between 2.60 and 2.75 mmol/L.

The preoperative preparation is as for thyroidectomy. Some surgeons use frozen section and others intra-operative (quick) PTH assay.

Operation. The approach and exposure are the same as for thyroidectomy. If an adenoma is found, it is removed. The surgical treatment of multi-gland hyperplasia is more difficult. The conventional management is subtotal parathyroidectomy (removal of three and a half glands), leaving half a gland in the neck. However, there is a chance of recurrence, and neck re-exploration is then more difficult and treacherous. Some surgeons now autograft the remaining half gland into the forearm. The graft survival rate is high (more than 90%) and further surgery in the neck is avoided. A third option is to cryopreserve some parathyroid tissue and delay its transplantation until hypocalcaemia is documented; however, graft survival is much lower. The fourth option is to excise all parathyroid tissue and place the patient on lifelong calcium and vitamin D supplements.

Postoperative care. Serum calcium concentration is measured the day after surgery. After a successful procedure, the calcium level often falls below normal before it rises to the normal range. If the calcium level does not fall, or returns to its original level after a transient decrease, the surgeon has failed to remove the disordered tissue.

The patient is questioned for early signs of hypocalcaemia such as paraesthesiae of the hands and lips. Trousseau's and Chvostek's signs may be elicited. It may be necessary to give oral calcium and vitamin D until the suppressed parathyroids recover.

Complications

PERSISTENT OR RECURRENT HYPERCALCAEMIA is the consequence of failure to remove an adenoma or enough hyperplastic tissue. Re-exploration must be carried out, but only by an experienced surgeon because the complication rate is much higher than for a first operation.

HYPOPARATHYROIDISM. Transient hypocalcaemia is common even after successful removal of a diseased gland but recovery occurs within a week. Permanent hypocalcaemia follows removal of too much parathyroid tissue. If cryopreserved tissue is available, some of it is implanted as already described; otherwise, the patient is treated with calcium and vitamin D for life.

Parathyroid carcinoma

This condition is very rare. Usually there is invasion of local tissues and recurrence after excision. Metastases are uncommon. Death is often caused by hypercalcaemia.

Clinical features. There may be symptoms of metastatic disease in addition to the progressive effects of hyperparathyroidism.Physical findings are of a mass in the neck which may be palpable; this should alert the surgeon to the possibility of carcinoma.

Investigation and management. The plasma calcium concentration is typically very high and is accompanied by a high level of PTH. CT of the neck demonstrates the local anatomy, and a chest X-ray should be taken to look for secondary spread.The surgical strategy is en-bloc resection of the tumour. Adjuvant oncotherapy should be considered, and bisphosphonates may be required to control the hypercalcaemia.

5. Materials for activating students during lectures (questions, problems, problem situations, etc.).

CASE SCENARIOS.

DIRECTIONS: Each item below contains a question or incomplete statement followed by suggested responses. Select the one best response to each question.

1. A 29-year-oldwoman the diagnosis of "diffuse toxic goiter, the IIIrd degree of enlargement" was established 3 years ago. She was being treated conservatively. In course of time a dense node in the right lobe of the gland which quickly enlarged in size has appeared. What kind of research should be performed to exclude thyroid cancer?

A. X-ray of the neck
B. Ultrasonic research of the thyroid gland
C. Intraoperative biopsy of the node
D. Scanning of the thyroid gland
E. Fine-needle puncture-aspiration biopsy

2

A 34-year-old female presents to the outpatient clinic with swelling in the lower anterior aspect of her neck. She does not complain of insomnia, weight loss, or increased appetite. She does not express decreased tolerance to heat or increased tolerance to cold. Clinical examination reveals a solitary nodule in the right lobe of the thyroid gland. The nodule is nontender and firm in consistency. No additional signs (e.g., lid lag, proptosis, tremulousness of the hands) are present. Which of the following would be the most likely indication that this nodule is malignant?

A. Evidence of a cold nodule on an iodine 131 (^{131}I) scan
B. Cystic on fine-needle aspiration
C. History of previous irradiation of the neck
D. History of hyperthyroidism
E. History of Hashimoto's thyroiditis

Explanation

The majority (60%) of solitary nodules in the thyroid gland are not neoplastic and represent cysts or goiter. Approximately 25% are follicular adenomas, and the remaining 15% are malignant. Factors that suggest malignancy in a solitary nodule are: a history of previous irradiation of the neck; any solitary nodule in a man or a child; a hard, irregular nodule with cervical lymphadenopathy, or one that is greater than 3 to 4 cm; serum thyroglobulin greater than 100 ng/dl; and a family history of a medullary carcinoma of the thyroid suggesting multiple endocrine neoplasia (MEN) IIa or IIb syndrome.

3. In a 26-year-old woman operated on due to diffuse toxic goiter, the IIIrd degree of enlargement and moderate thyrotoxicosis cramps in hands, feet and face have appeared on the 2nd day after operation. Chvostek's and Trusso's signs are positive. The patient complains of pains in the heart area. On ECG an elongation of Q-T interval is being detected. What kind of complication has developed in the patient?

A. Thyrotoxic storm
B. Hyperparathyroidism
C. Hypoparathyroidism
D. Laryngeal nerves palsy
E. Thyrotoxic myocardial dystrophy

4. A 35-year-old woman complains of pains in the heart area on the 2nd day after operation for mixed toxic goiter, the IVth degree of enlargement. On ECG an elongation of Q-T interval is being detected. Chvostek's and Trusso's signs are not being clearly defined. The initial diagnosis of latent

tetany has been established. What kind of research should be carried out for confirmation of the diagnosis?

A. To determine the concentration of thyrotropic hormone
B. To determine the concentration of calcium and phosphorus in the blood
C. To determine the concentration of potassium
D. To determine the concentration of sodium
E. To determine the concentration of thyroid hormones in the blood

6. A 30-year-old woman presents with hypertension, weakness, bone pain, and a serum calcium level of 15.2 mg/dL. Hand films below show osteitis fibrosa cystica. Which of the following is the most likely cause of these findings?

a. Sarcoidosis
b. Vitamin D intoxication
c. Paget disease
d. Metastatic carcinoma
e. Primary hyperparathyroidism

Explanation
The answer is e. (Brunicardi, pp 1377-1378.) Osteitis fibrosa cystica is a condition associated with hyperparathyroidism that is characterized by severe demineralization with subperiosteal bone resorption (most prominent in the middle phalanx of the second and third fingers), bone cysts, and tufting of the distal phalanges on hand films. These specific bone findings would not be present in sarcoidosis, Paget disease, or metastatic carcinoma. Vitamin D deficiency can lead to osteitis fibrosa cystica, but it would also be associated with hypocalcemia, not hypercalcemia.

7. A 35-year-old woman presents with a serum calcium level of 15.2 mg/dL and an elevated parathyroid hormone level. Following correction of the patient's hypercalcemia with hydration and furosemide, which of the following is the best therapeutic approach?

a. Administration of steroids
b. Radiation treatment to the neck
c. Neck exploration and resection of all 4 parathyroid glands
d. Neck exploration and resection of a parathyroid adenoma
e. Avoidance of sunlight, vitamin D, and calcium-containing dairy products

Explanation
The answer is d. (Brunicardi, pp 1381-1383.) Treatment for primary hyperparathyroidism in this setting is resection of the diseased parathyroid glands after initial correction of the severe hypercalcemia. Parathyroidectomy without preoperative localization studies have a high success rate and low complication rate. Neck exploration will yield a single parathyroid adenoma in about 85% of cases. Two adenomas are found less often (approximately 5% of cases) and hyperplasia of all 4 glands occurs in about 10% to 15% of patients. If hyperplasia is found, treatment includes resection of 3½ glands. The remnant of the fourth gland can be identified with a metal clip in case reexploration becomes necessary. Alternatively, all 4 glands can be removed with autotransplantation of a small piece of parathyroid tissue into the forearm or sternocleidomastoid muscle.

8. A 52-year-old woman sees her physician with complaints of fatigue, headache, flank pain, hematuria, and abdominal pain. She undergoes a sestamibi scan that demonstrates persistent uptake in the right superior parathyroid gland at 2 hours. Which of the following laboratory values is most suggestive of her diagnosis?

a. Serum acid phosphatase above 120 IU/L
b. Serum alkaline phosphatase above 120 IU/L
c. Serum calcium above 11 mg/dL
d. Urinary calcium below 100 mg/day
e. Parathyroid hormone levels below 5 pmol/L

Explanation
The answer is c. (Brunicardi, pp 1376-1381.) Elevated parathyroid hormone (PTH) levels in conjunction with elevated calcium levels are diagnostic for hyperparathyroidism. Primary hyperparathyroidism is a common disease, affecting 100,000 individuals each year in the United States. Essential to the diagnosis of hyperparathyroidism is the finding of hypercalcemia. Though there are many causes of hypercalcemia, hyperparathyroidism is by far the most prevalent. The majority of patients with primary hyperparathyroidism have a single parathyroid adenoma, which can be localized in 75% to 80% of patients with sestamibi scanning. Technetium 99m–labeled sestamibi is taken up by the parathyroid and thyroid glands. Hyperfunctioning parathyroid glands take up the sestamibi to a greater extent than normal glands, and therefore sestamibi scanning can be used to identify parathyroid adenomas. Patients with primary hyperparathyroidism have either normal or elevated urinary calcium. As the name suggests, patients with familial hypocalciuric hypercalcemia (FHH) have hypercalcemia. They also usually have elevated PTH, but urine calcium excretion is low (as opposed to normal to high as with a parathyroid adenoma). Surgery is not indicated in this relatively rare setting of hypercalcemia.

9. Which of the following patients with primary hyperparathyroidism should undergo parathyroidectomy?

a. A 62-year-old asymptomatic woman
b. A 54-year-old woman with fatigue and depression
c. A 42-year-old woman with a history of kidney stones
d. A 59-year-old woman with mildly elevated 24-hour urinary calcium excretion
e. A 60-year-old woman with mildly decreased bone mineral density measured at the hip of less than 2 standard deviations below peak bone density

Explanation
The answer is c. (Brunicardi, p 1380.) Patients with symptomatic primary hyperparathyroidism as manifested by kidney stones, renal dysfunction, or osteoporosis should undergo parathyroidectomy. However, management of "asymptomatic" patients is controversial. Indications for surgical intervention for asymptomatic primary hyperparathyroidism include age less than 50 years, markedly elevated urine calcium excretion, kidney stones on radiography, decreased creatinine clearance, markedly elevated calcium or 1 episode of life-threatening hypercalcemia, and substantially decreased bone mass.

6. **Methodological lecture support:**

- classrooms №1;
- Equipment - Multymedia;
- illustrative material - slides.

7. **Questions for self-control:**

1. Classification of the goiter.
2. Pathological and anatomical features of goiter.
3. Methods of inspection of the patients with goiter.
4. Tool methods of inspection of the patients with goiter.
5. Tactics in the patient with goiter.
6. Tactics in the patient with diseases of parahtyroids.
7. Clinical presentations of diseases of parahtyroids.

8. Treatment.

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Additional literature.

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   - Format Mixed media product | 244 pages
   - Publication date 15 Aug 2013
   - Publisher Elsevier Health Sciences
   - Publication City/Country London, United Kingdom

Lecture №__4

Theme: " Clinics, diagnostics and treatment of acute and chronic ischemia of the lower extremities. ".

I. Introduction:

As the age of the population in the United States increases, the prevalence of lower extremity ischemia secondary to atherosclerosis is increasing. The American life-style contributes to the development and progression of this disease. Increasing evidence supports the fact that appropriate diet, exercise, and smoking cessation can prevent or delay the onset of vascular disease. However, despite education by physicians and the media, many patients continue to maintain habits that put them at high risk for the development of atherosclerosis. In addition, the role of predisposing factors such as diabetes and genetics are not clearly understood, and lower extremity ischemia develops in many patients without clearly identified risk factors. With the advent of new radiologic and operative technologies, the physician has a large array of interventions to offer. As therapeutic options have increased, so has the knowledge of risks, benefits, and indications. Physicians must be equipped with this knowledge to be able to treat the patient with lower extremity ischemia more effectively

2. Aims of the Lecture:

TO KNOW

1. Anatomical features of structure of major arteries of the lower extremities.
2. Clinics and diagnostics of obliterative arteriosclerosis of vessels of the lower extremities.
3. Variants of treatment of obliterative arteriosclerosis of vessels of the lower extremities.
4. Clinics and diagnostics of endarteritis obliterans.
5. Variants of treatment of endarteritis obliterans.
6. Clinics, diagnostics and treatment of Raynaud's disease.
7. Clinics and diagnostics of diabetic angiopathy of the lower extremities.
8. Treatment of diabetic angiopathy of the lower extremities.

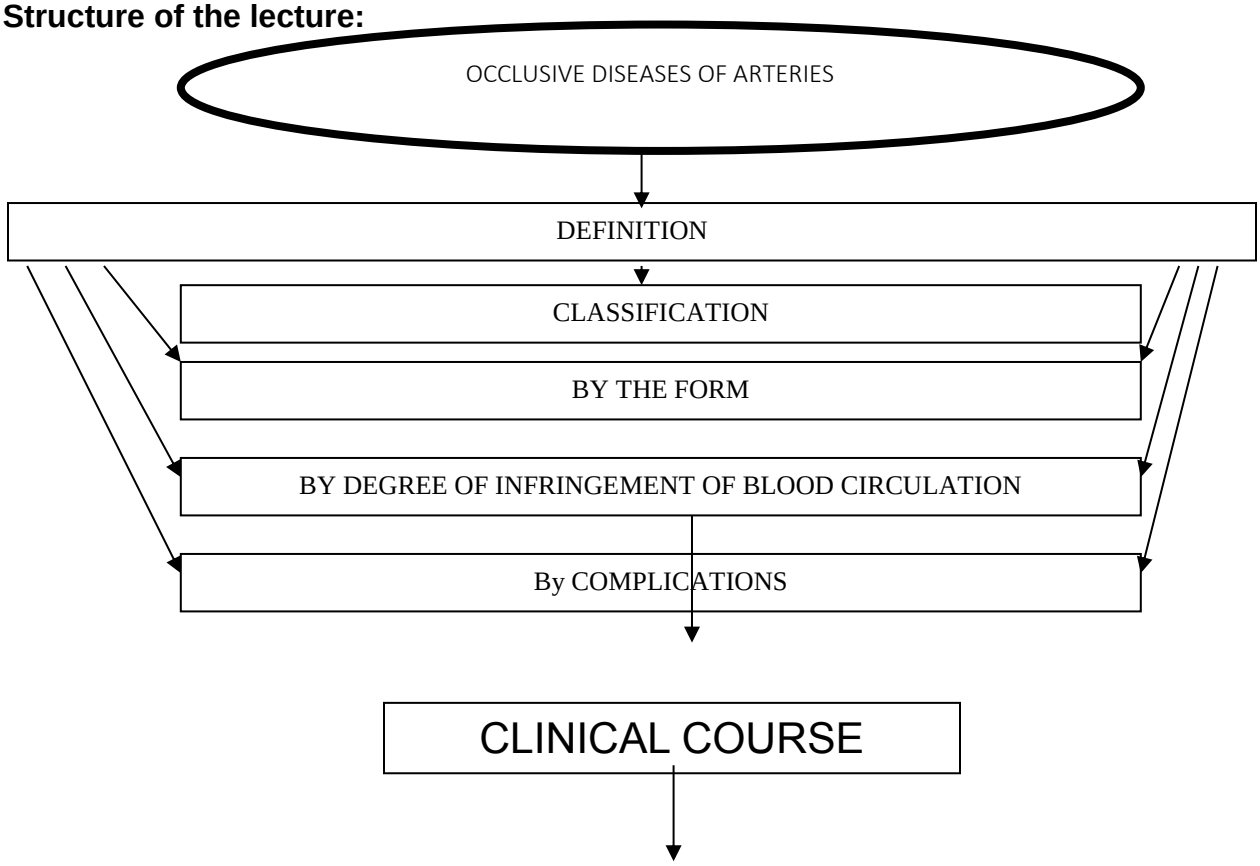
Basic concepts: obliterative arteriosclerosis. Endarteritis obliterans.Raynaud's disease. Diabetic angiopathy. *Diagnostic techniques. Treatment.*

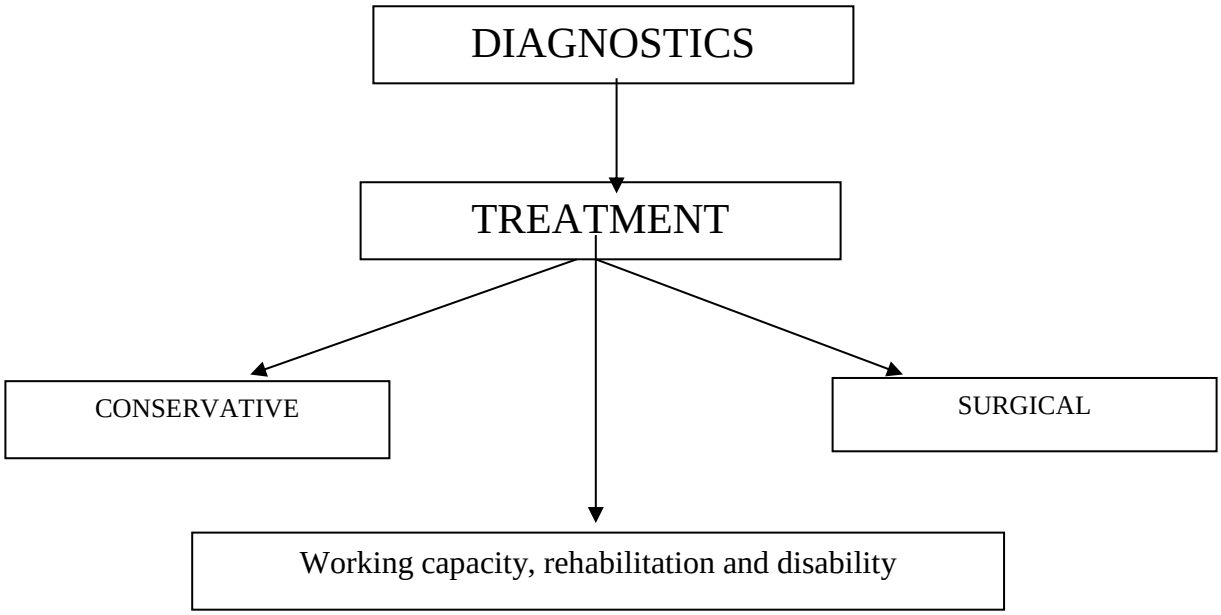
3. Plan and structure of lecture.

№№ of.	The basic units of the lecture.	The purposes in levels of abstraction.	Equipment of the lecture.	Time.
	Preliminary pert			
1.	Definition of educational purposes.	1-10	theme	3 %
2.	Maintenance positive motivations.	-"-	lecture	2 %
	The basic part			
3.	Text of the lecture . The plan		Tables,	90 %

	1. Anatomo-functional features of arteries of the lower extremities	-“-	codograms,	
	2. The general data of morbidity of population of Ukraine.	-“-	slides. Videofilm.	
	3. Classification.	-“-		
	4. Methods of inspection of the patients and diagnostics.	-“-		
	5. Clinical course of different forms and their complications	-“-		
	6. Conservative and surgical treatment.	-“-		
	8. working capacity,	-“-		
	The final part			**5 %**
4.	Summary of the lecture			
5.	Lecturer’s answers for questions.		The list of the literature	
6.	Tasks to self-study		tasks.	

