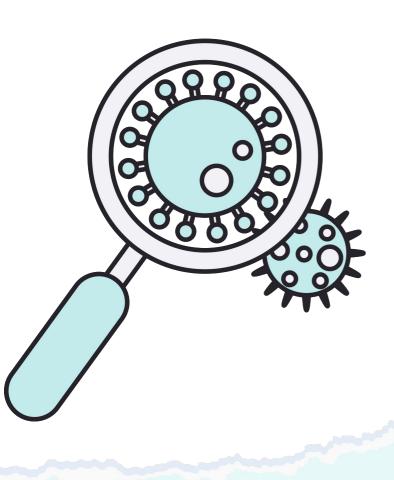


### Common infections in DM

### Prof.Hanan Habib & Prof.Ali Somily





Describe the reasons that patients with diabetes are at higher **risk** to develop infections.

Underline the common **infections** in diabetic patients ( **emphsizing on diabetic foot infection**).

Name the causative **organisms** and the **pathogenesis** of common infections in diabetic patients.

Discriminated between different clinical **presentations** of common infections In diabetic patients.

List the different laboratory and radiological **tests** used in common infections.

Identify the complications of diabetes mellitus ( diabetic foot ).

Select the appropriate **management plan** and antimicrobial therapy of common infections in diabetic patients.

Color Index: Main text Important Doctor Notes Males slide Females slide Extra



Diabetic patients are more susceptible to infections, nearly half of all diabetic patients had at least one hospitalization or outpatient visit for infections compared to non-diabetic patients. diabetic patients with infections have bad outcomes ie. higher morbidity and mortality

Why diabetic patients are at increased risk to have infections? Because of Host related factors & Organisms related factors



# Host Related Factors



HOST RELATED FACTORS ★				
Vascular insufficiency (1)	<ul> <li>Results in local tissue ischemia especially in small/medium sized blood vessels that :</li> <li>Enhances the growth of microaerophilic and anaerobic organisms.</li> <li>Suppression of the O2 dependent bactericidal functions of leukocytes → impairment of the local inflammatory response</li> <li>Decrease absorption of antibiotics.</li> </ul>			
Sensory peripheral neuropathy (2)	Minor local trauma $\rightarrow$ lack of sensation $\rightarrow$ development skin ulcers $\rightarrow$ diabetic foot infections.			
Autonomic neuropathy (3)	Diabetic patients may develop urinary retention $\rightarrow$ urinary stasis $\rightarrow$ predisposes to develop urinary tract infections.			
Hyperglycemia and metabolic derangements (4)	In diabetes may facilitate development of same infections.			
Immune defects	In diabetes such as: • Depressed Neutrophil function • Affected chemotaxis and phagocytosis • Depressed cell mediated immunity • Affected adherence to the endothelium • Compromised bactericidal activity			
Increased skin and mucosal colonization	<ul> <li>Diabetics on insulin have asymptomatic nasal and skin colonization with S. aureus particularly MRSA (6).</li> <li>Colonization predisposes to skin infection and transient bacteremia which may result in distal sites infection such as damaged muscle.</li> <li>In type-2 diabetes; mucosal colonization with C. albiacns is common. Vulvovaginitis (5) Caused by non-albicans Candida spp. is common in patients with poor glycemic control.</li> </ul>			
Surgical site infections	Associated with postoperative hyperglycemia which is related to deleterious effect on chemotaxis, phagocytosis and adherence of granulocytes.			



<b>Candida albicans</b> (7) yeast,Pseudohyphae	<b>Rhizopus spp</b> (9), (11) Mold Fungi
Glucose↑ inducible proteins promote → adhesion of <i>C. albicans</i> to buccal or vaginal epithelium(especially in pregnant)which in turn, → impairs <u>phagocytosis</u> , giving the organism advantage over the host.Leads to oral thrush and vaginitis.	Ketoacidosis (10) allow <i>Rhizopus</i> spp. which cause <b>Mucormycosis</b> (Zygomycosis) to thrive in high glucose acidic conditions .
Image: A product of the product of	Rhizopus colonies Rhizopus colonies CHE stain C.HE stain



## Common infections in diabetic patients



Upper & lower respiratory tract infections (URTI & LRTI)





