INTRODUCTION

In a short span of two and a half decade, HIV/AIDS has emerged as second largest killer disease that has affected mankind. The triple drug antiretroviral therapy (ART) has ensured a reasonably good quality of life to HIV infected individuals. However, it has been seen that HIV infection is diagnosed most of the times with one or the other opportunistic infection (OI), particularly in the developing countries. At time of diagnosis, most of the patients have advanced disease and are at a higher risk of serious OI and death.

Human immunodeficiency virus (HIV) infection is associated with several opportunistic infections/malignancies that may be life threatening and need quick intervention by health care workers. These emergencies could be related to

1. Opportunistic infections that are seen at presentation or that occur as the immune system gets weaker.
2. HIV induced diseases like enteropathy and wasting, diarrhea leading to dehydration and its sequel, neurologic complications like PML, etc.
3. Complications from the use of anti-HIV medication like lactic acidosis, pancreatitis, bone marrow suppression etc.
4. Immune reconstitution syndromes.

Emergencies in HIV-infected patients can occur at any stage of the disease. Opportunistic infections may lead to irreversible damage of organs such as the brain, the eye or the lung. The use of antiretroviral therapy may be associated with side effects of ARV drugs like jaundice, lactic acidosis, anaemia etc. The drug-drug interaction can frequently lead to severe symptoms such as nausea, diarrhoea and complications such as anaemia or leucopenia.

In a prospective study conducted in Cote d’Ivoire in 1999-2000, it was found that the most frequent reasons for emergency consultation were deterioration of general condition (62%), diarrhea (39.1%) and cough (20.5%). Illness was chronic in 54% of cases. Physical signs were severe weight loss (84%), fever (50%), pale conjunctivas (29%), respiratory signs (19.2%) and dehydration (19%). The most frequent organic involvement causing admission was digestive (39.7%), neurological (24.4%) and pulmonary (20.5%). Most medical emergencies related to the HIV infection in the adult involved opportunistic diseases.

An overview of the various emergencies in HIV infected individual are summarized in the following table:

Table 1: Emergencies in HIV infection

<table>
<thead>
<tr>
<th>Pulmonary emergencies</th>
<th>ARV therapy</th>
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<tbody>
<tr>
<td>Pneumocystis carinii pneumonia</td>
<td>lactic Acidosis</td>
</tr>
<tr>
<td>Bacterial pneumonias</td>
<td>Hepatic necrosis due to Nevirapine</td>
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</tbody>
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Central nervous system emergencies

1. Cerebral toxoplasmosis
2. Cryptococcal meningitis
3. Tubercular meningitis
4. PML
5. Primary CNS Lymphoma

Diarrheal Diseases

Ocular emergencies

1. Cytomegalovirus retinitis
2. Varicella zoster

Others

Lymphadenopathy due to IRIS causing Compression on trachea, spite etc

<table>
<thead>
<tr>
<th>Table 2: Relation of the occurrence of various OI with CD4 counts</th>
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<tbody>
<tr>
<td>Any CD4 level</td>
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<tr>
<td>&lt; 250/cmm</td>
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<tr>
<td>&lt;100/cmm</td>
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<td>&lt; 50/cmm</td>
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tem tends to weaken over time, it paves the way for the development of various infection termed opportunistic infections. Consequently, the site of infection determines the clinical presentation and hence the emergencies that may be encountered often become system specific, though they may involve more than one system.

B. EMERGENCIES DUE TO ANTIRETROVIRAL DRUGS

A. EMERGENCIES DUE TO OI

1. Pulmonary Emergencies

1.1 Pneumocystis carinii pneumonia:

This disease is caused by the organism pneumocystis jerovici, that is a fungus. The pneumonia caused is primarily an infiltrative pneumonitis and is one of the more commonly encountered emergency.