4. Structure of the lecture:





Contents of the theme:

ANATOMY

The abdominal aorta divides at the fourth lumbar vertebra to give rise to the right and left common iliac arteries. Each common iliac artery divides to form an internal and external iliac artery. The external iliac artery lies along the wall of the pelvis, and as it passes the inguinal ligament into the femoral triangle, it becomes the common femoral artery. The femoral triangle is bordered by the inguinal ligament superiorly, the sartorius muscle laterally, and the adductor longus muscle medially. The floor is made up of the iliacus, psoas major, and pectineus muscles. The femoral sheath courses through this triangle with its contents, the femoral nerve, common femoral artery, and femoral vein, laterally to medially.

The common femoral artery provides most of the blood to the lower extremity, although some collaterals are derived from the internal iliac artery. About 3 cm past the inguinal ligament, the common femoral artery divides to form the deep femoral artery laterally and posteriorly and the superficial femoral artery medially. The deep femoral artery gives off the medial and lateral circumflex arteries and three perforating arteries before terminating in the fourth perforating artery. Through these, the deep femoral artery provides most of the blood supply to the thigh muscles. Collaterals are found between these vessels and branches supplied by the internal iliac artery.

The superficial femoral artery travels deep to the sartorius muscle and then through the adductor (Hunter's) canal, where it becomes the popliteal artery. The superficial femoral artery gives off the descending genicular arteries. The popliteal artery exits the canal and travels posteriorly between the lateral and medial gastrocnemius heads. It gives off the superior lateral and medial genicular and inferior lateral and medial genicular arteries. These geniculate arteries form a complex collateral circulation at the knee with the descending branch of the lateral circumflex artery and branches of the anterior tibial artery.

Below the knee, the popliteal artery divides into the anterior tibial artery laterally and the posterior tibial-peroneal trunk medially. This trunk immediately divides into the posterior tibial artery medially and the peroneal artery laterally. These three arteries supply blood to the lower leg and foot. The anterior tibial artery begins at the lower border of the popliteus muscle and passes between the two heads of the tibialis posterior muscle and then through the interosseous membrane, where it courses alongside the deep peroneal nerve in the anterior compartment. It gives off the anterior and posterior tibial recurrent, fibular, anterior medial and anterior lateral malleolar, and muscular branches. It then passes the ankle joint, where it becomes the dorsalis pedis artery.

The posterior tibial artery lies posterior to the tibia and continues posteriorly to the medial malleolus and into the foot. It gives off the posterior medial malleolar, communicating, medial calcaneal, and muscular branches, and then in the foot it gives off the medial and lateral plantar arteries.

The peroneal artery lies between the tibialis posterior and flexor hallucis longus muscles. It gives rise to the perforating, communicating, lateral calcaneal, muscular, and nutrient branches. These various branches of the anterior and posterior tibial and peroneal arteries form multiple collaterals around the ankle joint and in the foot.

PATHOLOGY AND PATHOPHYSIOLOGY

Multiple causes of lower extremity ischemia are recognized, but by far the most predominant is atherosclerotic disease. Other causes include arteritis, antiphospholipid syndrome, popliteal aneurysms, adventitial cystic disease, popliteal artery entrapment, and trauma. The favorable anatomy of the lower extremity helps to prevent progressive ischemia. The collateral circulation allows for blood flow to all areas of the lower extremity in the face of localized occlusive disease. Also, through complex neurohumoral control, the muscle arterial resistance can be decreased to allow a large increase in blood flow. This is physiologic during exercise and compensatory during ischemia. However, as occlusive disease progresses, it usually involves multiple sites in the lower extremity vasculature. The first symptoms are noted by the patient during exercise because the leg is no longer able to increase blood delivery in the normal fashion. Claudication, which is reproducible lower extremity muscle pain on walking that is relieved by rest, develops. The site of pain depends on the arteries involved but in general is one level distal to the site of occlusion. Most commonly, it includes the calf. As ischemic disease progresses, blood flow is also decreased at rest. When the decrease limits normal metabolic function, a level of critical ischemia is reached. With critical ischemia, the patient experiences rest pain and wounds are unable to heal, so that the patient is predisposed to infection, gangrene, and limb loss. Those with gangrene and infection require emergent hospitalization, antibiotics, debridement, and revascularization. Otherwise, limb loss will occur within the next few weeks.

Rest pain initially begins in the forefoot (metatarsalgia) and toes and progresses proximally. Patients often notice a beneficial effect of gravity on their arterial blood flow. They complain of night pain and may let their legs hang over the side of the bed in a dependent fashion to increase the effect of gravity, which augments minimal perfusion and decreases pain. Conversely, symptoms of rest pain are provoked and worsened when the extremity is elevated. In patients with rest pain, ulcerations and infection usually develop during the ensuing 6 months and lead to amputation if no revascularization has been undertaken.

It should be noted that ischemic disease does not always progress. In fact, 75% of nondiabetic patients with mild to moderate claudication have no worsening of symptoms during the next 5 years, and only 5% to 7% require amputation. Thus, when evaluating a patient with claudication, the physician should limit the use of procedures; all are associated with a risk for mortality, and they may increase the limb threat. A clear judgment should be made regarding whether an intervention is required according to the degree that the patient's life-style is inhibited by the inability to walk.

Atherosclerosis

Atherosclerosis is the number one cause of lower extremity arterial disease. Atherosclerosis affects the arteries of the lower extremity frequently, whereas those of the upper extremity are rarely affected. The superficial femoral artery is the most frequent site of of multiple lesions, specifically in the area of the adductor canal, where early stenosis most often occurs. The arteries of the lower extremity are more subject to changes in flow velocity, depending on exercise, than other areas of the body, and the hydrostatic pressure is higher in these vessels. A lack of exercise may favor plaque formation as a consequence of lower flow rates. It has been postulated that because the adductor canal region of the superficial femoral artery is unable to dilate, intimal plaque causes a greater degree of constriction and thus hemodynamic effects that may lead to the development of atherosclerosis.

Atherogenesis, marked by the initiation and progression of processes followed by healing and remodeling, is not continuous. Thus, atherosclerosis may not always lead to stenosis or clinically significant complications. Why the disease progresses in some and not in others is still unknown. Much research is devoted to inhibiting progression and promoting regression by manipulating various predisposing factors.

Predisposing Factors

As with all vascular disease, multiple factors have been identified that affect the development and progression of atherosclerosis and thus arterial disease leading to ischemia of the lower extremity (Table 1). Heredity plays a role through both identified genetic diseases and less clearly identified mechanisms. Thus, a detailed family history of peripheral vascular disease, cardiac disease, cerebrovascular disease, and other stigmata of atherosclerosis can be helpful in identifying patients at risk for the development and progression of atherosclerosis.

Table 1 Risk factors for atherosclerosis

High risk factors
Smoking
Hypetension
Hyperlipidaemia (raised LDL)
High fat diets
Other probable risk factors
Diabetes mellitus (hyperglycaemia)
Elevated blood uric acid (gout)
Hypothyroidism
Renal disease
Familial history of premature atherosclerosis
Factors having an uncertain role
Sedentary life
Obesity
Anxiety
The degree of atherosclerosis may potentially be decreased by:
Low fat diets
Exercise
High levels of high density lipoprotein (HDL)

Tobacco use, especially cigarette smoking, is the number one preventable cause of peripheral vascular disease. It is known to promote atherosclerosis. Multiple factors have been identified within tobacco smoke that play a role in atherogenesis and peripheral vascular disease via hematologic, neurohormonal, metabolic, hemodynamic, genetic, and biochemical pathways. Cessation of smoking can halt progression of disease and has been shown to lead to regression over time. In fact, in one study, 11.4% of patients with claudication who continued to smoke required amputation, whereas none of those who quit smoking required amputation.

Buerger's disease (thromboangiitis obliterans), which affects small vessels of the hands and feet, is a rare cause of lower extremity ischemia in the United States, being more common in the Middle and Far East. It is a chronic inflammation of the neurovascular bundle that leads to blood vessel thrombosis and fibrosis. Buerger's disease usually affects men in the third and fourth decades and is always associated with tobacco use. Cessation of smoking stops progression of the disease.

Diabetes mellitus predisposes a person to the development of atherosclerotic disease. In the diabetic patient, atherogenesis occurs at a younger age and progresses at a faster rate than in the nondiabetic. Diabetic atherosclerosis affects the distal leg arteries more than the aorta and iliac arteries. Involvement of small vessels is often noted in diabetics. In combination with diabetic peripheral neuropathy, such involvement increases the frequency of foot lesions, infection, and limb threat. The evaluation of lower extremity vascular disease in diabetic patients is often complicated by the presence of calcific medial sclerosis, which prevents the accurate measurement of ankle pressures because the vessels cannot be compressed. Toe pressures can often be substituted to determine the severity of disease.

Hypercholesterolemia, hyperlipidemia, obesity, and hypertension have been shown to be predisposing factors for atherosclerosis and lower extremity ischemic disease. These conditions can be familial or specific to the individual patient. Dietary and drug therapies can lessen the progression of atherosclerosis in patients with these problems.

Hypercoagulable states may contribute to the development of peripheral vascular disease, although arterial thrombosis is much less common than venous thrombosis. When arterial thrombosis does occur, it predominantly affects patients over the age of 50 years with other risk factors. Thrombi develop at sites of vessel injury where shear stress is elevated. Histologically, they are composed mostly of platelets, and disorders of platelet function and the vessel wall predispose a patient to arterial thrombosis. Disease processes include homocystinuria, abnormalities of lipo protein(a), and fibromuscular dysplasia. A hypercoagulable state should be suspected in a patient with recurrent venous thromboembolism; unexplained thromboembolism before the

age of 45 years; intraperitoneal, retroperitoneal, or cerebral thrombosis; diffuse cutaneous microvascular thrombosis; or a family history of thrombosis.

PATIENT EVALUATION

A detailed, problem-oriented history and physical examination are vital in the evaluation of lower extremity ischemia. Patients usually present with specific complaints characteristic of peripheral vascular disease, and the history often suggests the diagnosis before the physical examination or any additional studies are performed. Pain is the most common complaint. The characteristics of the pain can indicate the urgency of the problem and the risk for limb loss or infection. Chronic ischemic complaints are usually either claudication or rest pain. In diabetic patients, peripheral neuropathy may decrease or even eliminate pain, and the chief complaint may be one of nonhealing ulcers, infection, or dry or even wet gangrene. Peripheral neuropathy can also cause a severe, burning dysesthesia that can be hard to differentiate from ischemic pain. However, the pain of peripheral neuropathy is usually constant and is present in a stocking distribution over both lower legs. In addition, neuropathic pain often involves the hands and upper extremities (stocking-glove distribution). The location of pain also assists in the diagnosis. The pain of claudication is usually one level distal to the occlusion. Thus, an occlusion of the superficial femoral artery may cause calf claudication. Proximal disease may influence a distal lesion and make it hemodynamically significant; for example, distal symptoms may be caused by aortoiliac disease.

Ischemic rest pain is often nocturnal. It usually involves the distal foot and progresses proximally. Proximal rest pain is rare without distal pain. Patients often describe sleeping with legs off the bed or in a recliner, rubbing the foot, or walking to decrease pain. While the “five ps” (pain, paresthesia, pallor, paralysis, and pulselessness) of acute ischemia are helpful in the evaluation of infrainguinal ischemia, they are not always evident in the patient with chronic lower extremity ischemia.

A careful cardiac history is important in the patient with suspected peripheral vascular disease. Cardiac disease in itself is a risk factor for lower extremity ischemia, and because atherosclerosis is a systemic disease, some coronary occlusive disease is found in almost all patients with lower extremity atherosclerosis. Also, as the median age of the population increases, the prevalence and extent of coronary artery disease will increase. This coexistence of coronary and peripheral vascular disease is important; a frequent complication during coronary bypass is symptomatic lower extremity ischemia. The complications of interventions for peripheral artery disease account for 70% of the associated morbidity and mortality. It is therefore important for the cardiac surgeon to evaluate the patient for peripheral artery disease and the vascular surgeon to evaluate the patient for coronary artery disease before intervention is undertaken.

The past medical history and family history should focus on diseases predisposing to ischemia. The social history should include an inquiry about tobacco use and the patient's normal activity level.

During the physical examination, a full vascular examination should be performed because vascular disease can present in multiple areas at once. Special attention should be given to the heart and aorta as possible sources of emboli, especially if blue-toe syndrome is noted. A bilateral examination of the lower extremities should be performed, and the two extremities should be compared and any differences noted. The examiner should assess the extremities for color (pallor or dependent rubor, a purplish erythema in the distal lower extremity during dependency that decreases on elevation in advanced ischemia), hair growth, muscle mass, deformities, and lesions. Decreased hair growth is one of the first signs of ischemia. Nail thickening may be noted. More advanced ischemic changes include skin atrophy or shine. Muscle wasting is often late, and unless it is unilateral, it may be difficult to identify. Ischemic lesions are very painful and tend to occur distally or on the dorsum of the foot. In contrast, the ulcers of venous stasis are usually on the lower third of the leg or over bony prominences and are not very painful. Neurotrophic ulcers tend to form under callus or at pressure points. On touch, temperature, capillary refill, and tenderness should be noted. Elevation of the lower extremity can result in the development of pallor, and dependency can cause the erythema of dependent rubor, seen in advanced ischemia, to return. Finally, the pulses should be examined for strength and bilateral equality. Specifically, the femoral, popliteal, dorsal pedal, and posterior tibial pulses should be examined. A hand-held Doppler probe can be used if the pulse is too weak to be palpated. Listening with a stethoscope for potential bruits can also aid in the detection of a suspected stenosis and can easily be done over the carotid and common femoral arteries and

the abdomen. By the end of the history and physical examination, a diagnosis can usually be reached. The level of stenosis can also be appreciated by a diminished or absent pulse just beyond the level of the lesion. Ischemia can be categorized as critical or noncritical. Further evaluation can then serve multiple purposes by confirming the level of stenosis, providing baseline values with which to detect progression or regression of disease, and indicating the appropriateness of operative treatment options.

Noninvasive Techniques

The Doppler examination can be used in infrainguinal occlusive disease to evaluate the blood supply of the lower extremity, confirm the presence of disease, and obtain a base measurement from which the evolution of disease and response to therapy can be monitored. In itself, it does not provide a precise measurement of the extent of disease; rather, it is a semiquantitative assessment of circulation in the lower extremity.

The ankle-brachial index (ABI) can easily be determined with the Doppler technique (Fig. 1). The ABI is a rough evaluation of blood flow and has been useful in predicting the likelihood of wound healing. In a study by Barnes et al. (3), amputations healed in all patients with an ABI above 70%, whereas healing did not occur in 25% of those with an ABI below 70%. Advantages in obtaining this test are that it is simple and inexpensive and can be performed at the bedside or in the vascular laboratory. It is an excellent means to evaluate and monitor claudication. It is not very specific and does not define the anatomy. Results in the diabetic patient are often unreliable because of abnormal wall calcification and noncompressibility. Toe pressures may be more reliable than the ABI in diabetic patients. A pneumatic or photoplethysmographic cuff is used to measure toe pressures. In normal persons, toe pressures are roughly 5 to 10 mm Hg lower than arm pressures. Rest pain usually develops below 20 to 30 mm Hg, although ischemic ulcers are usually present at somewhat higher levels.

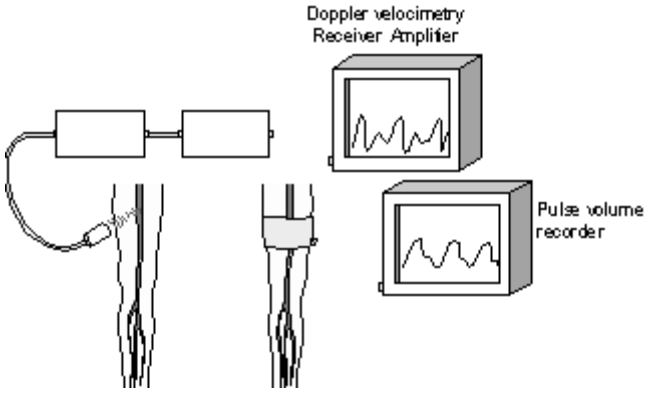


Fig. 1 Both Doppler velocimetry and plethysmography may be used to produce “pulse waveforms” which are used to assess severity of lower extremity arterial disease.

Additional information can be obtained by measuring pressures at various levels of the lower extremity. In this way, the location of a lesion can be approximated because gradients of more than 20 mm Hg are diagnostic of a hemodynamically significant lesion.

Duplex ultrasonography can be used to examine vessels from the distal aorta to the tibial branches. This modality measures the velocity of blood flow through the arteries and provides additional information on flow as well as ultrasonographic images of the vessels themselves. With advances in technology and more sophisticated ultrasonographic machines, this technique has improved such that its specificity and sensitivity in the diagnosis of lesions occluding the vascular lumen by more than 50% are in the 90% range. When peripheral vascular occlusive disease is suspected despite relatively normal resting ABI values, an exercise stress test can be performed. An increase in blood flow velocity through a fixed stenosis causes additional energy to be lost because of turbulence and the amplified hemodynamic effects of such lesions. If a cardiac condition or other circumstances preclude an exercise stress test, one can administer a reactive hyperemia stress test to the same end. At present, magnetic resonance angiography is of limited use in the lower extremity. In a patient who is a poor candidate for conventional angiography, magnetic resonance angiography may be an alternate choice.

Invasive Techniques

Angiography is the gold standard for evaluating lower extremity ischemic disease. It can visualize blood flow from the aorta to the distal foot arteries and defines the location and extent of arterial disease. Before a surgical bypass is undertaken, clear and precise anatomic knowledge from an arteriogram is vital. The aorta

and iliac arteries must be evaluated because disease in these areas may amplify the distal symptoms and influence the planned procedure. A runoff study to the level of the ankle or plantar arch is usually performed. Hemodynamically significant lesions are identified by a reduction in the cross-sectional area of 75% or more or a 50% decrease in diameter. Reactive hyperemia or pharmacologic angiography can increase blood flow and improve the study results. To visualize the entire lower extremity arterial tree properly, a substantial dye load and multiple exposures are necessary. In the patient with renal insufficiency, this can be problematic. Other risks include contrast hypersensitivity and local and distal complications. The risk for contrast hypersensitivity is less than 3%, and the rate of local puncture site complications (e.g., bleeding, hematoma, thrombosis, pseudoaneurysm, and the creation of an arteriovenous fistula between the artery and vein at the puncture site) is less than 1% to 2%. The risk for local thrombosis with limb-threatening ischemia is less than 1%. Distal complications can also develop, including embolism with subsequent thromboses, which can also lead to limb threat and loss. Although angiography is an important and vital part of the evaluation of the presurgical vascular patient, it carries real risk. Thus, careful thought is necessary before arteriography is attempted, and if intervention is not planned, angiography should not be performed. This is especially true in claudication. Conservative management of claudication does not include angiography.

TREATMENT

It is important to differentiate between infrainguinal disease that is causing claudication and limiting activity and infrainguinal disease that is threatening a limb. When limb-threatening ischemia is present, surgical intervention must be considered. In claudication, on the other hand, surgical intervention should be used only in those patients whose life-style is significantly compromised. The inability to work or carry out the normal activities of daily living is a reasonable indication for intervention in good-risk patients. In patients at high risk for operative morbidity, however, alternate strategies or less risky operations may be warranted. When a treatment plan is chosen, the patient's overall health, ways of using the extremity, and coexisting disease processes must be considered.