Periodontal infections

Genitourinary infections



Abdominal infections



Skin and soft tissue & diabetic foot infections

# Upper Respiratory Tract Infection

	Invasive (malignant) otitis externa (8)	Rhinocerebral mucormycosis	
Introduction	Uncommon but potentially life threatening.	A life threatening fungal infection associated with DKA.	
Cause	Involves P.aeruginosa . Slowly invades from the external canal into adjacent soft tissues, mastoid & temporal bone and eventually spreads across the base of the skull.	cent soft tissues, and eventually(Mucormycosis ) Rhizopus (has non-septate hyphae), Absidia and Mucor species.	
Signs/symptoms /Clinically	Patient presents with severe pain, otorrhoea, and hearing loss. Intense cellulitis and oedema of the ear canal.	<ul> <li>Sinus pain/sinusitis facial or ocular pain and nasal stuffiness, generalized malaise and fever. May be intranasal black eschars or necrotic turbinate.</li> <li>Fungal colonization can go to blood vessel and they can cause ischemia and spread to the base of the skull quickly ,because of this we call it → Rhinocerebral or Rhino Orbital.</li> </ul>	
Diagnosis	CT scan and MRI studies to define the extent of bone destruction.	Biopsy of the necrotic tissue .Direct smear examination for hyphae.	
Vianagement annuluius		Surgical debridement and prolonged IV therapy with Amphotericin B.	

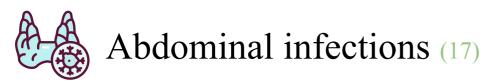


# Lower Respiratory Tract Infection

Pneumonia and Influenza (12)				
Introduction	Diabetic patients are 4 times more likely to die from pneumonia or influenza than non-diabetic patients.			
<b>Common</b> organisms	<ul> <li>Gram positive bacteria : S. aureus, S. pneumoniae.</li> <li>Gram negative bacteria: Enterobacteriaceae and Legionella.</li> <li>Other organisms: Influenza virus &amp; Mycobacterium tuberculosis.</li> </ul>			
Management	Routine pneumococcal and influenza vaccination recommended. (13), (14) (Can prevent it, especially: elderly, cardiovascular patients, and diabetics			

# Genitourinary infections (15), (16)

Cystitis (due to neuropathies )		Bilateral Pyelonephritis	Emphysematous Pyelonephritis	Vulvovaginitis Pyelonephritis
Introduction	Same as non-diabetics, incomplete bladder emptying and high incidence of unsuspected upper UTI.	Diabetes predisposes to a more severe infection of the upper urinary tract. alter kidney function→ end stage renal disease → hemodialysis	Exclusively an infection of diabetics (60%) and carries grave prognosis ( 30% fatal). emphysema = contain air	As mentioned earlier.
Organisms	Bacteria : - Gram negative rods - Group B Streptococcus (S.agalacteae ) fungi: - Candida albicans may be		_	
Diagnosis	-	_	Flank mass & crepitus . CT scan shows gas in the renal tissues.	-
Management important to be quick to prevent pus formation	-	_	Supportive & IV antibiotics , nephrectomy may be needed.	-



Severe fulminating Cholecystitis		
IntroductionGall stone or peritonitis may be present . Gas gangrene and perforation may occur.		
Common causes	Enteric Gram negative bacteria and anaerobes.	
Management	Cholecystectomy and broad spectrum antibiotics.	

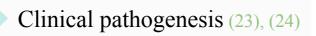


The most common and most important soft tissue infection in diabetic patient is diabetic foot infection, WHY? because it is related to peripheral neuropathy and compromised microvascular circulation (\blood supply) which limits the access of phagocytic cells (\immunity) to the infected area and poor concentration of antibiotics (due to decreased blood supply) in the affected area

Complicated by chronic osteomyelitis, gas gangrene, amputation and death.

The spectrum of foot infection ranges from superficial cellulitis to chronic osteomyelitis (22)

Combined infection involving bone and soft tissue may occur



A microvascular disease limits blood supply to the superficial and deep structures. Pressure from ill fitting shoes ,trauma compromises local blood supply predisposing foot to infection.

Infection may involve the skin, soft tissues, bone ,or all

Diabetic neuropathy may lead to incidental trauma that goes unrecognized. Sinus tract may be present.

