DM and Infection

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Case

- 87-year-old woman
- fever and drowsiness for two days
- She had a history of diabetes mellitus, atrial fibrillation and post-stroke global aphasia.
- she had diffuse abdominal tenderness.
- leukocytosis and bacteriuria,

- ??????

Case

- Suspicious to urinary tract infection.
- Blood and urine cultures were obtained,
- and she was given intravenous amoxicillin clavulanate.

Case
3rd admission day

-
- fever resolved,
- but hypochondrial guarding developed on her right side

- **????**

- A plain radiograph of the abdomen with the patient in a supine position suggested the presence of a dilated gallbladder with air in the lumen and wall. Computed tomography showed an air-liquid level in the gallbladder lumen, gas dissecting the entire gallbladder wall, and pneumoperitoneum

case

- Cholecystectomy was not performed because the patient was thought to be too frail.
- Instead, she was given piperacillin-tazobactam intravenously, and **percutaneous drainage** of the gallbladder was subsequently performed.
- **urine culture grew *Escherichia coli***,
- **blood and bile cultures from the drainage** were negative.
- The patient recovered and was able to eat at discharge

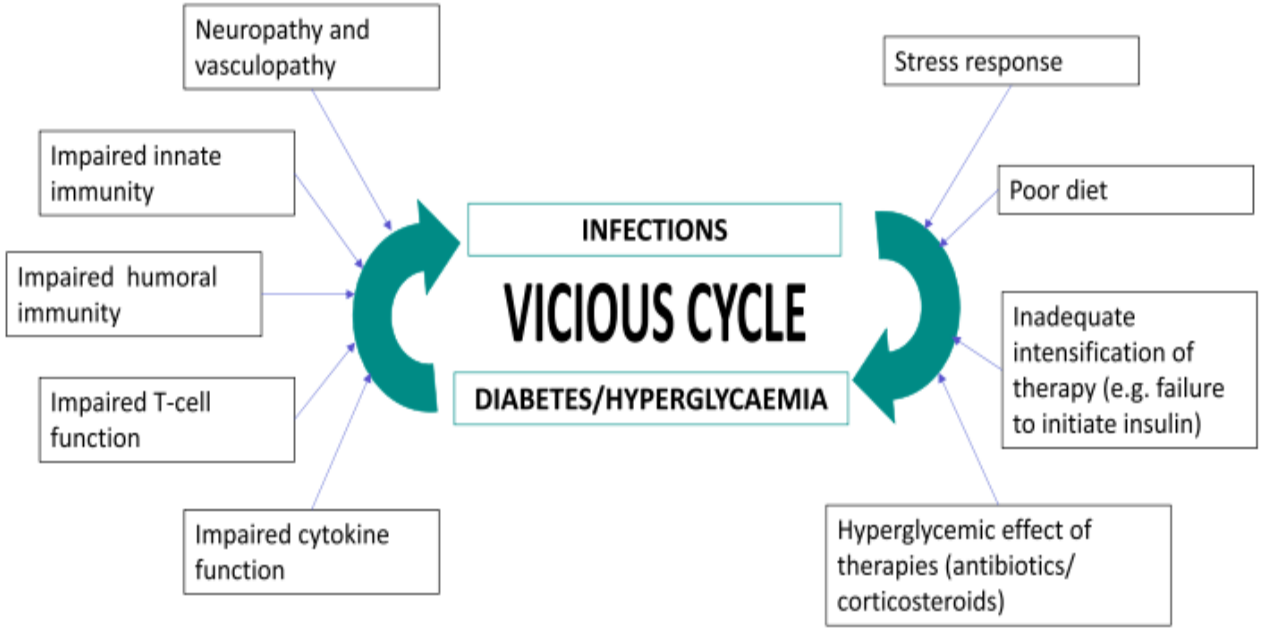

Fig. 1. Bidirectional relationship between diabetes/hyperglycemia and infection.