Conservative Therapy

Optimal control of all modifiable atherosclerotic risk factors, such as hypertension, lipid disorders, and diabetes, is desirable. All patients with peripheral vascular disease should be strongly urged to stop smoking. This alone is the most effective treatment for claudication. Quick and Cotton noted significant improvement in the ABI and distance walked (mean improvement of 214 to 300 m) when patients with claudication stopped smoking. In the study of Jurgens et al., 11.4% of patients with claudication who continued to smoke required amputation, whereas none of those who quit smoking required amputation. Patients should also be urged to begin a walking program. They often misinterpret their pain as a sign of impending damage and so decrease their activity level; they must be encouraged not to do this. Formal walking programs have been shown to increase the overall distance that patients can walk before pain begins. Various studies have shown the increase in distance walked to be between 80% and 234%. Creasy et al. showed the long-term benefits of exercise programs to be greater than those of angioplasty. Walking programs might, in theory, increase the number of collateral vessels and so increase blood delivery and relieve claudication, but this has never been shown to be the case, and ABI values do not increase. The alternative explanation for the increase in distances walked is an improvement in muscular oxygen extraction and metabolic efficiency.

Foot care in the diabetic patient is of vital importance in preventing the complications of peripheral vascular disease. Diabetic patients are predisposed to the development of foot lesions because of peripheral neuropathy, poor wound healing, and an increased susceptibility to infection. These factors are all compounded by poor blood flow. In addition to the early recognition and treatment of lesions, prevention is essential; patients must wear suitable shoes and examine their feet regularly. Regular visits to a podiatrist are helpful.

Optimal control of blood glucose in diabetic patients lessens the progression of peripheral vascular disease. Regular exercise and dietary adjustments to decrease elevated cholesterol levels and promote weight loss also slow the progression of disease in diabetics and nondiabetics alike.

Many of the above recommendations and treatments entail basic life-style changes, and good compliance is required for optimal effect. Programs for smoking cessation, support groups, and counseling by dietitians may help the patient to make the necessary changes.

Pharmacologic Therapy

Various drug therapies are being used in the treatment of lower extremity ischemia. Of note are hemorrheologic, antiplatelet, and metabolic enhancing agents.

Hemorrheologic drugs work on the basis that a decrease in viscosity will result in an increase in blood flow, as per Poiseulle's law. Red blood cell mass and fibrinogen are the major determinants of viscosity in vivo. Ernst et al. showed a reduction in claudication with a decrease in hematocrit. Therapeutic anemia is impractical in most cases but should be considered in polycythemia. A decrease in viscosity can also be achieved through pharmacologic means. If cessation of smoking and a walking program do not adequately relieve symptoms of claudication, a trial of pentoxifylline may be undertaken. Pentoxifylline is a theobromine derivative that has been shown to increase blood filtration and decrease platelet aggregation and plasma fibrinogen in vitro. In vivo, it increases blood flow in the lower extremity and increases muscle oxygen tension. In various trials, pentoxifylline relieved symptoms of claudication and enabled patients to increase their walking distance, although fewer than half of them doubled their walking distance. It has also been suggested that pentoxifylline promotes healing of ulcers. Side effects include dizziness and gastrointestinal complaints, especially nausea.

Cilostazol is a drug recently approved for the treatment of claudication. It is a phosphodiesterase inhibitor that suppresses platelet aggregation and also acts as a direct vasodilator. In a prospective, randomized trial that included 77 patients, the mean distance that patients could walk before the onset of claudication increased by 58%, and the increase in maximum distance walked was 63%. Further study of this drug in larger groups of patients with claudication are needed to confirm efficacy.

Antiplatelet agents include aspirin, nonsteroidal antiinflammatory drugs, calcium channel blockers, prostaglandins, ticlopidine, and thromboxane synthetase inhibitors. The most frequently used of these is aspirin. Aspirin blocks the production of thromboxane A2, which is a stimulus of platelet aggregation. Unlike the effects of other nonsteroidal antiinflammatory drugs, those of aspirin are irreversible. Although no direct benefit on lower extremity ischemia is known, aspirin has been shown to increase survival by reducing the incidence of myocardial infarction and stroke in patients with atherosclerotic disease.

Thromboxane synthetase inhibitors are vasodilators, and they inhibit platelet aggregation via a slightly different mechanism. Ticlopidine inhibits adenosine diphosphate receptors. It has been shown to decrease blood viscosity and may function via hemorrheologic effects. It has not been shown to relieve symptoms of claudication in clinical trials.

Metabolic enhancing agents enhance the metabolism of ischemic muscle. Carnitine is under investigation as a potential therapy for claudication. Carnitine acts to facilitate the entry of pyruvate into the citric acid cycle. Thus, it decreases lactate and increases adenosine triphosphate. Ischemic muscle is relatively deficient in carnitine, so that it is inefficient during anaerobic metabolism. Brevetti et al. demonstrated an increase in walking distance in patients with claudication. Further trials are under way.

Endovascular Therapy

Discrete stenotic lesions and acute thrombosis are amenable to endovascular therapy. Discrete lesions of the superficial and deep femoral arteries have been successfully treated with percutaneous transluminal angioplasty (PTA). In this technique, a catheter is inserted into the artery, usually via an ipsilateral or contralateral femoral artery approach. The catheter is equipped with a balloon that can be inflated at the site of the lesion. The balloon causes the atherosclerotic intima to rupture and stretches the media. Increased blood flow allows for continued patency. PTA can be complicated by neointimal hyperplasia, which can lead to partial or total reocclusion. The atherosclerotic lesion can also re-form over time. Success rates for PTA of the femoropopliteal arteries are about 85%, and a 5-year patency rate of 52% was noted by Rutherford et al. The use of stents to maintain patency distal to the iliac artery has actually proved to decrease patency and at this time is not warranted. The success of PTA depends on patient selection. Because it carries a

complication risk of about 4%, it should be reserved for patients in whom this risk is warranted; therefore, many patients with claudication are not candidates. Patients who are candidates for standard surgical therapy are potential candidates for PTA. The best results are observed in those with short focal lesions. The size of the vessel also must be taken into account; initial success rates are higher in larger vessels. Good runoff is important for patency. Thus, distal disease increases the risk for restenosis and failure, and the consequences would be devastating if acute thrombosis were to occur during the procedure.

In high-risk surgical patients with longer or multiple lesions, PTA may be a better alternative, even though success rates will be lower. PTA has also been used successfully as an adjunct to surgery to improve inflow for a more distal bypass and outflow for a more proximal bypass. Stenosis in bypass grafts is also amenable to PTA. Recently, PTA has been used to treat tibial artery stenosis and occlusion. Although results are not as yet well quantified, it is anticipated that patency and success rates will be lower than those for PTA in the femoropopliteal region. Percutaneous transluminal angioplasty offers several potential advantages. Hospital stay and expense are lessened, although the procedure may have to be repeated. Morbidity and mortality are less for PTA than for surgery. The risks of PTA are similar to those of angiography and include bleeding, thrombosis, infection, pseudoaneurysm or arteriovenous fistula formation, and distal embolization and possible thrombus formation. These are particularly important to consider when PTA is planned for a patient with non-limb-threatening ischemia. In the event of acute lower extremity ischemia, an immediate angiogram is optimal and fibrinolytic therapy may be warranted. The currently used fibrinolytic agents include streptokinase, urokinase, and tissue plasminogen activator. Other agents are being developed. Fibrinolytic agents function by stimulating the conversion of plasminogen to plasmin and thus triggering lysis of clot. In fibrinolytic therapy, a catheter is inserted into the clot and the fibrinolytic agent is infused into the clot during the ensuing hours along with heparin.

Complications of fibrinolytic therapy are similar to those of PTA, but hemorrhage is the major complication and patients must be monitored closely. An advantage of PTA is that it does not activate plasminogen outside the clot and so has less of a systemic effect. Streptokinase carries a risk for allergy and anaphylaxis, and hypothermia develops in one third of patients who receive streptokinase. Fever develops in only 2% to 3% of patients treated with urokinase. Contraindications to fibrinolytic therapy include a central nervous system ischemic or hemorrhagic event, history of bleeding or a coagulopathy, surgery within the previous 2 weeks, open wounds, and severe hypertension.

Surgical Intervention

The patient with peripheral vascular disease virtually always has multiple other medical problems. These should be optimized before surgery. Cardiac disease is almost universal, and the preoperative work-up should include an expert cardiac evaluation—even when cardiac disease is asymptomatic. Sepsis is a relative contraindication to bypass, and if urgent treatment is necessary, aggressive debridement or amputation may be necessary. In the nonambulatory patient, bypass surgery is rarely warranted, and amputation may be preferred. A clear evaluation of the patient's anatomy is necessary before surgical intervention, and traditionally this required an angiogram. Recently, however, some surgeons have been using duplex scanning alone or with intraoperative angiography to identify anatomy for surgical intervention. The surgical options are then thromboendarterectomy, bypass, or amputation.

Thromboendarterectomy was a common technique for femoropopliteal disease in the 1950s and 1960s. This procedure is similar to carotid endarterectomy; a longitudinal incision is made in the artery, and the plaque, intima, and inner media are removed. The artery is then closed with a vein or prosthetic patch. With the advent of vein graft bypasses, endarterectomy was mostly abandoned. Darling and Linton compared saphenous vein graft bypass with extended endarterectomy and found 5-year patency rates of 72% and 32%, respectively. The patency rate for endarterectomy increases with shorter, more discrete lesions and with larger arteries. The operation requires less time than bypass, and the surgical risk is less. Endarterectomy is still used for short, discrete lesions of the common femoral, superficial femoral, deep femoral, and popliteal arteries, especially in high-risk patients.

Infrainguinal bypass is the gold standard in the treatment of peripheral vascular disease (Fig. 2). It is indicated for the patient with critical ischemia and, in specific instances, the patient with claudication. Before a bypass is performed for claudication, both the physician and the patient must be certain that the disease is truly incapacitating and limits the activities of daily living, that conservative and medical management have been unsuccessful, and that the mortality risk and threat of limb loss as a complication of surgery are worth the possible relief of symptoms. It must be remembered that claudication progresses to critical ischemia and limb loss in relatively few cases, and that all interventions in the peripheral circulation can be complicated by limb loss.

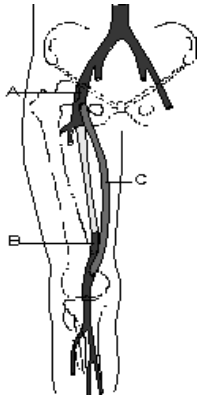


Fig. 2 Femoropopliteal bypass. A, common femoral artery; B, above knee popliteal artery; C, femoropopliteal bypass graft.

Before surgery, a clear delineation of the patient's anatomy must be obtained. This is usually accomplished with an angiogram. It is important to identify the critical stenoses that must be bypassed, and the inflow and outflow of blood must be good for the graft to remain patent. A bypass graft can in theory start and end at any site along the arterial tree, and various generalizations can be made regarding patency rates. Patency rates are better in shorter, large-caliber vein grafts placed in vascular beds with higher rates of flow; thus, relatively proximal grafts, grafts that do not pass the knee, and vein grafts rather than artificial grafts are preferred. Frequently performed procedures include femoral-to-popliteal above-the-knee and below-the-knee bypass, and femoral- or popliteal-to-distal bypass. Bypass can be accomplished with saphenous or other vein, or with an artificial graft. However, femoral- or popliteal-to-distal bypasses are almost exclusively performed with the vein because the combined effects of lower flow rate and smaller diameter decrease the patency of artificial grafts to an impractical level. When a femoral-to-popliteal bypass is performed, autogenous vein grafts are still preferred; however, multiple other uses of the vein, including coronary artery bypass and future distal bypass, may make artificial graft a reasonable choice in some cases.

Saphenous vein grafts can be either in situ or reversed. In situ saphenous vein grafts are left in place in the patient's leg, all valves are cut to allow for unimpeded blood flow through the vein, and all branches are ligated. The vein is anastomosed to the artery proximally and distally. In the reversed saphenous vein graft, the vein is removed from the body and all branches are ligated. The valves are not cut, and the graft is reversed and tunneled under the tissue and attached to the artery proximally and distally.

Following a revascularization procedure, an intraoperative evaluation of patency is important. This can be accomplished via angiography, angioscopy, or duplex scan. It is also important to document pulses postoperatively as a reference for further evaluation and postoperative management.

The complications of bypass surgery are significant. Many are the consequence of multiple comorbid conditions in patients with peripheral vascular disease. Perioperative mortality has been reported to be between 2% and 5%, depending on patient selection, and cardiac complications are the most frequent. Perioperative myocardial infarction rates have been reported as 3%, and if silent and unnoticed myocardial infarctions are included, they may be as high as 10% to 15%. Other complications include hemorrhage, hematoma, thrombosis, infection, and edema. Donaldson et al. documented graft thrombosis in 2% to 7% of procedures within the first 30 days. When bypass surgery carries a very high risk, or when a patient is not ambulatory or has unreconstructable anatomy, irreversible tissue compromise, or invasive infection, an amputation may be the best treatment. An important issue in selecting the level of amputation is the need to remove all painful, infected, and necrotic tissue. In addition, a level must be chosen that offers a good chance of healing, rehabilitation, and use of a prosthetic device.

The most common amputation procedures for patients with peripheral vascular disease are toe, ray, and transmetatarsal amputations for disease confined to the forefoot. Below-knee and above-knee amputation and occasionally a Symes amputation are used in patients with more extensive disease. Various methods to

estimate blood flow are used in planning the level of amputation, including the ABI or pressure measurements, skin temperature, and transcutaneous oxygen measurements.

Rehabilitation is important to all patients. It may be straightforward, or considerable effort may be required to enable use of a prosthesis. Many patients with severe peripheral vascular disease have limited muscle mass and poor exercise tolerance, which make the use of a prosthesis difficult. Ambulation with a below-knee prosthesis requires 40% more energy and with an above-knee prosthesis 70% more energy than normal gait. Although often quoted as higher, mortality from below-knee amputation has been shown to be 6%, and from above-knee amputation it is 11%. The difference can be accounted for by a difference in comorbidity. Immediate and later death is usually caused by cardiac disease. Life tables show that 50% of elderly persons who undergo a lower extremity amputation die within 3 years.

AORTOILIAC DISEASE

Atherosclerotic occlusive disease of the aorta and iliac arteries is one of the most common problems encountered by vascular surgeons. Alone or in combination with more common femoropopliteal/tibial occlusive disease, it is the most frequent cause of chronic lower extremity arterial insufficiency. Because a greater number of muscle groups are affected by aortoiliac atherosclerosis than by infrainguinal disease, the resulting symptoms may be particularly disabling. The treatment of symptomatic aortoiliac disease also represents one of the major success stories of modern vascular surgery. Since the first reconstructive procedures on the abdominal aorta were performed nearly five decades ago, treatment has undergone significant progress. Advances in noninvasive vascular diagnosis, arteriography, preoperative assessment, and anesthesia and critical care in addition to those in surgical technique have contributed to improved outcomes. Reconstructive procedures for aortoiliac disease have become routine, with low perioperative morbidity and mortality and excellent early and long-term outcomes. The excellent durability of such reconstructions is undoubtedly in large part related to the large caliber and high flow rates of the vessels involved. Depending on the pattern of the occlusive process and patient risk, a variety of revascularization techniques are currently available. Selection of a patient-specific treatment strategy from an increasing array of alternatives, although challenging, frequently will alleviate symptoms, avoid an amputation, and prevent or reverse organ dysfunction.

ANATOMY

The arteries supplying blood to the lower extremities are frequently divided into abdominal, or “inflow,” arteries (the aorta and iliac arteries) and infrainguinal, or “outflow,” arteries (the femoropopliteal/tibial arteries). The aorta enters the abdomen from the chest through the aortic hiatus, located between the 12th thoracic and first lumbar vertebrae, and ends at the level of the fourth lumbar vertebra, where it bifurcates into the right and left common iliac arteries. This terminal bifurcation roughly corresponds to the level of the umbilicus. Each common iliac artery curves posteriorly into the sacral hollow and divides into an internal and an external iliac branch. The external iliac then curves anteriorly and continues along the psoas muscle under the inguinal ligament to become the common femoral artery, which in turn bifurcates into the superficial and deep (profunda) femoral arteries. The internal iliac (hypogastric) artery follows the curve of the pelvic side wall and branches repeatedly to supply the pelvic viscera and gluteal musculature (Fig. 3).

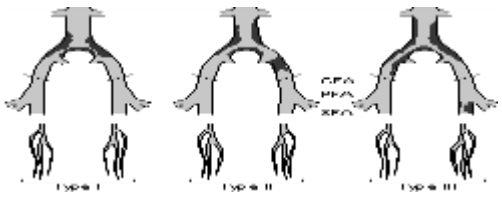


Fig. 3 Distribution of disease. Type I: disease localized to aortic bifurcation; type II: disease also involves external iliac arteries; type III: multilevel disease with infrainguinal arterial disease.

The branches of the abdominal aorta can be divided in three groups: (a) Three unpaired arteries to the gut arise from its anterior wall; the celiac trunk supplies the foregut, the superior mesenteric artery supplies the

midgut, and the inferior mesenteric perfuses the hindgut. (b) Arteries to the three paired genitourinary glands arise close together from the lateral wall of the aorta—the adrenal, renal, and gonadal branches. (c) Branches to the "roof" and walls of the abdominal cavity include the phrenic, lumbar, and median sacral arteries. These branches assume varying degrees of importance in the formation of collateral perfusion channels around occlusive lesions in the aorta and iliac arteries. Because the abdominal aorta and its iliac branches are retroperitoneal structures coursing through the deepest portions of the abdominal cavity, a sophisticated operative technique is required to expose them. The proximal (suprarenal) abdominal aorta is rendered particularly inaccessible by the overlying stomach, pancreas, and colon. Fortunately, occlusive lesions of this portion of the aorta are relatively uncommon in comparison with those of the distal (infrarenal) aorta. The crossing left renal vein serves as a useful surgical landmark defining the usual boundary between these two segments of the abdominal aorta. Although transabdominal exposure of the infrarenal aorta is fairly routine, it requires reflection of the transverse colon superiorly and of the small bowel and its mesentery and distal duodenum to the right. The iliac bifurcations can also be difficult to expose because of their location deep in the pelvis; in addition, the bifurcation of the left iliac artery lies directly behind the sigmoid colon.

PATHOPHYSIOLOGY

Although atherosclerosis is a generalized disease, the earliest and most severe lesions tend to occur at arterial bifurcations and in areas of relative fixation, where the disruption of normal laminar flow is greatest. The aortic bifurcation is in fact the location where the earliest atherosclerotic changes are first noted in most young adults. In persons predisposed to the development of more advanced disease, plaque gradually extends proximally into the infrarenal aorta and distally into the common iliac arteries, usually along the posterior wall first. With progressive worsening of the occlusive process, hemodynamic alterations lead to the enlargement of a network of auxiliary or collateral channels around the involved segments. Important collateral arterial pathways around the aortic bifurcation and common iliac segments are the following: (a) intercostal and lumbar arteries to circumflex iliac and iliolumbar arteries, (b) superior to inferior epigastric arteries, and (c) superior and inferior mesenteric arteries to rectal and internal pudendal arteries. Collateral pathways around occlusive lesions of the external iliac arteries include the hypogastric-to-circumflex femoral channels. With slowly developing occlusive lesions, this collateral network is usually sufficient to provide enough blood flow to meet the resting metabolic needs of the lower extremities. However, these channels do not have the capacity to increase blood flow to the levels necessary to meet the exercise demands of the leg musculature. Claudication (from the Latin verb claudicare, "to limp") is the term used to denote the characteristic exercise-induced, cramping pain in the muscles of the lower extremity that results. With acute arterial occlusions and multiple-level disease (occlusive disease in both the aortoiliac and infrainguinal segments), collateral pathways may be inadequate to meet even the basal metabolic needs of nonexercising tissue. The outcome is critical limb ischemia associated with pain at rest, tissue loss (gangrene, nonhealing ulceration), and threatened limb viability.