The clinical manifestation is sub acute to chronic in the immunocompromised individual and is characterized by the triad of – shortness of breath, fever and non productive cough in most instances. Occasionally, the cough may be productive, and the manifestations can be complication like pneumothorax or hemoptysis rarely. It may have associated extreme fatigability.

Diagnosis should be confirmed by sputum examination, if available. However, treatment should not be withheld for want of confirmation. The definitive diagnosis of PCP is confirmed by demonstration of the organism in pulmonary sections. The examination of sputum is a simple, inexpensive, and effective means to confirm the diagnosis. If sputum is not diagnostic, special medical procedures like a bronchoscopy with bronchoalveolar lavage (BAL) may be performed.

Chest X ray may be normal in large number of cases. The chest film typically shows diffuse interstitial or perihilar infiltrates but can be normal in at least one third of cases. Less commonly, lobar infiltrates, effusions or cavitary lesions mimic other pulmonary processes

Trimethoprim-sulfamethoxazole is the drug of choice for the treatment of PCP. It is given for 21 days followed by prophylactic therapy to prevent the high likelihood of PCP happening again.

In cases of severe PCP, the use of corticosteroids has clearly decreased clinical failures and lowered death rates. Prednisone is given as 21 day course as: 40 mg BD in first 5 days, 40 mg OD for 6-10 day and 20mg OD from eleventh to twenty first day. Oxygen supplementation should be initiated in cases with moderate and severe PCP.

Primary prophylaxis is recommended in patients with CD4 count <200 cells/mm3, or in the presence of any other AIDS-defining illnesses. Secondary prophylaxis should be given to all patients after an episode of PCP. One double-strength tablet of trimethoprim–sulfamethoxazole (TMP–SMX) (160/800 mg) daily is used for prophylaxis.

B.1.2 Bacterial Pneumonias

Pneumonia in HIV-infected patients is unique, differing from that in the general population with respect to possible causative agents, presentation, and management. Because the illness can be rapidly fatal when associated with HIV disease, it is very important to make the diagnosis quickly, identify the most likely pathogen(s), and initiate the appropriate therapy

Falco et al collected clinical and microbiological observations, as well as follow-up on human immunodeficiency virus (HIV)-infected patients with bacterial pneumonia, and compared pneumococcal pneumonia in patients with and without HIV infection. Fifty five HIV-infected patients, who had had 68 episodes of bacterial pneumonia, were

Table 3: Assessing the severity of Pneumocystis jerovici pneumonia

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough, sweats, exertional dyspnoea</td>
<td>Dyspnoea on minimal exertion, fever, cough</td>
<td>Dyspnoea at rest, tachypnoea, persistent fever</td>
<td></td>
</tr>
<tr>
<td>Blood gas analysis</td>
<td>PaO2 normal</td>
<td>PaO2 60-80 mmHg and falls on exertion</td>
<td>PaO2 &lt; 60 mmHg</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>Normal or minor perihilar markings</td>
<td>Diffuse bilateral interstitial shadowing</td>
<td>Extensive bilateral interstitial and alveolar markings</td>
</tr>
</tbody>
</table>

(Source: Guidelines for Prevention and Management of Common Opportunistic Infections/Malignancies among HIV-Infected Adult and Adolescent. May 2007, NACO)

The severity of the disease is important to be established as it often reflects on the management and sometimes the prognosis. The severity is established with the determination of the PaO2.
studied prospectively. Twenty one HIV-infected patients with pneumococcal pneumonia were compared to 69 non-HIV-infected patients with pneumococcal pneumonia. Aetiological diagnosis was established in 48 cases (71%). The most common causative agents were S. pneumoniae and H. influenzae. In this study, the overall mortality was 10%. Fifty five percent of patients with follow-up had recurrent episodes.