Types of infection

Common

- Respiratory tract
- Genitourinary tract
- Skin and soft tissue

Uncommon infection

- Malignant otitis externa
- Rhino cerebral mucormycosis
- Emphysematous cholecystitis
- Emphysematous pyelonephritis
- Necrotizing fasciitis (Fournier gangrene)
- Diabetic foot infections

Pathogen	Emerging disease	Main complications in diabetics	References
RESPIRATORY INFECTIONS			
Streptococcus pneumoniae	Pneumonia	Respiratory failure, pleural effusion, bacteremia, septic shock	(62–64)
Mycobacterium tuberculosis	Tuberculosis (TB)	Impaired cell-mediated immunity, renal failure, micronutrient deficiency and pulmonary microangiopathy	(65, 66)
URINARY TRACT INFECTIONS			
Escherichia coli and *Proteus* sp.	Pyelonephritis	Pherinephric and/or renal abscesses, emphysematous pyelonephritis, renal papillary necrosis, urosepsis, and hemolytic-uremic syndrome	(5, 29, 67–70)
GASTROINTESTINAL INFECTIONS			
Helicobacter pylori	Gastritis	Macroangiopathy, neuropathy, proteinuria and microalbuminuria	(71–74)
SKIN AND SOFT TISSUE INFECTIONS			
Staphylococcus aureus and *Staphylococcus epidermidis*	Foot infection	Amputation, osteomyelitis, and death	(13, 75–78)
Combination of one anaerobic and many aerobic microorganisms	Necrotizing fasciitis	Fulminant local tissue destruction, microvascular thrombosis, and systemic signs of toxicity	(79–81)
Escherichia coli, *Klebsiella* sp., *Proteus* sp., and *Peptostreptococcus*	Fournier gangrene	Sepsis, multiple organ failure, and death	(82, 83)
HEAD AND NECK INFECTIONS			
Pseudomonas aeruginosa	Invasive external otitis	Periostitis, osteitis, chondritis, osteomyelitis, multiple cranial nerve palsies, and facial paralysis	(84, 85)
Listeria monocytogenes	Listeriosis	Sepsis, meningitis, hydrocephalus	(86–88)

TABLE 2 | Main complications during viral infections in patients with diabetes.

Pathogen	Emerging disease	Main complications in patients with diabetes	References
RESPIRATORY INFECTIONS			
Influenza virus	Pneumonia	Risk of admission to the intensive care unit, fatal outcome after infection, increasing influenza severity, and secondary bacterial infections	(130, 135, 136)
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS CoV2) virus	COVID-19	Inflammatory storm in atherosclerotic plaques, increased viral secondary infection to lung, acute respiratory distress syndrome, acute renal failure, acute cardiac injury and heat failure, and increased risk for patient mortality	(137, 138)
LIVER INFECTIONS			
Hepatitis B virus[a]	Hepatitis B	Elevated serum triglyceride level, blood glucose abnormalities steatosis and cirrhosis	(22, 139)
Hepatitis C virus	Hepatitis C	Reduced rate of sustained virological response, progression to fibrosis and cirrhosis, and higher risk for development of hepatocellular carcinoma	(22, 140, 141)
OTHER INFECTIONS			
Human immunodeficiency virus	HIV/AIDS	Hypertension, dyslipidemia, and acute myocardial infarction	(142, 143)

TB

- The greater risk of contracting TB in diabetes,
- reactivation of latent TB: due to a combination of susceptibility to infection with **oxidative stress and increased tissue inflammation**.

- A recent systematic review on the co-prevalence of TB and diabetes in ***low and middle-income countries***; diabetes was found in 1.8- 45% of individuals diagnosed with TB, and 0.1- 6% of individuals with diabetes had TB.

DM depresses the immune response through:

impairing in :

- chemotaxis,
- phagocytosis
- antigen presentation
- T-cell function

facilitating infection and **progression to symptomatic disease**.

- .

Genitourinary infections in DM

- urethritis,
- vaginitis,
- cystitis,
- prostatitis.
- Common: Gram-negative bacteria (E. coli and Klebsiella) and fungi such as Candida.
- nearly 30% of individuals with positive urine culture were found to be asymptomatic; guidelines state that asymptomatic bacteriuria need not be treated, even among patients with diabetes

Skin and soft tissue infections

- furuncles, carbuncles, and cellulitis.