PRESENTATION

The risk factors for aortoiliac occlusive disease are those for atherosclerosis in general—smoking, hypertension, lipid abnormalities, diabetes mellitus, male sex, older age, and genetic predisposition. Smoking appears to be a particularly important risk factor for the development of lower extremity atherosclerotic occlusive disease. Patients with symptoms of aortoiliac occlusive disease usually present in their 50s and 60s, whereas patients with symptoms of infrainguinal disease are generally in their 70s. Patients with critical limb ischemia secondary to multiple-level disease are also generally in this older age group.

Claudication is the most common presenting symptom of patients with significant aortoiliac disease. Induced by ambulation and quickly relieved by rest, claudication is usually described as a cramping pain, tiredness, or easy fatigability of the involved muscle groups. Although patients with aortoiliac disease classically present with claudication of the thighs, hips, and buttocks, a significant minority may complain of only calf claudication. Erectile dysfunction in men secondary to reduced hypogastric perfusion is another common complaint. The combination of bilateral lower extremity claudication, atrophy of the leg muscles, impotence, and diminished or absent femoral pulses is known as Leriche's syndrome, after the French physician who

first described these classic manifestations of aortoiliac disease. Critical limb ischemia associated with rest pain or tissue loss may be a manifestation of aortoiliac occlusive disease but almost always occurs in combination with more distal femoropopliteal disease. In the absence of infrainguinal disease, aortoiliac collaterals are almost always able to maintain adequate resting tissue perfusion. An exception to this rule is atheroembolic disease, or “blue toe” syndrome. Degenerative plaque(s) in the aortoiliac (or any proximal arterial) segment can ulcerate or rupture to release platelet microthrombi and atheromatous debris into the arterial lumen. Downstream embolization into the microcirculation of the lower extremities can produce digital ischemia and gangrene and dermal discoloration in a characteristic reticular pattern (livedo reticularis) (Fig. 4). Such patients usually have palpable pedal pulses.

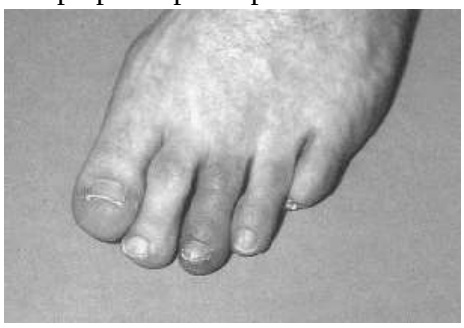


Fig. 4 An isolated ischaemic toe resulting from atheromatous embolism to the digital arteries

Physical examination typically reveals diminished or absent femoral pulses. Severely diseased, calcified femoral arteries may be palpable as firm, tubular masses. Normal femoral and distal pulses may be palpable, however, even in the presence of hemodynamically significant aortoiliac stenoses. Such pulses rapidly disappear following ambulation as the increased flow demands of the exercising leg muscles lead to lowered peripheral vascular resistance. Bruits heard over the lower abdomen or groins suggest the presence of turbulent flow resulting from occlusive plaque. Patients with long-standing aortoiliac atherosclerosis may have disuse atrophy of the lower extremity musculature. Other common signs of lower extremity arterial occlusive disease include trophic changes, such as hair loss on the legs or toes and thin shiny skin on the feet, in addition to rubor on limb dependency coupled with pallor on elevation. Such chronic advanced changes in addition to gangrene and nonhealing ulceration(s) are unusual in the absence of multiple-level disease. Different patterns of aortoiliac disease have been identified on preoperative arteriographic studies (Fig. 5). Disease confined to the distal infrarenal aorta and common iliac arteries, classified as type I, accounts for only 10% of patients with inflow disease. Patients with type I disease are younger and more frequently female than patients with other forms of aortoiliac disease, and they usually present with complaints of disabling claudication in the buttocks, hips, and thighs. Such localized disease may be amenable to endarterectomy or percutaneous transluminal angioplasty. More extensive disease is the rule; atherosclerotic plaque extends distally into the external iliac artery and not infrequently to the common femoral bifurcation in more than 80% of patients. In somewhat less than half this group, no significant occlusive disease is present in the femoropopliteal/tibial segments (type II disease). Such patients experience worse claudication than persons with more localized, type I disease. In the remaining patients, occlusive disease in the aortoiliac segment is combined with femoropopliteal/tibial disease (type III disease). As outlined previously, patients with such multiple-level disease are usually older than those in the other two groups and more frequently present with symptoms of critical limb ischemia.

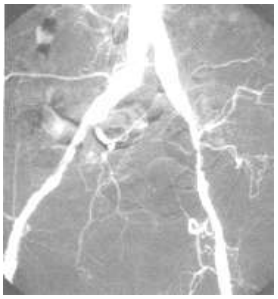


Fig. 5 Digital subtraction aortography by intra-arterial injection. Note the retrograde Seldinger catheter within the right iliac artery. The proximal left external iliac artery is stenosed.

In all three groups, the atherosclerotic process progresses unpredictably, but the end result in a small percentage of patients (approximately 5% to 6% in our experience) is occlusion of the terminal infrarenal aorta with propagation of clot proximally to the levels of the renal arteries. In the absence of significant renal artery stenoses, propagation proximally to the renal arteries is an unusual event. One other pattern worthy of mention is aortoiliac hypoplasia, an uncommon variant usually encountered in young to middle-aged women who smoke cigarettes. The infrarenal aorta and iliac arteries are unusually small in caliber and hence prone to significant narrowing, even with modest disease. Operative treatment in such patients can be particularly challenging.

EVALUATION

In the overwhelming majority of cases, a diagnosis of significant aortoiliac occlusive disease can be made on the basis of the history and physical examination alone. A clinical diagnosis can and should be supplemented by noninvasive vascular testing. Such testing provides valuable information to the treating clinician by confirming the presence of disease and objectively documenting the degree of ischemia and the arterial segment(s) involved. A baseline is established according to which the patient can be followed and interventions planned. Treatment results can be assessed by repeated testing. Such information is particularly useful in a patient with an equivocal history or pulse examination. Arteriography can then be reserved for those patients considered suitable candidates for operative or endovascular (catheter-based) intervention.

Segmental Pressure Measurements

Measurement of the systolic arterial pressures at different levels of the lower extremity with a hand-held, pencil-sized, continuous-wave Doppler flow probe is the simplest and most useful noninvasive method to assess arterial occlusive disease. The ratio of the ankle systolic pressure to the brachial systolic pressure is the ankle-brachial index (ABI), or pressure ratio, and is a good indicator of the degree of ischemia present. With the Doppler probe used as an ultrasonic stethoscope, the systolic pressures in the dorsalis pedis and posterior tibial artery are measured at the ankle, and each of these values is then the numerator of a simple fraction in which the higher of the two brachial pressures is the denominator. Normal ABIs are generally equal to or slightly greater than 1. Patients with claudication usually have ABIs ranging from 0.5 to 0.9, whereas patients with rest pain and tissue loss have ABIs of less than 0.5. Determination of limb systolic pressures at different locations (with the "four-cuff" technique, pressures are measured at the upper thigh, lower thigh, calf, and ankle) provides information about which arterial segment(s) are involved with occlusive disease. A pressure drop of more than 20 mm Hg between consecutive levels is indicative of significant disease within the intervening arterial segment. A reduced upper thigh pressure signifies occlusive disease in the aortoiliac or common femoral segments. In patients with extensive calcification in the walls of the tibial arteries (as is frequently seen in diabetes mellitus or end-stage renal disease), the ankle pressures may not be interpretable because the vessels are too "stiff" to be compressed by the externally applied cuff. In this situation, the pressure in the digital arteries of the great toe can be measured because these small vessels are generally spared calcification. A toe pressure of less than 30 mm Hg indicates severe ischemia. Inspection of the Doppler-derived arterial waveforms can provide additional information when tibial vessels are incompressible. Patients with claudication occasionally have normal or nearly normal ABIs. As described previously, in such cases the arterial stenosis is not severe enough to cause a pressure drop while the limb is at rest but does produce a hemodynamic effect under conditions of higher rates of flow, as during exercise. Higher rates of flow through a moderately stenotic segment increase the energy lost at the site, so that a

significant distal pressure drop results. Exercise stress testing can be used to evaluate patients suspected of having such disease. ABIs are measured before and after a treadmill exercise protocol; a drop of 15% or more in the ABI following exercise is indicative of hemodynamically significant occlusive disease.

Duplex Scanning

Duplex scanning of the aorta and iliac arteries has been advocated by some as a more precise noninvasive diagnostic tool (6). Some authorities have even suggested that duplex scanning can be used to plan therapeutic interventions without the need for arteriography. Imaging of the abdominal arteries, however, is difficult because of their deep retroperitoneal and pelvic locations. Many patients are not candidates for such studies because of body habitus and overlying bowel gas, and even in experienced hands, this procedure is quite time-consuming. These problems have limited the widespread use of this modality.

Differential Diagnosis

The diagnosis of aortoiliac disease is usually straightforward, but occasional diagnostic confusion may arise when other causes of lower extremity pain are present. Irritation of lumbosacral nerve roots by spinal stenosis or intervertebral disk herniation may cause buttock and leg pain that is associated with activity. However, such symptoms (“neurogenic claudication”) usually cannot be reproduced at the same level of activity and frequently occur when the patient is standing, so that the patient must sit or lie down to obtain relief. In addition, the pain is usually in a classic sciatic distribution. Degenerative arthritis of the hip joints may produce similar buttock, hip, and referred thigh pain. The physical examination typically reveals pain directly over the hip joint that is exacerbated by movement of the joint. Peripheral neuropathy, particularly that associated with diabetes mellitus, may masquerade as ischemic rest pain. In all these situations, segmental limb pressure measurements with or without stress testing can be extremely helpful in determining the contribution of arterial occlusive disease to the patient's symptoms.

TREATMENT

The aims of therapy in aortoiliac occlusive disease are to relieve symptoms and, in cases of critical limb ischemia, prevent limb loss. Medical therapy should be instituted in all patients with symptomatic disease but is obviously insufficient as sole therapy in patients with limb-threatening ischemia.

Medical Therapy

Risk factor modification, including smoking cessation and the follow-up and treatment of diabetes mellitus, systemic arterial hypertension, and hyperlipidemia should be an important component of primary care for all these patients. Although control of these factors will not reverse the atherosclerotic process, it may limit the progression of disease. Furthermore, some data indicate that smoking cessation lessens the severity of symptoms in many patients. Also, a daily exercise program of regular walking may improve collateral development and increase the anaerobic tolerance of ischemic skeletal muscle. Finally, pharmacotherapy with medications such as pentoxifylline and cilostazol can be a valuable adjunct in selected patients. Although the mechanisms of action of these agents are unclear, both have effected a modest but significant reduction in claudication symptoms in controlled trials. Some form of platelet inhibition, usually with aspirin, should also be considered for all patients. Although no specific data have demonstrated that antiplatelet therapy is helpful in the treatment of lower extremity arterial occlusive disease, abundant evidence has shown it to be beneficial in the treatment of atherosclerotic occlusive disease in other vascular territories (e.g., coronary and cerebral vessels).

Revascularization. Indications for Revascularization

Revascularization is clearly indicated in patients with critical limb ischemia; without intervention, the vast majority progress to limb loss in a fairly short period of time. Patients with significant or repetitive atheroembolism from an aortoiliac source represent another group who clearly benefit from operative therapy. Removal or bypass of the culprit lesion(s) eliminates the risk for further macroembolism and microembolism. The treatment for patients with claudication secondary to aortoiliac occlusive disease remains somewhat controversial and must be individualized. Patients with mild to moderate symptoms can

be treated medically with quite satisfactory results. Patients with severe, disabling, lifestyle-limiting symptoms of claudication can benefit from revascularization therapy. The current safety and long-term durability of direct aortic reconstruction make this approach acceptable even for older, higher-risk patients with significant symptoms. For patients who cannot tolerate such procedures, a variety of other methods of revascularization are available that have had good long-term success rates.

Arteriography

Once a decision has been made to proceed with revascularization therapy, contrast arteriography, either cut film or digital subtraction, is utilized for a detailed anatomic evaluation of the arterial circulation of the lower extremities. Such information is necessary to choose the most appropriate method of revascularization (operative or endovascular) and plan the procedure. Biplane abdominal aortography with demonstration of the arterial tree below the inguinal ligament ("runoff") is required. This procedure is most commonly performed from the femoral artery with the best pulse by means of a retrograde Seldinger technique. When neither femoral artery is available, a transaxillary or translumbar approach provides good access. Anteroposterior views of the aortoiliofemoral segments demonstrate the extent of the occlusive process and the pattern of collateral formation. Oblique views of the iliac and femoral arteries are frequently necessary to document posterior wall plaque and stenoses at the origins of the deep femoral arteries. Lateral aortography provides information about the origins of the visceral arteries, whereas anteroposterior views demonstrate the renal arteries. Views of the "runoff" to at least the midcalf level are required to assess the degree of associated occlusive disease; in cases of critical limb ischemia, visualization of the pedal circulation is usually necessary.

Occasionally, the hemodynamic effect of a stenosis or series of stenoses along an iliac arterial segment may be difficult to determine, even with oblique views. When the significance of a stenosis remains in question, pressures proximal and distal to the lesion(s) can be measured. A drop of more than 5 to 10 mm Hg across the stenosis is indicative of a hemodynamically significant lesion. For borderline cases, distal pressure measurements can be obtained before and after interarterial injection of a vasodilator, such as tolazoline (Priscoline), to simulate the hyperemic hemodynamics of exercise. A pressure drop of 20 mm Hg or more during hyperdynamic flow is considered to indicate hemodynamic significance. The information supplied by arteriography is crucial to the success of a revascularization procedure. In addition to providing a detailed "road map" of the exact arterial segments involved and the pathology present, arteriography identifies associated anatomic variations (e.g., accessory renal arteries) and aortic wall characteristics (e.g., extensive calcification, ulcerated plaque), which may alter the operative approach and the conduct of the procedure. For example, an operating surgeon who knows that the aortic wall just below the renal arteries is heavily diseased with ulcerated plaque may decide to control the aorta at a more proximal level rather than risk dislodging atheromatous debris with standard infrarenal aortic clamping. Similarly, documented occlusive lesions in the visceral or renal arteries (e.g., a patent inferior mesenteric artery with a large "meandering mesenteric artery") may best be addressed at the time of aortic reconstruction or require particular attention to avoid complications. The major risks of arteriography, allergic reactions and contrast-induced renal dysfunction, have been greatly reduced during the last several years by the introduction of newer non-ionic contrast agents and recognition of the importance of adequate hydration before the procedure. Nevertheless, interest has been increasing in the use of magnetic resonance (MR) imaging to avoid these and other complications of angiography. Unfortunately, current MR angiography technology, although promising, does not provide sufficient detail or accuracy to supplant traditional angiography in the evaluation of aortoiliac occlusive disease. We currently utilize MR angiography in patients with moderately severe renal dysfunction (serum creatinine ³ 3.0 mg/dL), for whom the burden of radioactive contrast in a complete aortogram with runoff study is considered too risky. Any questions remaining after MR angiography can be answered by a more focused arteriographic study with a smaller load of radioactive contrast.

Choice of Revascularization Technique

A variety of procedures, both endovascular and surgical, are available for revascularization of the patient with aortoiliac occlusive disease. Selection depends on a number of factors, including the pattern of the

occlusive process, patient risk, and surgeon experience. Commonly used techniques include (a) catheter-based balloon dilation with or without luminal stenting, (b) aortoiliac endarterectomy, (c) arterial reconstruction with an anatomically placed bypass prosthesis (aortofemoral or iliofemoral), and (d) arterial reconstruction with a remote or extraanatomically placed bypass prosthesis (axillofemoral/bifemoral, femorofemoral, thoracofemoral). Catheter-based techniques are best suited for focal lesions of the common iliac arteries. Endarterectomy is limited to good-risk patients with focal occlusive disease at the aortic bifurcation and common iliac arteries. Prosthetic aortobifemoral bypass is the procedure of choice for most patients with advanced, extensive aortoiliac involvement and is considered the gold standard technique for aortoiliac revascularization. Axillofemoral/bifemoral bypass is reserved for the small subpopulation of patients in whom standard direct aortic reconstruction is considered too risky, either for medical reasons (usually severe pulmonary or cardiac disease) or technical reasons (aortic reoperations, multiple prior abdominal procedures with dense adhesions, prior abdominal irradiation, prosthetic graft infections). The descending thoracic aorta can be considered as an alternative arterial source for the construction of a thoracofemoral bypass in good-risk patients with a "hostile" abdomen. Femorofemoral or iliofemoral bypass can be used in poor-risk patients with diffuse unilateral iliac disease or bilateral iliac involvement when the stenosis in one of the iliac arteries can be appropriately treated by balloon angioplasty with or without intraluminal stenting.

Preoperative Evaluation

The evaluation of patients for whom aortoiliac reconstruction is being considered should include a careful assessment of overall operative risk. Age per se is not a contraindication to a standard direct aortic reconstruction, if it is needed. A "lesser" procedure of more limited durability, however, may provide a similarly excellent outcome in a patient with reduced life expectancy. Patients with significant aortoiliac disease may have atherosclerotic occlusive disease in other vascular territories (e.g., coronary, cerebral) that affects their operative risk. The detection and treatment of significant coronary artery disease is particularly important because myocardial infarction is the leading cause of both perioperative and late mortality. More than 50% of patients with aortoiliac occlusive disease have clinical or electrocardiographic evidence of coronary disease. Selected patients may require cardiac catheterization and even occasional coronary angioplasty or bypass grafting before undergoing aortic reconstruction. Pulmonary and renal function should also be routinely assessed because of the higher mortality associated with postoperative dysfunction of these organ systems.

Endovascular Treatment

Since the very first transarterial dilation procedures, percutaneous transluminal angioplasty (PTA) has become the standard and in some cases the preferred therapy for iliac artery occlusive disease. Like operative reconstruction, PTA at this site is likely to be successful because of the large caliber of the vessels and high rates of flow in the aortoiliac segment. The best results are obtained with short, focal, nonocclusive lesions in the common iliac arteries. Occlusions, stenoses longer than 10 cm, and external iliac lesions respond less favorably. Initial success rates as high as 80% to 90% and long-term patency rates of 70% to 80% have been reported. Complications (thrombosis, dissection, perforation, and distal embolism) in experienced hands are uncommon and can frequently be remedied with intraluminal stenting or thrombolytic therapy. Stents have made it possible to apply angioplasty in a larger number of lesions (e.g., longer occlusions) and may improve long-term patency rates by reducing rates of restenosis. In our practice, approximately 20% to 25% of patients presenting with lesions in the aortoiliac segment can be effectively treated with iliac PTA with or without stenting. This technique is particularly useful in high-risk patients, those with critical ischemia secondary to multiple-level disease, and patients in whom iliac PTA can be combined with an infrainguinal bypass for limb salvage. Even in good-risk patients with focal iliac disease, however, PTA may be the preferred initial approach, with surgical intervention reserved for failures. If the presence of an appropriate lesion is suspected, PTA should be considered at the same time that the diagnostic arteriogram is performed. In the most recent development in the endovascular treatment of aortoiliac occlusive disease, stented

prosthetic grafts are placed in the diseased iliac segment through an open femoral artery cutdown. Early results are encouraging but far too preliminary to determine the eventual role of this new technique.

