20. HIV and Renal Function

By Ansgar Rieke

A quarter of the cardiac output is consigned to the perfusion of the kidneys – even though the kidneys amount to just 0.5% of the total body weight. Approximately every 20 minutes, i.e. 70 times a day, the entire blood plasma is filtered by the kidneys. Therefore, kidney glomeruli are target organs for every hematogenous infection. Viral infection can cause primary glomerulonephritis, whereas an immune reaction can lead to secondary glomerulonephritis. HIV infection, hepatitis B and C as well as bacterial infections are all typical causes of renal disease. Nephrotoxic agents precipitate renal diseases that affect the interstitium and the tubular apparatus in particular, and these have to be differentiated from glomerulonephritis.

Both forms can cause renal impairment and can lead to end-stage renal disease. While HIV-associated nephropathy (HIV-AN) is predominantly found in Afro-Americans (80-85%), in the HAART era the greater task will be to examine the renal safety of antiretroviral agents. However, only a small amount of literature is available on this subject to date.

Clinical manifestation/diagnosis of nephropathy

The major symptoms of glomerulonephritis are proteinuria and “nephritic sediment”. HIV-AN is diagnosed in cases of nephrotic syndrome with edema, hypoalbuminemia, hyperlipidemia and proteinuria of more than 3.5 g/day. However, even a mild proteinuria is possible. The occurrence of proteinuria and erythrocyturia is pathognomonic for glomerulonephritis (GN) and, together with a nephritic sediment, usually confirms the diagnosis. Under a polarizing microscope, a trained eye can easily identify the renal (glomerular) origin of the erythrocytes, on the basis of glomerularly deformed acanthocytes. More than 5 acanthocytes per field of vision is a significant sign for GN. Extensive erythrocyturia (bleeding) below the renal pelvis (tumor of the urinary tract collection system?) can be excluded by sonography and, if necessary, by cystoscopy.

The clinical symptoms are determined by the extent of proteinuria with loss of protein and imbalance, as well as loss of renal function. The severity of edema, tiredness, reduced performance, susceptibility to infections, hyperlipidemia, anemia, metabolic acidosis, problems with the calcium-phosphate metabolism, as well as venous thrombi and newly diagnosed arterial hypertension is limited by the length and intensity of the renal insufficiency. Nephrotic syndrome, acute nephritic syndrome (acanthocytes), rapid-progressive glomerulonephritis, asymptomatic proteinuria or hematuria and chronic glomerulonephritis can be clinically differentiated, and are treated differently.

An increase in serum creatinine is not to be expected until the glomerular filtration rate (GFR) is below 50%, and should be identified early by clearance measurements. Useful methods for estimating the GFR are the Cockroft formula or the MDR Clearance, as a urine collection over two 24-hour periods is difficult to organize.
Interstitial nephropathy, especially when caused by indinavir, can present as a sterile leukocyturia or – on proof of bacteria – as a bacterial-interstitial nephritis, and can also lead to a loss of renal function.

Leukocyturia must be microbiologically clarified (culture of mid-stream urine) in order to initiate treatment with antibiotics according to the resistance situation. Tuberculosis of the urinary tract should be considered as a possible cause of abacterial leukocyturia.

The symptoms of drug-induced Fanconi’s syndrome (tubulotoxic damage) are glucosuria + phosphaturia with a normal blood glucose (dropping the renal glucose limit) + hypophosphatemia. The patient feels tired and peaky, the symptoms are non-specific and an increase in serum creatinine is often delayed.

**Routine tests for renal impairment**

The routine investigation of an HIV-infected person should include tests for sodium, potassium, calcium, phosphate (every three months) and creatinine (creatinine clearance). The urine should be tested for glucosuria, proteinuria, erythrocyturia and leukocyturia every 3 months.

If there is a significant rise in proteinuria or serum creatinine, a nephrologist should be asked for advice. There is no time to waste in the case of a rapid increase of creatinine (rapid-progressive glomerulonephritis?), an increase of LDH connected with hyperbilirubinemia and thrombocytopenia (hemolytic uremia syndrome, HUS), or severe electrolyte imbalance (especially hyperkalemia), or acidosis that can no be controlled, which can also occur on therapy as lactacidosis.