- Infection is also an important component of Diabetic Foot Syndrome.
- Most cases of diabetic foot infection have been shown to be polymicrobial in nature, with a predominance of Gram-negative organisms.
- Prevalence of antimicrobial drug resistance was also found to be higher among patients with diabetes

Diabetes and COVID-19

- it appears that individuals with diabetes are not at higher risk of infection with SARS-CoV2 compared to the general population.
- they tend to have worse outcomes, with respect to the development of more severe illness and mortality risk, than individuals without diabetes.
- As individuals with diabetes tend to be older and to have a higher burden of cardiometabolic risk factors such as obesity and hypertension

New onset hyperglycemia during COVID infection

: can have multiple causes:

- weight gain following disordered diet and exercise during the lockdown,
- mental stress,
- unwarranted use of dexamethasone for mild to moderate cases of COVID.
-

Is covid, a diabetogenic cause?

- Direct invasion diabetogenic potential by way of its effects on the pancreas.
- The angiotensin-converting enzyme 2 (ACE2) receptor, by means of which SARS-CoV2 enters target cells, is also present on the pancreatic beta-cell.
- Infection of the beta cell may lead to acute impairment of insulin secretion or even destruction of the beta cell, as has been reported for human herpesvirus infection in Africa.

Rare infections

- Malignant otitis externa refers to Pseudomonal infection of the external acoustic meatus ad middle ear.
- Rhinocerebral mucormycosis is an infection of the nasal cavity and orbit by fungi such as Rhizopus, Mucor and Absidia.
- Emphysematous pyelonephritis refers to infection of the **renal parenchyma** by gas-forming micro-organisms such as E. coli.
- Renal papillary necrosis is a complication of UTI in diabetic patients characterized by necrosis and sloughing off of the renal papillae.
- Emphysematous cholecystitis is inflammation of the gall bladder due to infection by gas-forming micro-organisms.
- Necrotizing fasciitis is an uncommon infection of soft tissue caused by various combinations of Streptococci, Staphylococci, and anaerobes. Necrotizing fasciitis of the perineum is termed **Fournier's gangrene.**

Table 2
Recommendations for vaccination in individuals with diabetes [57–59].

Vaccine	Recommendation
Pneumococcus	• Children should be vaccinated with 13-valent pneumococcal conjugate vaccine (PCV13) before the age of 2 years • People with diabetes aged 2–64 years should receive 23-valent pneumococcal polysaccharide vaccine (PPSV23). Booster dose is needed after age 65
Influenza	• Annual vaccination with influenza vaccine (preferably quadrivalent vaccine) is recommended for all people 6 months of age and above
Hepatitis B	• Administer a 2- or 3-dose series of hepatitis B vaccine, depending on the vaccine, to unvaccinated adults with diabetes ages 18 through 59 years • Consider administering a 3-dose series of hepatitis B vaccine to unvaccinated adults with diabetes ≥60 years of age.
Other vaccines	Should be administered as appropriate for age

Pneumonia(Strep. Pneumonia-influenza)

- The **most frequent respiratory** infections associated with DM are caused by **Streptococcus pneumoniae** and **influenza virus**.

- Persons with DM are **six times** more likely to need **hospitalization** during influenza epidemics than non-diabetic patients.

- Diabetes is also a common coexisting condition and a risk factor for **complications in** patients with **H1N1** (pandemic influenza virus) infection.

Urinary tract infections

- Urinary tract infections (UTIs) are more prevalent in individuals with DM and may evolve into complications and/or serious manifestations.
- The main risk factors for UTI in DM are:

1. inadequate glycemic control,
2. duration of DM,
3. diabetic microangiopathy,
4. impaired leukocyte function,
5. recurrent vaginitis,
6. functional abnormalities of the urinary tract.

Asymptomatic bacteriuria

- Although women with DM have greater prevalence of asymptomatic bacteriuria,
- the data on the natural history of this condition in women with DM are conflicting.
- Some studies reported progression to pyelonephritis, whereas other suggested that this does not lead to serious complications.
- routine recommendation of antibiotic therapy for asymptomatic bacteriuria in diabetic is not necessary.

