

# GASTROINTESTINAL DISEASES IN HIV/AIDS

*Gastrointestinal disease is common among HIV-positive patients.*

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AIDS is one of the most devastating pandemics of modern society, with an estimated 65 million people believed to be infected and an estimated 14 000 new infections daily.<sup>1</sup> In sub-Saharan Africa the incidence of HIV is a staggering 10 - 20% of the population.<sup>1</sup> Gastrointestinal (GI) diseases account for a high proportion of HIV-related disease.<sup>2</sup> With the introduction of triple antiretroviral therapy the spectrum and complications of GI disorders have changed substantially.

## Historical perspective

In the late 1970s patients presented with *Pneumocystis carinii* pneumonia (currently *P. jiroveci*) (PCP), Kaposi's sarcoma and other rare immune deficiencies that could not be categorised. In 1981 the Centers for Disease Control (CDC) declared an epidemic of homosexual men with PCP.<sup>3</sup> At that stage a low CD4 T-lymphocyte count was identified in these individuals. Since 1995 antiretroviral therapy has been available.

Currently HIV-infected patients can be categorised as treatment naïve or antiretroviral experienced. For infected patients the CD4 count is a good risk indicator for opportunistic infections.<sup>4,5</sup> Evidence exists that viral load may also predict the risk for such infections.

## Gastroenterological problems

### Upper GI tract

Dysphagia or pain on swallowing due to oesophageal pathology is a very common complaint. The most common condition associated with this is candidiasis, followed by viral conditions that are included in the CDC classification as AIDS-defining conditions. Gastroscopy is a cornerstone investigation in patients with advanced immunodeficiency.<sup>6</sup> Upper GI endoscopy may yield a diagnosis in more than 75% of cases.

**Cytomegalovirus (CMV) is the most common cause of viral oesophagitis. These ulcers are usually present in the mid- and distal oesophagus.**

### Oesophagus

There is a very close relationship between the stage of immune suppression and oesophageal symptoms. Odynophagia is usually associated with *Candida* oesophagitis or an oesophageal ulcer.

The most common cause of dysphagia in HIV-positive patients is probably oesophageal candidiasis. Oral *Candida* is not always present and this lack of obvious infection should not deter one from investigating the oesophagus. Oral fluconazole is a very successful treatment for *Candida* oesophagitis. The dosage is 400 mg stat and then 200 mg for 14 days. Patients with documented refractory oesophageal candidiasis should be started on voriconazole.<sup>7</sup>

Cytomegalovirus (CMV) is the most common cause of viral oesophagitis. The ulcers are usually present in the mid- and distal oesophagus. A biopsy has to be taken to make a diagnosis. Histological diagnoses may be very difficult and a high index of suspicion is necessary. Treatment should be started empirically if the diagnosis is suspected. New agents in the treatment of CMV are ganciclovir, a derivative of acyclovir, and an experimental drug, phosphonformate.<sup>8</sup>

Herpes simplex virus and *Mycobacterium tuberculosis* are infectious causes that need to be excluded.

**Recent studies have demonstrated that the initial infection with HIV leads to a heavy involvement of the gut-associated lymphoid tissue (GALT), which may be permanently destroyed.**

### Enteritis and colitis

These are common problems in HIV patients. A variety of pathogens are implicated, such as mycobacteria, CMV, protozoa, fungi and neoplasms (Kaposi's sarcoma and non-Hodgkin's lymphoma).

Recent studies have demonstrated that the initial infection with HIV leads to a substantial involvement of the gut-associated lymphoid tissue (GALT), which may be permanently destroyed.<sup>9</sup> With a CD4 count of less than 50 opportunistic infections such as *Cryptosporidium* and *Microsporidium* play a significant role. The role of antibiotic-induced diarrhoea due to *Clostridium difficile* overgrowth should be kept in mind. In this setting we may also under-estimate the role of antiretroviral therapy in contributing to antiretroviral-associated diarrhoea. Studies on the role of the CD4 count in opportunistic infections showed that the infection was worse with a lower CD4 count.<sup>10</sup>

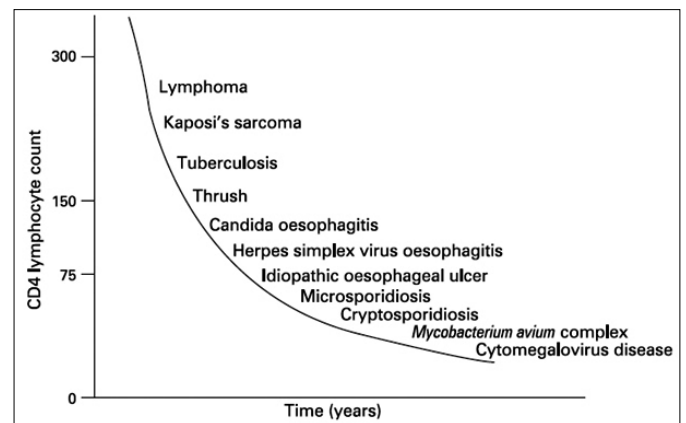


Fig. 1.

