



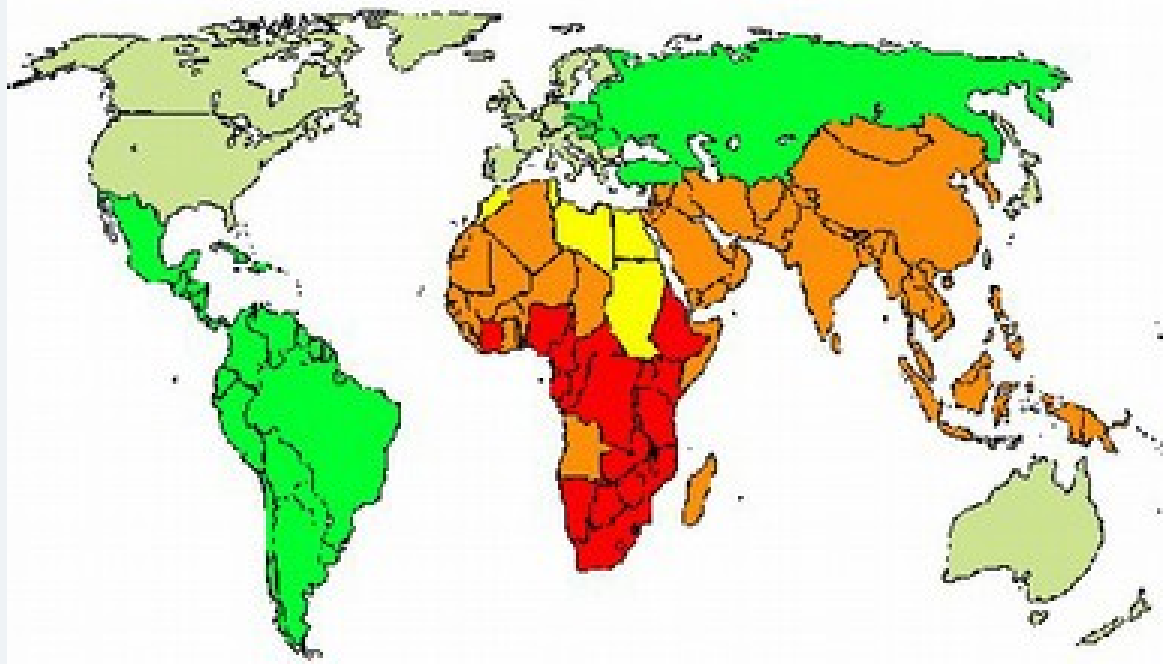
Renal Tuberculosis



Epidemiology



Global TB Incidence



Cases per 100,000:

