LECTURE 10

NECROSIS.GANGRENE.ULCERS. FISTULAS.

I.Actuality of theme. Knoweledge of the basic mechanisms of cells and tissue death, pathogenesis of arterial and venous insufficiency, diabetic tissue disoders has grown rapidly. A detailed knowledge of these mechanisms allows surgeon to influence healing and anticipate and prevent problems of infections and incomplete repair different type of wound (bedsore, diabetic ulcer ect) .

Vascular ulcers are a common cause of surgical consultation. For vascular surgeons, only painful extremities and swollen legs are more likely to trigger a consultation. The great majority of vascular ulcers are chronic and/or recurrent. They cause a considerable amount of morbidity among patients with peripheral vascular disease, including work incapacity. The burden placed on the patient and the health care system due to the care of chronic vascular ulcers is significant. Additionally, these nonhealing ulcers place the patient at much higher risk for lower extremity amputation. So, knowledge about diagnosis and treatment of leg ulcers is very important for all physicians.

II. Aims of lecture:

Educational:

- To expound the etiology, pathogenesis and classification of necrosis, gangrene, fistulas (β= II);
- To characterize the etiology and pathology of venous and arterial insufficiency, diabetic neuropathy; pathogenesis, classification, diagnosis, treatment of arterial, venous and diabetic ulcers (β= III);
- To describe of the etiology of pressure ulcers; pathogenesis and treatment of pressure ulcers (β= II);
- To describe clinical strategy in patients with different types of fistilas (β= III);
- To study the students the main principles of evidence-based medicine according the subject of lecture (β= IV).

Educative:

1. To educate for students sense of responsibility for every prescription, research, procedure, manipulation or surgery, for a health and renewal of capacity of patient, for the rightness of adequate estimation of the common state of patients and grant of timely effective treatment.
2. To form for students skills of clinical thought in the process of intercourse with the patients. To teach students to adhere to principles of medical deontology and bioethics in the process of socializing with a patient, his relatives, and also with colleagues.

III. Plan and organization of structure of lecture

№	Basic stages of lecture and their maintenance	Aims are in the levels of abstraction	Type of lecture, methods and facilities of activation of students, equipment	Division of time
1	**Preliminary stage**. Determination of educational aims and motivation.		Item I, II.	5%
2	**Basic stage. Teaching of lecture's material** Classification, diagnosis and treatment of necrosis and gangrene Arterial, venous and diabetic ulcers – pathogenesis, classification, diagnosis, treatment Etiology, pathogenesis and treatment of pressure ulcers Classification, diagnosis and treatment of fistulas	II II III II	Type of lecture – thematic (with controversial elements – critical analysis of results of meta-analyses, randomized controlled, trials, guidlines which are devoted for the problem of necrosis, gangrene, arterial, venous, pressure diabetic ulcers and fistulas). Facilities of activation of students are a questions, controversial situations, illustrative material	85%
3	Final stage (resume of lecture, general conclusions, answers to the possible questions, task for		List of literature, question, task for students	10%

	students for preparation for practical classes)			

IV. Subject of a lecture

Necrosis is the name given to accidental death of cells and living tissue. Necrosis is less orderly than apoptosis, which is part of programmed cell death. In contrast with apoptosis, cleanup of cell debris by phagocytes of the immune system is generally more difficult, as the disorderly death generally does not send cell signals which tell nearby phagocytes to engulf the dying cell. This lack of signalling makes it harder for the immune system to locate and recycle dead cells which have died through necrosis than if the cell had undergone apoptosis. The release of intracellular content after cellular membrane damage is the cause of inflammation in necrosis.

There are many causes of necrosis including injury, infection, cancer, infarction, toxins and inflammation. Severe damage to one essential system in the cell leads to secondary damage to other systems, a so-called "cascade of effects". Necrosis can arise from lack of proper care to a wound site. Necrosis is accompanied by the release of special enzymes, that are stored by lysosomes, which are capable of digesting cell components or the entire cell itself. The injuries received by the cell may compromise the lysosome membrane, or may initiate an unorganized chain reaction which causes the release in enzymes. Unlike apoptosis, cells that die by necrosis may release harmful chemicals that damage other cells. Biopsy material necrosis is halted by fixation or freezing.

There are seven distinctive morphologic patterns of necrosis:

- **Coagulative necrosis** is typically seen in hypoxic environments (e.g. myocardial infarction, infarct of the spleen). Cell outlines remain after cell death and can be observed by light microscopy.
- **Liquefactive necrosis** is usually associated with cellular destruction and pus formation (e.g. pneumonia). Curiously, ischemia (restriction of blood supply) in the brain produces liquefactive rather than coagulative necrosis.
- **Gummatous necrosis** is restricted to necrosis involving spirochaetal infections (e.g. syphilis).
- **Haemorrhagic necrosis** is due to blockage of the venous drainage of an organ or tissue (e.g. in testicular torsion).
- **Caseous necrosis** is a specific form of coagulation necrosis typically caused by mycobacteria (e.g. tuberculosis).
- **Fatty** necrosis results from the action of lipases on fatty tissues (e.g. acute pancreatitis, breast tissue necrosis).

- **Fibrinoid** necrosis is caused by immune-mediated vascular damage. It is marked by deposition of fibrin-like proteinaceous material in arterial walls, which appears smudgy and eosinophilic on light microscopy.

Avascular necrosis (AVN) is defined as cellular death of bone components due to interruption of the blood supply; the bone structures then collapse, resulting in bone destruction, pain, and loss of joint function. AVN is associated with numerous conditions and usually involves the epiphysis of long bones, such as the femoral and humeral heads and the femoral condyles, but small bones can also be affected. AVN of the jaw associated with bisphosphonate use was recently described. In clinical practice, AVN is most commonly encountered in the hip.

