



## *“Whoa, hold the amoxicillin!”*

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**A** 22-year-old student presents with a dramatic, intensely pruritic rash over most of her body, although it is most pronounced on her trunk. Her hands and feet have swollen to the extent that it hurts to walk. She has tried treating the rash with diphenhydramine, with no apparent effect.

The rash started a week after starting a course of amoxicillin, 500 mg three times daily, for a sore throat with a white tonsillar exudate. A monospot test comes back positive. She has taken penicillin before without problems. Apart from the rash (Figures 1 and 2), clinical exam is unremarkable .

### Questions:

1. What do we need to remember about mono?
2. How is mono diagnosed, and what is the monospot test?
3. Is this patient allergic to penicillin?
4. What else should we worry about?

### Answers:

#### **1.** *What do we need to remember about mono?*

The clinical triad of fever, tonsillar pharyngitis, and lymphadenopathy—usually following a short period of malaise and headache—characterizes infectious mononucleosis. It results from acute Epstein-Barr virus (EBV) infection, typically following intimate contact (usually via saliva) with a usually asymptomatic carrier 30 to 50 days before the onset of clinical symptoms. Although fatigue and lethargy may persist for months, acute symptoms resolve in one to two weeks. The virus persists asymptomatically for life, and can be cultured from the oropharynx for



Figure 1. Maculopapular rash on the patient's chest.



Figure 2. The rash on the patient's feet.

up to 18 months after clinical recovery. An EBV sero-positive result is found in 90% to 95% of adults (the vast majority having had a prior sub-clinical primary infection). Recovery usually leaves the patient with a high level of immunity from re-activation.

Table 1

## Other conditions that can cause mono-like symptoms

- Cytomegalovirus
- Toxoplasmosis
- Human herpesvirus
- Primary human immunodeficiency virus infection
- Hepatitis B
- Medication reactions (e.g. phenytoin, carbamazepine.)

Symptoms vary from none (most often), through mild pharyngitis or isolated lymphadenopathy, to the full-blown triad mentioned above. Classical symptoms are most common in adolescents and young adults. White or greyish-green tonsillar exudates are common with symmetrical lymphadenopathy, more pronounced in the posterior cervical chain, and often involve inguinal or axillary nodes.

*A rash following amoxicillin administration to patients with mono is a common reason for the misdiagnosis of penicillin allergy.*

Severe fatigue is frequent, as is splenomegaly and mild hepatitis.

A generalized maculopapular rash is occasionally seen at the onset of symptoms, and this differs from the far more common rash that follows the administration of antibiotics (usually ampicillin or amoxicillin). The amoxicillin is undoubtedly the cause of the rash in our patient.

Because symptoms of mono are felt to be related to the immune response to EBV, rather than viral

replication itself, treatment is generally symptomatic. Steroids can be used in severe cases, especially where airway compromise appears imminent. No clinical benefit of antiviral medication has been found.

## 2. How is mono diagnosed, and what is the monospot test?

Neither clinical nor whole blood count features of mono are specific enough to make the diagnosis. In most cases of pharyngitis, most differential diagnoses are self-limiting and benign, considering the practical disappearance of rheumatic fever in developed countries. Diagnostic testing rarely changes management, so is hardly ever needed. If antibiotic treatment is being considered to treat strep throat, physicians should be guided by the McIsaac Strep Throat score.<sup>1</sup> If antibiotics are used for pharyngitis, penicillin or erythromycin should be prescribed (unless guided otherwise by cultures).

The monospot tests for heterophile antibodies, which are both sensitive and specific for EBV. These antibodies are detectable in about 50% of patients in the first week of illness, climbing to about 90% at three weeks, and falling from about the fourth week. One year later, 20% to 75% of patients will still have positive results. Occasionally, patients confirmed EBV-positive by specific antibody testing remain heterophile antibody-negative throughout the course of illness.

If a firm diagnosis is desired, the monospot is the most useful test for mono, despite the aforementioned limitations; a positive result with a characteristic clinical picture is enough to clinch the diagnosis. Because other pathogens (Table 1) can cause a similar clinical picture to mono, specific antibody testing may be indicated in cases of high clinical suspicion with a negative monospot.

In most cases, however, the results will not change treatment.

### 3. *Is this patient allergic to penicillin?*

Not because of this rash! The characteristic rash that follows antibiotic administration to patients with mono is a common reason for patients being mistakenly labelled as allergic to penicillin. In most cases, the patients subsequently tolerate amoxicillin without problems.

### 4. *What else should we worry about?*

Apart from splenic rupture, which occurs in about 0.2% of cases (and almost exclusively in men), complications or dangerous manifestations of EBV infection are uncommon (Table 2). **Dr.**

Table 2

### Some of the rare complications of EBV infection

#### Neurologic:

- Guillain-Barré syndrome
- Meningoencephalitis
- Aseptic meningitis
- Peripheral neuritis
- Cranial nerve palsies
- Encephalomyelitis
- Optic neuritis

#### Hematologic:

- Hemolytic anemia
- Aplastic anemia
- Hemolytic uremic syndrome
- Thrombocytopenia
- Thrombotic thrombocytopenic purpura
- Disseminated intra-vascular coagulopathy

#### Gastrointestinal/Abdominal:

- Pancreatitis
- Severe hepatitis/jaundice/hepatomegaly/ascites
- Mesenteric adenitis

#### Miscellaneous:

- Myocarditis
- Myositis
- Acute renal failure
- Airway obstruction from massive lymphoid hyperplasia

Distortion of the cellular immune response to EBV infection is believed to be responsible for the development of a number of malignancies, most notably lymphoproliferative disorders.

EBV: Epstein-Barr virus

*This department covers selected points to avoid pitfalls and improve patient care by family physicians in the ED. Submissions and feedback can be sent to [diagnosis@sta.ca](mailto:diagnosis@sta.ca).*

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#### Reference

1. McIsaac WJ, White D, Tannenbaum D, et al: A clinical score to reduce unnecessary antibiotic use in patients with sore throat. CMAJ 1998; 158(1):75-83.