■ >300	■ 50-100
■ 200-300	■ <50
■ 100-200	

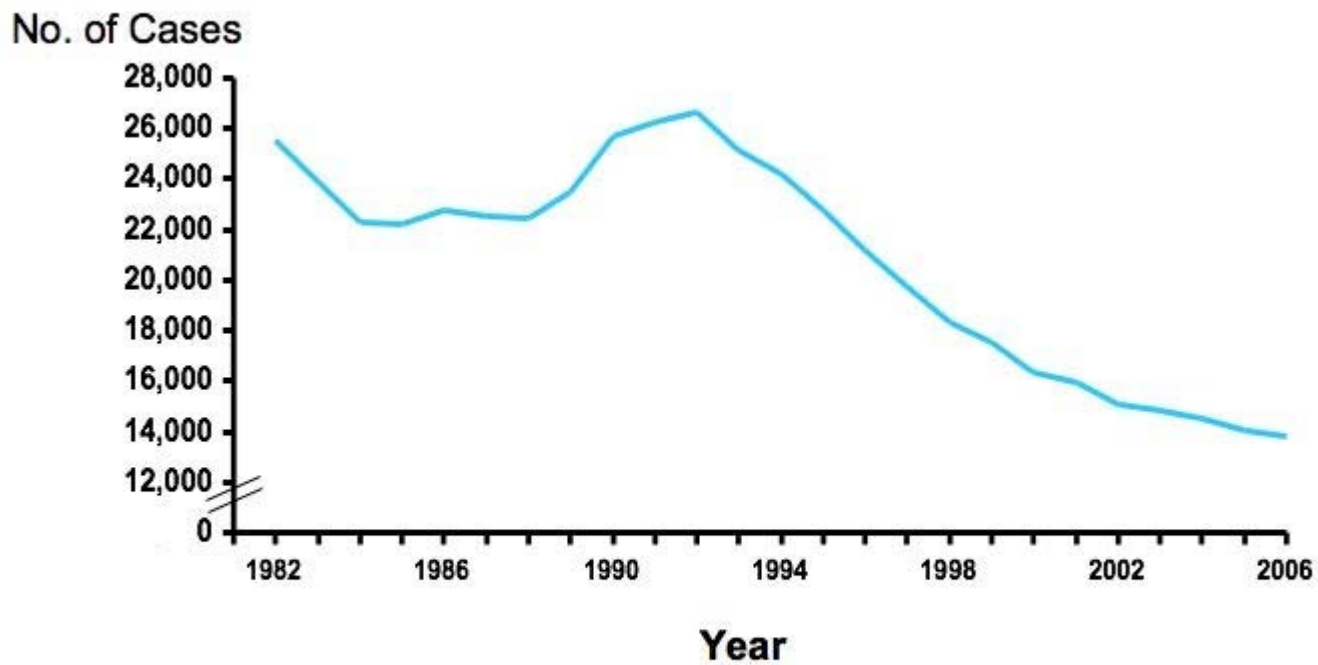


Figure 6. Reported TB Cases, United States, 1982-2006. Source CDC.

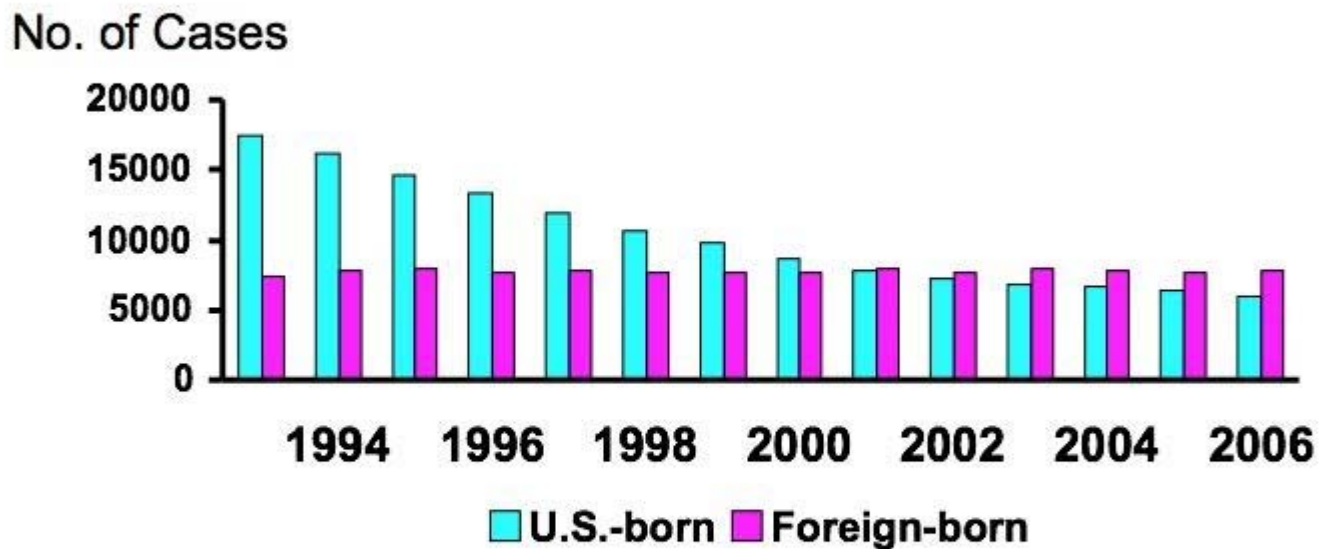


Figure 7. Number of TB Cases in US-born vs. Foreign-born persons, United States, 1993-2006. Source CDC.

