

# We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

**4,800**

Open access books available

**122,000**

International authors and editors

**135M**

Downloads

Our authors are among the

**154**

Countries delivered to

**TOP 1%**

most cited scientists

**12.2%**

Contributors from top 500 universities



**WEB OF SCIENCE™**

Selection of our books indexed in the Book Citation Index  
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?  
Contact [book.department@intechopen.com](mailto:book.department@intechopen.com)

Numbers displayed above are based on latest data collected.

For more information visit [www.intechopen.com](http://www.intechopen.com)



## Pathology of Renal Transplantation

Javed I. Kazi and Muhammed Mubarak  
*Sindh Institute of Urology and Transplantation, Karachi  
 Pakistan*

### 1. Introduction

Renal transplantation has become the treatment of choice for patients with end-stage renal disease (ESRD) resulting from a variety of causes. The short-term patient and graft outcomes have improved markedly over the recent years (Hariharan et al., 2000). Renal transplant recipients are subject to all those diseases which affect the general population. In addition, like all other allograft recipients, renal transplant recipients are also susceptible to a variety of unique pathological lesions not seen in the non-transplant population. These lesions may involve the transplanted organ or other native organs/systems of the transplant recipients. The focus of this chapter will be on the major pathological processes affecting the kidney allograft itself and are diagnosed on renal allograft biopsy. In this chapter we will present a brief but comprehensive overview of the pathology of the renal allograft seen on allograft biopsies supplemented by representative pictures.

### 2. Role of renal allograft biopsy in the management of renal transplant patients

The renal allograft biopsy plays an important role in the diagnosis and management of causes of renal allograft dysfunction (Al-Awwa et al., 1998; Colvin, 1996; Gaber, 1998; Mazzali et al., 1999; Matas et al., 1983; Matas et al., 1985; Parfrey et al., 1984). Regarding biopsy indications, it is befitting to state that it is always indicated to answer a clinical question. The question is formulated by the transplant physicians with the knowledge of the patient's clinical scenario, the results of relevant laboratory and imaging studies, and the response to any therapeutic measures already instituted to remedy the problem. The established indications for performing renal allograft biopsies are shown in Table 1.

- 
1. Delayed graft function (DGF) if worsening is seen in the renogram or DGF lasts longer than 2-3 weeks.
  2. Graft function lower than expected based on donor characteristics.
  3. A sudden rise in serum creatinine attributable to kidney disease.
  4. A progressive increase in creatinine levels (>20% from creatinine nadir).
  5. Proteinuria > 1 g.
  6. Urine sediment changes without apparent urological causes.
  7. Prior to changes in immunosuppressive treatment.
- 

Table 1. Established indications of renal allograft biopsies.

As is obvious from the table, renal allograft biopsy is indicated in both the acute and late dysfunction of the allograft as well as the investigation of recurrent/de novo glomerular disease. The causes of allograft dysfunction vary depending on the post-transplant duration, living vs. cadaveric source of organ, type of immunosuppression, underlying or primary disease, etc (Kazi & Mubarak, 2012). It is estimated that 30-50% of allografts develop dysfunction during the early period (John & Herzenberg, 2010). An accurate diagnosis of these is essential for the optimal management of the patients, as each of the major causes of renal allograft dysfunction requires different therapeutic approach (Colvin, 1996; Gaber, 1998).

### **3. Types of renal allograft biopsies**

Three important types of allograft biopsies are regularly and widely used in clinical transplant practice. These include; implantation biopsies, indication biopsies, and protocol biopsies. Each of these types of biopsy plays an important role in the optimal management of transplant patients if properly procured and interpreted (Racusen et al., 1999).

#### **3.1 Implantation biopsy, donor biopsy**

This is usually done after the allograft is anastomosed to the recipient's vessels, but before the clamp is removed. The Banff scheme recommends its routine use all over the world. It provides baseline information on the status of the donor organ and helps in the interpretation of subsequent dysfunctional renal allograft biopsies. Individual zero time biopsies have been shown to correlate with the graft outcome.

#### **3.2 Indication biopsy**

##### **3.2.1 Dysfunctional allograft biopsy**

These are the most common form of biopsies that are performed on the allograft and most challenging in their interpretation. These biopsies are most commonly performed during early post transplant period and their frequency decreases as the post transplant duration increases. The Banff schema has detailed guidelines on the processing and interpretation of morphological changes on renal allograft biopsies, which are periodically updated and revised.

##### **3.2.2 Allograft biopsy for proteinuria**

Although, majority of indication biopsies are done for a rise in serum creatinine, a significant proportion of biopsies are also performed for the investigation of proteinuria. The proportion of these biopsies increases as the post transplantation duration increases. Their optimal evaluation requires an approach similar to that used for native renal biopsies for the investigation of glomerular diseases, i.e., the use of immunofluorescence (IF), and electron microscopy (EM) in addition to light microscopy (LM).

##### **3.2.3 Protocol biopsies**

These are the renal allograft biopsies which are performed at pre-determined intervals after transplantation in normal functioning allografts. These biopsies have provided marked insights into the subclinical processes affecting the graft with implications for the long term graft outcome (Choi et al. 2005; Furness et al., 2003; Jain et al., 2000; Rush et al., 1998; Serón et al., 1997). Indeed, the concept of Banff classification of renal allograft pathology originated from the experience with the use of, and the publication of studies related to, protocol biopsies. However, these biopsies have been done at only a few centers in the world and are not universal.

#### 4. Causes of renal allograft dysfunction

The causes of renal allograft dysfunction can be conveniently divided into two categories depending on the time after transplantation; early and delayed, and generally follow the same pattern of etiologic factors as observed in native kidneys; pre-renal, renal, and post-renal types. The causes of renal allograft dysfunction according to time after transplantation are shown in table 2.

Acute or subacute renal allograft dysfunction generally manifests in the form of a sudden rise of serum creatinine. It is quite common and occurs in roughly half of all patients with kidney transplants. In the immediate post-transplant period, ischemic injury is the major cause, but acute rejection may occur during this period, especially acute antibody-mediated rejection (ABMR) in pre-sensitized recipients. However, majority of acute rejections manifest after one week. Over the first month, the risk of rejection is high and it gradually decreases over the ensuing few months. Acute rejection is rare after six months of transplantation. In contrast, acute ischemic injury can continue to occur at any time. Drug toxicity caused by calcineurin inhibitors (CNI) can occur at any time after transplantation and should always be in the differential diagnosis. Rarely, thrombotic microangiopathy (TMA) may occur, mainly caused by CNI toxicity, but has many other causes (Bergstrand et al., 1985; Pascual et al., 1999).

---

Acute (0-6 months after transplant)
Acute cellular rejection
Acute humoral rejection
Acute calcineurin inhibitor toxicity
Acute pyelonephritis
Acute ischaemic injury
Chronic (>6 months after transplant)
Chronic cellular rejection
Chronic humoral rejection
Chronic calcineurin inhibitor toxicity
Hypertension
Chronic obstruction/reflux
Chronic pyelonephritis
Polyomavirus nephropathy
Glomerular disease
Recurrent
De novo
Graft ageing, including:
Donor-related changes
Progression of perioperative injury
Post-transplant lymphoproliferative disorder
Interstitial fibrosis / tubular atrophy, not otherwise specified

---

Table 2. Causes of renal allograft dysfunction categorized according to time after transplantation.

Late or chronic allograft dysfunction is usually labeled when graft dysfunction develops after six months of transplantation, and generally presents with a slowly rising serum

creatinine. It is often also accompanied by low grade proteinuria and hypertension as the post transplant duration increases. This chronic allograft loss occurs at a relatively constant rate of 2-4% per year and is the major cause of graft failure throughout the world. It is caused by a multitude of causes; both the allo-immune and the non-immune causes contribute to this process. Chronic CNI toxicity and hypertension are among the major etiologic factors leading to chronic graft loss. In addition, chronic obstruction, reflux, and hyperlipidemia are also contributing factors. As post transplant duration increases, the risk of recurrence of original renal disease or de novo occurrence of the same also increases. More recently, chronic allo-immune injury has been identified as a major cause of chronic graft loss. An acute rise in serum creatinine may occur during late post transplant period, and in most instances is caused by stopping the drugs by the patients. Similarly, a chronically failing allograft may show an apparent acute rise in serum creatinine, resulting from diminished functional reserve, and precipitated by some acute insult (John & Herzenberg, 2010).

It is worth reiterating that the causes of renal allograft dysfunction vary depending on the induction protocol, maintenance immunosuppression, living vs. cadaveric organ source, and many other factors (D'Alessandro et al., 1995; Farnsworth et al., 1984; Matas et al., 2001; Mihatsch et al., 1985; Mishra et al., 2004; Ratnakar et al., 2002; Rizvi et al., 2011; Verma et al., 2007).

## **5. Procurement of renal allograft biopsy**

Renal allograft biopsy procurement should follow the same methodology, as the native renal biopsy, discussed previously in chapter 1, especially, if ABMR is suspected or proteinuria is the clinical indication. The timing of obtaining biopsy is also important, especially for dysfunctional graft biopsies. Ideally, the biopsy should be obtained before any attempt at treatment of the suspected rejection process. It should be planned as an elective procedure, and a technician from the histopathology department should be present in the biopsy suite to examine the removed tissue under the dissection microscope for the adequacy of the tissue removed and for apportioning the removed tissue for immunofluorescence (IF) and EM study, if the later are required. This allows fulfillment of adequacy criteria for the proper histopathological evaluation of the biopsy material and complete pathologic evaluation including IF study for complement fragment C4d and renal panel IF. Two cores of renal graft tissue including both cortex and medulla should be obtained. The sensitivity of rejection diagnosis increases with increasing number of cores. The rejection process can be patchy and can be missed if only a single core is obtained. The sensitivity for rejection diagnosis is estimated to be around 90% with one core, and reaches 99% if two cores of renal cortex are obtained. The sensitivity for rejection diagnosis varies from 75 to 80% if medulla alone is received. The specificity of diagnosis of rejection in the medullary tissue is even lower, as other causes of graft dysfunction such as infection, obstruction, or drug hypersensitivity may present with infiltrates and even tubulitis in the medulla (John & Herzenberg, 2010).