Bacterial pyelonephritis

- Acute pyelonephritis is 4–5 times more common in individuals with DM.
- Most infections are caused by Escherichia coli or Proteus sp.
- The clinical presentation is similar to that of non-diabetic individuals, except for the bilateral renal involvement.
- persons with DM are at increased risk for **complications**

1. perinephric and/or renal abscesses,
2. emphysematous pyelonephritis (EP),
3. renal papillary necrosis

Emphysematous pyelonephritis

- necrosis of the renal parenchyma with the presence of gas in the collecting system or in the perinephric tissues.
- It is most commonly observed in DM women.
- E. coli and Enterobacter aerogenes are the most frequent pathogens, (followed by Klebsiella sp., Proteus sp., Candida and Streptococcus sp).
- Fever, chills, mass and flank pain, nausea, and vomiting are the first symptoms.
- Crackles in the **flank or thigh** are less frequent.
- Abdominal computerized tomography allows the identification of gas in the urinary tract

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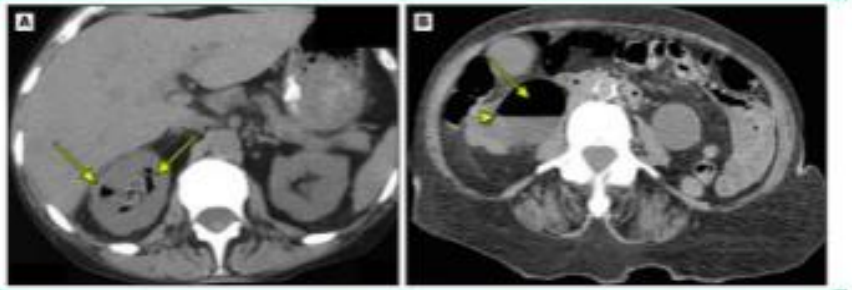
Emphysematous pyelitis on CT



An axial CT through the kidneys (A) shows air within the calyces of the right kidney (arrows). *Escherichia coli* was isolated from the urine. Image B shows air in the right renal pelvis (arrow) associated with an air-fluid level (arrowhead). The patient had a retrovesical fistula.

CT: computed tomography.

Graphic 94105 Version 3.0

Fungal cystitis

- Fungal infections are more common in DM, particularly those caused by Candida.
- The distinction between infection and colonization can be difficult.
- The presence of urinary symptoms or pyuria suggests infection.
- Fungal cystitis may result in the formation of "**fungal balls**" which may complicate urinary tract obstruction

Emphysematous cystitis

- Emphysematous cystitis affects persons with DM more frequently than non-diabetics.
- It is characterized by the presence of **gas in the bladder cavity** and infiltration of the **bladder wall** due to infection by bacteria that produce carbon dioxide.
- The most frequent pathogen is E. coli, followed by Enterobacter, Proteus, Klebsiella, and Candida Women are more affected than men.
- Computerized tomography is the standard diagnostic method.

Emphysematous cystitis

Perinephric abscess

- The main etiologies of renal and perinephric abscesses are enteric gram-negative bacilli (predominantly E. coli) or polymicrobial infection.
- Around one-third of perinephric abscesses occur in persons with DM.
- The initial clinical manifestations are fever, backache, dysuria, and/or polyuria.
- A palpable mass may be present.
- In individuals with DM, the clinical presentation is non-specific (diagnosis is usually late, contributing to a worse prognosis).

- ***This diagnosis should be considered in patients with acute pyelonephritis that does not get better after antimicrobial therapy***