Gangrene is defined as the gradual destruction of living tissue, due to an obstruction in the supply of blood and oxygen to an area of the body. Any part of the body can be affected by gangrene, but it most frequently occurs in the hands, fingers, feet and toes, particularly as these acral parts of the body seem to be the most susceptible to trauma. Gangrene of the skin is often called sphaceloderma.

Gangrene can also occur internally and is extremely dangerous if abdominal organs are involved. It does not generally discriminate between the sexes, although a predisposition to malnourished, elderly persons or those with diabetes mellitus or serious vascular impairment is recognised.

Gangrene can be divided into three categories:
1. Dry gangrene
2. Moist gangrene
3. Gas gangrene

Dry gangrene is a condition that results when one or more arteries become obstructed. In this type of gangrene, the tissue slowly dies, due to receiving little or no blood supply, but does not become infected. The affected area becomes cold and black, begins to dry out and wither, and eventually drops off over a period of weeks or months. Dry gangrene is most common in persons with advanced blockages of the arteries (arteriosclerosis) resulting from diabetes.
Moist gangrene may occur in the toes, feet, or legs after a crushing injury or as a result of some other factor that causes blood flow to the area to suddenly stop. When blood flow ceases, bacteria begin to invade the muscle and thrive, multiplying quickly without interference from the body's immune system.
Gas gangrene, also called myonecrosis, is a type of moist gangrene that is commonly caused by bacterial infection with *Clostridium welchii, Cl. perfringes, Cl. septicum, Cl. novyi, Cl. histolyticum, Cl. sporogenes*, or other species that are

capable of thriving under conditions where there is little oxygen (anaerobic). Once present in tissue, these bacteria produce gasses and poisonous toxins as they grow. Normally inhabiting the gastrointestinal, respiratory, and female genital tract, they often infect thigh amputationwounds, especially in those individuals who have lost control of their bowel functions (incontinence). Gangrene, incontinence, and debility often are combined in patients with diabetes, and it is in the amputation stump of diabetic patients that gas gangrene is often found to occur.

Other causative organisms for moist gangrene include various bacterial strains, including *Streptococcus* and *Staphylococcus*. A serious, but rare form of infection with Group A *Streptococcus* can impede blood flow and, if untreated, can progress to synergistic gangrene, more commonly called necrotizing fasciitis, or infection of the skin and tissues directly beneath the skin.

Chronic diseases, such as diabetes mellitus, arteriosclerosis, or diseases affecting the blood vessels, such as Buerger's disease or Raynaud's disease, can cause gangrene. Post-traumatic causes of gangrene include compound fractures, burns, and injections given under the skin or in a muscle. Gangrene may occur following surgery, particularly in individuals with diabetes mellitus or other long-term (chronic) disease. In addition, gas gangrene can be also be a complication of dry gangrene or occur spontaneously in association with an underlying cancer.

In the United States, approximately 50% of moist gangrene cases are the result of a severe traumatic injury, and 40% occur following surgery. Car and industrial accidents, crush injuries, and gunshot wounds are the most common traumatic causes. Because of prompt surgical management of wounds with the removal of dead tissue, the incidence of gangrene from trauma has significantly diminished. Surgeries involving the bile ducts or intestine are the most frequent procedures causing gangrene. Approximately two-thirds of cases affect the extremities, and the remaining one-third involve the abdominal wall.

Symptoms

Areas of either dry or moist gangrene are initially characterized by a red line on the skin that marks the border of the affected tissues. As tissues begin to die, dry gangrene may cause some pain in the early stages or may go unnoticed, especially in the elderly or in those individuals with diminished sensation to the affected area. Initially, the area becomes cold, numb, and pale before later changing in color to brown, then black. This dead tissue will gradually separate from the healthy tissue and fall off.

Moist gangrene and gas gangrene are distinctly different. Gas gangrene does not involve the skin as much, but usually only the muscle. In moist or gas gangrene, there is a sensation of heaviness in the affected region that is followed by severe pain. The pain is caused by swelling resulting from fluid or gas accumulation in the tissues. This pain peaks, on average, between one to four days following the injury, with a range of eight hours to several weeks. The swollen skin may initially be blistered, red, and warm to the touch before progressing to a bronze, brown, or

black color. In approximately 80% of cases, the affected and surrounding tissues may produce crackling sounds (crepitus), as a result of gas bubbles accumulating under the skin. The gas may be felt beneath the skin (palpable). In wet gangrene, the pus is foul-smelling, while in gas gangrene, there is no true pus, just an almost "sweet" smelling watery discharge.

Fever, rapid heart rate, rapid breathing, altered mental state, loss of appetite, diarrhea, vomiting, and vascular collapse may also occur if the bacterial toxins are allowed to spread in the bloodstream. Gas gangrene can be a life-threatening condition and should receive prompt medical attention

Diagnosis

A diagnosis of gangrene will be based on a combination of the patient history, a physical examination, and the results of blood and other laboratory tests. A physician will look for a history of recent trauma, surgery, cancer, or chronic disease. Blood tests will be used to determine whether infection is present and determine the extent to which an infection has spread.

A sample of drainage from a wound, or obtained through surgical exploration, may be cultured with oxygen (aerobic) and without oxygen (anaerobic) to identify the microorganism causing the infection and to aid in determining which antibiotic will be most effective. The sample obtained from a person with gangrene will contain few, if any, white blood cells and, when stained (with Gram stain) and examined under the microscope, will show the presence of purple (Gram positive), rod-shaped bacteria.

X-ray studies and more sophisticated imaging techniques, such as computed tomography scans (CT) or magnetic resonance imaging (MRI), may be helpful in making a diagnosis since gas accumulation and muscle death (myonecrosis) may be visible. These techniques, however, are not sufficient alone to provide an accurate diagnosis of gangrene.