### Organisms involved in diabetic foot infections (18)



Cellulitis	Beta-hemolytic streptococci (group A,B Streptococcus), S. aureus, Enterobacteriaceae (E. coli, Klebsiella, Proteus spp.) in chronic ulcers.	
Macerated ulcer or nail injury (sinus)	<b>P. aeruginosa.</b> because it is present in metal / wet object	
Deep soft tissue infections (necrotizing fasciitis, or myositis)	GAS & gas producing gram positive bacilli (Clostridium perfringens).	
Chronic osteomyelitis	GAS and Group B Streptococcus, S. aureus, Enterobacteriacae (E.coli, Proteus mirabilis, K.pneumoniae.) & Bacteroides fragilis.	

### Clinical Presentations of Diabetic Foot Infections

#### 1. Cellulitis

• Tender, erythematous non-raised skin lesion on the lower limb, may be accompanied with lymphangitis which suggests GAS.

• Bullae suggests S. aureus ,occasionally GAS.





#### 2. Deep skin and soft tissue infections

 $\circ$  Patient acutely ill, with painful inducation of the limb especially the thigh .

- Foot may be involved.
- Foul wound discharge suggest anaerobes.

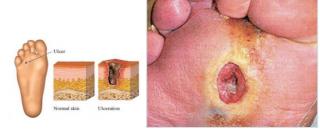
#### **3. Osteomyelitis** (25)

Acute osteomyelitis	Chronic osteomyelitis (26)	
Pain at the involved bone, fever and adenopathy.	Fever, foul discharge, may be pain, no lymphangitis, deep penetrating ulcer and sinuses on the planter surface of the foot.	

#### Factors that increases the development of Osteomyelitis

• Grossly visible bone or ability to probe to bone

- Ulcer size >2x2 cm
- $\circ$  Ulcer depth > 3mm
- ° Ulcer duration longer than 1-2 wks
- $\circ$  ESR >70 mm/hr





### Clinical Presentations of Diabetic Foot Infections

4. Skin and soft tissue infections				
Risk factors in diabetic patients	<ul> <li>Sensory neuropathy: no pain Dercention</li> <li>Atherosclerotic vascular disease</li> <li>Hyperglycemia: &gt;250 mg/ di increased risk</li> <li>History of cellulitis, peripheral vascular diseases, Tinea infection, and dry skin.</li> </ul>			
Organisms	<ul> <li>Streptococcus pyogenes (Group A Streptococcus (GAS))</li> <li>S. aureus. CA-MRSA (community acquired -MRSA) is of concern causes (77%) of skin and soft tissue infections. Resistance to (Methicillin, cloxacillin) Sensitive to (Vancomycin, sulfonamides, clindamycin)</li> </ul>			
	Necrotizing fasciitis(19), (27)			
Introduction	A deep –seated ,life threatening infection of subcutaneous tissue with progressive destruction of fascia, fat and muscles.			
Organisms	10% associated with Group A streptococci (S.pyogenes), with or without S. aureus, anaerobes may be involved Such as Clostridium perfringens.			
Clinically	<ol> <li>Pain of proportion of skin, anaesthesia of overlying skin, skin might not show severe redness (maybe mild edema and light redness only).</li> <li>Violaceous discoloration of skin purple color that evolves into vesicles and bullae bubbles.</li> <li>Crepitus</li> <li>Soft tissue gas seen in radiograph or CT scan.</li> <li>Fever, elevated WBC and, abnormal liver function test.</li> </ol>			
Management	Aggressive surgical debridement (28) & IV antibiotics. (if GAS was confirmed, penicillin and Clindamycin is an ideal choice)			











## Management of Diabetic Foot Infections

Diagnosis (20)				
	Thorough examination to evaluate the patient's vascular and neurological status.			
	Radiological examination including doppler ultrasonography, transcutaneous oximetry, MR angiography.			
	<b>CT scan, MRI</b> and gallium scan for soft tissue and bone evaluation.			
°°°	Exploration of ulcer to determine its depth and the presence of sinus tract.			
	Deep specimens (bone tissues) for culture and susceptibility testing.			
	Management &	& Treatment (21)		
<ul> <li>Control blood sugar and hydration.</li> <li>Evaluation of neuropathy and vasculopathy.</li> </ul>				
	Mild Cases Moderate to Severe Cases			
tissues the cau	<ul> <li>Surgical debridement of necrotic tissues and use of antibiotics according to the causative bacteria</li> <li>Moderate to Severe Cases may places the foot at risk of amputation (29) Team 42: So Antibiotics will be less effective in severe cases, so amputation may be required)</li> </ul>			

 eg. Cloxacillin, Cephalexin, Clindamycin, TMP-SMX (for CA-MRSA), Quinolones, Amoxicillin-clavulanic acid, Aminoglycosides.
 Needs hospitalization,IV antibiotics and surgical intervention as needed.