## Overview of abdominal pain

One of the general rules pertaining to HIV patients is that the clinical signs and symptoms are not always diagnostic.

The CD4 count dictates the specific pathogen responsible for the opportunistic infection, be it CMV, fungi or mycobacteria.<sup>11</sup> Multiple infections may occur simultaneously.

### Clinical manifestations

**Enteritis.** In both small and large bowel disease pain and diarrhoea are the significant symptoms. Bacteria (salmonella, shigella and

campylobacter), fungi (histoplasma), mycobacterial disease or other opportunistic infections also play a major role. Tuberculosis (TB) of the terminal ileum and peritoneum has become very important in recent years.<sup>12,13</sup> Kaposi's sarcoma may occur without any cutaneous signs and may present with pain, weight loss and GIT bleeding, but is mostly asymptomatic.<sup>14</sup>

**Intestinal perforation** usually occurs in the distal ileum or colon. Ileothypylitis is caused by the CMV and TB, which leads to chronic inflammation and subsequent perforation.<sup>15</sup>

**Tuberculosis (TB) of the terminal ileum and peritoneum have become very important in recent years.**

**Approach to diarrhoea**

The approach to diarrhoea should include a history concerning the duration of the condition, level of immunosuppression and drugs that could have complicated or introduced the diarrhoea. Essential tests that need to be done include a stool MC&S, *C. difficile* toxin and a CD4 count.

Endoscopy contributes to an accurate diagnosis and also points to the correct

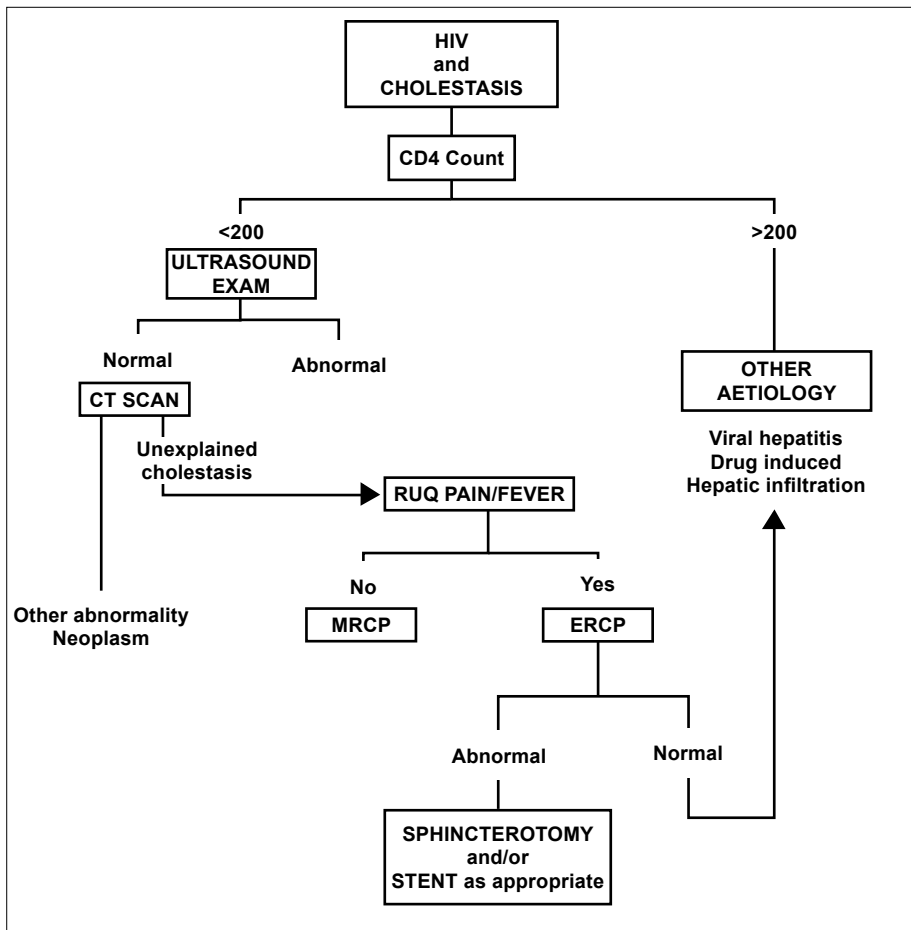


Fig. 2. Algorithm for the management of cholangiopathy.