Precise diagnosis of gas gangrene often requires surgical exploration of the wound. During such a procedure, the exposed muscle may appear pale, beefy-red, or in the most advanced stages, black. If infected, the muscle will fail to contract with stimulation, and the cut surface will not bleed.

Treatment

Gas gangrene is a medical emergency because of the threat of the infection rapidly spreading via the bloodstream and infecting vital organs. It requires immediate surgery and administration of antibiotics.

Areas of dry gangrene that remain free from infection (aseptic) in the extremities are most often left to wither and fall off. Treatments applied to the wound externally (topically) are generally not effective without adequate blood supply to support wound healing. Assessment by a vascular surgeon, along with x rays to determine blood supply and circulation to the affected area, can help determine whether surgical intervention would be beneficial.

Once the causative organism has been identified, moist gangrene requires the prompt initiation of intravenous, intramuscular, and/or topical broad-spectrum antibiotic therapy. In addition, the infected tissue must be removed surgically (debridement), and amputation of the affected extremity may be necessary. Pain medications (analgesics) are prescribed to control discomfort. Intravenous fluids and, occasionally, blood transfusions are indicated to counteract shock and replenish red blood cells and electrolytes. Adequate hydration and nutrition are vital to wound healing.

Although still controversial, some cases of gangrene are treated by administering oxygen under pressure greater than that of the atmosphere (hyperbaric) to the patient in a specially designed chamber. The theory behind using hyperbaric oxygen is that more oxygen will become dissolved in the patient's bloodstream, and therefore, more oxygen will be delivered to the gangrenous areas. By providing optimal oxygenation, the body's ability to fight off the bacterial infection are believed to be improved, and there is a direct toxic effect on the bacteria that thrive in an oxygen-free environment. Some studies have shown that the use of hyperbaric oxygen produces marked pain relief, reduces the number of amputations required, and reduces the extent of surgical debridement required. Patients receiving hyperbaric oxygen treatments must be monitored closely for evidence of oxygen toxicity. Symptoms of this toxicity include slow heart rate, profuse sweating, ringing in the ears, shortness of breath, nausea and vomiting, twitching of the lips/cheeks/eyelids/nose, and convulsions.

The emotional needs of the patient must also be met. The individual with gangrene should be offered moral support, along with an opportunity to share questions and concerns about changes in body image. In addition, particularly in cases where amputation was required, physical, vocational, and rehabilitation therapy will also be required.

Prognosis

Except in cases where the infection has been allowed to spread through the blood stream, prognosis is generally favorable. Anaerobic wound infection can progress quickly from initial injury to gas gangrene within one to two days, and the spread of the infection in the blood stream is associated with a 20-25% mortality rate. If recognized and treated early, however, approximately 80% of those with gas gangrene survive, and only 15-20% require any form of amputation. Unfortunately, the individual with dry gangrene most often has multiple other health problems that complicate recovery, and it is usually those other system failures that can prove fatal.

Prevention

Patients with diabetes or severe arteriosclerosis should take particular care of their hands and feet because of the risk of infection associated with even a minor injury. Education about proper foot care is vital. Diminished blood flow as a result of narrowed vessels will not lessen the body's defenses against invading bacteria.

Measures taken towards the reestablishment of circulation are recommended whenever possible. Any abrasion, break in the skin, or infection tissue should be cared for immediately. Any dying or infected skin must be removed promptly to prevent the spread of bacteria.
Penetrating abdominal wounds should be surgically explored and drained, any tears in the intestinal walls closed, and antibiotic treatment begun early. Patients undergoing elective intestinal surgery should receive preventive antibiotic therapy. Use of antibiotics prior to and directly following surgery has been shown to significantly reduce the rate of infection from 20-30% to 4-8%.

Specific gangrenes

- Noma is a gangrene of the face.
- Necrotizing fasciitis is attacking the deeper layers of the skin.
- Fournier gangrene usually affects the male genitals.

An **ulcer** is an open sore of the skin, eyes or mucous membrane, often caused, but not exclusively, by an initial abrasion and generally maintained by an inflammation, an infection, and/or medical conditions which impede healing. Or in other words, it is a macroscopic discontinuity of the normal epithelium (microscopic discontinuity of epithelium is called erosion). Other causes of skin ulcerations include pressure from various sources and venous insufficiency.

Ulcers are healing wounds that develop on the skin, mucous membranes or eye. Although they have many causes, they are marked by:

1. Loss of integrity of the area
2. Secondary infection of the site by bacteria, fungus or virus
3. Generalized weakness of the patient
4. Delayed healing

Ulceration due to vascular causes is often multifactorial and can be caused by both arterial and venous disease. Hypertension and atherosclerosis of the peripheral vessels lead to arterial disease associated with ischemic ulcers. Chronic venous insufficiency and the resulting venous hypertension cause venous ulcers. Vasculitides such as Buerger disease (thromboangiitis obliterans) or Takayasu disease can also be associated with ulceration. The former tends to manifest with arterial or ischemic-type ulcers, while the latter manifests with cutaneous disease such as pyoderma gangrenosum or erythema nodosum.

Table 1. Causes of leg ulcers
Vascular

- Venous—80-85% of all leg ulcers

- Arterial—atherosclerosis, arteriovenous malformation
- Vasculitis—systemic lupus erythematosis, rheumatoid arthritis, scleroderma, polyarteritis nodosa, Wegener's granulomatosis
- Lymphatic

Neuropathic

Diabetes, peripheral neuropathy—usually feet

Haematological

Polycythaemia rubra vera, sickle cell anaemia

Traumatic

Burns, cold injury, pressure sore, radiation, factitious

Neoplastic

Basal or squamous cell carcinoma, melanoma, Marjolin's ulcer, Bowen's disease

Others

Sarcoidosis, tropical ulcer, pyoderma gangrenosum

Chronic leg or vascular ulcers typically manifest as **arterial, neurotrophic, or venous ulcers.** They are distinct with regard to their location, appearance, bleeding, and associated pain and findings.