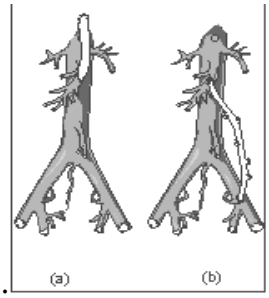
Endarterectomy

Endarterectomy was more commonly performed in the era before prosthetic graft conduits were developed. Currently, direct arterial repair is reserved for the management of focal atheroocclusive disease (type I) limited to the distal aorta and common iliac arteries (Fig. 6). When performed for this specific indication, aortoiliac endarterectomy can produce excellent long-term results, similar to those of aortofemoral grafting. Endarterectomy is less well suited for disease extending in the external iliac arteries and is to be avoided when aneurysmal degeneration complicates the primary atheroocclusive aortoiliac process

The aorta and common iliac arteries are exposed and vascular control is secured. During dissection, care is taken to preserve the autonomic nerves overlying the aortic bifurcation so that normal sexual function is not disturbed. The patient is then heparinized and atraumatic occlusion clamps or tapes are applied. Arteriotomies are made over the aorta and the common iliac arteries to expose the diseased lumen. The atherosclerotic plaque, along with the overlying intima and inner portion of the involved media, is removed. Good "breakoff" points for the removed plaques are needed to prevent postoperative thrombosis that results from the formation of an occluding flap of retained atheroma. The arteriotomies are closed by direct suture or with patch angioplasty, depending on vessel caliber.

Aortofemoral Prosthesis

Aortofemoral bypass is the most durable and reliable of all treatment options, for which reason it is the reference standard for the reconstruction of advanced aortoiliac occlusive disease (Fig. 7 and Fig. 8). The operative sequence starts with exposure of the abdominal aortic segment between the renal and inferior mesenteric arteries by means of appropriate retroperitoneal dissection and cephalad mobilization of the fourth portion of the duodenum and the left renal vein. Care is taken during dissection to avoid injury to the lumbar veins. Moreover, gentle handling of the dissected segment may lessen the risk for atheroembolism during the operation. The common, superficial, and deep femoral arteries are secured through separate groin incisions. Retroperitoneal tunnels are then developed between the exposed infrarenal aorta and the groins by means of blunt dissection. Care is taken to avoid injury to the bowel, particularly the rectosigmoid on the left. The tunnels are directed posterior to the ureter to avoid postoperative obstructive uropathy from graft limb compression of the ureter. A prosthesis of the appropriate size (polytetrafluoroethylene or Dacron) is selected, and the patient is heparinized. With an occluding clamp below the renal arteries and another just above the inferior mesenteric artery, the proximal anastomosis is performed as either an end-to-end or end-to-side graft to the aorta. The end-to-side technique has been found to be just as good, depending on the pattern of occlusive lesions and opportunity to perfuse the internal iliac arteries. The proximal anastomosis is placed as close to the renal arteries as practical to prevent future compromise of the bypass resulting from progression of atherosclerosis in the remaining infrarenal cuff. The limbs of the prosthesis are then delivered through the retroperitoneal tunnels into the groins. The distal anastomoses are performed to the common femoral arteries and may be carried into the deep femoral arteries as needed. The technique for distal femoral anastomosis is chosen to ensure adequate graft outflow, particularly if superficial femoral artery disease is present. In the patient with tissue loss secondary to type III or multiple-level aortoiliac disease associated with occluded superficial femoral arteries and compromised deep collaterals, concomitant distal reconstruction should rarely be required



. Fig. 7 (a) A bypass graft from the supracoeliac aorta to the superior mesenteric artery for revascularization in the management of intermittent mesenteric ischemia. (b) A bypass graft from the iliac to superior mesenteric artery, using a reversed segment of saph
enous vein, in the management of acute thrombosis with infarction.

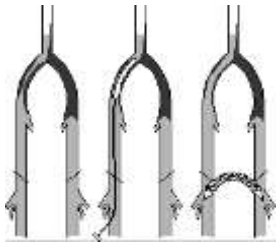


Fig. 8 Extra-anatomical bypass graft. Axillobifemoral bypass graft may be the procedure of choice in high-risk patients with aortic or bilateral iliac artery disease.Aortofemoral bypass has excellent 5- and 10-year graft patency rates of approximately 85% and 75%, respectively. Perioperative morbidity and mortality are reported to be below 10% and 5%, respectively, in many centers.

Axillofemoral Prosthesis

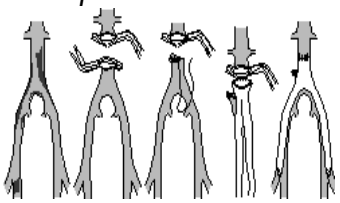


Fig.9 Method of aortobifemoral bypass graft: end-to-end proximal aortic anastomosis

Axillofemoral extraanatomic reconstruction has been utilized for revascularization in poor-risk patients or those with a hostile abdomen and has been reported to be an acceptable alternative to aortofemoral prosthesis. The axillary artery supplying the arm with the higher systolic blood pressure is usually chosen as the inflow vessel. The operative sequence starts with exposure of the most proximal part of the axillary artery through an infraclavicular incision and splitting of the pectoralis major muscle between its sternal and clavicular heads. The common, superficial, and deep femoral arteries are then dissected through groin incisions. The axillary or long limb of an externally supported polytetrafluoroethylene graft is then advanced behind the pectoralis major muscle and through a subcutaneous tunnel in the anterior axillary line connecting the axillary artery and the ipsilateral groin. Next, a crossfemoral-to-femoral limb of the graft is delivered through a subcutaneous suprapubic tunnel connecting the two groins. An anastomosis between the proximal axillary artery and the prosthesis is constructed in an end-graft to side-of-artery fashion. The graft is positioned parallel to the axillary artery and behind the pectoral muscles for the first 10 cm, before it enters the subcutaneous channel along the anterior axillary line. Following this plan seems to minimize traction on the anastomosis during arm movement and reduces the incidence of anastomotic disruption. The distal anastomoses are performed to the common femoral arteries and may be carried over or onto the deep femoral arteries to ensure adequate graft outflow.

The reported 5-year patency of the axillofemoral graft varies widely (30% to 80%) but is generally accepted to be lower than the patency of an aortofemoral prosthesis. The axillobifemoral bypass should therefore be reserved for patients with bilateral advanced aortoiliac disease who are either poor surgical risks or have a hostile abdomen.

Other Prosthetic Reconstructions

For high-risk patients with diffuse advanced disease limited to one iliac artery, unilateral femorofemoral or iliofemoral bypass may be employed to revascularize the ischemic extremity. If the contralateral iliac artery is normal or bears a lesion that is well treated by angioplasty/stenting, crossfemoral-to-femoral artery bypass is worthy of consideration. Iliofemoral bypass has a modest graft patency advantage over femorofemoral bypass (70% vs. 60%, respectively), but the main advantage is avoidance of a second groin incision and its associated complications. Femorofemoral bypasses are reserved for patients with occluded or heavily diseased common iliac arteries, in whom iliofemoral bypass is not advisable.

Angioplasty and Stenting

Since its introduction in 1963 by Dotter, the technique of intraluminal arterial dilation has evolved through various refinements and become more frequently applied. In a prospective, randomized trial comparing angioplasty and operative repair in the treatment of claudication (functional ischemia) secondary to iliac occlusive disease, operations produced successful outcomes at 3 years in 81% of the patients, versus 62% for angioplasty. When angioplasty was used to treat either functional or critical limb ischemia secondary to iliac occlusive disease, an overall success rate of 50% at 3 years was achieved. The same study identified four variables predictive of success. Specifically, angioplasty results were best when (a) performed for claudication, (b) limited to a common iliac lesion, (c) applied for stenosis rather than occlusion, and (d) good distal runoff was present. The results of angioplasty are suboptimal in cases with a residual pressure gradient, extensive plaque dissection, or significant recoil and residual stenosis, and the results can be improved by adding intraluminal stenting. In these cases, stenting may produce an incremental 10% improvement in the result of long-term angioplasty alone. Based on these findings, catheter-based interventions are currently reserved for the treatment of symptomatic short-segment stenoses of the common iliac arteries, either as primary treatment or as an adjunct to crossfemoral-to-femoral or femoral-to-distal graft reconstructions.

5. Materials for activating students during lectures (questions, problems, problem situations, etc.).

Case scenarios.

1. A 63-year-old car salesman is having difficulty doing his job. He works at a large, suburban used-car lot which is about 3 blocks long. When he walks about 1/2 a block, he gets severe cramping pain in his right calf, and must stop and rest for the pain to go away. As soon as he has walked another 1/2 block, pain recurs. He is the sole supporter of his family and he is about to be fired. He does not smoke. Establish the initial diagnosis.

A. Deep vein thrombosis
B. Protruded intervertebral disk.
C. Arthritis.
D. Intermittent claudication, from vascular disease.
E. Lerish's syndrome.

Explanation

Diagnosis: Intermittent claudication, from vascular disease.

2. A 25-year-old man is troubled by a periodic pain in legs. Objectively: on legs and thighs there are numerous cyanotic stains with phenomena of inflammation, local oedema which partly passes to the necrotic sites. Pulsation on the main arteries is saved. Ht: 45 %, prothrombin : 90 %, Fibrinogen A : 5,33 g/l, Fibrinogen B : ++. What from listed diagnoses is the most probable?

A. Thrombangitis obliterans
B. Atherosclerosis obliterans
C. Endarteritis obliterans
D. Raynaud's disease

E. Nodulated periarteritis

3. A 39-year-old man has been admitted with complaints to fast fatigability, cold sensation in the lower extremities and occurrence of a pain in the leg muscles at walking 300 m. The patient considers that he has been ill for 6 years and associates the onset of the illness with general overcooling. The patient's general state is satisfactory. P: 72 /min, is rhythmical. BP: 115/70 mmHg. Cardiac sounds are rhythmical. Skin of the lower extremities on the feet and on the lower third of the leg is with pale shade, is cold at touch, with poor hair growth on the leg; the skin is thin and dry. Pulsation on the arteries of the lower extremity is being defined on the femoral artery, on popliteal one it is weakened, on the feet arteries it is absent. Pulsation on the right femoral and popliteal arteries is satisfactory; on the foot arteries it is absent. What initial diagnosis is the most probable?

A. Nonspecific aorto-arteritis.
B. Atherosclerosis obliterans of the lower extremities.
C. Raynaud's disease.
D. Endarteritis obliterans of the lower extremities.
E. Diabetic angiopathy.

4. A 57-year-old man called the doctor of the ambulance at home because of acute pain, numbness, skin pallor, snap of the left limb suddenly appeared 40 minutes ago. Patient connects pain appearance with physical exertion (during digging in the kitchen garden). From the anamnesis it was found out, that he has been already marking difficult walking (a sign of «intermitting claudication") within 4 years. The doctor diagnosed acute arterial occlusion of the extremity. What is the cause of the disease in the patient?

A. Atherosclerosis obliterans of the extremity
B. Endarteritis obliterans
C. Deforming arthroso-arthritis of the extremity
D. Osteochondrosis of the lumbar compartment of the backbone
E. Chronic venous failure of the extremity

5. A 35-year-old man, a smoker, complains of periodic pains in fingers and toes after general overcooling of extremities that aggravate at excitement and during the cold year period. Objectively: the fingers and toes have cyanotic colour with insignificant oedema. Pulsation on the main arteries is saved. Blood glucose: 5,5 mmol/l. Establish the initial diagnosis.

A. Endarteritis obliterans
B. Thrombangiitis obliterans
C. Raynaud's disease
D. Atherosclerosis obliterans
E. Nodulated periarteritis

6. Methodological lecture support:

- classrooms №1;
- Equipment - media;
- illustrative material - slides.

7. **Questions for self-control:**

9. Classification of occlusive arterial diseases.
10. Pathological and anatomical features of arteries.
11. Methods of inspection of the patients with occlusive arterial diseases.
12. Tool methods of inspection of the patient with occlusive arterial diseases.

13. Tactics in the patient with occlusive arterial diseases.
14. Clinical presentations of occlusive arterial diseases.
15. Clinical presentations of complications. The indications, terms and types of treatment.

8. Literature used to prepare the lecture.

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Lecture №__5

Theme: " Ischemic abdominal syndrome. Mesenteric thrombosis. ".

1.Indroduction:

Mesenteric ischemia is classified as acute mesenteric ischemia (AMI) and chronic mesenteric ischemia (CMI). AMI is subdivided into occlusive and nonocclusive mesenteric ischemia. Occlusive mesenteric ischemia results from either thrombotic or embolic arterial or venous occlusion.

Approximately 80% of cases of AMI are occlusive in etiology, with arterial emboli or thromboses in 65% of cases and venous thrombosis in 15%. Arterial occlusions result from emboli in 75% of patients and in situ thrombosis cause the remaining 25%. Nonocclusive mesenteric ischemia is caused by low perfusion states and is responsible for 20% of AMI.

2. Aims of the Lecture: acquaint with aetiology and pathogenesis of mesenteric ischemia
- know variants of mesenteric ischemia and developments of haemodynamic infringements.
- know the basic attributes of these diseases.
- know additional methods of diagnostics.
- know opportunities of operative defects correction , indications to them and terms of performance of operation .

Basic concepts: mesenteric ischemia. Renal artery stenosis. Vascular disturbances in the gut. *Diagnostic techniques. Treatment.*

3.**Plan and structure of the lecture.**

#	Contents and units of the lecture.	Tasks in abstract levels.	Equipment of the lecture.	Time.
1	2	3	4	5
	Preliminary part			
1.	Determination of educational aims	I-10	Topic	3%
2.	Positive motivation	-“-	lecture.	2%
	Main part			
3.	Exposition of the lecture’s matter		Tables,	90%
	Plan:		schemes,	
	1. Definition of the pathology.	-“-	codograms,	
	2. General information about Mesenteric ischemia in Ukraine.	-“-	slides. Films.	
	3. Classification.	-“-		
	4. Methods of the patient’s examination and diagnostics of the Mesenteric ischemia.	-“-		
	5. Clinical course.	-“-		
	6. Organization of the surgical aid.	-“-		
	8. Working capacity. Rehabilitation.	-“-		
	Final part			5%
4.	Lecture summary			
5.	Lecturer’s answers to possible questions		Literature	
6.	Tasks for self-control		Questions.	

4.Contents of the theme

Chronic mesenteric ischaemia

The ability of the gastrointestinal circulation to develop collaterals ensures that the great majority of patients with arterial inflow obstruction are asymptomatic. It is generally believed that at least two of the three arteries which supply the gut (coeliac axis, superior and inferior mesenteric arteries) must be critically stenosed or occluded for symptoms to develop.

Clinical features. A typical complaint is of severe abdominal pain after eating – mesenteric angina. Fear of eating develops, so that mesenteric ischaemia is always associated with significant weight loss. This presentation mimics many other abdominal disorders, and frequently the patient has had numerous inconclusive investigations before the diagnosis is finally made. Apart from weight loss, which is universal, there are rarely any physical findings. Occasionally an epigastric bruit is present, but this is often audible in those who are otherwise normal.

Diagnosis and management. Although, in these slim patients, an experienced ultrasonographer can often identify mesenteric disease on duplex scanning, the diagnosis can only be made with certainty on angiography.

Surgical revascularisation is the mainstay of treatment, although balloon angioplasty and stent placement is playing an increasing role. The commonest operation is to take a graft from the aorta to the superior mesenteric artery and the coeliac axis. This is a major surgical undertaking and is associated with significant risk, but the long-term results are good. The alternative is often a slow and painful death from progressive cachexia.

Renal artery stenosis

Pathophysiological and pathological features. In most patients, renal artery stenosis (RAS) is asymptomatic and merely an incidental finding at postmortem or on angiography done for another indication. RAS leads to decreased renal perfusion and the release of renin from the juxtaglomerular apparatus. Renin converts angiotensinogen to angiotensin I, which is in turn converted to angiotensin II in the lung. Angiotensin II causes vasoconstriction and the release of aldosterone from the adrenal cortex. The renal excretion of sodium is reduced and blood pressure rises, which may in the short term return renal perfusion to normal. However, a progressive stenosis leads to worsening ischaemia, hypertension, loss of nephrons, atrophy and irreversible renal failure. The two main causes of RAS are atheroma (60%) and fibromuscular dysplasia (up to 40%). These two disease processes are quite different). Less common causes include renal artery aneurysm thrombosis and embolism arteritis and trauma. Angiogram showing almost compete occlusion of the left renal artery from atherosclerosis (arrow). This was successfully treated by percutaneous placement of a stent.

Clinical features. Renovascular hypertension affects a large number of people. For example, in the UK, approximately 10% of the adult population is hypertensive, and in these a renal cause is thought to be responsible for about 10%. Suggestive features are onset before the third and after the fifth decade and the presence of peripheral vascular disease. The hypertension is typically of abrupt onset, severe or malignant in nature and difficult to control with standard medical therapy.

Renal failure caused by RAS is much less common but it should always be considered in the differential diagnosis of renal failure, particularly when there is other evidence of peripheralvascular disease. Deterioration of renal function after administration of an angiotensin-converting enzyme (ACE) inhibitor may be the trigger for clinical detection because these drugs prevent the adaptive responses described above. Discontinuation of the ACE inhibitor usually returns renal function to pre-treatment levels.

Diagnosis. Renovascular hypertension can be successfully corrected by surgical and/or radiological means and will reduce the long-term complications of hypertension (stroke and heart failure), the need to continue lifelong anti-hypertensive medication and the risk of renal failure. Therefore it is important to make a precise diagnosis, but this can be difficult. Clinically suspected RAS is usually confirmed by angiography. Although many other less invasive and expensive investigations have been advocated, none is sufficiently sensitive or specific to be a satisfactory screening test. Occasionally the clinical significance of the diagnosis of RAS can only be confirmed by reduction in blood pressure and/or improvement in renal function after its correction.

Management. Medical. Drugs can control all but the most severe forms of hypertension and may limit hypertensive nephropathy in an unaffected contralateral kidney. However, medical treatment cannot arrest progression of stenosis, and information from non-randomised studies suggests that surgical correction is associated with an increased survival when compared with medical therapy. In particular, the risks of renal failure, stroke and myocardial infarction are reduced.
Surgical. Balloon angioplasty is now the first-line treatment of most cases of RAS, particularly that associated with fibromuscular dysplasia. Although restenosis is relatively common, the procedure can be repeated and is associated with less risk than open surgery. The long-term results of angioplasty are considerably better in non-ostial than in ostial lesions. Placement of a stent may offer better long-term patency in ostial disease. Open operation provides better long-term results than PTA but requires considerable surgical skill and is associated with a significantly greater morbidity and mortality. Operation is usually reserved for instances in which medical therapy and PTA have failed. The commonest operation is aortorenal bypass with long saphenous vein. Extra-anatomic renal revascularisation can also be achieved through hepatorenal and splenorenal bypasses. These procedures can be expected to provide long-term blood pressure control in 85–90% of patients with a mortality of less than 5% and a major morbidity of less than 10%. If there is a small non-functioning kidney, nephrectomy may be the only option. Acute thrombosis of a chronically stenosed renal artery may not lead to renal infarction, because of the development of collateral capsular supply, and surgical bypass or PTA with stenting can sometimes be successful.