Most HIV-infected patients with bacterial pneumonia have fever, cough, and sputum production, and the majority will have dyspnea. Patients with PCP present similarly, except that they usually do not produce sputum. Careful history taking also may help distinguish between bacterial pneumonia and PCP. Bacterial infection usually has an acute onset: on average, a patient presenting with bacterial pneumonia has been sick for 2 to 5 days. A patient who presents after 2 weeks of progressive symptoms more likely has PCP, which is more insidious. When taking the patient's medical history, it is important to ask about all his or her medications, particularly those for pneumonia prophylaxis. Prophylaxis with the combination of trimethoprim and sulfamethoxazole (TMP-SMX) has reduced the incidence of PCP and made it a disease that usually appears only in patients with very low CD4+ cell counts. However, PCP can still develop in a patient receiving PCP prophylaxis. Another important part of the patient's history regards drug use. The incidence of bacterial pneumonia in HIV-seropositive patients is about 10 times higher than in the HIV-seronegative population. When an HIV-infected patient also has a history of drug abuse, the likelihood of bacterial pneumonia increases.

Diagnosis of the bacterial pneumonia in HIV-infected needs to be prompt. Since the radiographic appearance of various pneumonias may overlap, radiographic findings provide only a differential diagnosis, not an absolute diagnosis, of the most likely causative organism. The goal is to decide, with some degree of confidence, what the most likely causative organisms are so that the appropriate therapy can be initiated. A lobar infiltrate generally suggests bacterial pneumonia, but it may also represent a fungal infection or even PCP. While diffuse infiltrates are more common in PCP, bacterial infection and tuberculosis (TB) can both result in this radiographic presentation. Linear or nodular infiltrates are associated with fungal, nocardial, and malignant diseases. Mycobacterial infection often shows a localized infiltrate, often apical, with hilar adenopathy. Small nodules may indicate TB, fungal infection, or neoplasm. Larger nodules suggest fungal infection or nocardial infection, and cavities may represent bacterial infection, fungal infection, TB, or neoplasm. Pleural effusions are most suggestive of bacterial infection but also occur with AIDS-associated malignancies, such as Kaposi's sarcoma and, rarely, with PCP. Finally, pneumothorax is more commonly seen with PCP than with other infections.

Treatment of bacterial pneumonia in HIV patients is similar to that in HIV-seronegative patients. Therapy should always begin empirically, without waiting for sputum or blood culture results. Results of sputum examination, though useful, often remains controversial. Many HIV patients with bacterial pneumonia can be treated as outpatients. Patients with poor immune status, very high fever (above 39.5 °C), poor compliance, signs of organ failure, CNS disorders (confusion) and poor vital signs (tachypnea, tachycardia, hypotonia), as well as older patients (above 65 years), should be hospitalized immediately.

For HIV-infected patients in whom bacterial pneumonia is suspected, it is recommended to initiate therapy with a second- or third-generation cephalosporin or b-lactam—lactamase inhibitor, which provides S pneumoniae and H influenzae coverage, or with TMP-SMX. The newer macrolides provide coverage for H influenzae and the atypical pneumonias, such as those caused by Chlamydia and Legionella. However, these are much less common in HIV-seronegative patients; therefore, the use of a macrolide as empiric therapy is not warranted unless these pathogens are suspected. Patients who are already hospitalized are more likely to have a gram-negative infection. In such cases, treatment depends on local resistance patterns and experience.

The antibiotic selection should include those used to treat patients with Pseudomonas infections; a regimen containing a third-generation cephalosporin plus an aminoglycoside is reasonable. HIV infection does not in itself determine prognosis.

2. Emergencies due to CNS Involvement

There are several neurological manifestations due to which the HIV infected person may present in the casualty. Many of them have features suggestive of stroke. The common causes are cerebral toxoplasmosis, tubercular meningitis, PML, cryptococcal meningitis, CNS lymphoma etc and are described.
2.1 Cerebral toxoplasmosis.
Toxoplasma gondii, a parasite, is the most common cause of focal brain lesions in people with AIDS. Most of the cases are a reactivation disease. The infection may have occurred much earlier, but was kept under control by the healthy immune system. The risk of reactivation increases as the T cells decrease, with the highest risk in persons with T cell counts less than 50.