Arterial ulcers

Arterial ulcers are often located distally and on the dorsum of the foot or toes. Initially they have irregular edges, but they may progress to have a better-defined appearance. The ulcer base contains grayish, unhealthy-appearing granulation tissue. With manipulation, such as debriding, these ulcers bleed very little or not at all. The patient may report characteristic pain, especially at night when supine, which is relieved by dependency of the extremity. Upon examination, characteristic findings of chronic ischemia, such as hairlessness, pale skin, and absent pulses, are noted.

Neurotrophic ulcers

Neurotrophic ulcers are characterized by a punched-out appearance with a deep sinus. These are often seen underlying calluses or over pressure points (eg, plantar aspect of the first or fifth metatarsophalangeal joint). They are commonly surrounded by chronic inflammatory tissue. Probing or debriding may lead to brisk bleeding. Because these patients usually have a neuropathy leading to hypesthesia and diminished positional sense or 2-point discrimination, these ulcers are frequently painless.

Venous ulcers

Venous ulceration is commonly noted in the “gaiter” region of the legs. This region is located circumferentially around the lower leg from approximately mid calf to just below the medial and lateral malleoli. Larger but shallower than other ulcers, stasis ulcers have a moist granulating base and an irregular border. This

base oozes venous blood when manipulated. The tissue surrounding these ulcers may exhibit signs of stasis dermatitis. Patients often report mild pain that is relieved by elevation. The main causes of venous hypertension are represented in table 2.

Table 2: Causes of sustained venous hypertension

• Venous disease:
Superficial venous incompetence—varicose veins
Deep venous incompetence
Primary Deep venous obstruction (rare)
Previous deep vein thrombosis
External compression
• Impaired calf muscle pump function:
Immobility
Joint disease
Paralysis
Obesity—immobility, femoral vein compression, high abdominal pressures
• Congestive cardiac failure

Imaging studies:

When noninvasive tests reveal unacceptable pedal perfusion, perform imaging studies of the lower extremity to identify the level of obstruction and to evaluate the distal runoff.

Angiography is performed when visualization of the vessels of the lower extremities is desired.

Magnetic resonance angiography (MRA) can also be useful when evaluating lower extremity disease. MRA is 94% accurate in evaluating lower extremity vessels when compared to conventional angiography or surgery.

Imaging tests for venous disease can also reveal important preoperative issues.

Doppler duplex scanning can detect venous reflux with a sensitivity greater than 75%, compared to approximately 40% for descending venography. Combining duplex scanning with air plethysmography helps differentiate severe venous disease from mild venous disease.

Ascending venography also may be considered to obtain detailed anatomic information. This study can reveal axial channel patency, perforator incompetence, obstruction, and the presence of deep venous thrombosis.

Other Tests:

Assess the vascular supply to the site of ulceration so that the likelihood of satisfactory wound healing may be estimated. Several methods of determining the adequacy of the pedal circulation are available.

Ankle-brachial indices (ABIs) and toe digital pressures with pulse volume recordings can provide good clues to the perfusion of the foot. Findings are also predictive of wound healing, although they may be misleading in patients with diabetes and calcified noncompressible arteries. An ankle pressure greater than 55 mm Hg suggests adequate leg perfusion. Research suggests that venous ulcers require a higher ABI for healing than arterial ulcers. The diagnosis of critical limb ischemia is supported by either an ankle systolic pressure of 50 mm Hg or less or digital pressures less than 30 mm Hg.

Xenon-133 clearance to measure blood flow can help estimate the chance of wound healing. A rate of 2.6 mL/100 g is believed adequate for healing.

Transcutaneous oxygen tension may be measured; however, a wide discrepancy exists with the minimal level below which wound healing does not occur. Most agree that a pressure of 30-35 mm Hg is sufficient for healing of more than 90% of wounds.

Management of the venous ulcer

Despite considerable research, little evidence of major benefits from modern interactive dressings has been published. An emphasis on education, training, and further development of compression systems is needed to improve patient care and ulcer healing. The basis for effective treatment of venous leg ulcers is outlined in **Table 3.**

Table 3: Effective treatment for venous leg ulcers

- Four layer compression bandaging
- Leg elevation
- Improve mobility
- Reduce obesity
- Improve nutrition
- Skin grafting in selected patients
- Venous surgery in selected patients

Treating the ulcer

The underlying causes need to be identified. Multiple pathologies are common, but patients with diabetes may have simple venous ulcers that are no more difficult to heal than in people without diabetes. As 80-85% of ulcers are associated with venous hypertension, compression remains the mainstay of treatment.

Dressing materials

Patients with leg ulcers are prone to contact sensitivity, particularly from wool alcohols, topical antibiotics, cetylstearyl alcohols, parabens, and rubber mixes, which are present in many dressings, ointments, and creams. Many entirely inadequate studies have examined the role of different dressing materials; most have shown that modern "designer" dressing materials have no additional effect on wound healing over that achieved by simple low adherence dressings under multilayer compression bandaging.

Compression treatment

Sustained graduated compression overcomes the effects of venous hypertension by reducing venous stasis and preventing (or treating) tissue oedema. The pressure within the veins on standing is largely hydrostatic, and the level of external pressure needed to counteract this decreases progressively up the leg.

Compression treatment has been covered in a Cochrane review on the cost effectiveness of both bandaging and stockings in the treatment of venous ulceration. Twenty two trials were identified and consistently showed that compression encouraged healing of ulcers. More ulcers were healed at 12-15 weeks with high compression systems than with low compression systems. No significant difference was found between the effectiveness of different high compression systems, but more ulcers healed at 24 weeks with four layer bandages than with a single layer.