Perinephric abscess

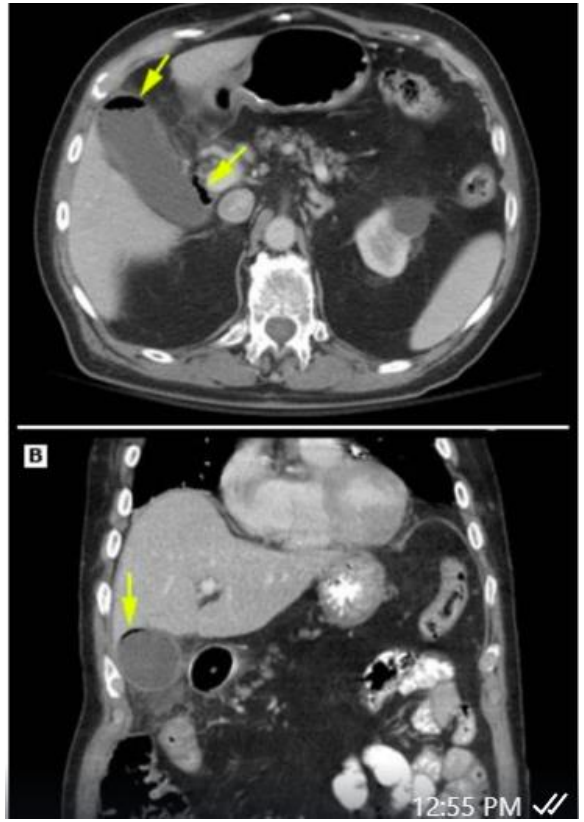
Oral and esophageal candidiasis

- The most common etiological agent is Candida albicans.
- Its pathogenesis is related to a combination of factors that increase its virulence;; production of **extracellular enzymes such as proteinase and phospholipase.**
- Candidiasis: median rhomboid glossitis or central papillary atrophy, atrophic glossitis, denture stomatitis, pseudomembranous candidiasis, and angular cheilitis.
- The diagnosis is **eminently clinical.**
- Esophageal candidiasis, endoscopy is needed.

Emphysematous cholecystitis

- emphysematous cholecystitis is more frequent in males with DM.
- The main pathogens are Salmonella enteritidis and Campylobacter.
- The clinical presentation is not different from that of non-complicated cholecystitis (e.g. right upper quadrant abdominal pain, vomiting, and fever).
- Clinical signs of peritonitis are usually not observed.
- **Crackles** can be felt on abdominal palpation, being associated with a worse prognosis.
- The diagnosis is made by the detection of gas inside the gall bladder, demonstrated in a **radiograph or computerized tomography scan**

Emphysematous cholecystitis



Skin and soft tissue infection

- Persons with DM are more predisposed to skin and soft tissue infections such as
- folliculitis,
- furunculosis
- subcutaneous abscesses.
- These infections may break out during the course of the disease or maybe the first sign of DM presentation, and can also be more severe in these populations

Foot infection

- the most important chronic complications of DM,
- one of the most common causes of hospitalization and often resulting in amputation, osteomyelitis, and death
- Moderate infections non-limb threatening are defined as superficial, with cellulitis less than 2.0 cm in the largest diameter, without evidence of serious ischemia, systemic toxicity, or bone and/or articular involvement.
- Serious infections limb-threatening." are defined as deep ulceration, with cellulitis equal to or greater than 2.0 cm in the largest diameter, with evidence of serious ischemia, systemic toxicity, or bone and/or joint involvement
- These infections can be monomicrobial or polymicrobial.
- Staphylococcus aureus and Staphylococcus epidermidis are isolated from around 60% of all the infected ulcers. Enterococci, streptococci, and enterobacteria are less frequent, and 15% of the infected ulcers have strict anaerobic bacteria.
-

Foot infection

- Infection in a very recently acquired superficial ulcer is likely to be monomicrobial due to aerobic Gram-positive cocci, such as staphylococci
- Long duration of ulceration and increased depth are likely to increase the chances of the wound, yielding both polymicrobial growth and resistant organisms.
- Simple clinical assessments are predictive of bone involvement, such as the size and depth of the ulcer.
- Ulcers larger or deeper than 2 cm^2 are more likely to be associated with underlying bone infection.
- radiological abnormalities are either observed 10–20 days after the beginning of the infectious process or when 40–70% of the bone is lost.
- Thus, the most sensitive tests are scintigraphy and magnetic resonance imaging

Necrotizing fasciitis

- fast and progressive necrosis of the ***fascia and subcutaneous*** tissue, causing fulminant local **tissue destruction**, **microvascular thrombosis**, and **systemic signs of toxicity.**
- Mortality occurs in approximately **40%** of the cases.
- The initial symptoms are fever and intense local pain, followed by areas of skin necrosis with small ulcers that drain a colourless fluid and have an unpleasant smell.
- Air in the soft tissues can be better detected by radiograph.
- The most affected sites are the thorax, abdominal wall, extremities, perineum, and groin.
- In DM, fasciitis is typically polymicrobial, with one anaerobic and many aerobic microorganisms.