An asymptomatic, slight proteinuria with no rise in creatinine in untreated patients is normally a consequence of the infection of the glomerulus or tubular apparatus with HIV/hepatitis-viruses and should be monitored quarterly.

A decrease in renal function in patients with an HIV infection could be interpreted as a symptomatic HIV infection, and in untreated patients antiretroviral therapy might be considered. The use of a contrast medium (CM) for the urinary tract should be avoided, especially in cases of renal insufficiency, proteinuria and all forms of low intravasal volume (including cirrhosis of the liver), in order to avoid causing CM-induced renal failure. If the administration of CM is unavoidable, the patient should receive a non-ionic contrast medium and be given 0.9 % NaCl intravenously at 1ml/kg/h, 12 hours before and 12 hours after receiving the contrast medium. The addition of acetylcysteine 600 mg before and after receiving the contrast medium is well documented as an effective protection for the kidneys and probably works as a free radical scavenger on CM-exposure.

**HIV-associated nephropathy (HIV-AN)**

HIV-AN is characterized by rapid loss of renal function, which is especially observed in Afro-Americans. The risk factors are genetic predisposition (97 % Afro-Americans), male gender and drug abuse.

Most patients have a poor immune status with < 100 CD4+ T-cells/µl (only 20 % have normal ranges). Individual cases of sudden renal insufficiency within an acute
HIV syndrome have been reported. But, there seems to be no correlation with HIV viral load and the duration of the HIV infection.

Nephrotic proteinuria usually presents clinically as more than 3.5 g/day, but a minor proteinuria is also possible. Progression is fast and can lead to end-stage renal disease (dialysis) in less than 10 months. The blood pressure is normal or slightly increased; the kidneys are within the normal size range when examined by ultrasound scan. Despite hemodialysis, the one-year-mortality rate is 50 %; on antiretroviral therapy it still reaches around 30 %.

The histological findings in biopsies mostly (70 %) correspond to a focal segmental sclerosing glomerulonephritis (FSGN), which is also frequently observed in “malignant hypertension” in Afro-Americans. However, other causes of a glomerulonephritis, such as an amyloid kidney are also possible with HIV (30 %). Single case descriptions with the histological course of disease have confirmed the direct infection of the glomerular basal membrane with HIV, and have documented an impressive positive effect of HAART on the histological changes.

Experience with other FSGN-forms has shown that only early intervention with HAART – before scaring of the glomeruli occurs due to the underlying disease – has a chance of success. The use of components of antiretroviral therapy should take into consideration the different means of renal elimination (adaptation of the dosing). ACE-inhibitors (captropil 6.25 to 25 mg bid, then change to a longer-term effective preparation such as enalapril 5 mg) should be added. The use of steroids is the subject of controversial discussion (1 mg/kg KG/day for 2 to 11 weeks).

**Post-infectious glomerulonephritis**

Many infections are able to trigger or support an acute post-infectious glomerulonephritis or other forms of chronic GN. Viral infections such as CMV, EBV, VZV, influenza, adenovirus, and parvovirus B19 do this as well as HIV. After syphilis and infections with staphylococci, pneumococci, legionella, salmonelli and other infectious agents, an acute post-infectious glomerulonephritis can also occur. An acute HIV infection can cause renal insufficiency.

Membranous glomerulonephritis is a special form of secondary glomerulonephritis, which can appear in malignant tumors and hepatitis (B and C). Chronic hepatitis C can lead to a membrano-proliferative GN; or through cryoglobulinemia can also cause vasculitis with renal involvement.

Irrespective of the liver histology, hepatitis C-associated GN can also be a reason for therapy with interferon/ribavirin (observe adaptation of the dosing intervals). However, ribavirin shouldn’t be used if the creatinine clearance is less than 50 ml/min/1.73 m² because of the danger of prolonged anemia.