The most effective level of compression to overcome venous hypertension has been determined to be around 40 mm Hg at the ankle. Correct application of bandages is essential to avoid pressure ulceration over bony high points and along the anterior border of the tibia. To achieve this pressure in a range of limb diameters, bandaging regimens must be adjusted according to ankle circumference.

As venous ulcer services improve, more patients have their ulcers healed and are then at risk of recurrence; recurrence rates of 26% at one year and 31% at 18 months have been quoted. A Cochrane review on the role of compression in the prevention of recurrence identified few adequate trials, but concluded that recurrence may be lower with higher compressions.

Limb elevation

Limb dependency, immobility, and oedema all contribute to venous hypertension. Limb elevation reduces oedema and enhances flow in the microcirculation, reducing trapping, sequestration, and activation of white cells—a necessary first step in the pathophysiology of ulceration. Leg elevation in hospital enhances healing.

Skin grafting

Split skin grafting is technically demanding and requires hospital admission. The

discharge from the surface of venous ulcers tends to dislodge continuous sheets of split skin, leaving a choice between mesh and pinch skin grafting.
Pinch skin grafts provide epithelial islands, from which epithelial growth may spread outwards as well as inwards from the ulcer margin. Pinch skin grafting has been done by district nurses in the community and has been found to be cost effective, accelerating healing when used with multilayer compression bandaging.

Bioengineered skin products, including bilayered skin constructs and frozen human allogeneic epidermal cultures, are being developed and may stimulate wound healing through the release of growth factors and cytokines. The numbers of patients recruited to such studies have been small, and most products are not yet available for clinical use. These new approaches have yet to be compared with pinch skin grafting, which is simple and inexpensive.

Growth factors
Wound fluid from non-healing ulcers contained higher concentrations of pro-inflammatory cytokines, interleukin-1, interleukin-6, and tumour necrosis factor- and had reduced proliferative responses compared with fluid from healing ulcers. Research on platelet derived growth factor, hepatocyte growth factor, and human keratinocyte growth factor-2 has been published, but these studies were small and often poorly designed.

Drug treatment
Antibiotics have little effect on ulcer healing but are needed for clinical infections with surrounding cellulitus. Pentoxifylline has been evaluated in clinical trials, but the largest placebo controlled, double blind, randomised study included only 80 patients; 88% were healed by 12 months on pentoxifylline compared with 44% on placebo. Oxerutins failed to improve ulcer healing or influence recurrence. Fibrinolytic agents such as stanozolol have also been disappointing. Studies on prostaglandin E_1 and micronised purified flavonoids were simply too small to influence clinical practice.

Venous surgery
Superficial venous surgery has been shown to improve ulcer healing in patients with only superficial venous incompetence. **Table 4** shows indications for superficial venous surgery.

Table 4: Indications for superficial venous surgery

- Patient fit for surgery (local anaesthesia if necessary)
- Sufficient mobility to activate calf muscle pump
- Prepared to attend hospital for investigation and surgery
- Obesity controlled (body mass index < 30)

- Superficial venous incompetence: no deep venous incompetence on duplex imaging, or predominantly superficial venous incompetence on ambulatory venous pressures with tourniquet occlusion of the superficial veins

Arterial ulcer management

In daily wound care a sharp wound debridement is not recommended. Compression therapy is contraindicated in arterial disease. The mainstay of treatment of arterial leg ulcers is surgical. The aim is to restore blood supply to compromised limbs. An optimal control of associated predisposing factors, such as hyperlipidemia, hypertension, and diabetes, as well as smoking cessation and an exercise program should be included in the management plan.

Neuropathic ulcer management

The goal of wound dressings is to provide a warm, moist environment that is free of external contamination. Saline wet-to-dry dressings and several types of commercially available occlusive dressings (eg, hydrocolloids, alginates, foams, and films) are effective. However, none is ideal for every situation. Various growth factors show promise. Becaplermin (Regranex), a recombinant human platelet-derived growth factor formulated into a gel, increases the incidence of and decreases the time needed for complete wound closure. All dressings and other wound care products are only adjuncts to careful local treatment measures, including reduction of pressure, sharp debridement of damaged tissues and control of infection.Restoration or optimization of blood supply, treatment of any active infection, and protection of the ulcerated areas should also be an integral part of the management. Off-loading the foot often requires the use of a protective plaster boot with a window cut out at the site of the ulcer. After complete healing of the wound, patients should be fitted with footwear designed to minimize trauma and protect bony prominences. Patient education about avoiding leg and foot problems is important in preventing recurrence after ulcer closure.

Diabetic foot ulcers occur as a result of various factors. Such factors include mechanical changes in conformation of the bony architecture of the foot, peripheral neuropathy, and atherosclerotic peripheral arterial disease, all of which occur with higher frequency and intensity in the diabetic population. Nonenzymatic glycosylation predisposes ligaments to stiffness. Neuropathy causes loss of protective sensation and loss of coordination of muscle groups in the foot and leg, both of which increase mechanical stresses during ambulation.

Overall, people with diabetes have a higher incidence of atherosclerosis, thickening of capillary basement membranes, arteriolar hyalinosis, and endothelial proliferation. Calcification and thickening of the arterial media (Mönckeberg sclerosis) also are noted with higher frequency in the diabetic population, although whether these factors have any impact on the circulatory status is unclear.

Diabetic ulcers tend to occur in the following areas:

- ✓ areas most subjected to weight bearing, such as the heel, plantar metatarsal head areas, the tips of the most prominent toes (usually the first or second), and the tips of hammer toes (ulcers also occur over the malleoli because these areas commonly are subjected to trauma.)
- ✓ areas most subjected to stress, such as the dorsal portion of hammer toes
- ✓ other physical findings include hypertrophic calluses, brittle nails, hammer toes, fissures.

Imaging studies:

Duplex scanning can provide images of arterial segments that help localize the extent of disease, and simultaneous Doppler measurement of flow velocity can help estimate the degree of stenosis. Duplex scanning is quite useful in visualizing aneurysms, particularly of the aorta or popliteal segments. Use of this technique probably is best left to the discretion of the vascular specialist.