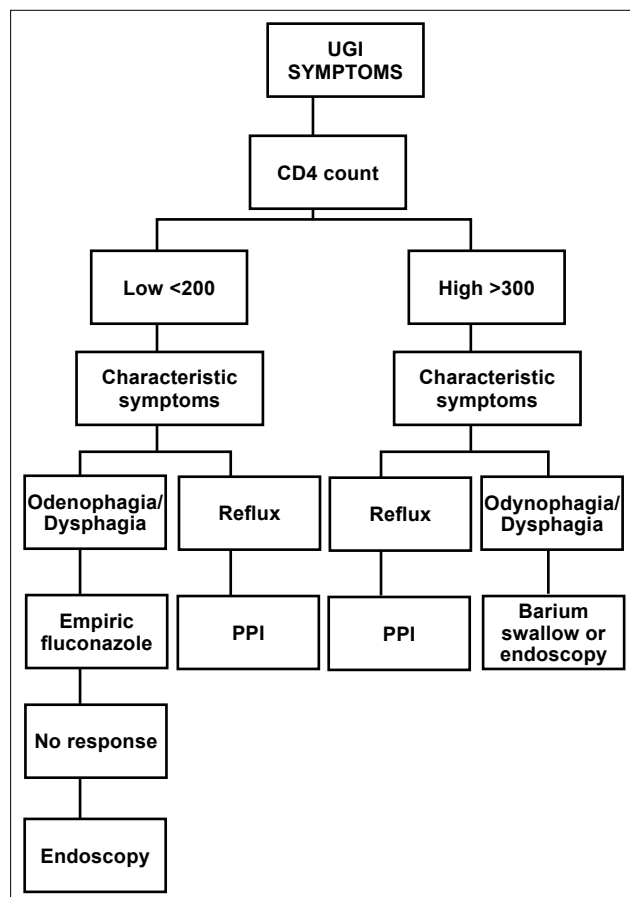


Fig. 3. Algorithm for the management of upper GI symptoms in HIV patients.

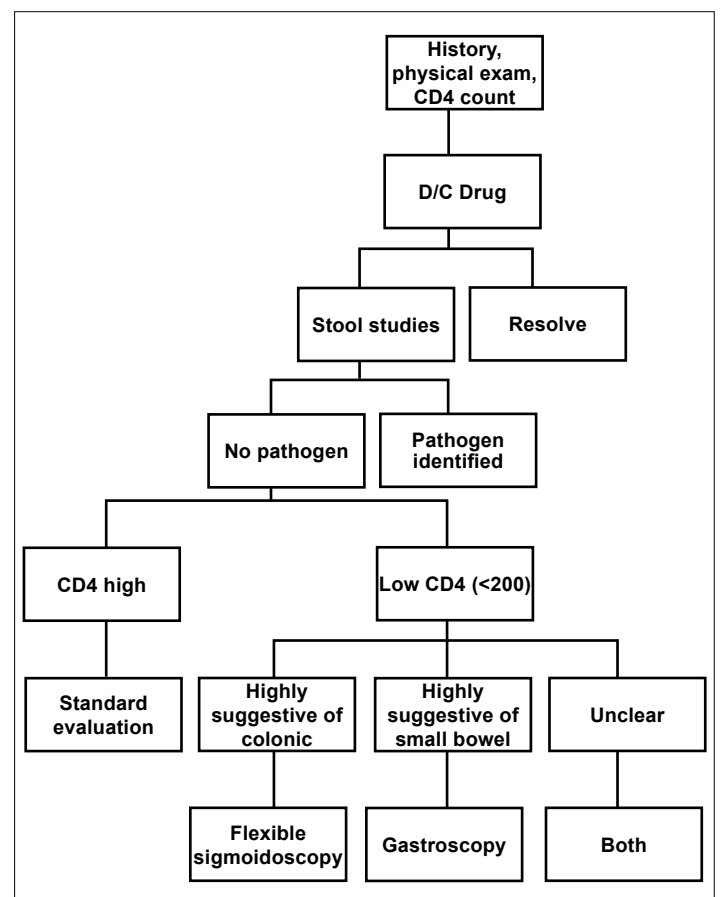


Fig. 4. Algorithm for the management of diarrhoea in HIV patients.

therapy. Upper endoscopy is essential when features suggestive of upper GI pathology are present.<sup>16</sup>

The indications for colonoscopy in HIV patients do not differ from those in healthy individuals. Symptoms such as fresh rectal bleeding, tenesmus or a change in bowel habits point to further investigation. An HIV-related diagnosis such as CMV colitis or pseudomembranous colitis may be made with endoscopy.