Vascular disturbances in the gut

The blood vessels of the gut have extensive anastomoses. In consequence, considerable vascular obstruction to mesenteric arteries or the portal venous system may exist without any clinical effects. Acute presentation is the rule. Relatively rarely, chronic insufficiency occurs Severe acute ischaemia, whether from arterial or venous causes, results in haemorrhagic infarction. Blood and extracellular fluid are lost into the affected loop, so producing hypovolaemia; the haemodynamic effects are potentiated by release of cytokines. Full-thickness ischaemia leads to gangrene with perforation and peritonitis.
A more gradual (subacute or chronic) reduction in arterial input may not have effects on the resting bowel, but with the increase in flow that accompanies digestion, the bowel contracts inappropriately and absorption is interfered with. The usual cause is an atheromatous plaque with narrowing at the ostium of the superior mesenteric artery.
Acute presentation. This is often an overwhelming and highly lethal event.
Clinical features. There is severe acute colicky abdominal pain, vomiting, rectal bleeding (usually dark, altered blood) and symptoms of hypovolaemia. There may be a past history of an underlying disorder such as heart disease which could give rise to an embolus.
Clinical findings are hypovolaemia and signs of strangulation in the abdomen. Investigation and management. Similar investigations are done as for intestinal obstruction. Contrast-enhanced CT scan may be diagnostic. Intestinal perforation is absent, but air may be seen in a swollen bowel wall. Arteriography is occasionally indicated, but the condition is usually so urgent that operation is required.
Management is by restoration of circulating blood volume and exploration of the abdomen. If possible, the gangrenous loop or loops are resected, but involvement of the whole small bowel (and often the right colon) carries a high mortality and very poor prognosis. Primary anastomosis may be done or the ends of the bowel are exteriorised until it is certain that further infarction has not taken place. If the cause is embolic, it is very occasionally possible to remove the clot and re-establish flow.
Subacute and chronic presentation.Clinical features. The history is often vague and the diagnosis is not made for some time. Features are: 1.diffuse pain shortly after eating – so-called abdominal angina 2.loss of weight – partly from malabsorption but also because the patient reduces intake to avoid pain 3.occasionally diarrhoea.
The physical findings are non-specific. An abdominal bruit is sometimes detected on auscultation, but many abdominal bruits are not associated with vascular obstruction. Investigation and management.If the condition is suspected on clinical grounds, contrast-enhanced CT scanning or selective

angiography is done to outline the origins of the mesenteric vessels and plan treatment. Untreated, the symptomatic patient often goes on to acute mesenteric infarction. A direct attack on the obstruction can be made either at operation or by balloon angioplasty. Alternatively, a bypass graft is sometimes feasible.

Mesenteric arterial embolism

1. The median age of patients presenting with mesenteric arterial embolism is 70 years. The overwhelming majority of emboli lodge in the superior mesenteric artery (SMA). Emboli originating in the left atrium or ventricle are the most common cause of SMA embolism.
2. Risk factors include advanced age, coronary artery disease, cardiac valvular disease, history of dysrhythmias, atrial fibrillation, postmyocardial infarction mural thrombi, history of thromboembolic events, aortic surgery, aortography, coronary angiography, and aortic dissection. A previous history of peripheral emboli is present in 20%.
3. The disorder usually presents as sudden onset of severe poorly localized periumbilical pain, associated with nausea, vomiting, and frequent bowel movements. Pain is usually out of proportion to the physical findings and may be the only presenting symptom.
4. The abdomen may be soft with only mild tenderness. Absent bowel sounds, abdominal distension or guarding are indicative of severe disease.
5. Blood in the rectum is present in 16% of patients, and occult blood is present in 25% of patients. Peritoneal signs develop when the ischemic process becomes transmural.

Mesenteric arterial thrombosis

1. Thrombosis usually occurs in the area of atherosclerotic narrowing in the proximal SMA. The proximal jejunum through the distal transverse colon becomes ischemic.
2. SMA thrombosis usually occurs in patients with chronic, severe, visceral atherosclerosis. A history of abdominal pain after meals is present in 20-50% of patients. Patients are often elderly, with coronary artery disease, severe peripheral vascular disease, or hypertension.
3. SMA thrombosis presents with gradual onset of abdominal pain and distension. A history of postprandial abdominal pain and weight loss is present in half of cases. Pain is usually out of proportion to the physical findings, and nausea and vomiting are common.
4. Signs of peripheral vascular disease, such as carotid, femoral or abdominal bruits, or decreased peripheral pulses are frequent. Abdominal distension, absent bowel sounds, guarding, rebound and localized tenderness, and rigidity indicate advanced bowel necrosis.

II. Diagnostic evaluation of acute mesenteric ischemia

Leukocyte count is elevated in most cases of mesenteric ischemia. In patients with SMA emboli, 42% have a metabolic acidosis. The serum amylase is elevated in half of patients.

Plain radiography. Abdominal and chest x-rays help to exclude the presence of free air or bowel obstruction. In rare instances, plain films of the abdomen reveal signs of ischemic bowel such as pneumatosis intestinalis, portal venous gas, or a thickened bowel wall with thumb- printing. However, plain films will be normal in the majority of cases.

Angiography is the gold standard for the diagnosis of AMI and is also used for therapeutic infusion of the vasodilator, papaverine. After obtaining plain abdominal films to rule out the presence of free air or obstruction, angiography must be obtained, especially in those patients
in whom there is a strong clinical suspicion for AMI.

III. Emergency management

Stabilization and initial management

1. Patients with significant hypotension require rapid fluid resuscitation, and vasopressors may be used.
2. If hemoglobin is low, blood should be given. Patients who appear acutely ill should receive parenteral antibiotics to cover for gram- negative enteric bacteria as well as anaerobes after blood cultures are drawn.

Papaverine
1. Intraarterial infusion of papaverine into the superior mesenteric artery will increase mesenteric perfusion by relieving mesenteric vasoconstriction.
2. Papaverine is started at angiography and continued postoperatively if laparotomy is performed. The dosing is 60 mg IV bolus, followed by a 30-60 mg/h continuous infusion at a concentration of 1 mg/mL. Papaverine improves survival by 20-50%.
Acute mesenteric infarction with embolism
1. Once embolism is confirmed at angiography, papaverine infusion is started, then laparotomy should be performed to evaluate bowel viability. Surgical intervention may involve arteriotomy with embolectomy and bowel resection if nonviable necrotic bowel is found. Postoperative anticoagulation is recommended for all patients.
2. Patients without peritoneal signs with minor emboli, who achieve pain relief with vasodilator infusion, may be managed nonoperatively with repeated angiograms.
Acute mesenteric infarction with thrombosis
1. Acute mesenteric ischemia secondary to thrombosis is treated initially with a papaverine infusion started at angiography. Patients without peritoneal signs with minor thrombi may be treated with papaverine only.
2. Patients with major thrombi with good collateral vasculature, without peritoneal signs, may be observed in the hospital without a papaverine infusion. Patients with peritoneal signs and documented thrombosis

5. **Materials for activating students during lectures** (questions, problems, problem situations, etc.).

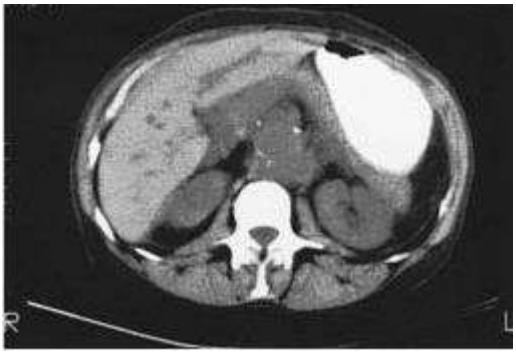
5.Case scenarios.

1. A 67-year-old woman with peripheral vascular disease, bilateral leg claudication, and hypertension comes to the clinic because of nausea and severe, diffuse abdominal pain that she rates as 7/10 in intensity for the past 2 days. The pain is related to meals, particularly lunch. She has smoked a pack of cigarettes per day for the past 30 years.
The patient has a temperature of 36.1 C/(97 F) with a pulse of 80/min and a blood pressure of 120/80 mm Hg. Abdominal examination demonstrates normal bowel sounds,
no tenderness, and no hepatosplenomegaly. Laboratory studies reveal a leukocyte count of 4,000/mm3 and a hematocrit of 47%. You should be immediately suspicious of
A. acute appendicitis
B. acute cholecystitis
C. malingering
D. mesenteric ischemia
E. ulcerative colitis

Explanation:
The correct answer is D. Mesenteric ischemia , although uncommon, must remain on the differential diagnosis of abdominal pain. The hallmark of mesenteric ischemia is pain out of proportion to physical exam findings. Mesenteric ischemia is especially likely in a patient with known vascular disease and a history of cigarette smoking. The next diagnostic step is a mesenteric angiogram. The superior mesenteric artery is the most often compromised vessel. Acute appendicitis (choice A) may

present with atypical symptoms in the elderly, but is usually present with a fever or elevated white blood cell count. Appendicitis is uncommon in the elderly.
Acute cholecystitis (choice B) should present with right upper quadrant pain and a positive Murphy's sign. Malingering (choice C) should be considered on the differential diagnosis for any patient complaint. It is, however, diagnoses of exclusion that must be entertained only when an extensive diagnostic work up is completed and is not suggestive of a disease process. Ulcerative colitis (choice E) should present with diarrhea, constipation, heme positive stools, and abdominal pain.

2. A 76-year-old woman is admitted with back pain and hypotension. A CT scan (shown below) is obtained, and the patient is taken to the operating room. Three days after resection of a ruptured abdominal aortic aneurysm, she complains of severe, dull left flank pain and passes bloody mucus per rectum. The diagnosis that must be immediately considered is



A. Staphylococcal enterocolitis
B. Diverticulitis
C. Bleeding AV malformation
D. Ischemia of the left colon
E. Bleeding colonic carcinoma

The answer is d. (Brewster, Surgery 109:447–457, 1991.) The CT scan reveals a fractured ring of calcification in the abdominal aorta with significant density in the paraaortic area. The inferior mesenteric artery (IMA) is always at risk in patients with the changes in the vessel wall characteristic of abdominal aneurysms, but particularly so in the presence of rupture and retroperitoneal dissection of blood under systemic arterial pressures. The incidence of ischemic colitis following abdominal aortic resection is about 2%. Blood flow to the left colon normally derives from the IMA with collateral flow from the middle and inferior hemorrhoidal vessels. The superior mesenteric artery (SMA) may also contribute via the marginal artery of Drummond. If the SMA is stenotic or occluded, flow to the left colon will be primarily dependent on an intact IMA. The IMA is usually ligated at the time of aneurysmorrhaphy. Those patients at highest risk for diminished flow through collateral vessels are those with a history of visceral angina, those found to have a patent IMA at the time of operation, patients who have suffered an episode of hypotension following rupture of an aneurysm, those in whom preoperative angiograms reveal occlusion of the SMA, and those in whom Doppler flow signals along the mesenteric border cease following occlusion of the IMA. Recognition of bowel ischemia at the time of operation should be treated by reimplantation of the IMA into the graft to restore flow.

3. A 67-year-old woman with peripheral vascular disease, bilateral leg claudication, and hypertension comes to the clinic because of nausea and severe, diffuse abdominal pain that she rates as 7/10 in intensity for the past 2 days.
The pain is related to meals, particularly lunch. She has smoked a pack of cigarettes per day for the past 30 years. The patient has a temperature of 36.1 C/(97 F) with a pulse of 80/min and a blood pressure of 120/80 mm Hg.
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Acute appendicitis (choice A) may present with atypical symptoms in the elderly, but is usually present with a fever or elevated white blood cell count. Appendicitis is uncommon in the elderly. Acute cholecystitis (choice B) should present with right upper quadrant pain and a positive Murphy's sign. Malingering (choice C) should be considered on the differential diagnosis for any patient complaint. It is, however, diagnoses of exclusion that must be entertained only when an extensive diagnostic work up is completed and is not suggestive of a disease process. Ulcerative colitis (choice E) should present with diarrhea, constipation, heme positive stools, and abdominal pain.

6. **Methodological lecture support:**

- classrooms №1;
- Equipment - Multymedia;
- illustrative material - slides.

7. **Questions for self-control:**

16. Classification of mesentery ischemia.
17. Pathological and anatomical mesentery ischemia.
18. Methods of inspection of the patients with mesentery ischemia.
19. Clinical presentations of mesentery ischemia.
20. Tactics in the patient with mesentery ischemia. The indications, terms and types of treatment.

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9. Clinical Anatomy and Operative Surgery=Клінічна анатомія і оперативна хірургія: Підручник для

мед. ун-тів, інст., акад. Рекомендовано Вченою радою Буковинського НМУ / О.М. Слободян, В.Ю. Єршов, Г.Ю. Костюк, В.І. Півторак; за ред. В.Ю. Єршова. — К., 2018. — 504 с.
13. Sabiston Textbook of Surgery. The Biological Basis of Modern Surgical Practice, 20th Ed. 2016
14. Hamilton Bailey's Physical Signs: Demonstrations of Physical Signs in Clinical Surgery, 19th Edition Paperback – Import, by John S.P Lumley (Author), Anil K. D'Cruz (Author), Jamal J. Hoballah (Author), Carol E.H. Scott-Connor (Author) 25 Feb 2016
15. Schwartz's Principles Of Surgery With DVD Hardcover – 2014 by F. Charles Brunicardi (Author), Dana K. Andersen (Author), Timothy R. Billiar (Author), David L. Dunn (Author), John G. Hunter (Author), & 2 More

Lecture №__6

Theme: " Diagnostics and treatment of acute and chronic diseases of peripheral veins of the upper and lower extremities. ".

1. Introduction:

Venous disorders are very common and especially affect the lower limb. Twenty per cent of the population suffer with varicose veins and 2 per cent have skin changes which may precede venous ulceration. At any one time 200 000 people in the UK have active venous ulceration. The provision of wound care and bandaging costs the National Health Service £600 million per annum.

2. Aims of the Lecture:

To know:

- anatomical and functional features of veins of the lower extremities;
- the general data of morbidity in Ukraine;
- classification of varicose disease of the lower extremities;
- clinical course and semiology of different forms of varicose diseases ;
- methods of patients' examination ;
- indications for conservative and surgical treatment ;
- methods of operative treatment;
- working capacity;
- rehabilitation of the patients.

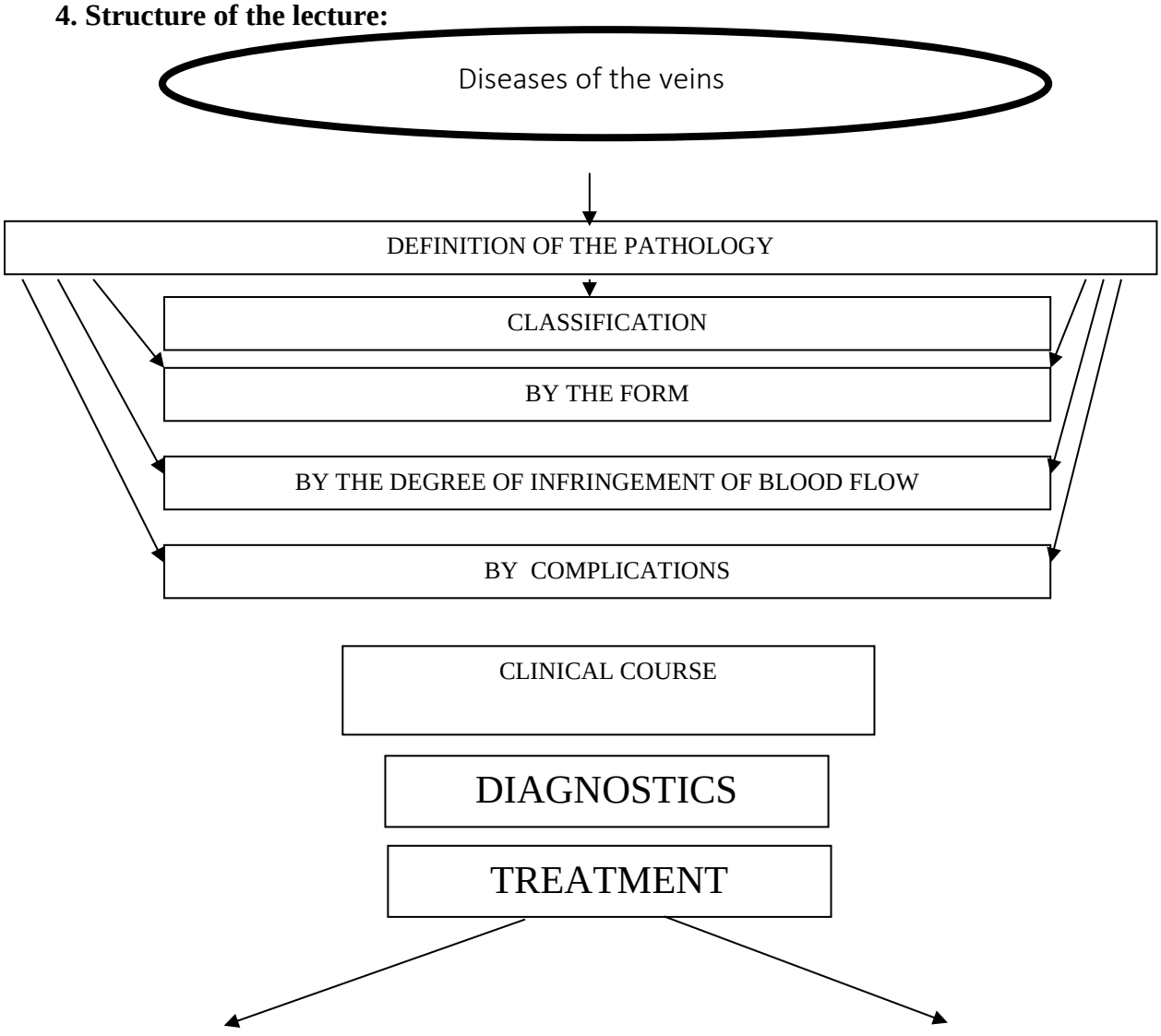
Basic concepts: veins of lower extremities. Venous pathophysiology. Venous Incompetence. Varicose Veins. Venous obstruction. *Diagnostic techniques. Treatment.*

3. Plan and structure of the lecture.

#	Contents and units of the lecture.	Tasks in abstract levels.	Equipment of lecture.	Time.
	Preliminary part			
1.	Determination of educational tasks		Theme of the lecture.	3%
2.	Positive motivation			2%
	Main part			

3.	Exposition of the lecture's matter Plan: 1. Anatomical and functional specifications of veins of lower extremities. 2. General information about morbidity in Ukraine. 3. Classification. 4. Methods of the patient's examination and diagnostics. 5. Clinical course of different forms and their complications. 6. Conservative and surgical treatment. 8. Working capacity .	 I-10 -"- -"- -"- -"- -"-	Tables, schemes, codograms, slides. Films.	90%
	Final part			5%
4.	Summary			
5.	Lecturer's answers to possible questions		Literature list	
6.	Tasks for self-control		Questions. Tasks.	