Plain x-ray studies of the diabetic foot may demonstrate demineralization and Charcot joint and occasionally may suggest the presence of osteomyelitis. Note that plain x-ray studies have no role in the evaluation of arterial disease. This is because arterial calcification observed on plain x-rays is not a specific indicator of severe atherosclerotic disease. Calcification of the arterial media is not diagnostic of atherosclerosis, and even calcification of the arterial intima, which is diagnostic of atherosclerotic disease, does not necessarily imply hemodynamically significant stenosis.

CT scan and MRI: Although an experienced clinician usually can diagnose a plantar abscess by physical examination alone, CT scan or MRI is indicated if a plantar abscess is suspected but not clear on physical examination.

Bone scans are of questionable utility because of a sizable percentage of false-positive and false-negative results. A recent study suggests 99mTc-labeled ciprofloxacin as a somewhat useful marker for osteomyelitis.

Contrast angiography is indicated if hemodynamically significant vascular disease precludes healing of the ulcer or is causing intractable pain at rest. Angiography is best ordered by the vascular or endovascular surgeon (not the generalist) to ensure that the study performed actually visualizes the entire segment of the arterial tree apropos to the potential vascular procedure.

MRA is an alternative for patients with renal compromise and patients who are allergic to contrast materials. MRA requires no iodinated contrast material but is contraindicated by hardware such as a hip prosthesis or a pacemaker, and the resolution often is inadequate for the vascular surgeon in planning reconstructive procedures, particularly in the smaller infrapopliteal arteries.

Staging: Stage diabetic foot wounds based on the depth of soft tissue and osseous involvement. Any ulcer that seems to track into or is deep to the subcutaneous tissues should be probed gently, and, if bone is encountered, osteomyelitis is likely.

Wagner's classification

This classification system is intended to rate the severity of diabetic foot ulcerations

- Grade 0 - Skin with prior healed ulcer scars, areas of pressure which are sometimes called pre-ulcerative lesion or the presence of bony deformity which puts pressure on an unguarded point.
- Grade 1-A - The wound is superficial in nature, with partial or full-thickness skin involvement but does not include tendon, capsule or bone.
- Grade 1-B - As above, the wound is superficial in nature, with partial or full thickness skin involvement but not including tendon, capsule nor bone; however the wound is infected. The definition of this wound implies superficial infection without involvement of underlying structures. If the wound shows signs of significant purulence or fluctuance, further exploration to expose a higher grade classification of infection is in order.
- Grade 1-C - As above but with vascular compromise.
- Grade 1-D - As above but with ischemia. Because ischemia is a type of vascular compromise, the distinction between these two grades is often difficult to make.
- Grade 2-A - Penetration through the subcutaneous tissue exposing tendon or ligament, but not bone.
- Grade 2-B - Penetration through the deep tissues including tendon or ligament and even joint capsule but not bone.
- Grade 2-C - As above 2B, but including ischemia
- Grade 2-D - As above 2C, but including infection
- Grade 3-A - A wound which probes to bone but shows no signs of local infection nor systemic infection.
- Grade 3-B - A wound which probes to bone and is infected.
- Grade 3-C - A wound which probes to bone is infected and is ischemic.
- Grade 3-D - A wound which probes to bone characterized by active infection, ischemic tissues and exposed bone.
- Grade 4 - Gangrene of the forefoot
- Grade 5 - Gangrene of the entire foot

Medical Care: Treatment of foot ulcers includes treatment of the diabetes itself. Management of contributing systemic factors, such as hypertension, hyperlipidemia, atherosclerotic heart disease, obesity, or renal insufficiency, is crucial. Management of arterial insufficiency, treatment of infection with appropriate antibiotics, offloading the area of the ulcer, and wound care are also

essential. In the presence of an intractable wound and associated noncorrectible ischemic arterial disease, hyperbaric oxygen therapy may be beneficial (in selected cases). The management of diabetic foot ulcers requires appropriate therapeutic footwear, daily saline or similar dressings to provide a moist wound environment, debridement when necessary, antibiotic therapy if osteomyelitis or cellulitis is present, optimal control of blood glucose, and evaluation and correction of peripheral arterial insufficiency. Wound coverage by cultured human cells or heterogeneic dressings/grafts, application of recombinant growth factors, and hyperbaric oxygen treatments also may be beneficial at times.

Charcot foot is treated initially with immobilization using special shoes or braces but eventually may require podiatric surgery such as ostectomy and arthrodesis. If neglected, ulceration may occur at pressure points, particularly the medial aspect of the navicular bone and the inferior aspect of the cuboid bone.

Surgical Care: All patients harboring diabetic foot ulcers should be evaluated by a qualified vascular surgeon and/or podiatric surgeon who will consider debridement, revisional surgery on bony architecture, vascular reconstruction, and options for soft tissue coverage.

Debridement: Surgical management is indicated for debridement of nonviable and infected tissue from the ulceration, removal of excess callous, curettage of underlying osteomyelitic bone, skin grafting, and revascularization. The wound usually requires an initial surgical debridement and probing to determine the depth and involvement of bone or joint structures. Visible or palpable bone implies an 85% chance of osteomyelitis.
Revisional surgery: Revisional surgery for bony architecture may be required to remove pressure points. Such intervention includes resection of metatarsal heads or ostectomy.
Vascular surgery: In general, the indications for vascular surgery in the presence of a reconstructible arterial lesion include intractable pain at rest or at night, intractable foot ulcers, and impending or existing gangrene. Intermittent claudication alone only infrequently is disabling and intractable enough to warrant bypass surgery.
Options for soft tissue coverage of the clean but nonhealing wound: Once a wound has reached a steady clean state, a decision has to be made about allowing healing by natural processes or expediting healing by a surgical procedure. Clinical experience and observation of the healing progress in each case dictate the appropriate management. Surgical options include skin grafting, application of bioengineered skin substitutes, and flap closures.
The autologous skin graft is the criterion standard for viable coverage of the partial thickness wound. The graft can be harvested under local anesthesia as an outpatient

procedure. Meshing the graft allows wider coverage and promotes drainage of serum and blood.
A cadaveric skin allograft is a useful covering for relatively deep wounds following surgical excision when the wound bed does not appear appropriate for application of an autologous skin graft. The allograft is, of course, only a temporary solution.