#### **Preventions (30)**

- $\circ$  Is the cornerstone of diabetic foot care.
- It is a multidisciplinary including family physician, social worker, home care nurse and specialist.
- Patient education about the control and complication of diabetes.
- Blood sugar should be controlled promptly (shift to insulin if oral hypoglycemic agents were not effective), weight reduction, a diet low in fat and cholesterol.
- $\circ$  Proper foot care, using protective footwear and pressure reduction.
- Self and family member examination of foot.



# Extra but helpful

Gram +ve				
S.aureus	-Cocci in <b>clusters</b> -Catalase: + -Coagulase: + - <b>Yellow</b> colonies on blood agar -DNAse +ve			
Strept. pyogenes (group A)	-Cocci in <b>chains</b> -Catalase: - -Coagulase; - - <b>β hemolytic</b> - Bacitracin <b>sensitive</b>			
Strept. agalactiae (group B )	-Cocci in <b>chains</b> -Catalase: - -Coagulase: - - <b>β hemolytic</b> -Bacitracin <b>resistant</b>			
Strept. pneumoniae	-Diplococci -Catalase: - -Coagulase: - -α hemolytic -Bile soluble -Optochin sensitive			
Clostridium perfringens	-Spore forming rods (bacilli) -Double zone of hemolysis -Transmission: foodborne and traumatic implantation			
	Gram -ve			
Enterobacteriaceae	-Oxidase: - -Catalase: + -Ferment <b>glucose</b>			
Legionella	-Gram stains poorly, use silver stain -Grow on <b>charcoal yeast extract medium</b> -Transmission: aerosols from environmental <b>water</b> source habitat (air conditioning systems) , no person-to-person transmission			
Pseudo. aeruginosa	-Bacilli -Non-lactose fermenter -Oxidase: +			
Bacteroides fragilis	-Reservoir: predominant anaerobe in the human <b>colon</b> -Transmission: endogenous from <b>bowel defect</b>			

Extra

Special thanks to team39



- 1. Regarding blood supply in diabetic patient :
- in normal healthy individual blood guides the immune cells towards the site of injury but in case of low blood supply, this mechanism will not happen. Also in case of low blood supply will lead to decrease oxygen and that will help bacteria to multiply
- 2. Regarding peripheral neuropathy: Can lead to infection because patients might have ulcer at the beginning and they do not feel it, which will then lead to complications.
- 3. Regarding Autonomic neuropathy :
  - 1- mainly affect internal organ ,like: GIT and urinary bladder.

2- normally in healthy person we are able to feel the distension of urinary bladder ,but in diabetic patient they do not sense bladder distension (Also they have other factors like they are elderly or have benign hyperprostatic hyperplasia ), because of these factors urine will remain in bladder longer than usual  $\rightarrow$  possibly lead to sepsis and infection.

(مثل المستنقع اللي الماء فيها راكد فيكون فيه Accumulation of all the organisms)

- 4. hyperglycemia itself can affect metabolism, immune system, healing process ,can affect so many things.
- 5. Candida normal flora in GIT ,it can cause infection in pregnant women and diabetic patient( later on we will teach you Candida vulvovaginitis very common in diabetic patient)
- 6. MRSA (Methicillin-resistant staphylococcus aureus) : they are colonized In diabetic patients more than in non diabetic patient
- 7. Candida is a simple infection we do not worry about it ,but it might lead to candidemia ,or might be annoying to the patient because he won't be able to eat due to oral thrush .and in diabetic patient this would be more severe.
- 8. if you are diabetic and you are injured or exposed to water "مثل لما تلبسوا سماعه واذنكم فيها مويه" that contain organism → it will cause very bad infection like: edema, discharge, redness, very severe pain (why feel pain? cuz it the nerve has been affected) and this infection can extend and go to the bone and skull.
- 9. Rhizopus is a mold like aspergillus , and both of them present in nature in the air, to be more specific in dust, so once a diabetic patients (uncontrolled) is expose to this organism , they develop something we call diabetic ketoacidosis
- 10.
- pathophysiology of ketoacidosis :

normally once insulin is secreted it helps in taking up glucose by organs (like liver, muscle, ect) in order to be used to produce energy, in case there is no glucose uptake (which consider the first source of energy) our body will undergo gluconeogenesis ( another way to get ATP) so blood will undergo acidosis due to production of ketone bodies which will be elevated in blood and excreted in urine ,This acidity that have been produced is favored by mucoid Rhizopus.