## **6. Preparation of the biopsy for evaluation**

After the adequacy criteria are fulfilled, the graft biopsy material should be prepared with great care and dexterity. The biopsy should be processed and prepared according to the

guidelines for allograft biopsy handling by the most experienced technologists. The quality of biopsy material available for pathologic study is of utmost importance in the correct interpretation of the abnormalities in the tissue (Serón et al., 2008). Many centers process the biopsy by urgent methods, including microwave oven method (John & Herzenberg, 2010). We also process the allograft biopsies by the rapid method using auto-processor and report the biopsies on the same day. The quality of reagents is also very important. According to Banff schema, it is recommended to prepare at least seven slides, with multiple sections mounted on each slide. Three of these should be stained with hematoxylin and eosin (H&E), three with periodic acid-Schiff reagent (PAS), and one with a Masson's trichrome stain. The PAS and/or silver stains are very useful in delineating tubular basement membranes (TBMs) and in defining the severity of tubulitis, and for evaluating glomerulitis. The PAS stain is also useful in the identification of arteriolar hyalinosis (ah) and tubular atrophy and their semi-quantitative scoring. Trichrome stains help in assessing the chronic sclerosing changes in the interstitium and in the arterial intima. Banff schema recommends cutting tissue sections at a thickness of 3 to 4 microns for an accurate semiquantitative assessment of the morphological lesions in the biopsy sections (Racusen et al., 1999).

## **7. Pathologic evaluation of allograft biopsy**

The accurate pathologic evaluation of renal allograft biopsy requires a well trained renal pathologist with a thorough knowledge of renal transplant pathology, and also of renal and transplant medicine in order to correlate the morphologic abnormalities with the detailed clinical information. The importance of correlation of morphological findings on the renal allograft biopsy with clinical data and a close liaison between the nephrologists and pathologists cannot be overemphasized and is self-explanatory. However, the biopsy should be examined by the pathologist initially, without reference to the available clinical information and a morphological diagnosis formulated. This morphological diagnosis should be an objective and unbiased record of all abnormalities seen under the microscope. An attempt should then be made to correlate the clinical details provided with the morphological changes and preferably following discussion with the clinicians. A final diagnosis is then made and any treatment available, given. Further, in an ideal situation a follow up on the patient's progress is also communicated to the pathologist so that the predictions made from the biopsy can be confirmed or corrected if possible. Renal allograft biopsy interpretation is therefore developed out of a discussion between a clinician and the renal pathologist and is a learning process for both based on the patient's clinical course. In this context, it is worth emphasizing that transplant pathology is the youngest discipline of surgical pathology and is continuously evolving rapidly (John & Herzenberg, 2010).

## **8. Diagnosis of acute graft dysfunction**

Acute graft dysfunction may be caused by acute ischemic injury, acute rejection, or drug toxicity. Rare causes include; infections, surgical complications, vascular complications, or obstruction. Acute ischemic injury with delayed graft function (DGF) is more common in the cadaveric setting and is recognized by degenerative and regenerative changes in the tubular epithelium.

Renal graft biopsy is the gold standard test to identify many of these lesions. However, it is invasive, and not without risks (Vidhun et al., 2003; Wilckzek, 1990). Renal allograft biopsies are of three major types according to their indications: time zero biopsies or implantation biopsies; dysfunctional graft biopsies; and protocol biopsies. Among these, the second category is obviously the most common type in most of the centers around the world. Many centers do not perform routine implantation or protocol biopsies.

### **8.1 Diagnosis of acute rejection**

Renal allograft biopsy is the gold standard procedure for the diagnosis of acute rejection. Acute rejection was traditionally classified on the basis of rapidity and severity of the process, as hyperacute, accelerated acute, and acute rejection. Banff classification tried to classify the rejection on the basis of pathological and pathogenetic mechanisms with considerable refinements in the classification over the past 20 years (Solez et al., 1993; Racusen et al., 1999; Racusen et al., 2003; Solez et al., 2007; Solez et al., 2008). More recently, the Banff classification has categorized acute rejection on pathogenetic mechanisms, as acute ABMR and acute T cell mediated rejection (TCMR). Each of these types of rejection has unique morphological, immunohistochemical, and clinical features and different responses to therapy. Acute TCMR is diagnosed on the concurrent fulfillment of two key thresholds: significant interstitial lymphocytic infiltration (i2) associated with significant tubulitis (t2). If only one of these features is present, the diagnosis is made of borderline rejection. The borderline category exists only in type I or TCMR. Once a diagnosis of acute TCMR is made, its severity is assessed mainly on the basis of severity of tubulitis as Type IA and IB. Acute TCMR may also manifest as varying degrees of arterial inflammation and necrosis. It most often causes intimal arteritis, but occasional cases may manifest as V3 lesion. Often the vascular involvement is accompanied by tubulo-interstitial inflammation.

### **8.2 Mechanisms of rejection**

Rejection is a complex and somewhat redundant response of the specific and innate immune systems to the allograft tissue. The major targets of this response are the major histocompatibility complex (MHC) antigens, which are known as human leukocyte antigens (HLAs) in humans. The HLA genes on the short arm of chromosome 6 encode two structurally distinct classes of cell-surface antigens, known as class I (HLA-A, -B, and -C) and class II (-DR, -DQ, -DP). The T lymphocytes recognize allograft antigens by one of two mechanisms; direct and indirect allorecognition. In the direct pathway, T cells recognize intact allogenic MHC molecules on the surface of allogenic donor cells. The T-cell response that results in early acute TCMR is caused mainly by direct allorecognition. In the indirect pathway, T cells recognize processed alloantigens in the context of self antigen presenting cells (APCs). Indirect presentation may be important in maintaining and amplifying the rejection response, especially in chronic rejection.

In both pathways, T lymphocytes recognize foreign antigen only when the antigen is associated with HLA molecules on the surface of APCs. Helper T lymphocytes (CD4) are activated and they proliferate, differentiate, and secrete a variety of cytokines. These cytokines increase expression of HLA class II antigens on the allograft tissues, stimulate B lymphocytes to produce antibodies against the graft antigens, and help cytotoxic T cells (CD8), macrophages, and natural killer cells to develop effective specific and innate immunity against the graft (Nankivell & Alexander, 2010).

### 8.3 Semiquantitative assessment of histological changes – The mainstay of Banff schema

The semiquantitative scoring of the acute and chronic structural changes in different compartments of the graft parenchyma forms the mainstay for the Banff classification of renal allograft pathology (Solez et al., 1993; Racusen et al., 1999; Racusen et al., 2003; Solez et al., 2007; Solez et al., 2008). Altogether, five categories of acute and four of chronic changes are assessed. These are given in table 3.

Acute changes:	
g	0, 1, 2, 3 No, mild, moderate, severe glomerulitis (g3 = mononuclear cells in capillaries of all or nearly all glomeruli with endothelial enlargement and luminal occlusion)
i	0, 1, 2, 3 No, mild, moderate, severe interstitial mononuclear cell infiltration (in rejection edema & lymphocyte activation usually accompany mononuclear cell infiltration: i3 = >50% pf parenchyma inflamed)
t	0, 1, 2, 3 No, mild, moderate, severe tubulitis (t3 = >10 mononuclear cell per tubule or per 10 tubular cells in several tubules)
v	0, 1, 2, 3 No, mild, moderate, severe intimal arteritis (assessed in most involved vessel) (v3 = severe intimal arteritis and / or transmural arteritis and / or hemorrhage and recent infarction)
ah	0, 1, 2, 3 No, mild, moderate, severe nodular hyaline afferent arteriolar thickening suggestive of cyclosporine toxicity (ah3 = severe PAS-positive thickening in many arterioles)
Chronic changes:	
cg	0, 1, 2, 3 No, mild, moderate, severe chronic transplant glomerulopathy (% glomeruli).
ci	0, 1, 2, 3 No, mild, moderate, severe interstitial fibrosis, often with mononuclear cell inflammation (% total interstitial area).
ct	0, 1, 2, 3 No, mild, moderate, severe tubular atrophy and loss (% tubular area).
cv	0, 1, 2, 3 No, mild, moderate, severe fibrous intimal thickening often with elastica fragmentation (cv3 indicates occlusion( (cg and cv lesions suggest the presence of chronic rejection) (assessed in most damaged vessels).

Table 3. Semiquantitative scoring of acute and chronic changes in different compartments of renal graft parenchyma.

The focus of acute rejection diagnosis in Banff schema is on the tubulitis and intimal arteritis. However, it is worth emphasizing that with the exception of arteritis, there is no single specific feature of rejection. The diagnosis of rejection depends on the concurrence of interstitial inflammation of at least i2 (>25% to <50% of the unscarred parenchyma) and a tubulitis of grade t2 (4 -10 lymphocytes invading the tubule), as shown in Figures 1 and 2.



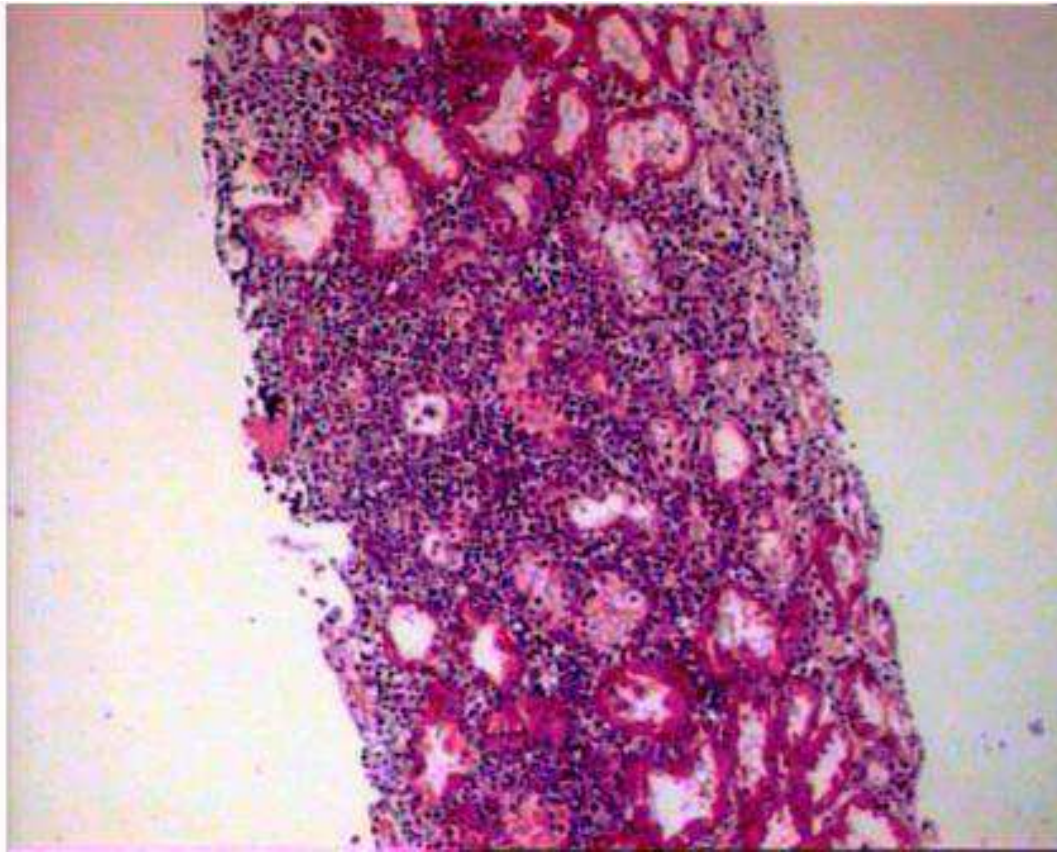


Fig. 1. Low-power view showing almost diffuse, dense, lymphocytic infiltrate in the interstitium. This is highly suggestive of acute T cell mediated rejection. (H&E,  $\times 100$ ).