Patients with cerebral toxoplasmosis complain of headache, confusion or altered mental status, and fever (in about half the cases). Up to 50% of patients with this infection may develop seizures as an initial sign of the disease, and even more will have a stroke.

The diagnosis is based on the clinical findings, low T cell count, evidence of the infection in the blood (positive IgG antibodies against Toxoplasma), and CT scan or MRI of the head. CT scan or MRI may reveal typical ring enhancing lesions with a predilection to involve the basal ganglionic region.

Treatment for cerebral toxoplasmosis consists of a combination of pyrimethamine, sulfadiazine, and folinic acid. Alternative therapies for patients with allergies to sulfa drugs include pyrimethamine and folinic acid, in addition to one of the following: clindamycin, clarithromycin, dapsone, or azithromycin. Improvement is expected after 7 to 10 days of therapy. The duration of treatment is 4-6 weeks.

The presence of multiple brain lesions in a T gon-dii-seropositive, HIV-infected patient with a CD4 T-cell count <100/µL who is not receiving anti-T gondii prophylaxis is still considered highly predictive of toxoplasmic encephalitis. Neurologic response is noted in 51% of patients by day 3, and in 91% of patients by day 14. Thus, brain biopsy should be considered when there is no clinical improvement by 10-14 days of therapy. The duration of treatment is 4-6 weeks.

2.2 Cryptococcal meningitis.
Cryptococcus neoformans is the most common fungus responsible for infections in patients with AIDS. The most severe type of cryptococcal infection is chronic meningitis. The symptoms may include headaches, fever, altered mental status, nausea, and vomiting.

A serum cryptococcal antigen test may be used to screen HIV-infected patients with these nonspecific symptoms and low T cell counts. A spinal tap is the preferred diagnostic procedure. The level of cryptococcal antigen in cerebrospinal fluid (CSF) or a CSF fungal culture provides a definite diagnosis.

Treatment of HIV-associated cryptococcal meningitis is with intravenous amphotericin B for two weeks with or without flucytosine, followed by oral fluconazole for 8 to 10 weeks. Once this therapy is finished, patients will have to stay on suppressive therapy with oral fluconazole. Increased intracranial pressure (pressure inside the head) may be frequent and could be a life-threatening complication of acute cryptococcal meningitis that may require a series of spinal taps or the placement of a special shunt to help relieve pressure.

Treatment success is monitored based on the clinical course and repeated lumbar punctures. When this is the case, maintenance therapy or secondary prophylaxis can be started, though not sooner than after four weeks of acute therapy. If there is increased intracranial pressure, CSF drainage may become necessary.

2.3 Progressive Multifocal Leukoencephalopathy (PML)
This is a demyelinating disease of the central nervous system, caused by the JC virus. The disease manifests as a result of the reactivation of the virus due to impaired cell mediated immunity.

PML can occur at any level of immunosuppression. It is more common after the CD4 count falls below 100/cmm, but has been reported even with CD4 count more than 200/cmm.

There is a broad spectrum of PML symptoms due
to the variety of localized areas of demyelination. Cognitive disorders are frequent and range from mild impairment of concentration to dementia. Additionally, focal neurological deficits are very typical of PML. Mono- and hemiparesis are observed most frequently, as well as speech and even visual deficits. These deficits may be isolated and initially present as discrete changes in coordination, rapidly leading to considerable disabilities. Epileptic seizures may occur.

The diagnosis of PML often requires advanced radiological evaluation. MRI is more useful and may reveal small discrete areas of demyelinated usually involving white matter. It is important to note that often, the lesions are asymmetrical. MRI also helps in differentiating PML from the characteristic findings of cerebral toxoplasmosis or CNS lymphoma.

Specific PML treatment is not available. The absolute priority should currently be to optimize ART in cases of PML. It was supported in past by numerous studies that prognosis significantly improved under HAART although results vary from case to case.