-Rhizopus and ketoacidosis:

sinusitis + mucoid Rhizopus only  $\rightarrow$  no problem

but in case with ketoacidosis  $\rightarrow$  organism will go and spread within hours and start invading blood vessel ,if we opened the blood vessel we will see colonization that looks like cotton.



- 11 we have to take a sample quickly once we suspect ( Rhizopus ) by doing:
  - $\circ$  staining  $\rightarrow$  non septeaded (flabby colonies like cotton, and it is grey-white in color)  $\circ$  culture
  - $\circ$  microscopic  $\rightarrow$  hyphae , but once we take the slide section it will be broken.
  - Characteristic of Rhizopus :

wider than Aspergillus, non septeaded , the margins is right angle (زاوية قائمة) or greater, non diacomitic hyphae

#### 12.

- Severe pneumonia infection in diabetic patient may lead to high mortality rate, so we have to know there is a way to prevent infection by getting a vaccine.
- pneumococcal vaccine must be given routinely  $\rightarrow$  if they do not have it they must have it, whatever polysaccharide or conjugate vaccine.
- -polysaccharide  $\rightarrow$  it has a capsule, but recently they found that it is not effective in young children, so they created diphtheria conjugate vaccine, and it's more immunogenic.
- In summary, The conjugate is important for children, but for adult it depends in availability
- 13. Indication for getting influenza vaccine:
  - 1- diabetic patient  $\rightarrow$  must get the vaccine annually
  - 2- people who are older than 50 years
  - 3- people who have chronic lung disease
- 14. What the difference between annual and routine??
  - annual  $\rightarrow$  every year
  - routine  $\rightarrow$  we give it to people depending on scaling ( $\neq \ell \ell$ ) and depend on indication .

#### 15.

- UTI is very serious condition in diabetic patient ,because it may lead to renal failure due to diabetic neuropathy ( creatinine level in blood is very high).

once diabetic patients are infected, they will lose one kidney in pyelonephritis or abscess that lead to dialysis. you do not want this to happen to your patient ,so you must take this condition seriously by excluding GI intolerance ,knowing if it is upper or lower ,and assessing radiological.

- Why should we take the situation seriously? Because sometimes the patient might be hypothermic (not febrile) and doesn't complaining of anything or any pain, But unfortunately frequent infection if not treated well, the patient will end up having scars (renal scar)
- 16. you know the kidney is retroperitoneal, so severe infection may turned into flank of mass (collection of abscess) you have to dain it or do surgery to remove it ,if you keep it ,it will go to the blood and kill the patient
- 17. for abdomen  $\rightarrow$  severe cholecystitis and gangrene , same as we said in kidney with the same organism.



مهم جدًا تفرقوا بينهم :18. Diseases in the skin

1- Cellulitis : involves subcutaneous (fat)

mainly caused by strep and staph ,and might be by gram negative anaerobes, pseudomonas

Sakean

- 2 Ulcer or wound ,and it depends on the location, and might lead to abscess.
- 3 Necrotizing fasciitis : involves the facia, and it has two types : type 1 : mixed → Clostridium perfringen , group A strep , may gram negative. type 2 : group A strep
- 4 Myositis: involve the muscle mainly caused by : group A strep or clostridium perfringens ( can cause gas gangrene due to presence of alpha toxin phospholipase)
- 5 Osteomyelitis : involve the bone
  - Note: we have to consider about the possibility of overlapping or combination of these diseases, for example a patient might present with cellulitis and necrotizing fasciitis or osteomyelitis with necrotizing fasciitis and so on.
- 19. Regarding necrotizing fasciitis :
  - Similar to cellulitis but the difference is that the patient has \*\*severe pain\*\*and systemic disease like: hypertension , elevated liver enzyme (blood test), multiorgan failure
  - treatment: penicillin or ceftriaxone
  - in case it is type two  $\rightarrow$  penicillin with clindamycin
  - if we suspected type 1 (mixed)  $\rightarrow$  we use broad spectrum antibiotic like pip tazo or meropenem and we add clindamycin