The tubulitis grading is carried out on the most severely involved tubule. Most difficulty is encountered in the diagnosis of Type I acute cellular rejection, i.e., the tubulo-interstitial type, especially during very early stages of the process. The process starts and builds gradually with interstitial accumulation of progressively increasing numbers of inflammatory cells which later invade and attack the tubules. Thus if the biopsy is done at very early stage, tubulitis may not be found (Kazi et al., 1998). The rejection also begins as a patchy process, which in later stages becomes diffuse. The clearly defined threshold of rejection diagnosis, especially interstitial inflammation and tubulitis, has helped in improving the interobserver reproducibility of diagnosis (Furness et al., 1997; Furness et al., 1999). The rationale behind this threshold setting is that some inflammatory changes are to be expected in any allograft, but do not signal rejection. At the same time, this has resulted in lower sensitivity of diagnosis of very early acute TCMR. For this reason, various investigators have tried alternative approaches for increasing the sensitivity of diagnosis of early acute TCMR. One such approach involves the use of a computer program, known as Bayesian Belief Network (BBN) to record and analyze multiple biopsy features to diagnose more accurately the cases of early acute rejection. In one study involving 21 difficult cases of early acute rejection, the use of computer program resulted in higher correct diagnoses than any of the pathologists using the Banff criteria (Furness et al., 1999; Kazi et al., 1998). Moreover, there are interinstitutional differences in the quality and quantity of inflammatory infiltrates of rejection (Furness & Taub, 2001; Furness et al., 2003; Kazi et al., 1999). In spite of these limitations, Banff schema has become the international benchmark for the pathologic interpretation of renal allograft biopsies.

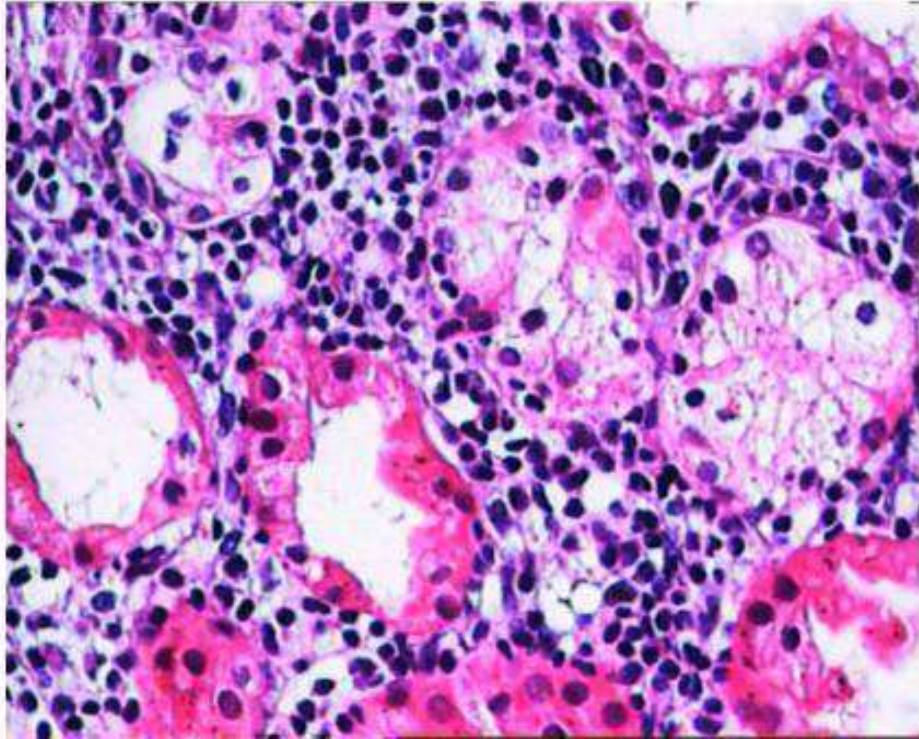


Fig. 2. Medium-power view showing almost diffuse, dense, lymphocytic infiltrate in the interstitium associated with foci of significant tubulitis (t2). This is highly suggestive of acute T cell mediated rejection. (H&E,  $\times 200$ ).

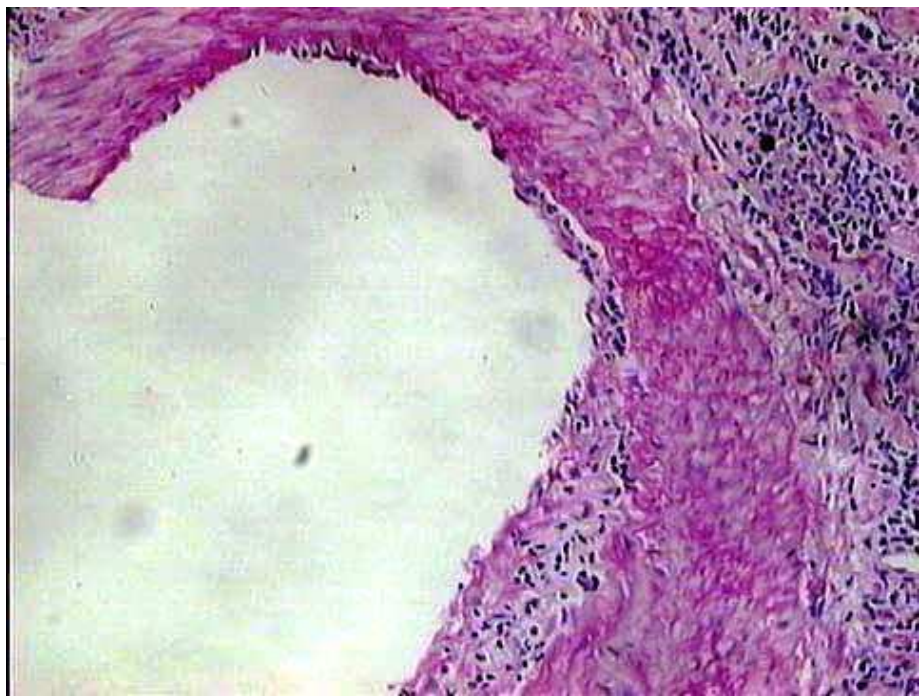


Fig. 3. Medium-power view showing part of wall of artery with focal intimal arteritis consistent with acute vascular rejection: Banff category, IIA. There is also dense lymphocytic infiltrate in the surrounding interstitium. (PAS stain,  $\times 200$ ).

The diagnosis of acute vascular rejection (AVR) is most often straight forward. Detection of even a single lymphocyte in the arterial intima (intimal arteritis) is sufficient to diagnose a case as AVR. The severity of rejection is also graded on the basis of V scores. AVR may be a manifestation of TCMR or antibody-mediated rejection (ABMR). The later mechanism of rejection most often results in V3 lesions, while the former pathway causes V1 and V2 lesions (Figures 3 to 7).

Significant tubulointerstitial inflammation and vasculitis may also be a manifestation of recurrent or de novo development of renal disease in the allograft. A good pretransplant clinical history is highly valuable in resolving this differential, the occurrence of which increases with increased post-transplant duration.

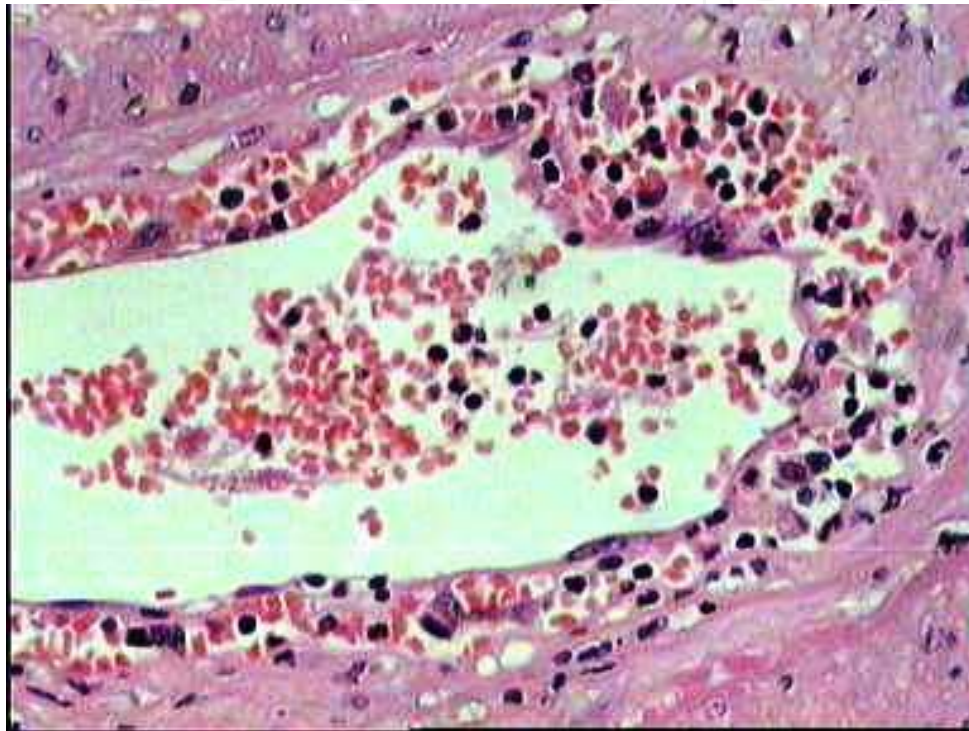


Fig. 4. High-power view showing numerous lymphocytes invading the arterial intima. Many red blood cells are also seen in the intima. (H&E stain,  $\times 400$ ).

