BHIVA guidelines on the management of opportunistic infection in people living with HIV: The clinical management of pyrexia of unknown origin 2023: non-technical summary

HIV and pyrexia of unknown origin (PUO)

The British HIV Association (BHIVA) produces medical guidelines about HIV treatment. Each guideline reviews the evidence for the best care. Although these guidelines are for clinicians, it is important that you know how these guidelines may affect your care.

This non-technical summary gives you the main points from the chapter on pyrexia of unknown origin (PUO) in the opportunistic infection guidelines. You can check the full guidelines for more detail at https://www.bhiva.org/OI-guidelines-PUO.

Key messages:

- Pyrexia of unknown origin (PUO) is when you have had a high temperature or fever on several occasions and been ill for several weeks, but doctors have not yet been able to find the cause.
- There are many infections and other health conditions that might cause this.
- It may also be seen in people living with HIV. It is less common now that we have successful antiretroviral therapy (ART) for HIV.
- It is important to find the cause so that you get the right treatment.
- Your doctors will ask about your lifestyle and travel history, as well as doing a range of tests. You may need to be admitted to hospital for some of these tests.
- Treatment is not usually started before the cause is known, though it may be needed in some cases.
- If you have PUO and are diagnosed with HIV, your HIV treatment will usually not be started until the cause of PUO has been found.
- HIV treatment may need to be started if you are at risk of other infections, or very unwell.

What are opportunistic infections?

These are infections that occur in people with a weakened immune system. They can be severe. They were often seen before there was good HIV treatment. But they are less common now because of the use of effective antiretroviral therapy (ART) for HIV.

What is PUO?

Pyrexia of unknown origin (PUO) is the term used when:

- You have had a high temperature (a fever) on several occasions AND
- You have been ill for about 4 weeks at home or for several days if you are so unwell that you have been admitted to hospital AND
- Doctors have not yet been able to find out the cause, even after you have had initial diagnostic tests.

But it can be seen in many diseases. Some examples are:

- Tuberculosis (TB) that has not yet been confirmed
- Some cancers
- Some autoimmune diseases such as rheumatoid arthritis, lupus or multiple sclerosis (MS)
- A wide range of infections.

PUO may also be seen in people living with HIV. It is not seen very often now because of the use of effective ART for treating HIV. When taken as prescribed, ART will reduce the HIV in your blood to levels that are extremely low (this is called an undetectable viral load). The health of your immune system will return to or remain within normal levels.

What causes PUO in people living with HIV?

The cause can be hard to find. Lots of tests may be needed to try and find out what is or is not causing it. The causes seen most often are:

- TB
- Non-tuberculous mycobacteria (NTM)
- Visceral leishmaniasis (in some parts of the world)
- Cytomegalovirus (CMV)
- Lymphoma (a type of cancer).

The diagnosis and treatment of many of these conditions is discussed in other chapters of the BHIVA opportunistic infection guidelines (https://www.bhiva.org/OI-guidelines) and the BHIVA TB guidelines (https://www.bhiva.org/TB-guidelines).

A wide range of other bacterial infections may also cause PUO and there are many other less commonly seen causes.

How is PUO managed in people living with HIV?

It is important to try to find out what is causing PUO, so that the right treatment can be given. The causes may vary, so your doctors will need to ask about your lifestyle and where you have been travelling. This will help them decide what tests to do. This will include sexual health screening. Your doctor will also examine you and do a number of different tests. Some of these may need to be repeated. The process may take a few weeks. You may need to be admitted to hospital while these tests are done.

If your immune system is weak, or if you are very ill, you may be offered treatment for the most likely causes even before it is confirmed. This will depend on your particular circumstances.

You may have been newly diagnosed with HIV as part of the testing to try to find out the cause of your PUO. In these cases, it is usually better to wait until the cause of PUO has been found before starting ART. But if you are very ill, or at risk of other infections, it may be necessary to start ART even if the cause of PUO has not been found. Your HIV team may ask for expert opinions from other specialists before making any decision about this. They need to be sure that they have considered and tested for all relevant causes, including those unrelated to HIV. If ART is started, your healthcare team will monitor you closely. There may be a risk of immune reconstitution inflammatory syndrome (IRIS). This is where your condition might worsen because of inflammation caused by the immune system improving. This would need to be treated carefully.

Further information and support

Community organisations in the UK that produce information and resources about HIV treatment include HIV i-base (https://www.i-base.info), Terrence Higgins Trust (https://www tht.org.uk) and NAM (https://www aidsmap.com).

About BHIVA

The British HIV Association (BHIVA) is an organisation for health professionals in the UK. Members include doctors, nurses, researchers, pharmacists and community advocates. Since 1995, BHIVA has been committed to providing excellent care for people living with and affected by HIV. BHIVA is a national advisory body on all aspects of HIV care and provides a national platform for HIV care issues. To help promote and monitor high standards of care, BHIVA publishes a range of clinical guidelines: https://www.bhiva.org/guidelines. Information about how BHIVA guidelines are developed can be found at: https://www.bhiva.org/clinicalguidelines.