Data suggest that individuals with HIV develop colorectal cancer at an earlier age, which is more advanced at the time of diagnosis.<sup>17</sup> The appropriate age at which colorectal screening should be done is not clear and further studies are needed. Early colonoscopy should be done on patients with distressing symptoms and screening should probably be started at an earlier age.

**In HIV-positive patients, there may be concurrent infection with hepatitis B virus (HBV) and hepatitis C virus (HCV) because of the similar mode of transmission.**

### Liver disease

In HIV-positive patients there may be concurrent infection with the hepatitis B virus (HBV) and hepatitis C virus (HCV) because of the similar mode of transmission. Five to ten per cent of HIV-positive patients

have active hepatitis B and 35% have HBV core antibodies. Concurrent infection with HCV varies from 13% to 80%.<sup>18</sup>

It is very important to note that there is a more rapid progression to liver cirrhosis in HCV-positive HIV patients. Recent studies show that there is a decrease in liver-related mortality when antiretroviral therapy is initiated.<sup>19,20</sup>

Treatment of HIV-positive patients with HCV infection with peginterferon and ribavirin should be started after antiretroviral therapy has been introduced and the CD4 count has increased.<sup>21</sup> In active HBV infection treatment should be carefully planned because of HIV drug resistance when treatment aimed at HBV is commenced.

The following factors play a role in cholestasis: antiretroviral therapy, antimycobacterial medication, liver infection and HIV-related cholangiopathy. In HIV-associated cholangiopathy opportunistic infections play a major role, with pain and jaundice being prominent features. Management is difficult because cholangiopathy is often associated with AIDS. Essential treatment entails antiretroviral therapy, medically targeted therapy and endoscopic retrograde cholangiopancreatography (ERCP) for severe cholestasis or cholangitis.<sup>22</sup>

Other causes for liver infection must also be kept in mind, e.g. an increase in amoebic liver abscess has been noted in HIV-positive individuals.<sup>23</sup>

TB – a chronic infectious disease – causes hepatic granulomatous hepatitis with abnormally high alkaline phosphatase levels.

A CT scan of the abdomen demonstrates the omental cake, ascitis and liver lesions caused by TB granulomas.<sup>24</sup>

Lastly, there is an increase in the incidence of hepatocellular carcinoma (HCC),<sup>25</sup> mainly because of concurrent HCV and HBV infections causing liver cirrhosis, with a 75% incidence of HCC.<sup>26</sup> With such a high incidence of liver cirrhosis and the associated risk of HCC, hepatitis C and B should be treated and ultrasound screening and alpha-fetoprotein determination should be done every 6 months.<sup>27</sup>

### Pancreatitis

In the pre-antiretroviral era, 4.7% of patients with HIV had pancreatitis.<sup>28</sup> It is usually caused by disseminated infection or an infiltrative process such as Kaposi's sarcoma or lymphoma.<sup>29,30</sup> With the introduction of antiretroviral therapy an increase in drug-introduced pancreatitis has occurred.<sup>31</sup> The management of these patients does not differ from that of patients without HIV and the prognosis correlates with an APACHE score.<sup>32</sup>

References available at [www.cmej.org.za](http://www.cmej.org.za)

## IN A NUTSHELL

- Gastrointestinal disease in HIV-positive patients occurs frequently.
- Starting with determining the CD4 count is a good option to dictate treatment. The lower the CD4 count, the more pronounced the opportunistic infections.

## SINGLE SUTURE *Eye tests for Alzheimer's disease*

Eye tests could one day be used for the early detection of Alzheimer's disease, thanks to the discovery of a link between the amount of a characteristic protein in the brain and levels of the same protein in the eye.

Virtually everyone with Down syndrome goes on to develop Alzheimer's disease. When Lee Goldstein and colleagues of the Boston School of Medicine examined lens and brain tissue during post-mortems of people with Down's, they found that brain levels of amyloid correlated with those in the eye.

Clumps of amyloid protein in the brain are associated with Alzheimer's in the rest of the population, so Goldstein et al. suggest that scanning people's eyes might be a non-invasive way to diagnose Alzheimer's before other symptoms become apparent.

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