4. Structure of the lecture:



CONSERVATIVE

SURGICAL

WORKING CAPACITY AND REHABILITATION

Text of the lecture

Anatomy of the venous system in the limbs

Arterial blood flows through the main axial arteries to the upper and lower limbs. It returns via the deep and superficial veins. In the upper limb the superficial veins are more important in carrying blood back to the heart. In the lower limb, the superficial veins carry only about 10 per cent of the blood, while the remainder passes via the deep veins. The superficial veins lie superficial to the muscle fascia of the limb. The principal superficial veins in the leg are the long and short saphenous veins (Fig. 1).

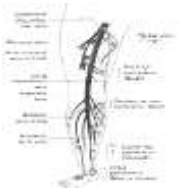


Fig. 1 The superficial veins of the lower limb.

In the arm, the cephalic and basilic veins are the principal superficial veins.

Interestingly, venous diseases occur much more frequently in the lower limb than in the upper limb, and most often in the superficial veins. The deep veins of the lower limb may be the site of life-threatening venous thrombosis or venous valvular incompetence resulting in leg ulceration. Each major axial artery has at least one and often a pair of accompanying veins named after the artery (Fig. 2).

Fig. 2 The main deep veins of the lower limb.

The superficial and deep veins join at a number of points. The short saphenous vein terminates at the saphenopopliteal junction (SPJ) and the long saphenous vein at the saphenofemoral junction (SFJ) in the groin. Here the flow in the superficial veins joins that in the deep veins. There is, in addition, a number of places in the calf and thigh where flow in the superficial veins may also join that in the deep veins. These is the ankle, calf and thigh communicating or perforating veins (Fig. 3).

Fig. 3 Lower limb perforating veins – points at which blood should flow from the superficial to the deep veins.

The names of these veins come from their course from the superficial to the deep venous system in which they perforate the deep fascia of the leg. Near the ankle are the Cockett perforating veins, near the knee the Boyd perforators and in the thigh the Hunterian perforating vein. All veins in the upper and lower limbs contain valves every few centimetres which ensure that blood flows towards the heart.

Venous pathophysiology

Blood flows into the leg because it is pumped by the heart along the arteries. By the time it emerges from the capillaries it is at a low pressure (about 20 mmHg), but this is enough for the blood to return to the heart. Blood from the muscles of the leg returns through the deep veins. Blood from the skin and superficial tissues, external to the deep fascia, drains via the long and short saphenous veins — SFJ and SPJ — and communicating veins into the deep veins. Valves prevent the flow of blood from the deep to the superficial system.

The venous pressure in the foot vein on standing is equivalent to the height of a column of blood, extending from the heart to the foot. However, the same is true of the arterial system so that on standing the arterial blood pressure at the ankle rises by 80—100 mmHg, depending on the height of the person. So the blood continues to circulate, even in the absence of muscle activity. However, we

also have a sophisticated series of muscle pumps that act as peripheral hearts in the venous system. These are made up of the deep veins of the calf and thigh which are surrounded by muscle. In addition, there is a foot pump which ejects blood from the plantar veins as pressure is placed on the foot during walking. On exercise the calf and thigh muscles contract compressing the veins and ejecting blood towards the heart. The direction of venous blood flow is controlled by the venous valves. The pressure within the calf compartment rises to 200—3 00 mmHg during walking and this is more than enough to propel the blood in the direction of the heart. During the muscle relaxation phase, the pressure within the calf falls to a low level and blood from the superficial veins flows through the perforating veins into the deep veins. The consequence of this is that the pressure in the superficial veins falls during walking. This can be monitored by a cannula placed in a superficial vein of the foot and connected to a pressure transducer. Normally the pressure in the superficial veins of the foot and ankle falls from a resting level of 80—100 mmHg to about 20 mmHg.

This ability to reduce the pressure in the superficial venous system is crucial to the health of the lower limb. Patients with damage to the veins in whom the superficial venous pressure does not fall during exercise may develop varicose eczema, skin damage and, eventually, leg ulceration.

Venous Incompetence - varicose Veins

One of the most common problems with the veins of the leg is failure of their valves. This occurs frequently in the superficial venous system resulting in varicose veins, which affect 10—20 per cent of the adult population in Westernised countries. In developing countries, where a primitive way of life is maintained, there is a very low incidence of varicose veins. The reasons for this difference are unclear but are probably related to differences in diet. A further major factor is inheritance: women in whom neither parent has varicose veins have a 10 per cent risk of developing varices, but when both parents are affected there is an 80 per cent chance. Men are affected less frequently than women.

The mechanisms that cause the superficial vein valves to fail have not been fully established. What appears to happen is that first a small gap appears between the valve cusps at the commisure (where the valve leaflets join the vein wall). This gap widens and more reverse flow (venous reflux) is allowed. The valve cusps degenerate and holes develop in them. Eventually they disappear completely (Fig. 4). The vein below the valve responds by dilating. Varicose veins may eventually reach five times their usual size if left to develop for long enough.

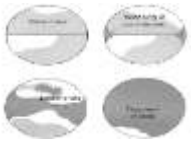


Fig. 4 Stages of development of venous valvular incompetence.

In the past it was thought that varicose veins were caused by anatomical abnormalities in the deep vein valves. It is now clear that this is not true. Varicose veins often develop in the calf when the veins above are normal. This seems to be a process where congenital and environmental factors accumulate to cause valve failure.

Varicose veins are thought to develop more often in people who stand during their work. People who sit or walk are at less risk of developing varices. They often develop during pregnancy under the influence of oestrogen and progesterone which cause the smooth muscle in the vein wall to relax.

Clinical features

Varicose veins are very common; they may either give no symptoms or cause aching and discomfort in the legs. Varices are recognised as tortuous dilated veins in the leg, but physiologically speaking a varicose vein is one which permits reverse flow through its faulty valves. Varices of the major tributaries of the saphenous veins or the saphenous veins themselves are large (5—15 mm diameter) and usually start in the calf (Fig. 5).

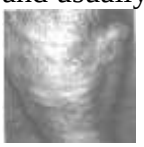


Fig. 5 Varicose veins.

Later varices of the long saphenous system may also appear in the thigh. Patients may develop much smaller varices. These range from 0.5-mm diameter vessels in the skin, which are commonly referred to as thread veins or dermal flares, and are usually purple or red in colour. Slightly larger veins (1—3

mm diameter) lying immediately beneath the skin may also present as small varicosities. These are usually referred to as reticular varices. The association of thread veins and reticular varices is frequently seen, and these probably reflect a type of varicose veins which is confined to the smallest size of vein. These tiny veins are associated with superficial venous incompetence in about 30 per cent of cases. They require different treatment from large varices. The combination of small varicosities and much larger truncal and tributary varices is often seen, but each type may occur on its own. The symptoms reported by patients affected by either type of varices are very numerous. Often there are no specific symptoms but the cosmetic appearance is unsatisfactory. Patients may also report aching especially on standing, itching, 'restless legs' and ankle swelling. The severity of the symptoms is unrelated to the size of the veins, and is often more severe during the early stages of development of varices.

Complications of varicose veins

Occasionally complications of varicose veins may develop. These include thrombosis, which is referred to as superficial thrombophlebitis. Usually this remains in the superficial veins and may cause considerable discomfort. Sometimes thrombosis extends into the deep venous system to cause deep vein thrombosis, although this is infrequent. Spectacular haemorrhage can occur when large superficial varices are damaged. This is easily controlled by lying the patient down, elevating the leg and applying a compression bandage. The most serious problem is venous ulceration which complicates varicose veins in less than 5 per cent of patients. However, it is a troublesome and painful condition which requires careful management if the ulcer is to heal.

Venous incompetence — deep vein incompetence

Valvular incompetence of the deep veins may develop in the same way as in the superficial venous system, with the degeneration of the valve cusps resulting in reverse flow in these veins. In other patients it may develop following a deep vein thrombosis. When the deep veins• fill with thrombus a new channel appears (recanalisation) after a number of weeks or months. However, the deep vein valves are destroyed by this process and, although the veins carry blood, the valves no longer work and reverse flow is allowed. Some veins are severely scarred by the recanalisation process so that they also become very narrow and ineffective at carrying blood. Occasionally veins fail to recanalise at all. This is sometimes seen following a venous thrombosis in the iliac veins. Under these conditions the blood must find an alternative way round the blockage and collateral veins develop. In the leg the long and short saphenous veins may act as collateral channels and may double in size to accommodate the additional blood flow. In patients with chronic iliac vein occlusion large suprapubic or abdominal varices may be seen carrying the collateral flow.

Clinical features of deep vein incompetence

A number of patients with severe deep vein damage has little to show for their problems. In patients with venous valvular incompetence the calf muscle increases in size, apparently in response to the greater work in returning blood from the leg. There may be some ankle oedema, especially in those patients who have persistent venous obstruction. A proportion of patients develops skin complications. These may range from mild eczema to severe ulceration. An early sign of skin injury is brown pigmentation due to haemosiderin deposition in the skin. This occurs because the high venous pressures which result from damage to the muscle pumping mechanism cause red blood cells to be forced out of capillaries in the skin where their haemoglobin breaks down to form haemosiderin. A later and more serious stage is lipodermatosclerosis in which palpable induration develops in the skin and subcutaneous tissues. This particularly affects the gaiter area of the leg, just above the malleoli, and may be the precursor of leg ulceration. Contraction of the skin and subcutaneous tissues is seen and the ankle becomes narrower. The combination of a narrow ankle and prominent calf is often referred to as a 'champagne bottle leg' (Fig. 6). Atrophie blanche may also develop. In this condition the superficial blood vessels are lost from the skin and white patches develop. These indicate that the skin has been severely damaged by the venous valvular incompetence. Venous ulceration may develop in these areas.

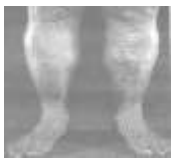


Fig. 6. Lipodermatosclerosis (scaring) and haemosiderosis (brown pigmentation of the skin) in a patient with venous disease.

Patients may remain untroubled by many of these symptoms and may not seek medical advice until venous ulceration develops. Even then, it is thought that less than half of the patients with venous leg ulcers are known to their general practitioners (Fig. 7).

Fig. 7 Venous ulceration.

Effects of deep and superficial venous
incompetence on the vascular physiology of the leg

When the venous valves fail, the ability of the muscle pumps to reduce the pressure in the leg is decreased. Following muscle contraction blood may return to the leg rapidly by flowing in the reverse direction along deep or superficial veins. Incompetence of the deep veins usually has a more severe effect on the venous physiology than does superficial venous incompetence as the deep veins are much larger than the superficial veins. The effect of reverse flow in the deep or superficial veins is to prevent the superficial venous pressure from falling during exercise. This is referred to as 'ambulatory venous hypertension' and is the main cause of venous leg ulceration. Persistently raised venous pressure tracks back to the microcirculation of the skin and causes skin damage that eventually may result in venous ulceration.

In some patients veins remain permanently blocked following a deep vein thrombosis leading to the blood experiencing difficulty leaving the leg. This usually causes worse symptoms than venous valvular incompetence alone. Swelling of the leg, especially ankle oedema, is often a feature in patients with persistent venous obstruction. In many cases the passage of time allows deep veins to recanalise and the ankle oedema may then become less severe. However, the recanalised veins are likely to be incompetent and the features of venous hypertension may then predominate.

How does ambulatory venous hypertension cause leg ulceration?

The damage caused by venous hypertension in patients with venous disease is confined to the skin and subcutaneous tissues. The main focus of the damage is in the capillaries in the skin. These increase in size and length, and become very convoluted and are described as 'glomerulus like'. The amount of capillary endothelium is increased in the skin and many more capillary loops are cut on histological sections of damaged skin. This results in the development of a fibrotic process affecting the skin and subcutaneous fat which comprise the condition of lipodermatosclerosis. Around the capillaries are many inflammatory cells, especially macrophages. The combination of capillary proliferation and inflammation accounts for the appearance of liposclerotic skin, which looks inflamed. A perivascular cuff is present around the capillaries, which is made up of many connective tissue proteins including fibrin, collagen IV and fibronectin. This perivascular cuff is probably the result of chronic inflammation and occurs in many other types of inflammatory processes. It was originally thought that the fibrin cuff acted as a barrier to diffusion preventing nutrient exchange between the capillaries and the tissues. The 'flbrin cuff' hypothesis was accepted for many years as the explanation for venous ulceration. Research and theoretical calculations have shown that there is no physical barrier to the diffusion of nutrients to the tissues in this condition.

The factors which cause the inflammatory process have been sought. It has been shown that venous hypertension causes leucocyte sequestration in the microcirculation of the leg. Patients with chronic venous disease resulting in lipodermatosclerosis and venous ulceration trap more leucocytes than do subjects with normal limbs. It has been shown that these 'trapped' leucocytes become activated and release the proteolytic enzymes that are normally used in defence against infection. This, in turn, causes injury to the capillary endothelium. It seems likely that inappropriate activation of leucocytes instigates the series of events that results in leg ulceration. The frill mechanism is incompletely understood and further investigation of the processes involved may eventually lead to the development

of better treatments for venous ulceration. This mechanism is referred to as the 'white cell trapping hypothesis' and was first proposed in 1988.

Investigation of venous disease

A full history should always be taken, enquiring about any injury to the leg or swelling which may suggest a previous episode of deep vein thrombosis. Patients report a wide range of symptoms associated with venous disease. These include tiredness, aching, tingling and ankle swelling which get progressively worse towards the end of the day and are relieved by elevating the leg. Sometimes patients report cramps in the legs, which are usually worse at night. Patients with more severe venous disease may notice the skin changes that occur. Pain in the calf on walking is usually attributable to lower limb arterial disease, referred to as intermittent claudication. Patients with severe deep vein obstruction may also develop bursting pain in the calf on walking, due to the very high venous pressures that may occur under these conditions.

A clinical examination carried out with the patient standing will reveal the extent of any varicose veins and whether they are associated with the long or short saphenous systems. Further information may be gained by using a tourniquet test (Brodie, 1846; Trendelenburg, 1890) to determine the source of varices. The tourniquet is often replaced by the hand of the examiner used to compress the long or short saphenous vein. The patient lies and the leg is elevated to empty the veins. The tourniquet is applied high on the thigh and the patient stands again. The speed at which the varices fill is observed. In the case of varices from the long saphenous vein these fill within a few seconds without a tourniquet, but with the trunk of the long saphenous vein compressed in the thigh much slower filling takes place over 15 or 20 seconds. If filling is not controlled by an above-knee tourniquet, then a tourniquet is applied to compress the short saphenous vein, just below the knee. If the varices now fill slowly then the source of venous reflux is from the SPJ. If the varices continue to fill rapidly some further source must be the cause. The patient may have incompetent deep veins or a calf perforating vein. The success of tourniquet tests lies in the ability of the examiner to assess the varices and their rate of filling. This may be easy in the case of large varices, but can be vary difficult with smaller varices. Considerable practice is required for successful application of these tests (Fig. 8).

Fig. 8 Tourniquet tests used in the diagnosis of superficial venous incompetence.

The clinical examination should continue by noting the presence and extent of any skin changes or ulceration at the ankle. An examination of the peripheral pulses should be carried out. Venous and arterial disease of the lower limb often coexist, especially in more elderly patients. An abdominal examination completes the clinical examination in patients presenting with lower limb varices, as these may occasionally be the result of an abdominal neoplasm causing venous obstruction.

More detailed information than can be obtained from clinical examination is useful in the management of patients with primary varicose veins and essential in the management of patients with recurrent varices, a history of lower limb venous thrombosis or venous leg ulcers.

Doppler ultrasound

A Doppler assessment is now the minimum level of investigation required before treating somebody with venous disease. A Doppler flow probe can be used to exclude arterial disease and to determine the patency of a vein, and a bidirectional flow probe used to detect venous reflux. This investigation is carried out with the patient standing. The Doppler probe is first placed over the SPJ and the blood flow assessed to locate the venous flow in the common femoral vein. With one hand the examiner gently squeezes the calf to produce an acceleration of blood flow in the veins. This is heard as a 'whoosh' from the loudspeaker of the Doppler machine. The calf compression is released and any reverse flow in the veins sought. With practice it is possible reliably to identify venous reflux in the SFJ. The examination may be repeated with the probe held over the long saphenous vein in the mid-thigh region, to confirm that the venous reflux lies in the superficial vessels. Some surgeons use a tourniquet to occlude the superficial veins, in the same way as when performing a Trendelenburg test. The probe may also be held over the SPJ while the calf is compressed and released to test the

competence of veins in this region. In the popliteal fossa it is more difficult to distinguish between deep and superficial venous incompetence (Fig. 9).

This method is very useful when examining patients with primary varicose veins, especially those which are thought to result from SFJ incompetence. The popliteal fossa contains many veins and if venous reflux is heard it is difficult to be certain from which veins it arises. However, in patients with primary varices saphenopopliteal incompetence is usually readily identified. All surgeons who regularly treat patients with varicose veins should be competent at this type of investigation. Where the source of recurrent varices or a leg ulcer is sought, duplex ultrasonography is usually more reliable.

Fig. 9 Doppler ultrasound examination of the venous system of the lower limbs.

Photoplethysmography and other plethysmographic techniques

In this investigation a probe is attached to the skin to assess venous filling of the surface venules by measuring light transmission of the skin. The filling of these vessels reflects the pressure in the superficial veins of the leg. The patient sits quietly until the trace stabilises. Then he or she performs a series of 10 dorsiflexions at the ankle. The venous pressure falls in the superficial veins of the leg and the skin venules empty, so the photoplethysmography (PPG) trace falls. The patient then sits and the veins refill. Under normal conditions venous refilling occurs through arterial inflow alone, a slow process taking 20 or 30 seconds when the limb is at rest. In patients with venous incompetence the veins also fill via venous reflux, which speeds the refilling process. Fast refilling times mean that one or more veins in the leg are incompetent. The test can be repeated after the application of a tourniquet above the knee to occlude the long saphenous vein, and then below the knee to occlude both the long and short saphenous veins. This helps to establish which set of superficial veins is incompetent (Fig. 10).

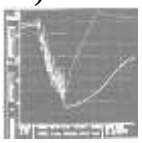


Fig. 10 Photoplethysmography traces demonstrating normal refilling. Lower trace: abnormal refilling in a patient with superficial venous insufficiency.

A number of other plethysmographic tests is used t evaluate the venous system physiology including the ai plethysmograph, light reflex rheography and strain gaug plethysmograph. These are usually used by vascular surgeon in vascular laboratories or by specialists in venous diseases All are used to quantify the impairment of venous function caused by obstructed or incompetent venous valves.

Duplex ultrasound imaging

This technique involves the use of high-resolution B-mode ultrasound imaging and Doppler ultrasound to obtain images of veins and simultaneously measure flow in these vessels. It allows direct visualisation of the veins and provides functional, as well as anatomical, information. Modern duplex ultrasound machines represent blood flow as a colour map which is superimposed on the greyscale image of the vessel. This technique is highly reliable in the investigation of arteries and veins, and is the most appropriate investigation to use when detailed analysis of the anatomy and physiology of the venous system is required.