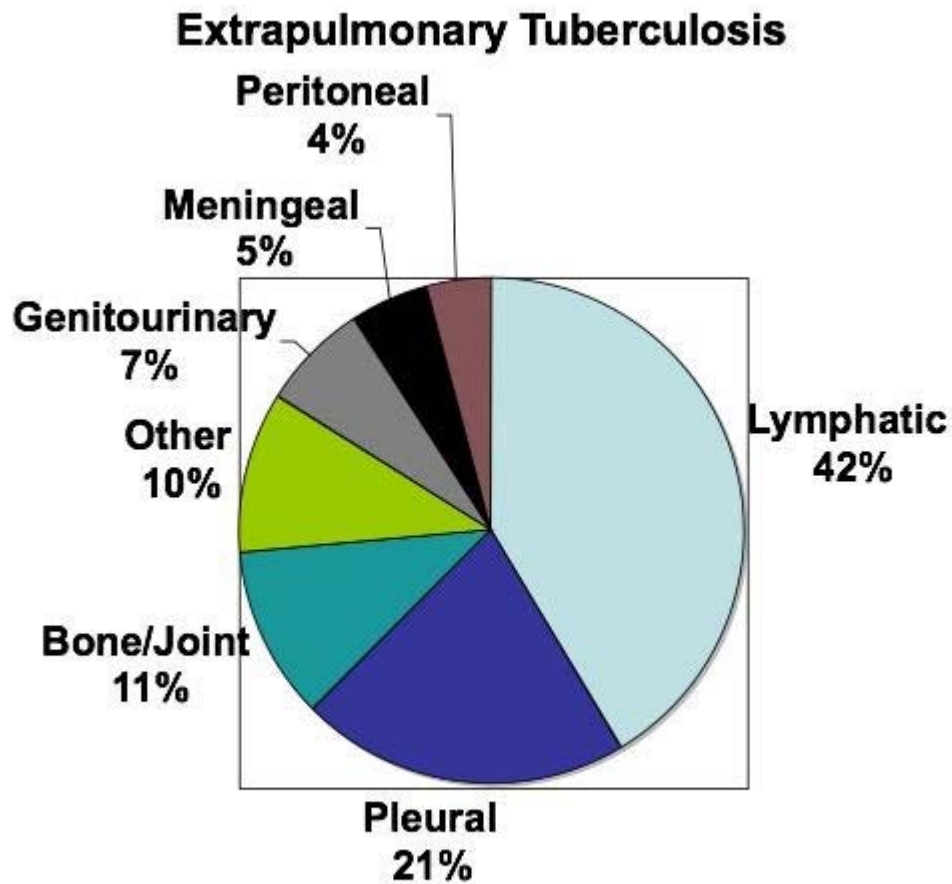


Figure 1: Frequency of different forms of extrapulmonary tuberculosis. Source CDC.



- Globally, tuberculosis is a common disease, with 8 to 10 million new cases annually and a rising incidence, particularly in regions with a high incidence of HIV infection
- Genitourinary disease is a common form of nonpulmonary tuberculosis



- By far the most common causative organism is the human tubercle bacillus, *M. tuberculosis*, but the bovine tubercle bacillus, *M. bovis*, occasionally can be responsible
- Other species within the genus *Mycobacterium* are free-living environmental saprophytes and are commonly found in water, including piped water supplies



- Some of these environmental mycobacteria occasionally cause human disease, particularly in immunosuppressed individuals, including recipients of renal transplants
- Because they occur in water, environmental mycobacteria readily contaminate the lower urethra and external genitalia and, thus, often are isolated from urine samples



- The kidney usually is infected by hematogenous spread of bacilli from a focus of infection in the lung
- In most cases, at the time of presentation there is no evidence of active pulmonary disease suggesting that renal involvement occurs as a result of reactivation after a period of dormancy



- If a tuberculous lesion in the lung gains access to the vascular system by erosion of the wall of a vessel, usually a vein, then emboli containing organisms may be disseminated throughout the body
- However, the bacilli have stringent growth requirements and generally tend to proliferate only in a small number of sites, including the kidney, epididymis, fallopian tube, bone marrow, and brain, particularly the hindbrain



Clinical features



- Many patients present with lower urinary symptoms typical of conventional bacterial cystitis
- Other symptoms that sometimes occur include back, flank, and suprapubic pain, frequency, and nocturia