2.4 Tubercular Meningitis

Extrapulmonary tuberculosis occurs predominantly in co-infected patients with CD4+ T-cell counts of less than 200/µl. The most common feature of extrapulmonary tuberculosis is cervical lymphadenopathy. Tuberculous meningitis often presents with unspecific prodromal symptoms, such as headache, nausea and vomiting followed by elevated temperature and clinical signs of meningeal irritation. In case of doubt, a lumbar puncture should be performed without delay. The diagnosis is established with a lumbar puncture. The pressure is high, the protein elevated, the sugar low. There is a pleocytosis with predominantly lymphocytes. Acid fast staining may not demonstrate the organisms.

Anti tuberculous therapy with the standard drugs should be given for 1 year. Treatment of TBM follows in line with the treatment of the TB in HIV sero negative individuals. The national guidelines for India for management of OI recommend anti tuberculous therapy with the standard drugs to be given for 1 year. As TBM belongs to WHO Stage IV for HIV, the anti retro viral therapy should be initiated as soon as possible, correlating with the CD4 levels. There is considerable drug interaction between various classes of the ARV and the ATT. The changes in drug levels need to be addressed adequately to prevent sub optimal treatment.

3. Diarrheal Diseases in HIV

Diarrhoea is among the most common symptoms of HIV infection and is experienced by over 90% of patients with AIDS. It becomes more frequent as immune deficiency progresses. Some of these diarrhoeal diseases are likely to be severe, recurrent and persistent, and associated with extra-intestinal disease. Diarrhoea and weight loss are independent predictors of mortality.

Diarrhoea in HIV-infected individuals may be either acute (<7 days), or chronic (three or more liquid stools daily for >14 days). Chronic diarrhoea leads to mal-absorption, malnutrition and contributes to mortality. Initial clinical evaluation should include assessment of hydration, skin elasticity, weight, pulse, blood pressure, respiration, eyes, mucous membranes and urine output. Chronic diarrhoea is a very frequent and frustrating problem in PLHA; at least 50% experience it sometime during the evolution of the disease. Diarrhoea is often accompanied by nausea, weight loss, abdominal cramps and dehydration. There is often an intermittent watery diarrhoea, without blood or mucus. In one-third to two-thirds of cases, no cause is identified. Wherever possible, establish the cause and give specific treatment. The step-up diagnostic approach consists of examination of the stool for ova and parasites (with special stains – modified AFB, trichome and monoclonal stains) and endoscopic biopsy (gastroscopic/colonoscopic) if referred. The key to good management is rehydration including replacement of electrolytes. High-energy and high-protein intake reduces the degree of muscle wasting.

Prevention consists of attention to personal hygiene, hand-washing, drinking boiled water and eating only thoroughly cooked meat and vegetables.

An overview of the common causative opportunistic agents and the management is provided in the following table:

4. Ocular emergencies: Amongst the various ocular manifestations of HIV, the two condition that need to be promptly identified and treated are:- Cytomegalovirus infection and varicella zoster infection.

4.1 Cytomegalovirus infection: It is the most common ocular fatality. It can occur as pre ART OI or as an immune reconstitution manifestation. It usually occurs with CD4 less than 50 /cmm. When occurring as an IRS, it typically, like any other IRIS, should appear anytime between 6 weeks to 6 months of initiation of ART.

The manifestation of retinitis are due to reactivation of the CMV infection and symptomatically
leads to blind spots, visual field loss, flashing lights, floaters, or decreased or blurred vision. Peripheral retinal lesions may be asymptomatic, but the central lesions on the macula leads to development of decreased acuity of vision and central field defects. Diagnosis of CMV retinitis can readily be made by fundoscopy performed by an experienced ophthalmologist. The fundus examination reveals peripheral, whitish exudates. These should not be confused with the cotton wool spots that are sometimes seen with patients with high HIV levels. The bilateral involvement is not very commonly seen. There is often perivascular fluffy yellow–white retinal infiltrates, and focal necrotizing retinitis with or without preretinal haemorrhage. In the absence of HAART or specific anti-CMV therapy, retinitis progresses and causes a characteristic brushfire pattern, usually within 10–21 days after presentation. A granular, white leading edge forms, eventually resulting in an atrophic and gliotic scar leading to blindness.