**Principles of therapy of glomerulonephritis**

The underlying cause of a post-infectious glomerulonephritis should be treated first, including hepatitis B, C and HIV infection.

Particular attention should be paid to the adjustment of blood pressure: target values are < 130/80 mm Hg or, in the presence of proteinuria < 120/80 mm Hg. ACE-
inhibitors as well as AT-II-receptor-antagonists are used to control blood pressure, usually in combination with diuretics.

Proteinuria should be treated with an ACE-inhibitor, also at high doses, if necessary, irrespective of the blood pressure, and should be combined additionally with AT-II-receptor-antagonists if the proteinuria is more than 0.5 to 1 g/day. The protein intake is reduced to 0.6-0.8 g/kg/day (low protein diets like the Mediterranean diet might be helpful).

Fluids should be restricted to 1.5 to 2 l/day and adapted according to the body weight and amount of edema. Forced drinking of large amounts, or rather the alleged “flushing” of the kidneys or the use of high-ceiling diuretics in combination with increased fluid flow rate, only has a limited effect on renal function. Not smoking is of vital importance because nicotine causes an increase in the risk of progression of glomerulonephritis.

Hyperlipidemia should be treated after dietary arrangements have been exhausted. HMG-CoA reductase inhibitors are ideal, provided that they can be combined with the antiretroviral therapy (see chapter on drug interactions). Fibrates or fibrates in combination with statins may only be used carefully when renal function is reduced (cumulation).

Analgesics should be waived as far as possible, which applies especially to the “small” analgesics, such as ASA and paracetamol. At the latest, when the creatinine clearance reaches a value of less than 50 ml/min/1.73 m², treatment should be managed by a nephrologist.

**Treatment of hypertension**

Please take note of the specific side effects of antihypertensive drugs. Note hyperkalemia with ACE-inhibitors; at a creatinine count of 1.4 mg/dl do not use potassium-saving diuretics; at creatinine > 1.8 mg/dl high-ceiling diuretics such as furosemid or torasemid should be used.

**Table 1: Blood pressure adjustments**

<table>
<thead>
<tr>
<th>Category</th>
<th>Drug</th>
</tr>
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<tbody>
<tr>
<td>ACE-inhibitors</td>
<td>Lisinopril, Benazepril-HCL, Fosinopril sodium, Enalapril, etc.</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>Metoprolol, Bisoprolol</td>
</tr>
<tr>
<td>AT II-receptor-antagonists</td>
<td>Valsartan, Candesatan, Telmisartan, etc.</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Hydrochlorothiazide + Triamterene</td>
</tr>
<tr>
<td>Ca-antagonists</td>
<td>Amlodipine</td>
</tr>
</tbody>
</table>

**Renal safety of antiretroviral therapy**

The spectrum of an allergic or autoimmune reaction in the kidney is no different from the skin. Reactions can be humoral or T-cell-mediated and can lead to renal insufficiency. The spectrum ranges from the type I immune reaction (acute interstitial nephritis after exposure to medication) to the type IV T-cell-mediated reaction
(special forms of a chronic interstitial nephritis). It is, therefore, important to know that even the one-off use of an analgesic (e.g. ibuprofen) can lead to renal failure. In principle, this is possible with antiretroviral drugs. Any change of treatment should be followed by a check of renal function.

The typical side effects of antiretroviral therapy are:

**Indinavir-associated nephropathy**

As indinavir was established in 1996 and administered at the hight dosage of 3 x 800 mg, the renal side effects ranged from asymptomatic crystalluria to renal failure. In different studies, the cumulative occurrence of the symptomatic nephrolithiasis in indinavir was indicated to be over 10 %.

Boosted indinavir (800 mg + 100 mg ritonavir) does not reduce the rate of nephrolithiasis, and brings about the interruption of therapy in to 6-9 % of cases. The classic symptoms of hematuria and flank pain, increasing to renal colic, indicates nephrolithiasis. Special risk factors are crystalluria, a high specific weight of the urine (higher than 1,025 mg/l, dehydration), an alkaline urine with a pH value > 6, little absorption of fluid (less then 2-3 l/day), obstructive uropathy, male gender, history of nephrolithiasis and a body mass index below 20.