#### 8.4 Antibody-mediated rejection (ABMR)

Recently, more attention is focused on antibody mediated rejection (ABMR) as a common cause of graft loss, and it is increasingly being recognized as an important cause of both acute and chronic renal allograft injury (Mauiyyedi et al., 2001; Mauiyyedi et al., 2002). This has been made possible with the discovery and the widespread use of C4d as a marker of ABMR. The detailed diagnostic criteria and classification of ABMR have been developed during recent updates of the Banff classification. A category of C4d negative ABMR has also been included in Banff 07 classification.

The definite diagnosis of ABMR requires fulfillment of three criteria; the histological evidence of graft injury, the immunohistochemical evidence of C4d positivity, and the presence of donor specific antibodies (DSA). If only two of these criteria are present, the case is labeled as presumptive ABMR. The pathological changes of ABMR may coexist with other categories of alloimmune or non-immune injuries of the graft (Racusen et al., 1999; Racusen et al., 2003; Solez et al., 2007; Solez et al., 2008).

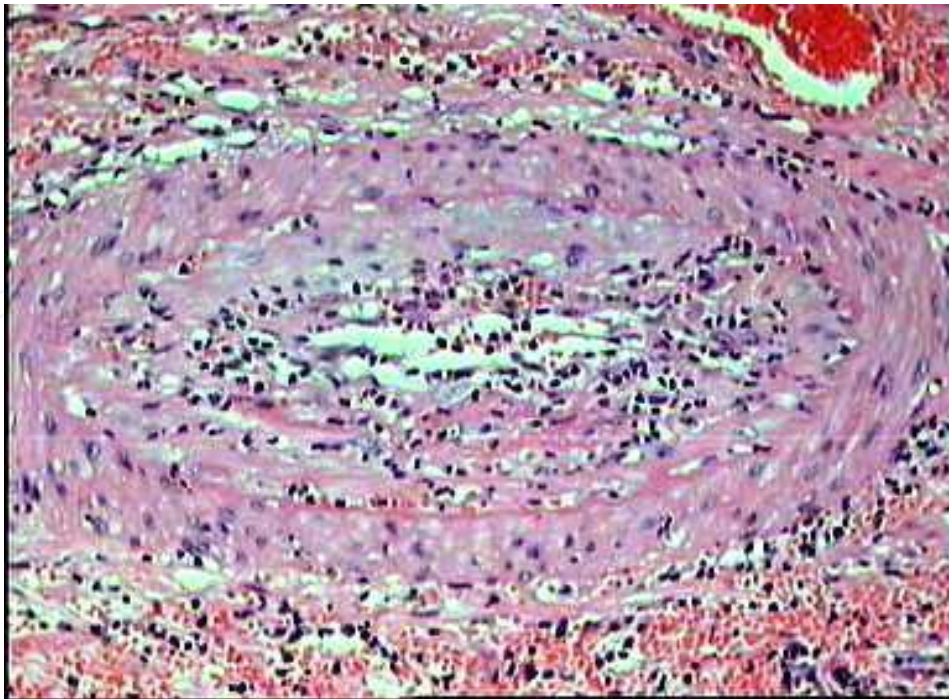


Fig. 5. Medium-power view showing severe/circumferential intimal arteritis, consistent with acute vascular rejection; Banff category, IIA. (H&E,  $\times 200$ ).

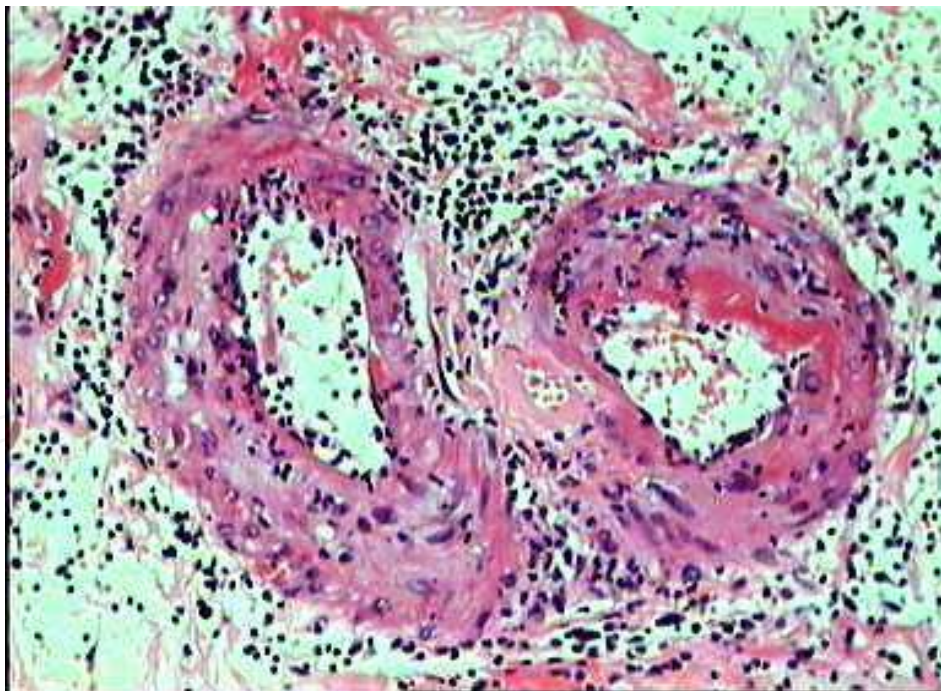


Fig. 6. Medium-power view showing two small arteries showing transmural arteritis along with a small area of fibrinoid necrosis in one of the arteries. This is consistent with V3 lesion and is categorized as acute vascular rejection; Banff category, III. Although, this morphological change may be seen in acute cellular rejection, this lesion is typically seen in cases of antibody mediated rejection (H&E,  $\times 200$ ).

A variety of morphological changes have been described, which, although, not entirely specific, are found more commonly in cases of ABMR. These changes include; polymorphonuclear glomerulitis, peritubular capillaritis, fibrin thrombi in glomerular capillaries, and fibrinoid necrosis of arteries. More recent Banff updates have formulated criteria for scoring the peritubular capillaritis and C4d positivity. These are undergoing clinical validation studies in many transplant centers in the world (Racusen et al., 1999; Racusen et al., 2003; Solez et al., 2007; Solez et al., 2008).

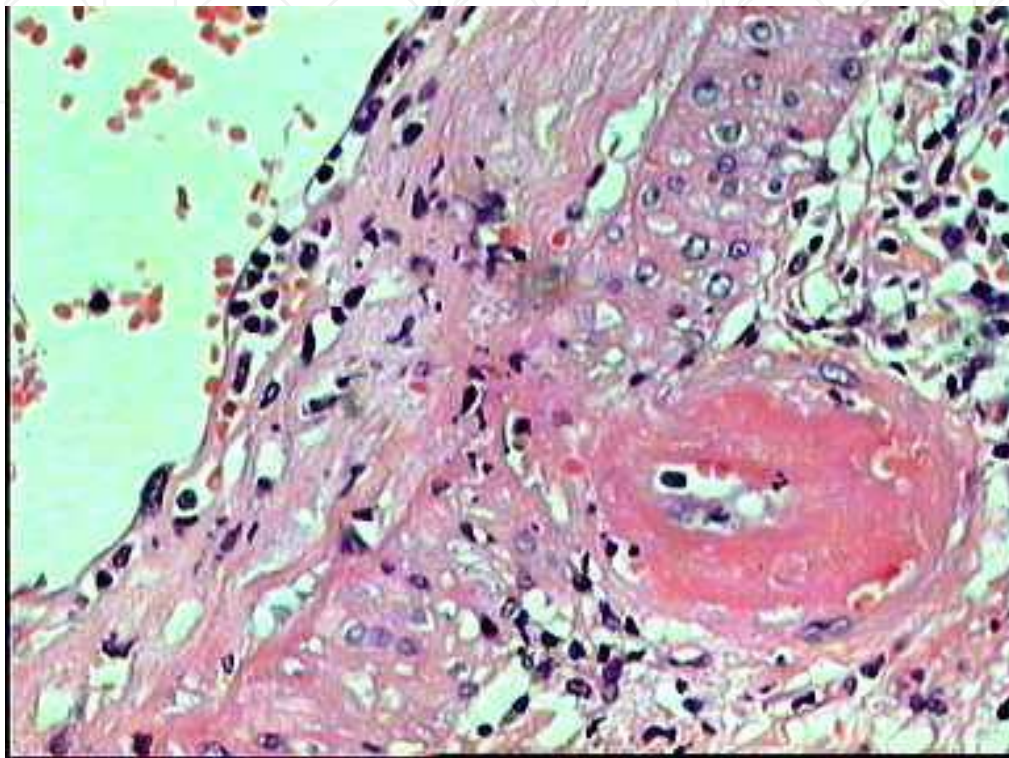


Fig. 7. Medium-power view showing fibrinoid necrosis of the wall of one small artery, characteristic of antibody mediated rejection. The wall of adjacent large artery shows intimal arteritis. (H&E,  $\times 200$ ).