It is important to understand that none of the medicines used in the treatment of CMV retinitis reverses the disease. They are only helpful in halting the diseases progression, and hence, time is vital in treating and preventing blindness. The drugs used are gancyclovir, foscarnet and cidofovir.

Treatment for CMV retinitis can be given intravenously, orally, or directly into the eye(s). It consists of two phases: induction therapy and maintenance therapy. Induction therapy usually takes two or three weeks.

Treatment is given by intravitreal injection of 0.1 ml ganciclovir at a dose of 200–4000 ìg thrice weekly for induction and 200–4000 ìg weekly for maintenance. The induction dose of foscarnet is 1.2–2.4 mg twice weekly, and maintenance dose 1.2 mg/week. The dose of cidofovir is 20 ìg/5 weeks in divided doses for induction and maintenance.

Maintenance therapy is intended to prevent the
virus from causing a relapse. This may be discontinued once the CD4 count increases to more than 200 cells/mm³ for at least 6 months following HAART. The treatment of choice is ganciclovir 5 mg/kg twice daily IV (induction) followed by capsules (maintenance), and can treat all forms of CMV disease. IV ganciclovir is given twice daily for two to three weeks and then IV once daily 5–7 days a week. Oral treatment is given as 1000 mg capsules three times daily.

4.2 Varicella Zoster Infection:

It is caused by the Varicella zoster virus (VZV) or herpesvirus type 3. Herpes zoster occurs in 8–11% of HIV-infected individuals. The incidence of herpes zoster is 15–25 times higher in HIV-1-infected persons than in the general population. The symptoms of zoster start with a burning, sharp pain, tingling, numbness, itching or aching in or under the skin of one side of the body or face. However, sometimes, the infection may effect the visceral organs spreading to lungs, liver or nervous system. When the ophthalmic division of the trigeminal nerve is involved, it may lead to dangerous affliction of the eye.

Treatment is usually intravenous acyclovir 10 mg/kg q8h is given for 7–10 days and continued until the lesions are clearly resolving.

B. EMERGENCIES DUE TO ANTIRETROVIRAL THERAPY

The advent of anti retro viral drugs have remarkably modified the course of the illness and HIV disease, particularly after the advent and use of HAART, after mid nineteen nineties. The anti retroviral drugs that are currently used belong to seven classes.

1. Lactic Acidosis

The term “mitochondrial toxicity” describes a group of different clinical conditions that happen because of damage to parts of the cell called mitochondria. (The mitochondria are the energy factories inside cells.) One possible cause of damage to mitochondria may be anti-HIV drugs known as nucleoside reverse transcriptase inhibitors (NRTIs).

The most serious condition that can result from such damage is lactic acidosis (an increase of lactic acid in the blood). Lactic acidosis has been reported in patients receiving NRTI regimens including combinations of Zidovudine (AZT) or stavudine (d4T) with didanosine (ddI), or rarely lamivudine (3TC). Lactic Acidosis is therefore an important ‘class’ specific side effect for the NRTI group.

The initial symptoms may include nausea, vomiting, abdominal pain, weight loss, malaise, fatigue (feeling tired), shortness of breath and occasionally fever. In addition, the patient may experience diarrhea, tachycardia and tachypnea.

Laboratory tests usually show a high amount of lactic acid in blood, somewhat abnormal liver function tests, and moderate to severe acidosis.