The proof of typical indinavir crystals in the urine alone is no reason to discontinue indinavir therapy, as 80 % of these patients are clinically inconspicuous. Even so, these cases should be monitored. In our clinic, the patients with indinavir nephropathy are examined by ultrasound scan. If there is no obstruction, they receive fluid i.v. or orally. The combination of 1,000 ml fluid with spasmolytics and NSAR (Novaminsulfon) can control the situation.

If there is an obstruction and fever, urological intervention is necessary (double-J-catheter). The urine should be acidified to a pH value of 4-5. This works best with buttermilk, yoghurt, coke and avoidance of fruit juice. A brief interruption of indinavir, therapeutic drug monitoring and a conversion of the therapy to e.g. 600/100 mg should be considered.

When evaluating the triggering agent, it must be observed that other medicaments could have caused the crystalluria, and only resulted in nephrolithiasis on combination with indinavir (e.g. ampicillin, acyclovir, aspirine, ciprofloxacin, methotrexate, vitamin C, sulfonamide and also other drugs that lead to an increase in uric acid).

On abdominal x-ray, an indinavir stone is not usually apparent. However, in combination with calcium it can become radio-opaque, and could be confused with a calcium-oxalate-stone. Urate stones are transparent on x-rays.

Elevation of creatinine under long-term indinavir therapy was already observed at the end of the 90s. Typical signs of indinavir nephropathy include sterile leukocyturia and an echogenic transformation of the renal parenchyma in otherwise normal kidneys. Discontinuing indinavir leads to a normal function in most cases. One should pay heed to the possibility of tuberculosis in the urinary tract in sterile leukocyturia.
**Tubulotoxic side effects of ART, Fanconi’s syndrome**

Fanconi’s syndrome is characterized by generalized disturbance of tubular function, while glomerular filtration is not primarily affected. The limited capacity of transportation and reabsorption of amino acids, glucose, phosphate, and bicarbonate leads to the loss of these components in the urine. The results are hypophosphatemia, hypocalcemia, osteoporosis and acidosis. The most prominent example is the glucose threshold of the kidneys (180 mg/dl).

The main symptoms of Fanconi’s syndrome are the loss of phosphate, amino acids and glucose in the urine, a low phosphate value in the blood, or glucosuria at normal blood glucose levels. In the past, a drug-induced Fanconi’s syndrome on cidofovir, tenofovir and adefovir has been observed. Because mitochondrial toxicity is discussed as a potential reason, this side effect is possible with any other NRTI.

In case reports, renal failure was above all described in patients with other reasons for renal insufficiency, mostly under boosted PI-regimes with tenofovir as well as secondary disorders and cirrhosis of the liver or hepatitis. Nephrologists advise caution in selecting antiretroviral therapy for patients with proteinuria, nephritic syndrome, cirrhosis of the liver, and/or dyslipoproteinemia. Nephrotoxic substances such as cidofovir, adefovir and tenofovir should be avoided in these patients. According to the current data, there is no reason to categorize the one or the other substance as nephrotoxic ahead of time or to discourage patients from using them. A recently published overview concerning changes in the renal function under antiretroviral therapy saw no advantage of one particular therapy with regard to nephrotoxicity. Therefore, only careful monitoring of serum creatinine, proteinuria, erythrocyturia and serum phosphate is advised.

**Tenofovir and the kidney**

In the past few years, a number of studies have investigated the kidney function on tenofovir. It must be emphasized in advance that, in comparison to other NRTIs, the licensing studies revealed no differences with regard to nephrotoxicity. However, cohort analyses and case studies reported tubular damage suggestive of Fanconi’s syndrome. This was almost always diagnosed in conjunction with hypophosphatemia, glucosuria (renal diabetes mellitus with normal blood sugar), and a mild proteinuria (not nephrotic). In the cohort studies, the serum creatinine increased on average to 2.7 mg/dl (0.9-7.8) and decreased again to a creatinine level that was slightly higher than the starting level, at 1.2 mg/dl (0.7-2.1), once tenofovir was discontinued.