## 9. Pathological changes not related to allo-immune mechanisms

### 9.1 Calcineurin inhibitor (CNI) drug toxicity

Calcineurin inhibitors (CNIs) including cyclosporine (CsA) and tacrolimus form the mainstay of maintenance immunosuppression. The discovery of CsA in 1979 has revolutionized the iatrogenic immunosuppressive protocols and the overall success rate of solid organ transplantation. However, the drugs are also potentially nephrotoxic, causing both acute and chronic nephrotoxicity. Acute CNI toxicity is one of the important causes of acute graft dysfunction. It also frequently poses differential diagnostic problems with acute TCMR. Toxic effects of CsA have been studied in detail, however, the toxicity profile of tacrolimus is still being defined. Both the mechanism of action and the toxicity profile of the two drugs also shows overlapping features (Figures 8 to 10). Acute tubular injury (ATI) is the most common lesion, accompanied by isometric vacuolization of tubular epithelial cell cytoplasm. This change is observed in both the proximal and distal convoluted tubules, and focal coalescence of vacuoles may yield larger vacuoles. Both the drugs are also associated

with microvascular toxicity characterized by damage to glomerular capillaries and renal arterioles. Acute arteriolar damage manifests in a variety of ways: there may be endothelial cell swelling, mucinous intimal thickening, nodular hyalinosis, and focal medial necrosis. Marked vacuolization of media of arterioles is also frequently observed (Figure 9). Sometimes, CNI toxicity manifests itself in the form of thrombotic microangiopathy (TMA). Chronic CNI toxicity results in nodular arteriolar hyalinosis, characterized by hyaline, eosinophilic deposits encroaching onto the media. These deposits consist of fibrin, IgM, C3, and C1q. This nodular hyalinosis differs from the circumferential arteriolar hyalinosis limited to the intima, and found in aging, hypertension, and diabetes mellitus. We have observed nodular arteriolar hyalinosis in CNI toxicity as early as one week after transplantation (unpublished data). Drug induced vasculopathy leads to ischemic injury accentuated in the medullary rays, leading to striped or diffuse interstitial fibrosis (Myers et al., 1984).

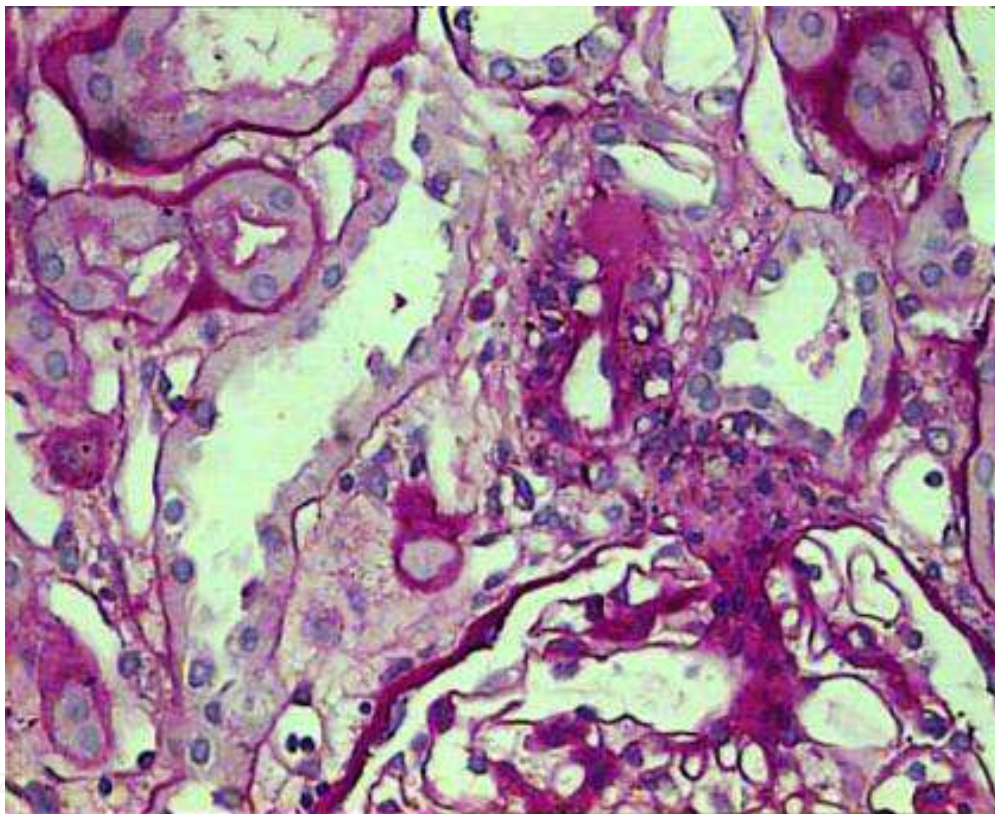


Fig. 8. Medium-power view showing part of a glomerulus with an arteriole, showing nodular hyalinosis. The hyaline is replacing the media and adventitia. This is highly suggestive of cyclosporine toxicity. (PAS,  $\times 200$ ).

## 9.2 Infections

The iatrogenic immunosuppression induced in renal transplant patients predisposes these patients to a variety of infections. The etiologic agents and the site of infections varies depending on a number of factors. Among the different infective agents affecting renal transplant recipients, bacterial, fungal, protozoal, and viral infections are common. Urinary tract infections are common in renal transplant patients in the early post-transplant period. The infective agents may affect the allograft or the native organs of the recipient. Bacterial infections may involve the graft and may be diagnosed on renal allograft biopsy. Bacterial

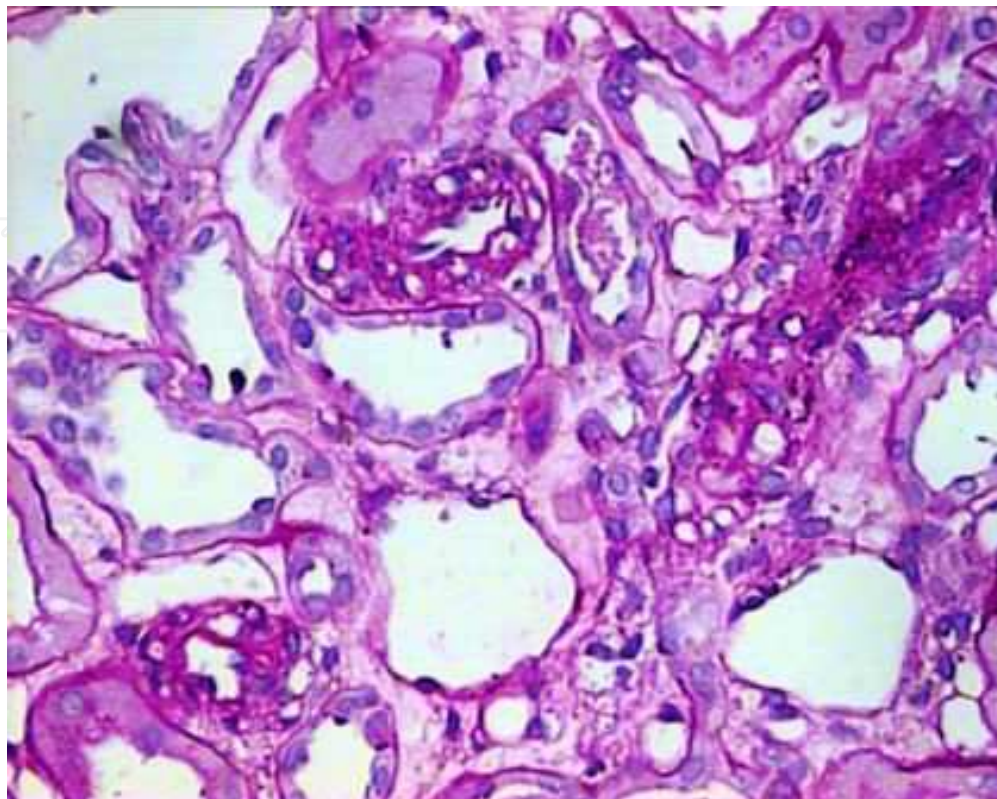


Fig. 9. Medium-power view showing three arterioles with marked vacuolization of medial muscle fibers. This change is also suggestive of cyclosporine toxicity. (PAS,  $\times 200$ ).

infections result in a mixed inflammatory cell infiltrate in the interstitium with a predominance of neutrophils, associated with tubular microabscesses (Figures 11 and 12). The infiltrate is usually localized in the medulla but may be found in the cortex. Sometimes, the infection may not be picked up on urine culture (Imtiaz et al., 2000; Oguz et al., 2002). Among the viral infections affecting the graft, CMV and polyoma viruses are of paramount importance (Nickeleit et al., 1999).

### 9.3 Posttransplant Lymphoproliferative Disorder (PTLD)

Although rare, this disorder is an important differential diagnosis with acute cellular rejection, especially as the posttransplant duration increases. An early diagnosis of this complication is necessary for its successful management. Although, typically the disorder occurs many months to years after transplantation, there are many examples of its occurrence during early posttransplant period.

On light microscopy, PTLD is characterized by a monomorphic or polymorphic lymphocytic infiltrate containing plasma cells, many of which are atypical. There is typically a diffuse interstitial infiltrate without associated tubulitis or arteritis, the later features help in its differential diagnosis from rejection. Occasionally, the two processes may be concurrent. Immunophenotyping of lymphocytes helps in the definite diagnosis of this concurrence.

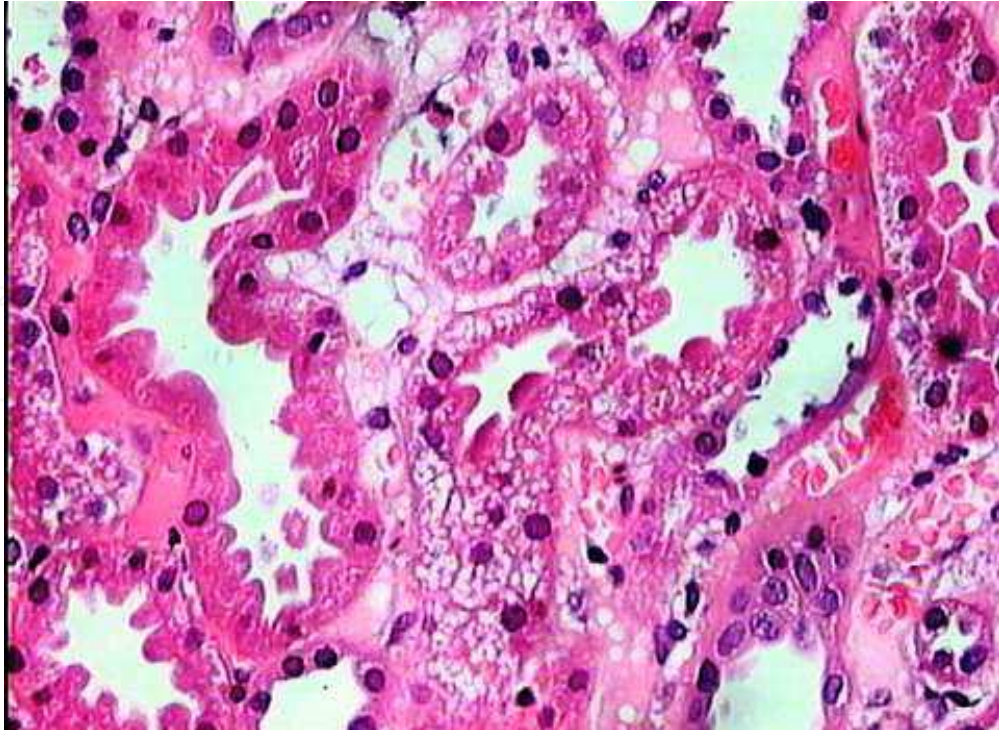


Fig. 10. High-power views showing prominent isometric vacuolization of tubular epithelial cells in two tubules in the center of the field. Although, no specific, this is highly suggestive of cyclosporine toxicity. (H&E,  $\times 400$ ).