Tissue-cultured skin substitutes

Dermagraft (Smith & Nephew) is a cryopreserved human fibroblast–derived dermal substitute produced by seeding neonatal foreskin fibroblasts onto a bioabsorbable polyglactin mesh scaffold. Dermagraft is useful for managing full-thickness chronic diabetic foot ulcers. It is not appropriate for infected ulcers, those that involve bone or tendon, or those that have sinus tracts. Apligraf (Organogenesis) is a living, bilayered human skin substitute. It is not appropriate for infected ulcers, those that involve tendon or bone, or those that have sinus tracts. Allergic reactions to the agarose shipping medium or its bovine collagen component have been reported.

The use of bioengineered skin substitutes has been questioned because the mechanism of action is not clear, the efficacy is questionable, and the cost is high.

Xenograft: Oasis (Healthpoint, Ltd) is a xenogeneic, acellular collagen matrix derived from porcine small intestinal submucosa in a way that allows an extracellular matrix and natural growth factors to remain intact. This provides a scaffold for inducing wound healing. Do not use this for patients with allergies to porcine materials.

Surgical wound closure: Delayed primary closure of a chronic wound requires well-vascularized clean tissues and tension-free apposition; it usually requires undermining and mobilization of adjacent tissue planes by creation of skin flaps or myocutaneous flaps. The basic principle of topical wound management is to provide a moist, but not wet, wound bed. After debridement, apply a moist sodium chloride dressing or isotonic sodium chloride gel (eg, Normlgel, IntraSite gel) or a hydroactive paste (eg, Duoderm). Optimal wound coverage requires wet-to-damp dressings, which support autolytic debridement, absorb exudate, and protect surrounding healthy skin. A polyvinyl film dressing (eg, OpSite, Tegaderm) that is semipermeable to oxygen and moisture and impermeable to bacteria is a good choice for wounds that are neither very dry nor highly exudative.

The risk of ulceration and limb amputation in people with diabetes can be improved by routine preventive podiatric care, appropriate shoes, and patient education. Diabetic clinics should screen all patients for altered sensation and

peripheral vascular disease. Of diabetic foot ulcers, 85% are estimated to be preventable with appropriate preventive medicine.

A pressure ulcer is any injury usually caused by unrelieved pressure that damages the skin and underlying tissue. Pressure ulcers are also called "decubitus ulcers," "bed sores," or "pressure sores," and their severity ranges from reddening of the skin to severe, deep craters that have formed down to muscle and bone.

Classification of Pressure Ulcers

Research indicates that there are several stages to the severity and condition of pressure ulcers. The following stages are adapted from the Agency for Health Care Policy and Research (1994) guidelines:

- Stage 1: Non-blanchable erythema of intact skin, the heralding lesion of skin ulceration. In individuals with darker skin, discoloration of skin, warmth, edema, induration, or hardness may also be indicators. Assessment of Stage 1 pressure ulcers is difficult in patients with darkly pigmented skin. In lighter-skinned people, a Stage 1 pressure ulcer may change skin color to a dark purple or red area that does not become pale under fingertip pressure. In dark-skinned people, this area may become darker than normal. The affected area may feel warmer than surrounding tissue. When an eschar is present, accurate staging is not possible.
- Stage 2: Partial thickness skin loss involving epidermis, dermis or both (e.g., abrasion, blister, or shallow crater).
- Stage 3: Full thickness skin loss involving damage to or necrosis of subcutaneous tissue that may extend down to, but not through, underlying fascia (deep crater with or without undermining). The ulcer presents clinically as a deep crater with or without undermining adjacent tissue.
- Stage 4: Full thickness skin loss with extensive destruction, tissue necrosis, or damage to muscle, bone, or supporting structures (e.g., tendon or joint capsule).

Treatment of pressure ulcers

Treatment of pressure ulcers should center on the following intervention activities:

- Management of tissue loads (i.e. pressure, friction, and shearing)
- Nutritional assessment and support
- Ulcer care
- Management of bacterial colonization and infection

Assessment of pressure ulcers should focus upon the following factors:

- Location and stage of ulcer (Stage 1 to 4)
- Size of ulcers (i.e. length, width and depth)
- Presence of tracts or undermining
- Ulcer bed appearance
    - Granulation tissue

    - Yellow slough
    - Eschar
    - Drainage
    - Presence of rolled wound edges
- Odor
- Peri-wound skin condition