According to the cases available at present, it can be assumed that tubular acidosis, hypokalemia, hypophosphatemia and glucosuria will all recede after tenofovir has been discontinued. Kidney biopsies performed on patients with Fanconi’s syndrome who were taking tenofovir showed a proximal acute tubular necrosis without any glomerular, vascular or interstitial changes, corresponding to the clinical course of restitution ad integrum after discontinuation of tenofovir. Therefore, tenofovir should not be withdrawn immediately in the case of mild proteinuria or hypophosphatemia. In such cases, the kidney function can (and indeed should!) continue to be monitored.
The differential diagnosis of tenofovir-induced kidney damage and HIV-AN is very important. Low serum phosphate, glucosuria and a mild proteinuria all tend to point to side effects of tenofovir. In this differential diagnosis, asking for a simple urine disc electrophoresis can answer the question of selectivity of proteinuria, which can differentiate between the non-selective glomerular (HIV-AN), and the selective tubular (TDF) form of damage.

According to a number of cohort studies, the risk factors for tenofovir-associated impairment of kidney function are: advanced HIV infection (low CD4+ T-cells), limited kidney function at the beginning of treatment (increased serum creatinine), history of kidney disease, or arterial hypotonia – but, interestingly enough, not diabetes mellitus.

The measurement of serum creatinine alone identifies at least mild impairment of the kidney function on tenofovir in about 2% of patients. When the more sensitive MDRD clearance is applied, the occurrence is 13%. We therefore recommend a combination of serum creatinine and urine status/sediment to check progress in cases of tenofovir intake, as well as with other antiretroviral therapies. To be particularly thorough, this can be supplemented by a calculated MDRD clearance. We consider urine collection to be less useful, for there is nothing more unreliable than a 24-hour urine collection at home by a patient who has not been given precise instructions beforehand.

In the case of tubulotoxic damage, an overlapping toxicity of tenofovir with boosted PIs due to a blockade of the MRP2-efflux-transport-protein of the tubule cell by ritonavir is possible. The increased AUC levels of tenofovir combined with atazanavir/r or ddI could also have a cytotoxic effect on tubule cells, but this is still hypothetical. At present, the clinical data do not justify to categorically abandon such combinations. However, for combinations of ddI, tenofovir and boosted PIs (especially atazanavir), the kidney function should be monitored carefully, as an increase in the tenofovir level can be expected.

Acute kidney failure or acute tubular necrosis is also possible when taking acyclovir, ganciclovir, adefovir, aminoglycosides or pentamidine. Tubular dysfunctions can also occur when taking ddI, d4T, or 3TC. An acute allergic interstitial nephritis can arise in the context of the hypersensitivity reaction with Abacavir. Membranoproliferative glomerulonephritides have been described in connection with atazanavir and enfuvirtide (T-20).

Thus, all that remains is the reminder to always perform routine checks on kidney function where HAART is involved. On the other hand, from a nephrological viewpoint, there is no reason at present to issue a general warning about one substance or another.

Nephroprotection

In view of the prolonged use of antiretroviral medication, long-term renal side effects are to be expected. This applies especially to the discussion about hyperlipidemia and lipodystrophy. Similar to experiences with diabetes mellitus and diabetic nephropathy, the principles of therapy should be particularly emphasized: adjustment of blood pressure values to < 130/80 mm Hg and no smoking. However, they have not yet been scientifically investigated in relation to HIV infection. The con-
sequent adjustment of diabetes mellitus or change of therapy to avoid a metabolic syndrome are in principle advantageous and will probably have a long-lasting positive side effect on renal function. On the basis of current data, the viral changes of the glomeruli and the renal tubules due to HIV infection should be reason enough to start/maintain an antiretroviral therapy in a symptomatic patient, rather than to worry too much about potential nephrotoxic side effects.

Estimating the GFR

According to Cockroft and Gault: \[((140-\text{age}) \times \text{kg body-weight}) \div (\text{serum creatinine, mg/dl} \times 72)\). For women, the result is multiplied by 0.85.