ماراح أسألكم عنها بس مهم تعرفوها ?why we add clindamycin

1-to stop toxin 2- it has a good bioavailability 3- it acts on lactines

- 20. Example: a diabetic patient presents with pain in his leg and he has ulcer in his sole, What will you do?
  - 1- History( presenting illness) :
  - ask about DM, if his suger controlled or not
  - ask about the pain (SOCRATES)
  - 2 -Whole physical examination: Blood test, X-ray, systemic examination, CVS examination, abdomen(ischemic bowel disease)
  - 3- foot examination=> sensation examination, movement of muscle, blood supply, hair (people who have ischemia tend to lose hair)
- 4- palpation of the artery=> arteries that supply the leg: dorsalis pedis and posterior tibia.
- 5- Examine the ulcer=> redness, size, depth, the bone is involved or not?
- 6- After that we decide what further investigation we need=> radiology(mainly MRI), blood test (urea, creatinine, CPC), culture (blood culture/ urine culture/ ulcer aspiration deep sample cuz it is colonized/tissue biopsy)
- 21. treatment: antibiotics and debridement.



- 22. Diabetic foot wide spectrum, pathogenesis  $\rightarrow$  in diabetic patient, it will start with mild infection(so it is important to ask when the infection started) and then progress into chronic osteomyelitis and the patient might not feel the pain.
- 23. Always serious infections happen mainly due to three reasons:
  - Bacteremia
  - adjacent organ (soft tissue can go to the bone)
  - External ( like a glass caused injury)
- 24. accumulation of water inside shoes will lead to colonization of candida , and once the diabetic patient wears them , it can invade the skin and cause infection.
- 25. the ulcer is big and deep  $\rightarrow$  think about osteomyelitis
- 26. in chronic osteomyelitis : the patient is not very sick , because it is chronic .
- 27. In necrotizing fasciitis:

If the patient conscious  $\rightarrow$  he will complain from acute severe pain , very sick if the patient is unconscious  $\rightarrow$  we will find abnormal liver function test and hypotensive.

- 28. After performing surgery on a patient with necrotizing fasciitis, we keep the wound open, in order to provide an oxygenated environment and to make sure everything have been cleaned
- 29.
  - diabetic patients who suffer from gangrene will undergo amputation .
  - gangrene does not always occur due to infection ,it might be due to stoppage of blood supply.
  - amputation is considered as a big problem in necrotizing fasciitis , because the two risk factors for developing facia necrotizing are : 1- wound 2- presence of clostridium in GIT
- 30. Prevention: by controlling diabetes, how can we control diabetes?
  - social support
  - understand the complication
  - $\circ$  foot care => must be taken by family member , check the medication , exame the foot and wearing proper sheo.



Q1 - Which of the following antibiotics used only in lower tract / Not used in upper tract ?						
A) Ciprofloxacin	B) Ceftriaxone	C) Nitrofurantoin	D) Sulphonamides			
Q2 - Which one is a comm	Q2 - Which one is a common cause for mucosal colonization in type two diabetic patients?					
A) Pseudomonas aeruginosa	B) C. albicans	C) E.coli	D) legionella			
Q3 - Which of the followin	ng organisms most likely cau	uses UTI (Cystitis)?				
A) Group B streptococcus	B) Pseudomonas aeruginosa	C) S.aureus	D) Clostridium perfringens			
Q4 - Cellulitis which is ten	der, erythematous non-raise	ed skin lesion on the lower li	mb, may be accompanied			
with lymphangitis might c	aused by which organism?					
A) Strept. pyogenes (GAS)	B) C. albicans	C) Clostridium perfringens	D) Pseudomonas aeruginosa			
Q5 -Invasive (malignant) o	otitis externa mainly caused	by				
A) E.coli	B) S.aureus	C) Group B streptococcus	D) Pseudomonas aeruginosa			
Q6 - Rhinocerebral Mucor	rmycosis is mainly associate	d with which medical condit	ion?			
A) Urinary tract infections.	B) Diabetic ketoacidosis	C) Peripheral Neuropathy	D) lymphadenopathy			
1						
A 19 year-old man with a	negative past medical	Mention the clinical <b>p</b>	resentation of diabetic foot			

A 19 year-old man with a negative past medical and surgical history was diagnosed with aggressive rapidly progressive necrotizing fasciitis of left lower extremity, after examination we found that the organism is group A streptococcus only , what is the appropriate treatment?



- 4- Skin and soft tissue infection
- 5-Necrotizing fasciitis

Penicillin with Clindamycin.





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Any future corrections will be in the editing file, so please check it <u>frequently</u>