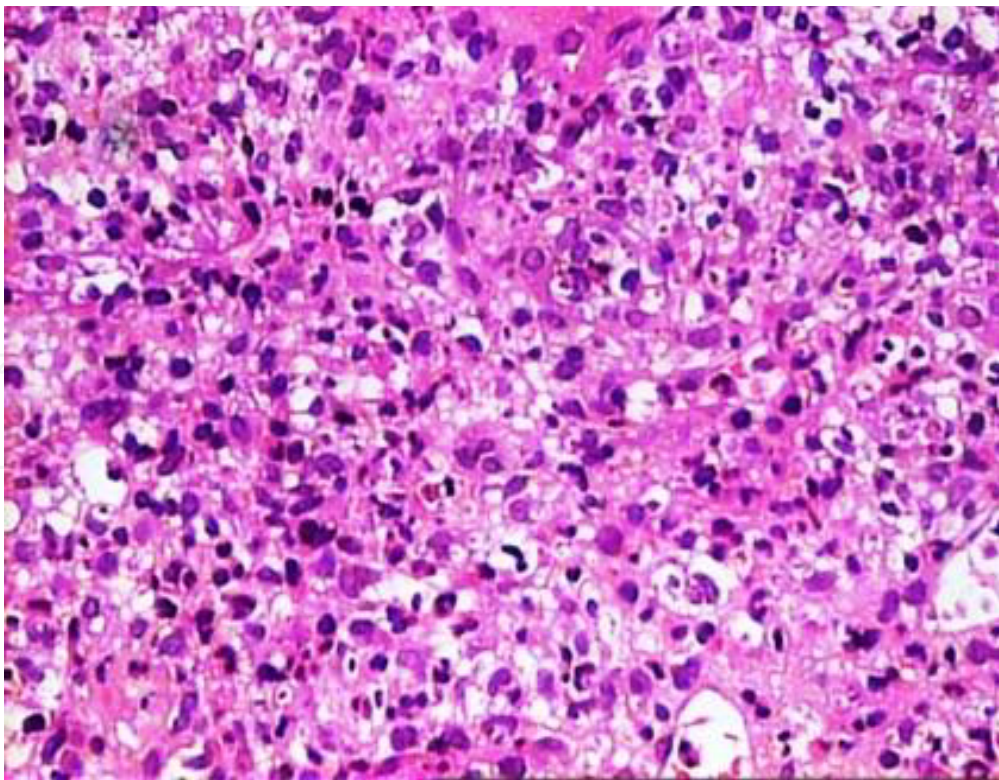


Fig. 11. Medium-power view showing dense, mixed inflammatory cell infiltrate with predominant neutrophils. This is strongly suggestive of infection. (H&E,  $\times 200$ ).



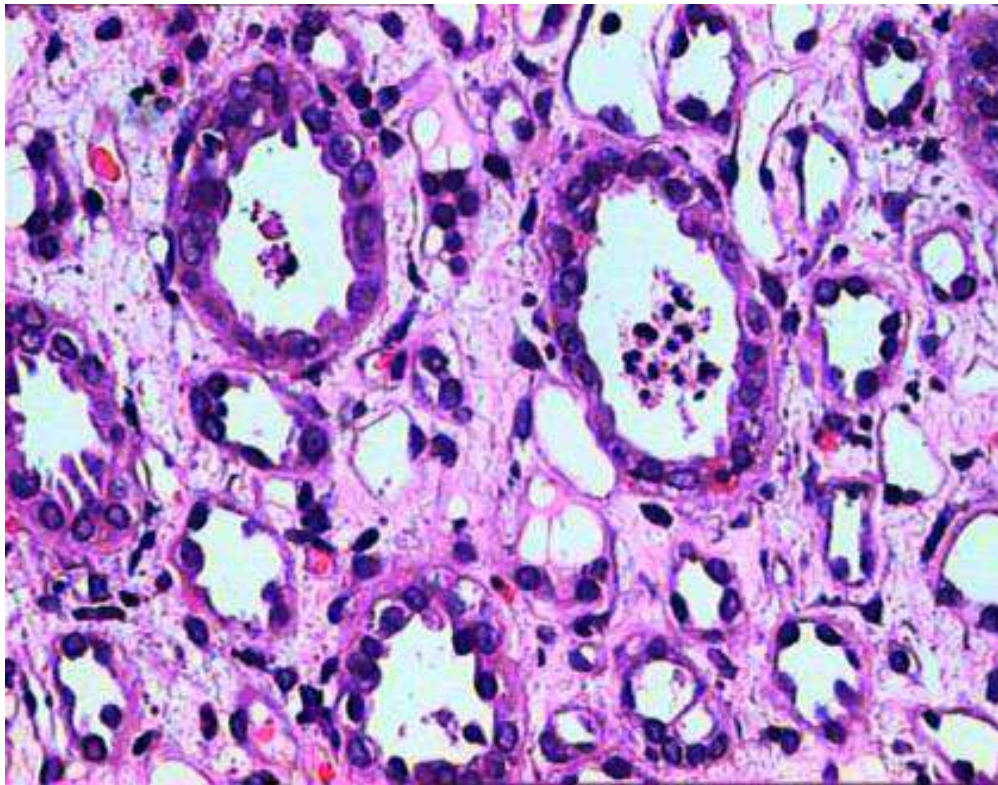


Fig. 12. High-power view showing accumulation of polymorphonuclear neutrophils in the tubular lumina, so called tubular microabscesses. These are highly suggestive of infection. (H&E,  $\times 400$ ).

#### 9.4 Acute Tubular Necrosis (ATN)

Acute tubular injury (ATI) or ATN is a common finding in renal biopsies from transplanted kidneys, especially in the cadaveric setting. It is the main cause of primary nonfunction of the allograft in this setting. ATI results from a multitude of causes and situations, including in situ injury in the donor; ischemia during organ harvesting, storage, or transportation of the organ; and ischemic injury incurred perioperatively in the recipient. The morphological picture is similar to that seen in the native kidneys and spans the whole spectrum from mild injury, which is difficult to identify, to severe flattening and loss of tubular epithelium from the tubular basement membrane. These degenerative changes in the tubular epithelial cells are accompanied by signs of regeneration, including mitoses. There may be accompanying interstitial edema, and mild mixed inflammatory cell infiltration. Tubulitis is typically absent or only trivial. Other changes include tubular cell vacuolization and blebbing, and tubular dilatation reflecting downstream tubular obstruction. There are also deposits of calcium salts in tubular lumina in the form of dystrophic calcification.

There is a poor correlation between the morphological changes of ATN and the allograft function. Although, the morphological lesions of ATI or ATN in the transplanted kidneys are similar to those of native kidneys, some authors have noted a few differences in the morphological profile.

#### 9.5 Acute Tubulointerstitial Nephritis (ATIN)

Non-immune related ATIN may occur in the transplanted kidneys and may be very difficult to distinguish from the tubulointerstitial rejection. The disorder may result from a variety of

insults to the transplanted kidneys, such as infection, drug hypersensitivity, viral infection, etc. A predominance of neutrophils in the mixed inflammatory cell infiltrate in the interstitium, especially if associated with tubular microabscesses or leucocyte casts favor the possibility of infection. A predominance of eosinophils raises the possibility of drug hypersensitivity. Viral infections are accompanied by appropriate viral cytopathic effects in addition to the infiltrate. It may be reiterated here that neutrophils and eosinophils may also be seen in rejection, and sometimes the above lesions are superimposed on underlying rejection reaction.

## 10. Diagnosis of chronic allograft dysfunction

As is evident in table 2, the causes of late allograft dysfunction are more varied than those of acute allograft dysfunction. The late graft dysfunction may manifest as an acute rise in serum creatinine or a slowly increasing serum creatinine, and the causes vary accordingly. An advanced failing allograft may show an apparent acute decline of graft function due to diminished renal reserve, as in native kidneys. Renal allograft biopsy is essential to diagnose the causes of late allograft dysfunction.

In the past, all cases of chronic allograft dysfunction were labeled as “chronic allograft nephropathy” by the pathologists, a “paper wastebasket” for all forms of chronic allograft damage (Cornell & Colvin, 2005; Ivanyi et al., 2001; Nankivell et al., 2003). This was mainly because the morphological features of various diseases were not clearly defined, as well as, the loss of features of primary pathology in advanced stages of sclerosing process. The main morphological changes of specific causes of chronic allograft dysfunction are shown in table 4.

The diagnosis of interstitial fibrosis/tubular atrophy, not otherwise specified, is reserved only for those cases, which show no evidence of specific causes after a detailed and meticulous investigation of the allograft biopsy by morphology, immunohistochemistry, electron microscopy, and molecular genetic methods.

## 11. Recurrent and de novo renal diseases

There are many renal diseases, especially glomerular diseases, which can recur in the transplanted kidneys after a variable period of time (Hariharan, 2000). Currently, glomerular diseases account for approximately 10-20% of cases of ESRD undergoing transplantation, and overall approximately 20% of these patients experience recurrence. The same disease can also occur as de novo disease in the transplanted kidneys. Disease characteristics of the recurrent disease are similar to those of the original disease, but are usually mild in nature. This may be due in part to the use of immunosuppressive agents in the transplant patients. De novo diseases generally occur later than the recurrent diseases. Almost all diseases that occur in the native kidneys can occur de novo in transplant kidneys. However, the two most common diseases are membranous glomerulonephritis and focal segmental glomerulosclerosis. The work up of renal allograft biopsies in cases suspicious for recurrent or de novo glomerulopathies should follow the approach used in native renal biopsy investigation.

One important non-glomerular disease that frequently recurs in transplanted kidneys is the primary hyperoxaluria, if kidney transplantation is carried out without concomitant liver transplantation.