- Persistent hematuria and pyuria should mandate evaluation of the genitourinary system that should include upper tract imaging, extensive microbiologic studies, cystoscopy, and tissue biopsy
- Renal colic is uncommon, occurring in fewer than 10% of patients, and constitutional symptoms such as fever, weight loss, and night sweats also are unusual



- A tuberculous kidney may become calcified and nonfunctioning
- If the gross anatomic distortion is advanced and bilateral, the GFR will fall and, in some patients, there is progression to end-stage renal failure



Diagnosis



- A microbiologic diagnosis of tuberculosis usually is made by isolation of the causative organism from urine or biopsy material
- Acid-fast bacilli may be seen on microscopy of centrifuged urine



- Because the Mycobacterium tuberculosis organisms are excreted intermittently, a minimum of 3 (preferably 5) consecutive early morning urine samples must be sent for culture
- The urine culture for TB takes 6-8 weeks for a definite result



- In early disease, it is often possible on intravenous urography to detect changes in a single calyx with evidence of parenchymal necrosis, and typically there is calcification on the plain film
- In more advanced disease, urography will show calyceal distortion, ureteric strictures, and bladder fibrosis

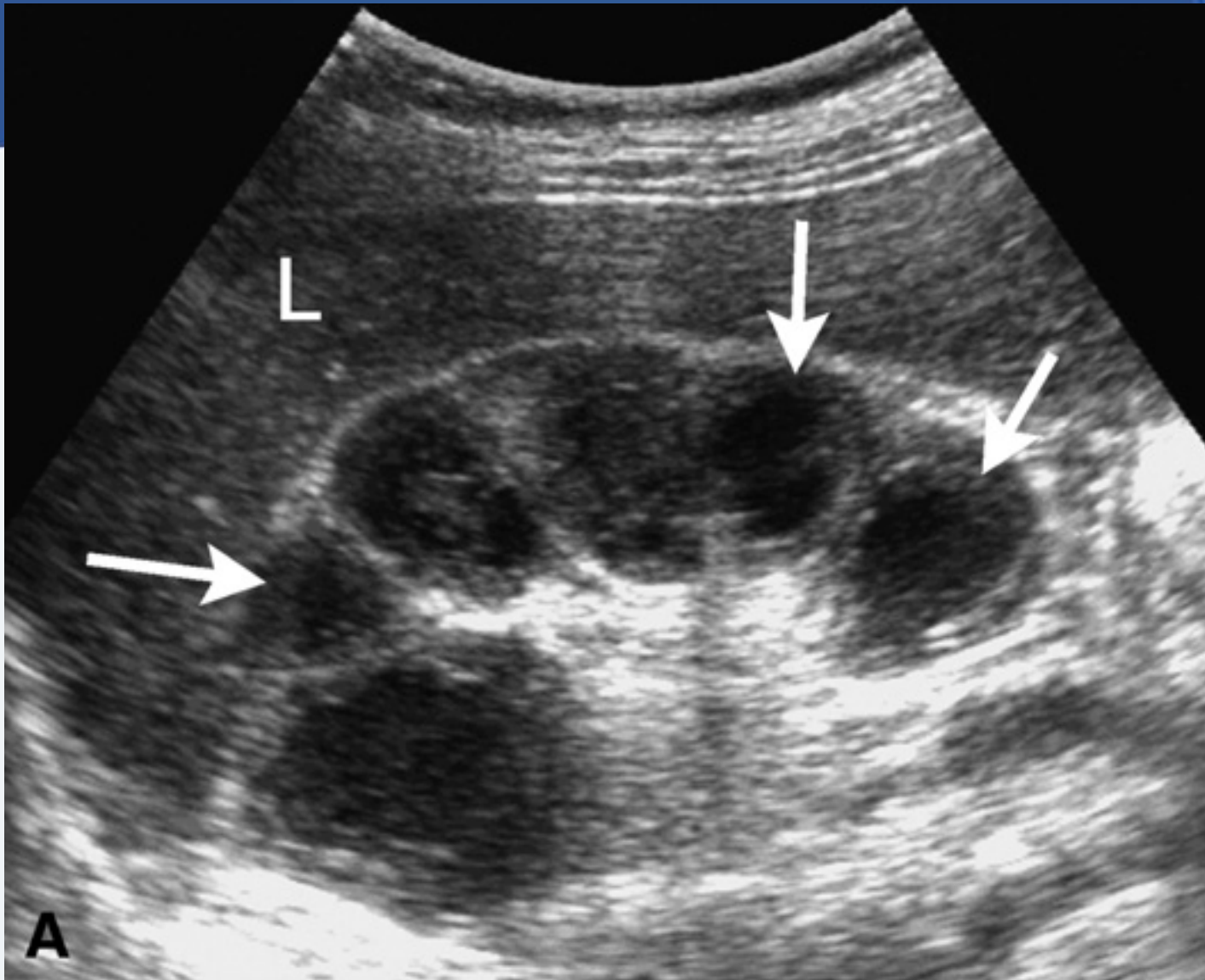
US findings

- Calcifications may be appreciated in the areas of caseating necrosis
- Tuberculosis involvement of the ureter can result in ureteral strictures, which cause a urographic appearance of a rigid, irregular, “pipestem” ureter
- Granulomatous mass lesions in the renal parenchyma can be seen as masses of mixed echogenicity, with or without necrotic areas of caseation and calcifications