Ensure adequate dietary intake to enhance healing. Request a consult from a dietitian and develop a nutrition plan. The stage of the wound is correlated with the severity of nutritional deficits, especially low protein intake or a below-normal serum albumin. Remove necrotic tissue with sharp, mechanical, autolytic, or enzymatic debridement. Autolytic and enzymatic debridement methods generally are specific to necrotic tissue and do not harm healthy tissue. However, they may be slow to debride the necrotic tissue. Sharp debridement is the most expedient at removing devitalized tissue, but does require specially trained personnel to perform. Cleanse with normal saline or commercially prepared wound cleanser at each dressing change. For the majority of wounds, isotonic saline is adequate to cleanse the wound surface. In those instances when the wound surface is more heavily laden with surface debris, a commercial wound cleanser may be used. Healing cannot occur until all inflammatory foreign material is removed. Use enough irrigation pressure to cleanse wound without causing trauma. Safe and effective ulcer irrigation pressures range from 4 to 15 pounds per square inch (psi). Avoid use of antiseptics (e.g., povidone iodine, iodophor, hydrogen peroxide, acetic acid). Apply dressings that maintain a moist wound environment. Examples of moist dressings include, but are not limited to, hydrogels, hydrocolloids, saline moistened gauze, transparent film dressings. The ulcer bed should be kept continuously moist. Keep the surrounding (periwound) intact skin dry while keeping the ulcer bed moist. If the ulcer does not progress toward healing, the patient should be evaluated to determine if osteomyelitis is present. If diagnosed, the infection must be treated if the ulcer is to heal. Adjuvant wound therapies such as hyperbaric oxygenation, negative pressure wound therapy, and electrical stimulation may be considered on an individual basis for those wounds that do not respond to more traditional therapies and osteomyelitis has been ruled . Consider a 2 week course of topical antibiotics for clean pressure ulcers that do not heal or continue to produce purulent exudate after 2 to 4 weeks of care as outlined in this protocol. The antibiotic should be effective against gram-negative, gram-positive, and anaerobic organisms. After initial treatment of pressure ulcers begins, the size of the ulcer may increase, especially when the ulcer initially contains necrotic tissue. However, the ulcer should become clearer and cleaner despite the increase in size. The treatment simply exposes more of the ulcer, thereby leading to the increased size. If the ulcer increases in size and does not become cleaner and clearer, then the

treatment needs to be altered, as the ulcer is not healing appropriately. Protect from further injury to the ulcer or additional ulcer formation by utilizing interventions outlined for patients at risk.

Fistulas

A fistula is any connection between an organ, vessel, or intestine and another structure in the body. Fistulas are usually the result of trauma or surgery, but can also result from infection or inflammation.

Types of Fistulas

- Blind (Open on one end only, but connects to two structures)
- Complete (Has both external and internal openings, as in a standard piercing with two distinct exit points)
- Horseshoe (Usually occurs when a connection develops between anus and one or more points on the surface of the skin after going around the rectum as in Crohn's disease and sever ulcerative colitis)
- Incomplete (A tube from the skin that is closed on the inside and does not connect to any internal organ or structure as in a healed transdermal implant).

Gastrointestinal (GI) fistulas are generally named according to their participating anatomic components, and virtually every imaginable combination has been reported in the medical literature. It is useful to separate congenital and acquired causes, since their clinical settings and implications obviously differ greatly. Congenital GI fistulas are best understood by realizing their embryologic origin and include such entities as branchial, tracheoesophageal, and omphalomesenteric fistulas. Acquired GI fistulas can be categorized as external or cutaneous if they communicate with the skin surface or internal if they connect to another internal organ system or space, including elsewhere along the GI tract itself. Internal GI fistulas can be further divided into two types: intestinal and extraintestinal. Intestinal fistulas refer to a gut-to-gut connection and may consist of any combination of stomach, small bowel, and colon. An enteroenteric fistula may refer to any intestinal fistula in the generic sense, although some may restrict this term to small-bowel fistulas only. Extraintestinal internal fistulas imply communication of the GI tract with another organ system such as the genitourinary system, biliary tree, or respiratory tract. Complex fistulas contain both internal and external components.

Underlying causes of acquired GI fistulas are diverse and can include virtually any process resulting in bowel perforation from within or bowel penetration from an extraintestinal process. The majority of external (cutaneous) fistulas represent a complication of recent abdominal surgery. The leading causes of internal fistulas in the industrialized world are Crohn disease, diverticulitis, malignancy, or a

complication of treatment of these entities. Not surprisingly, many cases are the result of multiple contributing factors; common examples include cancer patients who have undergone radiation therapy and patients with Crohn disease who have undergone prior bowel surgery. The specific location and type of fistula can often suggest certain causes, as will be seen when individual GI fistulas are covered more in depth. Some general features of the more common inflammatory causes will briefly discussed in the following paragraphs. Most of the remaining noninflammatory causes listed in will be covered in more detail in upcoming sections.

Fistula formation is a hallmark of Crohn disease, occurring in up to 20%–40% of patients described in surgical series. Sinus tracts and fistulas often involve the distal small bowel, and peritoneal abscess or phlegmon may be an associated finding. The clinical and radiologic manifestations vary widely because these internal fistulas can involve nearly any organ system, but ileocolic and enterovesical fistulas are the most common types. External fistulas are also common, especially in the perianal region. Fistula formation is considerably less common in ulcerative colitis, which, unlike Crohn disease, is not a transmural process. Rectovaginal fistula is the most frequent spontaneous GI fistula that develops in ulcerative colitis, followed by rectovesical fistula.

Diverticulitis is a common cause of colonic fistula formation, with the fistula most often communicating with the urinary bladder. Colovaginal fistulas are also relatively common in women with sigmoid colon diverticulitis, particularly after hysterectomy. Fistulas are seen in up to 20% of cases of surgically treated diverticular disease. Another relatively common finding in diverticulitis is a fistulous tract that parallels the colonic lumen, representing a localized form of colocolic fistula that has been termed "double tracking." Not surprisingly, fistula formation of the sigmoid colon predominates in diverticular disease, but other colonic segments are occasionally involved. Other than Crohn disease and diverticulitis, other less common inflammatory causes of GI fistulas include atypical infections, cholecystitis, pancreatitis, and appendicitis. Among the various atypical infectious causes that have been reported are tuberculosis, histoplasmosis, actinomycosis, xanthogranulomatous pyelonephritis, amebiasis, echinococcosis, and lymphogranuloma venereum.

V. Materials of activation of students

(questions, tasks, controversial situations, illustrative materials and other).

VI. Materials of selftraining of students on the topic of lecture: literature, questions, tasks.

Literature

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