**Chronic hypertension:** fibrous thickening of the arterial intima with reduplication of elastic lamina, and arteriolar hyalinosis.

**Chronic calcineurin inhibitor toxicity:** nodular peripheral arteriolar hyalinosis, and striped interstitial fibrosis

**Chronic obstruction:** prominent tubular dilation, and ruptured tubules with extravasated casts

**Chronic pyelonephritis:** chronic interstitial inflammation and fibrosis, out of proportion to vascular or glomerular changes, in the context of clinical history of recurrent urinary tract infections

**Polyomavirus nephropathy:** tubular epithelial viral infection evidenced by typical viral inclusions on H&E stain, or positive staining for SV40-large T antigen

**De novo/recurrent renal diseases:** morphological features of respective diseases

Table 4. The morphological features of specific causes of chronic allograft dysfunction, other than chronic allo-immune causes.

## 12. Conclusion

In conclusion, renal transplant pathology is a complex and rapidly evolving field, in which significant improvements have taken place in recent years in both the characterization and categorization of allo-immune mechanisms of injury. More refinement is expected to take place in near future with the inclusion of molecular genetic and image analysis techniques into the Banff classification.

## 13. References

- Al-Awwa I, Hariharan S, & First M. (1998). The importance of allograft biopsy in renal transplant recipients. *Am J Kidney Dis*, Vol. 31, No.6, pp. S15-S18.
- Bergstrand A, Bohman SO, Farnsworth A, Gokel JM, Krause PH, Lang W, Mihatsch MJ, Oppedal B, Sell S, & Sibley RK. (1985). Renal histopathology in kidney transplant recipients immunosuppressed with cyclosporine A: results of an international workshop. *Clin Nephrol*, Vol. 24, No. 3, pp.107-19.
- Choi BS, Shin MJ, Shin SJ, Kim YS, Choi YJ, Kim YS, Moon IS, Kim SY, Koh YB, Bang BK, & Yang CW. (2005). Clinical significance of an early protocol biopsy in living-donor renal transplantation: ten-year experience at a single center. *Am J Transplant*, Vol. 5, No. 6, pp. 1354-60.
- Colvin RB. The renal allograft biopsy. (1996). *Kidney Int*, Vol. 50, No. 3, pp. 1069-82.
- Colvin RB, Cohen AH, Saiontz C, Bonsib S, Buick M, Burke B, Carter S, Cavallo T, Haas M, Lindblad A, Manivel JC, Nast CC, Salomon D, Weaver C, & Weiss M. (1997). Evaluation of pathologic criteria for acute renal allograft rejection: Reproducibility, sensitivity, and clinical correlation. *J Am Soc Nephrol*, Vol. 8, No. 12, pp.1930-41.
- Cornell LD, & Colvin RB. Chronic allograft nephropathy. (2005). *Curr Opin Nephrol Hypertens*, Vol. 14, No. 3, pp. 229-34.
- D'Alessandro AM, Sollinger HW, Knechtle SJ, Kalayoglu M, Kicken WA, Uehling DT, Moon TD, Messing EM, Bruskewitz RC, Pirsch JD, & Belzer FO. (1995). Living related and unrelated donors for kidney transplantation- a 28-year experience. *Ann Surg*, Vol. 222, No. 3, pp. 353-64.

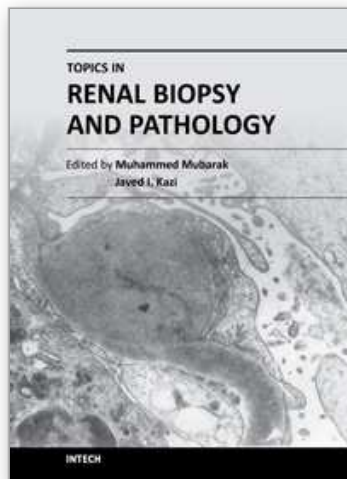
- Farnsworth A, Hall BM, Ng AB, Duggin GG, Horvath JS, Sheil AG, & Tiller DJ. (1984). Renal biopsy morphology in renal transplantation. A comparative study of the light-microscopic appearances of biopsies from patients treated with cyclosporin A or azathioprine prednisone and antilymphocyte globulin. *Am J Surg Pathol*, Vol. 8, No. 4, pp. 243-52.
- Furness PN, Kirkpatrick U, Taub N, Davies DR, & Solez K. (1997). A UK-wide trial of the Banff classification of renal transplant pathology in routine diagnostic service. *Nephrol Dial Transplant*, Vol. 12, No. 5, pp. 995-1000.
- Furness PN, Kazi JI, Levesley J, Taub N, & Nicholson M. (1999). A neural network approach to the diagnosis of early acute allograft rejection. *Transplant Proc*, Vol. 31, No. 8, pp. 3151.
- Furness PN, Levesley J, Luo Z, Taub N, Kazi JI, Bates WD, & Nicholson ML. (1999). A neural network approach to the diagnosis of early acute renal transplant rejection. *Histopathology*, Vol. 35, No. 5, pp. 461-7.
- Furness PN, & Taub N: Convergence of European Renal Transplant Pathology Assessment Procedures (CERTPAP) Project. (2001). International variation in the interpretation of renal transplant biopsies: report of the CERTPAP Project. *Kidney Int*, Vol. 60, No.5, pp. 1998-2012.
- Furness PN, Philpott CM, Chorbajian MT, Nicholson ML, Bosmans JL, Corthouts BL, Bogers JJ, Schwarz A, Gwinner W, Haller H, Mengel M, Seron D, Moreso F, & Cañas C. (2003). Protocol biopsy of the stable renal transplant: a multicenter study of methods and complication rates. *Transplantation*, Vol. 76, No. 6, pp. 969-73.
- Furness PN, Taub N, Assmann KJ, Banfi G, Cosyns JP, Dorman AM, Hill CM, Kapper SK, Waldherr R, Laurinavicius A, Marcussen N, Martins AP, Nogueira M, Regele H, Seron D, Carrera M, Sund S, Taskinen EI, Paavonen T, Tihomirova T, & Rosenthal R. (2003). International variation in histologic grading is large, and persistent feedback does not improve reproducibility. *Am J Surg Pathol*, Vol. 27, No. 6, pp. 805-10.
- Gaber LW. (1998). Role of renal allograft biopsy in multicentre clinical trials in transplantation. *Am J Kidney Dis*, Vol. 31, No. 6, pp.S19-S25.
- Hariharan S, Johnson CP, Bresnahan BA, Taranto SE, Mcintosh MJ, & Stablein D. (2000). Improved graft survival after renal transplantation in United States; 1988-1996. *N Eng J Med*, Vol. 342 No. 9, pp. 605-12.
- Hariharan S. (2000). Recurrent and de novo diseases after renal transplantation. *Semin Dial*, Vol. 13, No. 3, pp. 195-9.
- Imtiaz S, Akhtar F, Ahmed E, Khan M, Kazi JI, Naqvi A, & Rizvi A. (2000). Acute graft dysfunction due to pyelonephritis, value and safety of graft biopsy. *J Nephrol Urol Transpl*, Vol. 1, No. 1: 127-9.
- Ivanyi B, Kemeny E, Szederkenyi E, Marofka F, & Szenohradzky P. (2001). The value of electron microscopy in the diagnosis of chronic renal allograft rejection. *Mod Pathol*, Vol. 14, No.12, pp. 1200-8.
- Jain S, Curwood V, Kazi JI, White SA, Furness PN, & Nicholson M. (2000). Acute rejection in protocol renal transplant biopsies-institutional variations. *Transplant Proc*, Vol. 32, No. 3, pp. 616.
- John R, & Herzenberg AM. (2010). Our approach to a renal transplant biopsy. *J Clin Pathol*, Vol. 63, No. 1, pp. 26-37.

- Kazi JL, Furness PN, & Nicholson M. (1998). Diagnosis of early acute renal allograft rejection by evaluation of multiple histological features using a Bayesian Belief Network. *J Clin Path*, Vol. 51, No. 2, pp. 108-13
- Kazi JL, Furness PN, Nicholson M, Ahmed E, Akhtar E, Naqvi A, & Rizvi A. (1999). Interinstitutional variation in the performances of Bayesian Belief Network for the diagnosis of acute renal graft rejection. *Transplant Proc*, Vol. 31, No. 8, pp. 3152.
- Kazi JL, & Mubarak M. (2012). Biopsy findings in renal allograft dysfunction in a live related renal transplant program. *J Transplant Technol Res*, Vol. 2, No. 1, pp. 108. doi:10.4172/2161-0991.1000108
- Matas AJ, Sibley R, Mauer M, Sutherland DE, Simmons RL, & Najarian JS. (1983). The value of needle renal allograft biopsy. I. A retrospective study of biopsies performed during putative rejection episodes. *Ann Surg*, Vol. 197, No. 2, pp. 226-37.
- Matas AJ, Tellis VA, Sablay L, Quinn T, Soberman R, & Veith FJ. (1985). The value of needle renal allograft biopsy. III. A prospective study. *Surgery*, Vol. 98, No. 5, pp. 922-6.
- Matas AJ, Payne WD, Sutherland DE, Humar A, Greessner RW, Kandaswamy R, Dunn DL, Gillingham KJ, & Najarian JS. (2001). 2,500 living donor kidney transplants: a single-center experience. *Ann Surg*, Vol. 234, No. 2, pp. 149-64.
- Mauiyyedi S, Crespo M, Collins AB, Schneeberger EE, Pascual MA, Saidman SL, Tolkoff-Rubin NE, Williams WW, Delmonico FL, Cosimi AB, & Colvin RB. (2002). Acute humoral rejection in kidney transplantation: II. Morphology, immunopathology, and pathologic classification. *J Am Soc Nephrol*, Vol. 13, No. 3, pp. 779-87.
- Mauiyyedi S, Pelle PD, Saidman S, Collins AB, Pascual M, Tolkoff-Rubin NE, Williams WW, Cosimi AA, Schneeberger EE, & Colvin RB. (2001). Chronic humoral rejection: identification of antibody-mediated chronic renal allograft rejection by C4d deposits in peritubular capillaries. *J Am Soc Nephrol*, Vol. 12, No. 3, pp. 574-82.
- Mazzali M, Ribeiro-alves MA, & Alves FG. (1999). Percutaneous renal graft biopsy: a clinical, laboratory and pathological analysis. *Sao Paulo Med J*, Vol. 117, No. 2, pp. 57-62.
- Mihatsch MJ, Thiel G, Basler V, Ryffel B, Landmann J, von Overbeck J, & Zollinger HU. (1985). Morphological patterns in cyclosporine-treated renal transplant recipients. *Transplant Proc*, Vol. 17, No. 4 (suppl 1), pp. 101-16.
- Mishra MN, Saxena VK, Narula AS. (2004). Differences in renal transplantation in India and first world countries. *Int J Hum Genet*, Vol. 4, No. 2, pp. 161-5.
- Myers BD, Ross J, Newton L, Luetscher J, & Perlroth M. (1984). Cyclosporine-associated chronic nephropathy. *N Engl J Med*, Vol. 311, No. 11, pp. 699-705.
- Nankivell BJ, & Alexander SI. (2010). Rejection of the kidney allograft. *New Engl J Med*, Vol. 363, No. 15, pp. 1451-62.
- Nankivell BJ, Borrows RJ, Fung CL, O'Connell PJ, Allen RD, & Chapman JR. (2003). The natural history of chronic allograft nephropathy. *N Engl J Med*, Vol. 349, No. 24, pp. 2326-33.
- Nickeleit V, Hirsch HH, Binet IF, Gudat F, Prince O, Dalquen P, Thiel G, & Mihatsch MJ. (1999). Polyomavirus infection of renal allograft recipients: From latent infection to manifest disease. *J Am Soc Nephrol*, Vol. 10, No. 5, pp. 1080-9.
- Oguz Y, Doganci L, Bulucu F, Can C, Oktenli C, Yenicesu M, & Vural A. (2002). Acute pyelonephritis causing acute renal allograft dysfunction. *Int Urol Nephrol*, Vol. 34, No. 3, pp. 299-301.