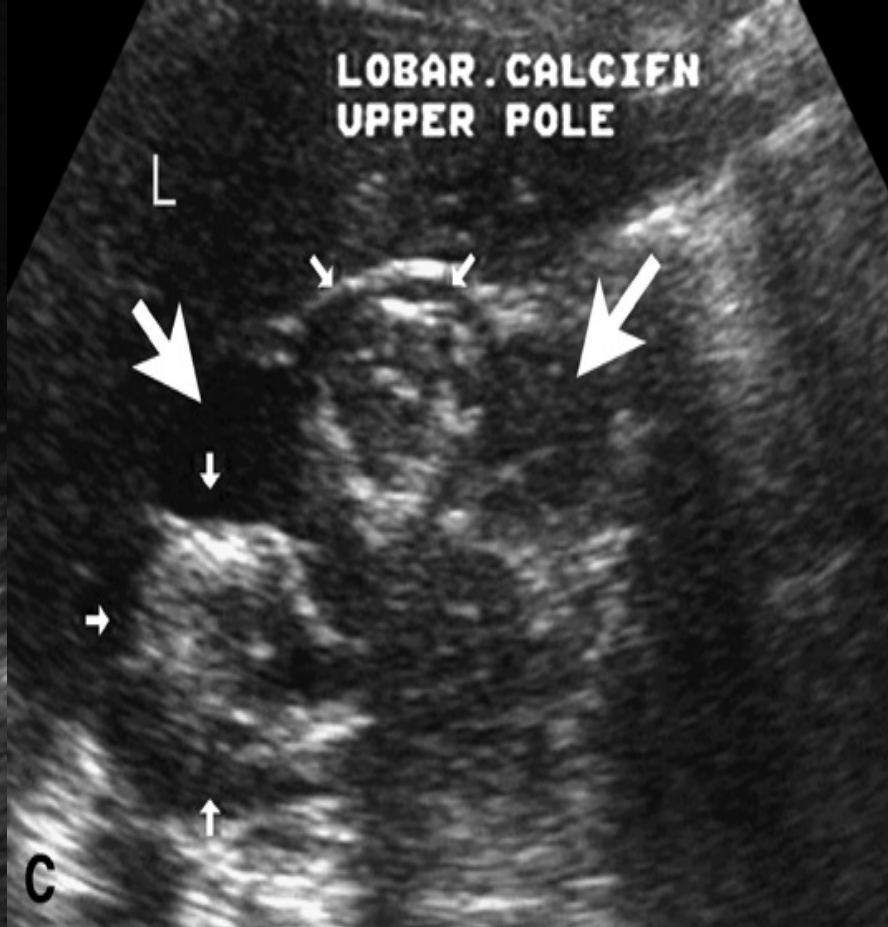
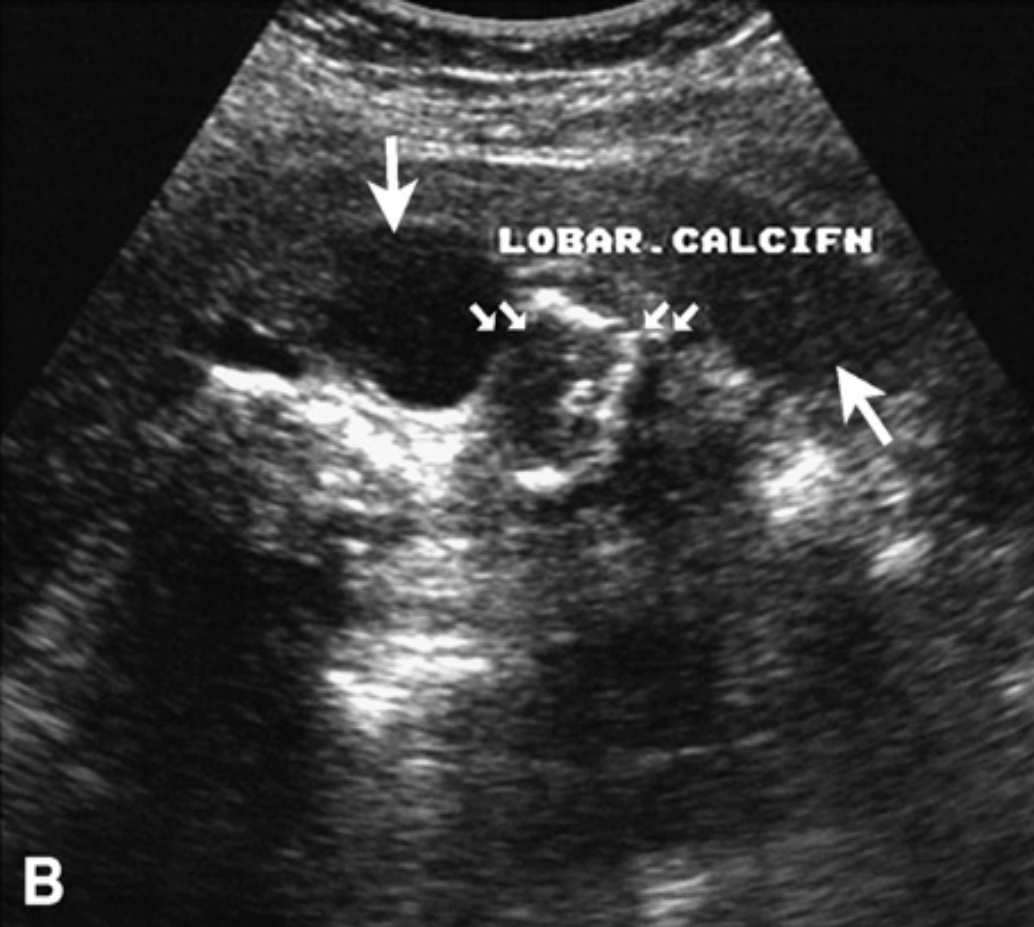


- Mucosal thickening and stenosis of the calyces is detectable by ultrasonography
- In addition, findings of mucosal thickening of the renal pelvis and ureter, ureteral stricture, and hydronephrosis are seen
- Finally, bladder changes such as mucosal thickening and reduced capacity are commonly detectable



Hypoechoic areas (arrows) in the renal cortex suggestive of lobar caseation





Hypoechoic areas of caseous necrosis (large arrows)
with dense peripheral calcification (small arrows)

Pathology



- Tuberculosis may involve the kidney as part of generalized disseminated infection or as localized genitourinary disease
- Tuberculosis can cause renal failure by two mechanisms that involve intrinsic infection within the renal parenchyma or obstructive uropathy



- The kidney frequently is involved in miliary tuberculosis where blood-borne miliary tubercles are seen throughout the renal substance
- The lesions measure up to 3 mm in diameter and usually are pale or white
- Organisms usually can be demonstrated microscopically within these lesions but sometimes are difficult to find



- Following an initial, acute, inflammatory response with polymorphonuclear leukocytes, a chronic inflammatory process develops with macrophages and the subsequent development of granulomas with Langhans giant cells, lymphocytes, and fibroblasts
- In time, the inflammatory foci coalesce with formation of central caseous necrosis