Fournier gangrene

- Fournier gangrene is a fasciitis that affects the genitalia.
- The most common etiologic agents are E. coli, Klebsiella sp., Proteus sp., and Peptostreptococcus.
- The aetiology can also be polymicrobial, involving Clostridium, aerobic or anaerobic streptococci, and Bacteroides.
- Up to 70% of the patients with this infection have DM.
- It usually involves the *scrotum but can be extended to the penis, perineum, and abdominal wall*.
- Contrary to the general belief, the **testicles** are usually spared

Head and neck infections

- The two most serious head and neck infections in diabetic persons:

1. invasive external otitis

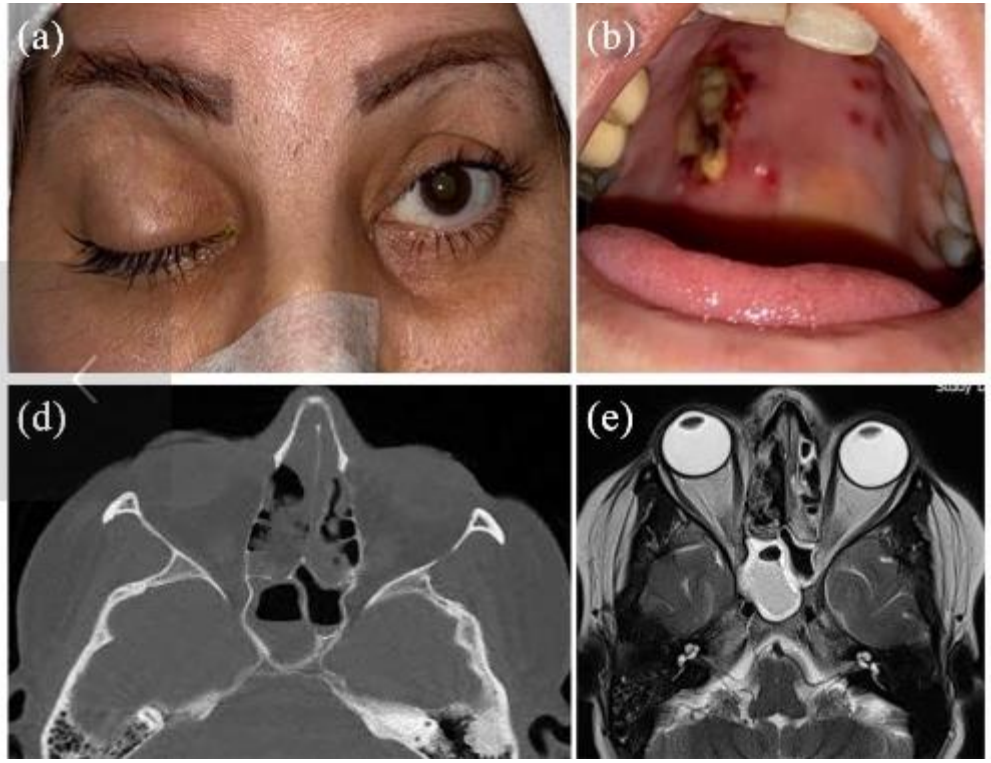
1. Rhinocerebral mucormycosis

Invasive external otitis

- external auditory canal that can extend to the skull base and adjacent regions.
- It often affects elderly diabetic individuals and the etiologic agent is usually Pseudomonas aeruginosa.
- Excruciating pain, otorrhea, and hearing loss are the characteristics.
- Skull base osteomyelitis and cranial nerve involvement may occur.
- Facial paralysis occurs in 50% of the cases.
- The best diagnostic method is the **magnetic resonance imaging**

Rhino cerebral Mucormycosis

- Mucormycosis is a rare opportunistic and invasive infection caused by fungi of the class Zygomycetes.
- This infection occurs in approximately 50% of the cases in individuals with DM due to the greater availability of glucose to the pathogen that causes mucormycosis,
- the decrease in serum inhibitory activity against the Rhizopus in lower pH, and the increased expression of some host receptors that mediate the invasion and damage to human epithelial cells by Rhizopus.
- The mucormycosis can be acute and chronic.
- The **classical triad :** paranasal sinusitis, ophthalmoplegia with blindness, and unilateral proptosis with cellulitis.
- Facial or eye pain and necrotic wound of the palate of the nasal mucosa may occur.
- Black necrotic eschar in the nasal cornets is a characteristic sign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THANK YOU