The management of lactic acidosis should include stopping anti-HIV drugs, and correction of these abnormalities. Patients may need to receive bicarbonate and glucose intravenously. Treatment with riboflavin might help in some cases. As many as 60% of patients with lactic acidosis can die from it. Recovery, sometimes may take few months. Long term residual effects are common.

2. Abacavir Hypersensitivity Reaction

The use of the NRTI abacavir can cause a serious hypersensitivity reaction in a small number of patients (4-9 % range). Median onset 9 day of abacavir initiation, 90% develop in first 6 weeks. Genetic predisposition is defined for some patients and possibly has a role in most.

The symptoms of abacavir hypersensitivity include fever, skin rash, nausea, vomiting, diarrhea, abdominal pain, malaise, and lethargy (sleepiness). Usually a hypersensitivity reaction will start within the first six weeks of taking abacavir. If a patient develops these symptoms, the abacavir should be stopped immediately. Whether hypersensitivity is suspected or confirmed, abacavir should never be restarted, as it may cause a more severe hypersensitivity reaction along with hypotension (low blood pressure), tachycardia (fast heart beat), and even death.

3. Indinavir-Induced Nephrolithiasis

Indinavir belongs to the protease inhibitor group of anti retro viral drugs. It tends to form crystals in the kidneys. These crystals can form kidney stones made up almost completely of this protease inhibitor. This can happen in 5% to 35% of patients treated with the standard dose of indinavir (800mg three times a day). Patients with indinavir stones can feel like those with other kind of kidney stones: pain on the sides, hematuria (blood in urine), nausea, and vomiting.

The confirmation of kidney stones may be difficult because indinavir-containing stones are not visible using plain radiography or non-contrast CT scans. Most patients will respond to conservative treatment that includes intravenous fluids, pain control, monitoring kidney function, and discontinuation of indinavir. Most people replace indinavir with some other agent.
To prevent kidney stones caused by indinavir, patients should take more liquids -- a minimum of 1.5 liters per day of non-caffeinated, non-alcoholic liquids.

4. **Marrow suppression by zidovudine**

The Marrow suppression by zidovudine manifests as neutropenia and/or anemia after weeks or months of therapy. Anemia has been reported with 1-4% and neutropenia with 2-8% cases. Risk is said to be more with advanced stage of HIV disease.

Zidovudine should be discontinued immediately. Erythropoetin and Granulocyte stimulating factor G-CSF may be needed for anemia and neutropenia respectively. Blood transfusions are often required.

5. **Hepatic necrosis with Nevirapine**

It has been reported in 1-2% of all recipients of Nevirapine. It has been observed that the rate of symptomatic hepatitis is almost 11% in females with CD4 count more than 250/cmm and 6% in males with baseline CD4 count more than 400/cmm. The drug should be promptly discontinued. Role of anti histaminics and steroids is doubtful. The side effect may progress even after the discontinuation of the drug.

6. **Rash by Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)**

6.1 Maculopapular rash.

NNRTIs sometimes can cause a maculopapular rash (a rash made up of small, well-defined bumps on the skin). NNRTIs include delavirdine, nevirapine, and efavirenz. The rash can affect the trunk, face, arms, and legs. It usually appears within the first four to six weeks of taking the medication.

6.2 Stevens-Johnson syndrome.

This is the most serious form of rash caused by NNRTIs. This severe and life-threatening rash can affect the skin but also mucosal surfaces (like inside the mouth or nose). It is sometimes known as toxic epidermal necrolysis. It is seen in 0.5-1% patients on Nevirapine and 0.1% on efavirenz. The symptoms are a diffuse rash with peeling of large areas of the skin, blistering inside of the mouth, conjunctivitis (swelling and reddening of the eyes), bronchitis, and general symptoms including fever, myalgia (muscular pain), arthralgia (joint pain), and malaise. This condition is an extreme emergency and most of the time patients are treated in burn units where close medical observation is necessary. IV fluids, and antibiotics may be required. Role of steroids is controversial.

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