- The site of preference is the renal medulla, where caseous necrosis occurs, leading to local tissue destruction
- The infection may cause vascular insufficiency of the papillae by damaging vessels, and papillary necrosis may ensue
- Calyces become ulcerated



Tuberculous infection involving renal papillae with associated papillary necrosis. There is also the dilation and irregularity of the ureter, which also is involved



- Spread to the renal pelvis produces a tuberculous pyelonephritis that may even progress to a pyonephrosis-like lesion, also known as a "cement" or "putty" kidney
- Scarring develops within the renal pelvis with calcification in 24% of cases, identifiable as renal or ureteric stones in up to 19% of cases



Tuberculous
"pyonephrosis" with
extensive caseous
necrosis and renal
parenchymal destruction





Right kidney showing a nodular contracted appearance



Cut surface showing total replacement of the renal parenchyma with whitish mortar-like material





- Infection frequently spreads down the ureters into the bladder, producing mucosal and mural granulomatous lesions associated with scarring
- Ureteric involvement also may produce irregular ureteric strictures and segmental dilation, leading to obstruction and/or reflux
- The clinical consequences of an extensive renal lesion include autonephrectomy



- When the patient is immunosuppressed, the granulomas may be less well formed and organisms may be more readily demonstrated
- In some patients with pulmonary or disseminated tuberculosis, there is evidence of renal failure without typical miliary involvement or localized genitourinary lesions
- Renal histology can reveal chronic tubulointerstitial nephritis with granuloma formation and caseation (Tuberculous Interstitial Nephritis)



- Chronic tuberculosis sometimes is complicated by amyloidosis
- There are a number of case reports of tuberculosis associated with various forms of glomerulonephritis



TB in ESRD patients



- Dialysis patients are at an increased risk for TB worldwide with reports showing 6.9–52.5-fold increased risk
- ESRD and uremia is a known contributor to immunosuppression
- The causative factors of the immunosuppression are complex and disrupt the cell-mediated immune (CMI) response
- T-cells are primarily responsible for CMI and their functions include identification and killing of intracellular pathogens such as *M. tuberculosis*

Risk factors

- Race and ethnicity with whites having the lowest rate and Asians and Hispanics having the highest rate of infection
- Age
- Unemployment
- Reduced BMI
- Ischemic heart disease
- Smoking history
- Illicit drug use
- Reduced serum albumin





- The prevalence of latent TB infection is higher in ESRD patients, and those who become infected are at high risk of developing active disease
- Therefore, screening for LTBI in this population is recommended to prevent progression to active TB and secondary contamination of others



- Tuberculin skin test consists of intradermal injection of tuberculin material which stimulates a delayed type hypersensitivity response mediated by T lymphocytes and causes induration within 48-72 hours
- However it has poor sensitivity (because of a high prevalence of anergy in dialysis patients) and specificity

IGRA

- The QuantiFERON-TB Gold® test (QFT-G) is an ELISA-based test that measures production of IFN- γ by sensitized lymphocytes after whole blood is stimulated with specific TB antigens
- The T-SPOT.TB is an enzyme-linked immunospot (ELISPOT) assay performed on separated and counted peripheral blood mononuclear cells; it also uses TB antigens. The result is reported as number of IFN-gamma producing T cells (spot forming cells)





- These new tests use proteins encoded by a unique genomic segment which is absent from all strains of *Mycobacterium bovis*, BCG, and most nontuberculous mycobacteria but is present in *M. tuberculosis*
- Many countries (at least 17 so far) have developed new national guidelines for the detection of LTBI, including IGRAs in this process



- In immunocompetent persons, the vast majority of these guidelines recommend a two-step approach (TST followed by IGRA to confirm TST-positive cases)
- In immunocompromised individuals in whom the TST may be falsely negative, almost all existing guidelines recommend using IGRAs



- The IGRAs are more sensitive and specific than the TST for detecting LTBI in dialysis patients
- The IGRAs also have operational advantages over the TST
- The rate of indeterminate results of IGRA tests is rather low
- Chronic dialysis patients should be screened for LTBI by using an IGRA test, if available, instead of TST