The MDRD-formula (http://nephron.com/cgi-bin/MDRDSI.cgi) is more exact. It just needs laboratory data (creatinine, urea, albumin), age and sex but no urine collection (the adjustment for dark-skinned persons can be disregarded). The formula is:

\[
\text{Creatinine-clearance [MDRD]} = 170 \times \text{Crea [mg/dl]}^{0.999} \times \text{age}^{-0.176} \times \\
(\text{urea [mg/dl]} \times 0.46)^{-0.170} \times \text{albumin [g/dl]}^{0.318} \quad \text{(for women: x 0.762)}
\]

The original formula displays SUrea (= Urea-nitrogen), which is the reason for the conversion “x 0.46”.

Dosage of antiretrovirals in renal insufficiency

In each case, the technical information of the individual substances must be taken into consideration. Because NNRTIs and PIs are almost exclusively hepatically eliminated, a dose rate adjustment is normally only necessary for the NRTI, unless a coexistent insufficiency of the liver is present.

Within the scope of hepatitis C therapy, ribavirin should be omitted in patients with renal insufficiency (note: prolonged anemia) if the creatinine clearance is under 50 ml/min/1.73 m². T-20 (Fuzeon™) can be used up to an endogenous creatinine clearance of 30 ml/min/1.73 m² without dose reduction; no data is available for more severe renal insufficiency.
OIs and renal insufficiency

Pneumocystis pneumonia

As cotrimoxazole is nephrotoxic as a high-dose therapy, its use must be carefully considered. Systemic administration of pentamidine should also be avoided in patients with renal insufficiency.
### Table 3: PCP treatment in renal insufficiency

<table>
<thead>
<tr>
<th>GFR</th>
<th>GFR &gt; 50 ml/min</th>
<th>GFR 10-50 ml/min</th>
<th>GFR &lt; 10 ml/min</th>
<th>Dose adaptation for HD/CAPD/cont. NET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cotrimoxazole</td>
<td>960 mg 3 x 3/die</td>
<td>960 mg 2 x 3/die</td>
<td>960 mg 1.2 x 3/die</td>
<td>480 mg 1 x 3/die</td>
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<tr>
<td></td>
<td>(total of 120 mg/ kg daily)</td>
<td>(100 % every 12 h)</td>
<td>(100 % every 12-24 h)</td>
<td>(50 % every 24 h)</td>
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<tr>
<td>Dapsone</td>
<td>100 mg every 24 h</td>
<td>50-100 % 50 %</td>
<td>avoid</td>
<td>avoid</td>
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<tr>
<td>Atovaquone</td>
<td>750 mg every 12 h</td>
<td>100 %** 100 %**  100 %**</td>
<td>HD: no adaptation</td>
<td>CAPD: no adaptation*</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>CAVH: (GFR &lt; 10)**</td>
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<tr>
<td>Pentamidine</td>
<td>4 mg/kg every 24 h</td>
<td>100 % 100 %</td>
<td>100 % every 24-36 h</td>
<td>100 % every 48 h see text !!!</td>
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</table>

* no studies available, normal dosage recommended.
** no studies available, dosage as for GFR < 10 ml/min recommended.
(cont. NET = continuous dialysis, HD = intermittent hemodialysis, CAPD = continuous ambulant peritoneal dialysis; CAVH = continuous arterio-venous hemofiltration, CVVHD = continuous veno-veno hemodiafiltration).