- Parfrey P, Kuo Y, Hanley J, Knaack J, Xue Z, Lisbona R, & Guttman RD. (1984). The diagnostic and prognostic value of renal allograft biopsy. *Transplantation*, Vol. 38, No. 6, pp. 586-90.
- Pascual M, Vallhonrat H, Cosimi AB, Tolckoff-Rubin N, Colvin RB, Delmonico FL, Ko DS, Schoenfeld DA, & Williams WW Jr. (1999). The clinical usefulness of the renal allograft biopsy in the cyclosporine era: a prospective study. *Transplantation*, Vol. 67, No. 5, pp.737-41.
- Ratnakar KS, George S, Datta BN, Fayek AH, Rajagopalan S, Fareed E, Al Tantawi M, Al Arrayed S, & Al Arrayed A. (2002). Renal transplant pathology: Bahrain experience. *Saudi J Kidney Dis Transplant*, Vol. 13, No. 1, pp.71-6.
- Rizvi SAH, Naqvi SAA, Zafar MN, Hussain Z, Hashmi A, Hussain M, Akhter SF, Ahmed E, Aziz T, Sultan G, Sultan S, Mehdi SH, Lal M, Ali B, Mubarak M, & Faiq SM. (2011). A renal transplantation model for developing countries. *Am J Transplant*, doi: 10.1111/j.1600-6143.2011.03712.x
- Serón D, Anaya F, Marcén R, del Moral RG, Martul EV, Alarcón A, Andrés A, Burgos D, Capdevila L, Molina MG, Jiménez C, Morales JM, Oppenheimer F, Pallardó L, Fructuoso AS. (2008). Guidelines for indicating, obtaining, processing, and evaluating kidney transplant biopsies. *Nefrologia*, Vol. 28, No. 4, No. pp. 385-96.
- Racusen LC, Solez K, Colvin RB, Bonsib SM, Castro MC, Cavallo T, Croker BP, Demetris AJ, Drachenberg CB, Fogo AB, Furness P, Gaber LW, Gibson IW, Glotz D, Goldberg JC, Grande J, Halloran PF, Hansen HE, Hartley B, Hayry PJ, Hill CM, Hoffman EO, Hunsicker LG, Lindblad AS, Marcussen N, Mihatsch MJ, Nadasdy T, Nickerson P, Olsen TS, Papadimitriou JC, Randhawa PS, Rayner DC, Roberts I, Rose S, Rush D, Salinas-Madrigal L, Salomon DR, Sund S, Taskinen E, Trpkov K, & Yamaguchi Y. (1999). The Banff 97 working classification of renal allograft pathology. *Kidney Int*, Vol. 55, No. 2, pp. 713-23.
- Racusen LC, Colvin RB, Solez K, Mihatsch MJ, Halloran PF, Campbell PM, Cecka MJ, Cosyns JP, Demetris AJ, Fishbein MC, Fogo A, Furness P, Gibson IW, Glotz D, Hayry P, Hunsickern L, Kashgarian M, Kerman R, Magil AJ, Montgomery R, Morozumi K, Nickleit V, Randhawa P, Regele H, Seron D, Seshan S, Sund S, & Trpkov K. (2003). Antibody-mediated rejection criteria – an addition to the Banff 97 classification of renal allograft rejection. *Am J Transplant*, Vol. 3, No. 6, pp. 708-14.
- Rush D, Nickerson P, Gough J, McKenna R, Grimm P, Cheang M, Trpkov K, Solez K, & Jeffery J. (1998). Beneficial effects of treatment of early subclinical rejection: a randomized study. *J Am Soc Nephrol*, Vol. 9, No. 11, pp. 2129-34.
- Serón D, Moreso F, Bover J, Condom E, Gil-Vernet S, Cañas C, Fulladosa X, Torras J, Carrera M, Grinyó JM, & Alsina J. (1997). Early protocol renal allograft biopsies and graft outcome. *Kidney Int*, Vol. 51, No. 1, pp. 310-6.
- Solez K, Axelsen RA, Benediktsson H, Burdick JF, Cohen AH, Colvin RB, Croker BP, Droz D, Dunnill MS, Halloran PF, Hayry P, Jennette CJ, Keown PA, Marcussen N, Mihatsch MJ, Morozumi K, Myers BD, Nast CC, Olsen S, Racusen LC, Ramos EL, Rosen S, Sachs DH, Salomon DR, Sanfilippo F, Verani R, Willebrand EV, & Yamaguchi Y. (1993). International standardization of criteria for the histologic diagnosis of renal allograft rejection: the Banff working classification of kidney transplant pathology. *Kidney Int*, Vol. 44, No. 2, pp. 411-22.

- Solez K, Colvin RB, Racusen LC, Sis B, Halloran PF, Birk PE, Campbell PM, Cascalho M, Collins AB, Demetris AJ, Drachenberg CB, Gibson IW, Grimm PC, Haas M, Lerut E, Liapis H, Mannon RB, Marcus PB, Mengel M, Mihatsch MJ, Nankivell BJ, Nicleleit V, Papadimitriou JC, Platt JL, Randhawa P, Roberts I, Salinas-Madruga L, Salomon DR, Seron D, Sheaff M, & Weening JJ. (2007). Banff '05 Meeting Report: differential diagnosis of chronic allograft injury and elimination of chronic allograft nephropathy (CAN). *Am J Transplant*, Vol. 7, No. 3, pp. 518-26.
- Solez K, Colvin RB, Racusen LC, Haas M, Sis B, Mengel M, Halloran PF, Baldwin W, Banfi G, Collins AB, Cosio F, David DS, Drachenberg C, Einecke G, Fogo AB, Gibson IW, Glotz D, Iskandar SS, Kraus E, Lerut E, Mannon RB, Mihatsch M, Nankivell BJ, Nicleleit V, Papadimitriou JC, Randhawa P, Regele H, Renaudin K, Roberts I, Seron D, Smith RN, & Valente M. (2008). Banff' 07 classification of renal allograft pathology: updates and future directions. *Am J Transplant*, Vol. 8, No. 4, pp. 753-60.
- Verma PP, Hooda AK, Sinha T, Chopra GS, Karan SC, Sethi GS, Badwal S, & Kotwal A. (2007). Renal transplantation- an experience of 500 patients. *MJAFI*, Vol. 63, No. pp. 107-11.
- Vidhun J, Masciandro J, Varich L, Salvatierra O, Jr., Sarwal M. (2003). Safety and risk stratification of percutaneous biopsies of adult-sized renal allografts in infant and older pediatric recipients. *Transplantation*, Vol. 76, No. 3, pp. 552-7.
- Wilckzek HE. (1990). Percutaneous needle biopsy of the renal allograft. A safety evaluation of 1129 biopsies. *Transplantation*, Vol. 50, No. 5, pp. 790-7.

IntechOpen



## **Topics in Renal Biopsy and Pathology**

Edited by Dr. Muhammed Mubarak

ISBN 978-953-51-0477-3

Hard cover, 284 pages

**Publisher** InTech

**Published online** 04, April, 2012

**Published in print edition** April, 2012

There is no dearth of high-quality books on renal biopsy and pathology in the market. These are either single author or multi-author books, written by world authorities in their respective areas, mostly from the developed world. The vast scholarly potential of authors in the developing countries remains underutilized. Most of the books share the classical monotony of the topics or subjects covered in the book. The current book is a unique adventure in that it bears a truly international outlook and incorporates a variety of topics, which make the book a very interesting project. The authors of the present book hail not only from the developed world, but also many developing countries. The authors belong not only to US but also to Europe as well as to Pakistan and Japan. The scientific content of the book is equally varied, spanning the spectrum of technical issues of biopsy procurement, to pathological examination, to individual disease entities, renal graft pathology, pathophysiology of renal disorders, to practice guidelines.

### **How to reference**

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Javed I. Kazi and Muhammed Mubarak (2012). Pathology of Renal Transplantation, Topics in Renal Biopsy and Pathology, Dr. Muhammed Mubarak (Ed.), ISBN: 978-953-51-0477-3, InTech, Available from: <http://www.intechopen.com/books/topics-in-renal-biopsy-and-pathology/pathology-of-renal-transplantation>

**INTECH**  
open science | open minds

### **InTech Europe**

University Campus STeP Ri  
Slavka Krautzeka 83/A  
51000 Rijeka, Croatia  
Phone: +385 (51) 770 447  
Fax: +385 (51) 686 166  
[www.intechopen.com](http://www.intechopen.com)

### **InTech China**

Unit 405, Office Block, Hotel Equatorial Shanghai  
No.65, Yan An Road (West), Shanghai, 200040, China  
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元  
Phone: +86-21-62489820  
Fax: +86-21-62489821



© 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen