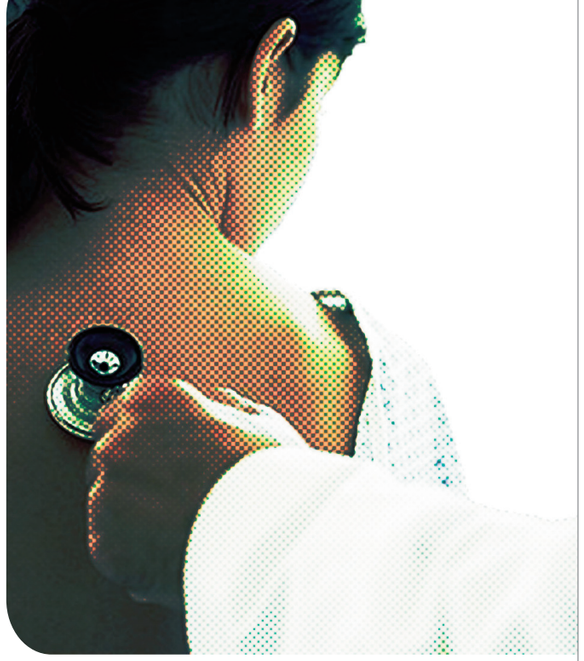

The information in this booklet is given as a guideline only and is not intended to be exhaustive.
It in no way binds bioMérieux S.A. to the diagnosis established or the treatment prescribed by the physician.

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7 What is EBV serology?

Performing an EBV serology consists of interpreting a profile obtained using a **combination of EBV-specific markers**. Generally, three EBV markers (VCA IgM, VCA IgG and EBNA IgG) are necessary to clearly determine the stage of infection (primary, past or absence of infection):

- **Primary EBV infection** is defined by a positive VCA IgM result, a positive or negative VCA IgG result depending on the sensitivity of the method, and a negative EBNA IgG result.
- **Past infection** is, in most cases, indicated by a negative VCA IgM result and positive VCA IgG / EBNA IgG results.
- Some indeterminate profiles require further serological analysis, such as immunofluorescence, immunoblots or even quantitative PCR to distinguish primary infection from past infection.

8 What is the monospot test and why choose serology?

The monospot (or heterophile antibody) test detects antibodies, which, although not directed against EBV, are highly indicative of IM when present. A negative result does not, however, make it possible to exclude IM. 20-30% of EBV IM are not diagnosed by this test.

Some heterophile antibody tests have an excellent positive predictive value, but the quality of the tests available on the market varies widely.

As a result, when faced with an incomplete IM clinical picture, it is **recommended to perform EBV serological tests** since heterophile antibodies are often absent. This is particularly applicable for young children.

ABBREVIATIONS:
EA IgG: Early antigen IgG - **EBNA IgG**: Epstein-Barr nuclear antigen IgG
VCA IgG / IgM: Viral capsid antigen IgG / IgM

9 Is patient monitoring important?

The complications of IM are rare, and therefore close clinical surveillance is not necessary.

Nevertheless, general practitioners should be aware of the most frequent complications and be able to advise the patient:

- **Contact sports** can result in a ruptured spleen.
- There is a **risk of airway obstruction** due to tonsillar enlargement that may require corticosteroid therapy if the Ear-Nose-Throat (ENT) signs worsen.
- **Hospitalization**, with specific medical management, is of course necessary in the case of symptoms suggesting encephalitis, liver failure, severe hematologic disorders (profound thrombopenia, agranulocytosis, haemo-phagocytic syndrome).

10 What about EBV reactivation?

After infection, EBV persists for life and can reactivate periodically. It may be associated with the presence of anti-EA IgG together with high anti-VCA IgG levels.

However, there is no need to follow reactivation in **immunocompetent patients**, as reactivation in these patients generally occurs without clinical symptoms.

Reactivation in **immunocompromised patients** can be more problematic with a risk of EBV-associated lymphoma.

Currently, molecular tools such as quantitative PCR in blood are the techniques recommended for the diagnosis and monitoring of EBV reactivation, especially in **transplant patients**. Immunocompromised patients are generally managed in hospitals by specialised teams.

INFECTIOUS MONONUCLEOSIS

10 QUESTIONS AND ANSWERS

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INFECTIOUS MONONUCLEOSIS

Why is diagnosis of this benign disease important for patient management?

This document answers some of the most frequently asked questions about this commonly encountered disease, that primarily affects adolescents and young adults.

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1 What is Infectious Mononucleosis?

Infectious Mononucleosis (IM) is the **main clinical manifestation of primary EBV (Epstein-Barr Virus) infection**.

It is also known as the "**kissing disease**" because it occurs mainly via exchange of saliva between teenagers or young adults.

2 What are the signs and symptoms?

The classic **clinical symptoms** of IM are sore throat with pharyngitis, malaise, fever, lymphadenopathy and fatigue. These symptoms are non-specific and can be found in other pathologies. This explains why tests may be necessary to establish a diagnosis of IM.

All of these symptoms can appear from the mildest form (e.g. a simple cold) to the most severe (e.g. profound fatigue, acute airway obstruction due to tonsillar adenoid enlargement, severe hepatitis).

The classic **biological signs** consist of lymphocytosis with atypical lymphocytes and a moderate rise in liver transaminases.

3 Who is at risk of IM?

Anyone, regardless of age, can become infected with EBV. However, the typical clinical symptoms of the disease are most frequently encountered in **pre-adolescents, adolescents and young adults**.

EBV primary infection is often asymptomatic in young children (under 10) and rare in subjects over 40, in whom it is associated with more atypical clinical signs that can delay diagnosis.

4 What is the duration of contagiousness?

The virus can be excreted in the saliva for months after the clinical signs disappear. As a result, infected patients remain contagious for a long period of time.

5 Why is it important to establish an accurate diagnosis?

It is important to establish a diagnosis of IM when faced with **non-specific symptoms** which can be found in other infectious etiologies (such as **cytomegalovirus, rubella, toxoplasmosis, and HIV primary infection**) and also when the clinical picture can suggest a **more severe illness**, such as a **hematologic malignancy** or **severe bacterial infections**.

Confirming a diagnosis of IM helps to rule out these pathologies.

It also enables to **reassure the patient** - since IM is usually benign - and to **provide better patient care**:

- explain that the fatigue may last for several weeks or months,
- give general recommendations: get lots of rest, avoid contact sports,
- explain that antibiotics are inappropriate because they have no effect on the virus and, particularly in the case of aminopenicillins, may result in skin rashes.

6 How is a diagnosis of IM established?

Complete EBV serological testing makes it possible to establish a **serological profile**, and should be performed as soon as possible. If the profile is found to be negative or is indicative of a past infection, then screening for other infectious etiologies (CMV, rubella, toxoplasmosis or possibly HIV primary infection) should be carried out.

It is also important to take into account the **age of the patient** and the **complete clinical picture** when establishing the diagnosis.