### Toxoplasmosis encephalitis

### Table 4: Treatment of cerebral toxoplasmosis with renal insufficiency

<table>
<thead>
<tr>
<th>GFR</th>
<th>GFR &gt; 50 ml/min</th>
<th>GFR 10-50 ml/min</th>
<th>GFR &lt; 10 ml/min</th>
<th>Dose adaptation for HD/CAPD/cont. NET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrimethamine</td>
<td>50-75 mg every 24 h</td>
<td>100 %</td>
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<tr>
<td>Clindamycin</td>
<td>150-300 mg every 6 h</td>
<td>100 %</td>
<td>100 %</td>
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<tr>
<td>Sulfadiazine</td>
<td>2 g every 6 h</td>
<td>Avoid</td>
<td>Avoid</td>
<td>Avoid</td>
</tr>
</tbody>
</table>

* = no studies available, dosage as for GFR < 10 ml/min recommended.
(cont. NET = continuous dialysis, HD = intermittent hemodialysis, CAPD = continuous ambulant peritoneal dialysis; CAVH = continuous arterio-venous hemofiltration, CVVHD = continuous veno-veno hemodiafiltration).
## CMV, HSV, VZV infection

### Table 5: Treatment of CMV, HSV, VZV in renal insufficiency

<table>
<thead>
<tr>
<th>Drug</th>
<th>GFR normal</th>
<th>GFR &gt; 50 ml/min</th>
<th>GFR 10-50 ml/min</th>
<th>GFR &lt; 10 ml/min</th>
<th>Dose adaptation for HD/CAPD/cont. NET</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acyclovir</strong></td>
<td>5-10 mg/kg every 8 h</td>
<td>5 mg/kg every 9-12 h</td>
<td>5 mg/kg every 12-24 h</td>
<td>2.5 mg/kg every 24 h</td>
<td>HD: Dose after dialysis CAPD: GFR &lt; 10 CAVH: 3.5 mg/kg every 24 h CVVHD: 6.5-15 mg/kg every 24 h</td>
</tr>
<tr>
<td><strong>Ganciclovir</strong></td>
<td>5 mg/kg every 12 h</td>
<td>3 mg/kg every 12 h if GFR 25-50 ml</td>
<td>3 mg/kg every 24 h if GFR 10-25 ml</td>
<td>15 mg/kg every 24 h</td>
<td>HD: Dose after dialysis CAPD: GFR &lt; 10 CAVH: 3.5 mg/kg every 24 h CVVHD: 2.5 mg/kg every 24 h</td>
</tr>
<tr>
<td><strong>Valgan-ciclovir</strong></td>
<td>900 mg every 12 h</td>
<td>GFR 40-59 ml/min 450 mg every 12 h GFR 25-39 ml/min 450 mg every 24 h GFR 10-24 ml/min 450 mg every 48 h for induction</td>
<td>unknown</td>
<td>unknown</td>
<td></td>
</tr>
<tr>
<td><strong>Foscavir</strong></td>
<td>90 mg/kg every 12 h</td>
<td>50-100 %</td>
<td>10-50 %</td>
<td>avoid</td>
<td>HD: Dose after dialysis CAPD: 60 mg/kg every 48-72 h CAVH: GFR 10-50</td>
</tr>
<tr>
<td><strong>Cidofovir</strong></td>
<td>5 mg/kg every 7 days</td>
<td>100 %</td>
<td>0.5-2 mg/kg every 7 days</td>
<td>avoid</td>
<td>HD: GFR 10-50 CAPD: GFR 10-50 CAVH: avoid</td>
</tr>
<tr>
<td><strong>Famciclovir</strong></td>
<td>250 mg every 8 h p.o.</td>
<td>Every 12 h</td>
<td>Every 48 h</td>
<td>50 % every 48 h</td>
<td>HD: Dose after dialysis CAPD: ? CAVH: GFR 10-50</td>
</tr>
</tbody>
</table>

(Cont. NET = continuous dialysis, HD = intermittent hemodialysis, CAPD = continuous ambulant peritoneal dialysis; CAVH = continuous arterio-venous hemofiltration, CVVHD = continuous veno-veno hemodiafiltration).

### References

2. Arribas J, et al. Superior outcome for tenofovir, FTC & efavirenz compared to fixed dose AZT/3TC (Combivir) & efavirenz in antiretroviral naive patients. 18th International Conference on Antiviral Research 2005, Barcelona.


8. Gallant et al. (TDF) Compared to Nucleoside Reverse Transcriptase Inhibitors (NRTIs): IAS 2005: Abstract TuPe2.3C18.