The examination is performed with the patient standing. In this position the veins are filled and easily seen on the ultrasound image. The flow in the veins is assessed in exactly the same way as when using a hand-held Doppler probe. The examiner images the vein that he or she wishes to study and compresses the calf with his/her hand to produce forward flow. This results in upward flow towards the heart in a normal vein, and is shown as blue in the colour flow map. The calf is then released to test the competence of the valves. Competent veins show no flow, but incompetent veins allow reverse flow which is represented as red in the colour flow map. All lower limb veins may he imaged with ease using modern ultrasound machines, and therefore the patency and competence of all lower limb veins may be tested. The examiner steadily works his/her way from the groin to the ankle testing each major deep and superficial vein along the limb. This allows a comprehensive map of the veins to the leg to be constructed. Blocked or incompetent veins can be readily identified by a skilled vascular

technologist. The origin of varicose veins and venous ulceration can be identified, and in patients with suspected deep vein thrombosis the presence of thrombus can be seen (Figs 11,12).

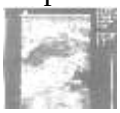


Fig. 11 Deep vein thrombosis in the popliteal vein. Blood attempting to flow round the thrombus, seen here as a filling defect.

Fig. 12 Flow through the popliteal vein. Forward flow is demonstrated on the left. On release of the calf compression reverse flow is seen on the right indicating venous reflux.

Venography

This investigation is the X-ray equivalent of duplex ultrasonography. Historically it preceded ultrasonography and has been widely used in the past for the assessment of patients with vein problems. An ascending venogram is performed by canulating a vein in the foot in order to inject X-ray contrast medium. A narrow tourniquet is applied just above the malleoli to direct blood flow into the deep veins and an injection of nonionic contrast material given to outline the veins. The technique provides excellent anatomical information but gives much less information about the veins where the valves have failed. It is a useful examination for suspected deep vein thrombosis where ultrasonography is not available.

Incompetent veins can be shown by descending venography. Here a cannula is inserted in the femoral vein and contrast material injected with the patient standing. The contrast material is heavier than blood and flows down the limb though incompetent valves. Both ascending and descending phlebography is required to establish as much information as is provided by duplex ultrasonography. The source of recurrent varicose veins may be identified by a varicogram. Contrast material is injected into one of the varicosities and followed to identify its source. Again, duplex ultrasonography has largely replaced this investigation (Fig. 13).

Fig. 13 Example of a venogram.

<u>Management of patients with varicose veins</u>

A history should be taken from the patient to find out how long the varices have been present and if any event seemed to cause them. A history of previous lower limb deep vein thrombosis should be sought. Venous thrombosis may follow lower limb fractures, so this also should be asked about. Superficial varices which develop after a venous thrombosis may be the only route of venous drainage in the lower limb and should not be removed until the patency of the deep veins of the limb has been shown. Patients may also have received previous surgical or other treatment for their varices. Any previous treatment may greatly alter the surgical management of the patient. When the SFJ has been ligated previously, a further operation here is technically much more demanding for the surgeon and should not be performed unless recurrence at the previous operation site has been conclusively demonstrated. Unfortunately, patients often have only a vague recollection of their previous vein operations and therefore diagnostic ultrasound imaging or venography is essential to establish the anatomy and source of varices in patients with recurrent varicose veins.

Clinical examination should establish the extent and size of varices, as well as the presence of any associated skin changes. Tourniquet tests should be used to decide the location of venous incompetence. All patients considered for surgical treatment of their varices should be examined using a hand-held Doppler ultrasound device to confirm the source of the varices.

Patients with recurrent varices or a history suggestive of previous venous thrombosis and any patient with skin changes should be fully investigated using duplex ultrasonography or venography. The presence of ankle pulses should be confirmed by palpation or, if necessary, by measuring the ankle blood pressure using Doppler ultrasound.

The treatment of varicose veins following a proper assessment may include reassurance, the use of elastic compression stockings, injection sclerotherapy or surgical treatment. The treatment of choice depends on the size of the varices, their extent and the symptoms that they produce.

Compression stockings

The symptoms of varicose veins may be relieved by the use of compression stockings. These are available for the treatment of venous disease in three grades of compression, classes 1—3. Light compression stockings may be helpful in the early stages of varicose veins but do not prevent the development of more varices or result in the disappearance of veins.

Injection sclerotherapy

This treatment is best used in the management of small varices and those where the main long and short saphenous veins, and their major tributaries, are competent. This type of treatment is also effective where the larger varices have been removed surgically and only small varices remain. In the past, sclerotherapy has been used in the management of incompetence of the main saphenous trunks. Evidence suggests that varicose veins managed in this way recur much more rapidly than following surgical treatment.

The basis of sclerotherapy is that a solution which destroys the endothelial lining of the veins is injected. In the UK the most widely employed drug is sodium tetradecyl (STD), which chemically is a soap. To be effective, the sclerosant has to be given into an empty vein that is compressed immediately after the injection has been given to avoid the development of thrombosis within the vein. It is easy to produce thrombophlebitis which can recanalise and result in the recurrence of the varices. The aim is to produce sclerosis with the vein being replaced by a fibrous cord, incapable of recanalisation and recurrence.

Complications

The complications of this treatment include skin pigmentation and ulceration if the sclerosant is not injected within a vein. Small regions of thrombophlebitis are often seen during a course of sclerotherapy. Deep vein thrombosis develops only rarely.

Microsclerotherapy

Thread veins and reticular varices may he treated by injection through a very fine needle, a treatment referred to as ‘microsclerotherapy’. Very dilute sclerosing solutions are used. The most frequently employed drugs used for this are STD and polidocanol. A skilled practitioner can insert a 30G needle into dermal flares and successfully eradicate these tiny veins. Compression bandaging is usually applied after this treatment for 1—5 days. Treatment of these veins is normally regarded as a cosmetic procedure.

Surgical treatment of varicose veins

Surgical treatment of varicose veins is widely used and is effective in removing varicose veins of the main saphenous trunks, as well as their tributaries, down to a size of about 3 mm. Veins smaller than this are best treated by sclerotherapy. Surgical removal of varices is inappropriate where these form a major part of the venous drainage of the limb, for example where a deep vein thrombosis has destroyed the main axial limb veins and the patient relies on the superficial veins. This possibility may be suggested by the patient’s medical history and can be confirmed by duplex ultrasonography or venography.

The main principles of surgical treatment are to ligate the source of the venous reflux (usually the SFJ or the SPJ) and to remove the incompetent saphenous trunks and the associated varices. Sapheno-femoral ligation alone, sometimes referred to as a ‘Trendelenburg procedure’, is associated with a high

rate of recurrence of varices. Recent research has shown that it is necessary to remove the long saphenous vein to ensure that as much venous reflux as possible is eliminated. Similarly, communications between the many deep veins in the popliteal fossa and the short saphenous vein mean that some patients develop recurrences in the short saphenous vein due to the re-establishment of reflux from these veins. This problem may be eliminated by removing the short saphenous vein. Removal of the saphenous veins has the disadvantage that both veins are accompanied by a nerve that may be damaged in the vein stripping operation. To avoid nerve injury the long saphenous vein should not be removed below mid-calf level and great care should be exercised in removing the short saphenous vein.

Venous anatomy is particularly variable, and for some veins preoperative vein localisation is very helpful. The termination of the short saphenous vein may lie from 2 cm below the knee to 15 cm above the knee. Its course and termination can be readily identified by ultrasound imaging and marked on the skin with an indelible pen before the operation, reducing the risk of damage to nerves and arteries in the popliteal fossa. Perforating veins in the calf and thigh, and residual segments of the saphenous veins left after previous venous surgery, can also be localised in this way.

Technique of saphenofemoral junction ligation

An oblique incision is made in the groin commencing over the femoral artery and extending 4 cm medially. The long saphenous vein is exposed and the common femoral and superficial femoral veins are identified before dividing the long saphenous vein. Having divided the long saphenous vein, all branches should then be isolated and divided. The SFJ should be tied flush with the femoral vein. Any tributary of the saphenous vein or femoral vein left in this operation may be the source of a future recurrence, so it is important that all are ligated and divided. It is important that the femoral vein is inspected carefully for at least 1 cm above and below the SFJ, and any tributaries ligated and divided. The conventional way of removing the saphenous vein is with a Babcock stripper. This consists of a flexible wire which is passed down the long saphenous vein. The end is identified in the upper third of the calf and a 2-mm incision is made to retrieve the stripper. An olive about 8 mm in diameter is attached to the upper end and the saphenous vein is removed by firm traction on the wire in the calf. More recently ‘inverting’ or ‘invaginating’ stripping has become popular. The aim here is to reduce the damage to the tissues around the vein leading to less bleeding and postoperative pain. This may be done in a number of different ways. A rigid metal ‘pin-stripper’ has recently been developed (Fig. 14).

Fig. 14 Oesch pin-stripper. A small notch at the back (above) indicates the direction of the small tip (below).

This is passed down the inside of the saphenous vein and recovered through a small incision in the upper part of the calf. A strong suture is attached to the end of the stripper and firmly ligated to the proximal end of the vein (Fig. 15).

Fig. 15 The vein does not directly attach to the end of stripper and this allows the vein to be inverted.

Pulling gently on the stripper, the long saphenous vein will invert and can be delivered through a 2-mm incision in the mid-calf region (Fig. 16.). No olive is used and the technique relies on the strength of the vein. Should the vein break, an instrument with a small olive on one end is used to recover the remaining saphenous vein.

Fig. 16. This figure illustrates recovery of the metal stripper through a small 1.5-mm incision.

Technique of saphenopopliteal junction ligation

Accurate preoperative ultrasound localisation of this junction makes the operation easy, as the position of the SPJ is notoriously variable. A skin incision is made over the junction and the deep fascia incised to reveal the short saphenous vein beneath. The vein is followed to the SPJ, where the short saphenous vein enters the side of the popliteal vein. The vein can then be ligated and divided

close to the popliteal vein. This operation may not be enough to eliminate venous reflux in the short saphenous vein because communication with the gastrocnemius (muscle) veins in the calf is often present and may lead to further varicosities arising from the short saphenous vein. Many surgeons now routinely strip the short saphenous vein to prevent this problem. This is best done using an inverting technique as the sural nerve lies close to the vein and may be damaged if a large olive is used.
A pin-stripper (Oesch) is passed down the short saphenous vein as described above for the long saphenous vein. This is recovered through a 2-mm incision made at the mid-calf level. A heavy suture is used to attach the vein to the upper end of the stripper and gentle traction applied to the stripper. The inverted vein appears in the calf incision.

Removing superficial varices

Varicose veins do not disappear following saphenous vein stripping and should be removed through small incisions. It was standard practice to insert artery forceps through the incision in order to remove varices. However, this necessitates long incisions in the leg which require suturing and are unsightly. European phlebologists have developed instruments to minimise the size of incision required for this procedure. The technique is referred to as 'hook phlebectomy' and uses small hooks which may be inserted through incisions of only 1—2 mm. The hook is used to capture a small section of a varicosity and bring it to the surface where is may be grasped using a large artery forceps; the remaining vein is then teased through the tiny incision. The aim is to remove all the varicosities through incisions that require no suture. Closure of the incisions is achieved using adhesive strips or dressings. The cosmetic outcome from this procedure is excellent.
The results of varicose vein surgery depend on the care taken with the preoperative assessment, the preoperative marking and the determination of the surgeon to remove all the superficial varicosities. Patients may complain of symptoms of varicose veins, but most remain unsatisfied until they achieve a good cosmetic result following treatment!

Postoperative management

Compression bandaging is applied to the limb at the end of the operation to prevent excessive bruising. In fact, some surgeons apply compression to the limb before stripping the long saphenous vein. After 1 or 2 days the bandages may be replaced by a thigh-length high compression stocking (class 2 compression is appropriate). This can usually he removed easily to allow the patient to take a shower and can then be reapplied.

Complications of varicose vein surgery

Bruising and discomfort are common following removal of varices, especially where the veins were of very large diameter. However, the pain usually requires only mild analgesics.

Sensory nerve injury is seen occasionally after removal of varicose veins. The saphenous nerve and its branches accompany the long saphenous vein in the calf, the suraJ nerve accompanies the short saphenous vein. Damage to the main part of these nerves occurs in about 1 per cent of operations, but small areas of anaesthesia may occur more frequently (in up to 10 per cent of patients). The adoption of inverting stripping techniques and avoidance of stripping the long saphenous vein below mid-calf level have reduced the risk of damage to these nerves. All patients should be warned before surgery that they may experience small areas of numbness and tingling after the operation. These changes are usually reversible but can be quite persistent.
Motor nerve injury is an uncommon complication of varicose vein surgery and may occur during exploration of the popliteal fossa if care is not taken to protect the nerves in this region. Preoperative ultrasound localisation of the short saphenous vein helps in limiting the extent of the dissection in this region and risk to the nerves during dissection. Venous thrombosis is often seen in residual varices following varicose vein surgery and resolves without the need for specific treatment. The risk of this is reduced if all visible varices are removed at the time of surgery. Deep vein thrombosis occurs in about one operation per 1000 following varicose vein surgery. The factors which result in increased risk are described below. Patients who have previously suffered a deep vein thrombosis seem to be particularly at risk and should receive full prophylactic measures, usually low-dose subcutaneous heparin in addition to compression stockings. Patients receiving oestrogen treatment may also be at increased risk of venous thrombosis, and heparin prophylaxis should be considered.

Venous reconstructive surgery

Surgery to the deep veins is limited by the absence of suitable prosthetic grafts or any satisfactory way of creating a venous valve. Surgery may be carried out for venous occlusion and for deep venous insufficiency. Patients who might be considered for these procedures include those who have persisting swelling of the lower limb after a previous venous thrombosis, even when a number of years has passed and collateral veins have had the opportunity to develop. The presence of a functional obstruction must be confirmed using direct venous pressure measurements. In the case of suspected iliac vein obstruction, the pressure in the femoral vein is measured with the patient lying supine. If there is a substantial rise in venous pressure during exercise then venous obstruction is confirmed. An alternative method is to measure the venous pressure in the hand and foot veins with the patient lying supine (the Raju test). Normally the foot venous pressure is the same as the hand venous pressure or no more than 5 mmHg greater. If venous obstruction is present the pressure difference is greater, with pressure differences of 10—15 mmHg indicating significant venous obstruction

Venous obstruction

In patients with venous obstruction venous bypass procedures can be performed. Simple bypass with vein or prosthetic material may be used in the larger vessels, such as the iliac veins and vena cava. One problem is to find a vein of large enough calibre to insert in this region. These are sometimes constructed from opened out sections of saphenous vein reconstructed as a spiral graft. Alternatively a Palma operation can be carried out. This involves mobilising the long saphenous vein in the opposite leg, tunneling the distal end of the long saphenous vein across suprapubically and inserting it into the femoral vein below the obstruction. Blood then drains from the affected leg via the long saphenous vein into the femoral vein in the opposite leg (Fig. 17).

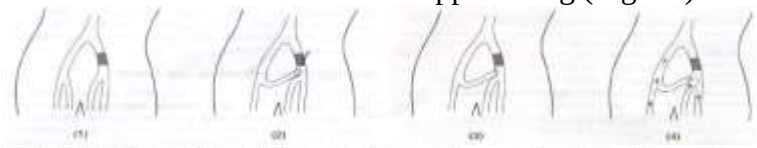


Fig. 17 Palma procedure – a femorofemoral vein graft constructed from the saphenous vein.

In patients who have obstruction of the superficial femoral vein, the long saphenous vein may be connected to the popliteal vein in the same limb, allowing blood to flow along the superficial veins more easily (May—Husni procedure). However, in the majority of patients with chronic superficial femoral vein obstruction, the blood flows along the long saphenous vein to reach the groin and therefore this operation is not required.

Venous incompetence

The surgical treatment of deep venous insufficiency remains a difficult problem that is dealt with in a few centres. Venous valves in the deep veins may be repaired if their incompetence is a consequence of primary valve failure. Kistner has described two methods of repairing incompetent valves, and successful completion of this operation may lead to long-term maintenance of leg ulcer healing. However, the operations are technically difficult and there is a risk of thrombosis which may destroy the reconstructed valve (Fig. 18). In patients who have previously suffered a deep vein thrombosis, transplantation of a segment of axillary vein has been carried out. This is usually attempted in patients who have damage to the deep veins following a previous venous thrombosis. The risk of further episodes of venous thrombosis makes the likely success of such operations as low as 50 percent

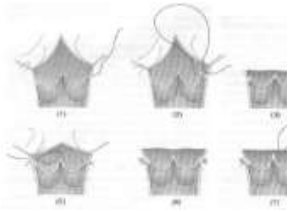


Fig. 18 Kistner-type valve repair f

5. Materials for activating students during lectures (questions, problems, problem situations, etc.).

Case scenarios.

1. In a 60 years old who suffers from varicose veins of the lower extremities a pain and oedema has appeared in the left leg in a day later after insignificant trauma of the leg. The body temperature increased to 37,5°C . Along the big subcutaneous vein on the leg a hyperaemia and a painful cordlike site of induration is being defined. Establish diagnosis.
   A. Haematoma
   B. Acute phlebitis
   C. Lymphangitis
   D. Acute thrombophlebitis
   E. Erysipelas inflammation

2. In a 42-year-old woman primary varicose dilatation of the right big saphena vein with valve insufficiency was diagnosed. What kind of operation is the most rational?
   A. Troyanov – Trendelenburg's, Babcock's, Narat's operation,
   B. Troyanov – Trendelenburg's operation
   C. Madelung's operation
   D. Madelung's, Troyanov – Trendelenburg's operation
   E. Linton's, Kocket's, Narat's operation

3. A 30- years- old woman is troubled by a strong pain in the left lower extremity, its fast fatigue, in particular in a vertical position. A varicose dilatation of the superficial veins on the left leg appeared about one year ago. On inspection an insufficiency of valves of superficial and perforating veins has been revealed. Your variant of treatment.
   A. Venectomy by Narat
   B. Operation by Troyanov - Trendelenburg.
   C. Venectomy by Babcock.
   D. Operation by Kocket.
   E. All listed methods of treatment.

4. In a 46 years old with varicose illness of the lower extremities profuse bleeding from varicose node in the lower third of the leg in trophic ulcer zone was diagnosed. What kind of first aid is the most correct?
   A. Arterial tourniquet proximally of the ulcer
   B. Tourniquet distally of the ulcer, a bandage
   C. Tourniquet proximally of the ulcer, a bandage
   D. A bandage, manual pressing of varicose node
   E. Elevated position of the extremity, aseptic compression bandage

5. Two children's Mother complains of softly-elastic nodes on the external surface of the left thigh with spread to the leg and oedema on the foot at the end of a day. After night sleep oedema disappears. The beginning of illness she links with pregnancy and childbirth. She wears elastic stockings. Establish the initial diagnosis.
   A. Acute thrombophlebitis of deep veins of the left leg
   B. Varicose dilatation of subcutaneous veins of the left leg
   C. Acute thrombophlebitis of superficial veins of the left leg
   D. Endarteritis obliterans of the left lower extremity
   E. Elephantiasis of the left lower extremity

6. **Methodological lecture support:**
- classrooms №1;
- Equipment - Multymedia;
- illustrative material - slides.

7. **Questions for self-control:**

1. Classification of diseases of veins.
2.Pathological and anatomical features of veins.
3.Methods of inspection of the patients with diseases of veins.
4.Tool methods of inspection of the patient with diseases of veins.
5.Tactics in the patient with diseases of veins.
6.Clinical presentations of diseases of veins.
7.Clinical presentations of complications. The indications, terms and types of treatment.

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