

Jarisch-Herxheimer Reaction

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Introduction

The Herxheimer reaction (also known as Jarisch-Herxheimer, JHR or Herx) is an acute febrile reaction accompanied by headaches, myalgia, rash and hypotension that occurs when large quantities of toxins are released into the body as bacteria (typically Spirochetal bacteria) die, due to antibiotic treatment or rapid detoxification. It usually occurs within one to two hours of treatment, peaks at eight hours and typically resolves within 24 to 48 hours.

Both Adolf Jarisch, an Austrian dermatologist, and Karl Herxheimer, a German dermatologist, are credited with the discovery of the Jarisch-Herxheimer reaction. Jarisch described the reaction in 1895 followed by Herxheimer and Krause about 7 years later. Both of them observed reactions in patients with syphilis treated with mercury.

This reaction was first seen following treatment in early and later stages of syphilis treated with Salvarsan, mercury, or antibiotics but can occur in any stage (1). It can also be seen in other diseases, such as borreliosis (Lyme disease and tick-borne relapsing fever), bartonellosis, brucellosis, typhoid fever, Myalgic Encephalomyelitis, and trichinellosis and Q fever (2).

Pathophysiology

JHR is a systemic reaction resembling gram negative sepsis. It is known to occur as an “all or none” principle that is determined by a certain unknown number of spirochetes. If that specific number is not reached, the reaction will not occur (3). Different theories have been proposed as far as the exact pathogenesis of this reaction. One theory proposed that the death of bacteria and the associated release of endotoxins occurs faster than the body can remove the toxins via the natural detoxification process performed by the kidneys and liver leading to the reaction (4).

Studies have also shown an increase in inflammatory cytokines during the reaction, including tumor necrosis factor alpha, interleukin-6 and interleukin-8 leading to activation of kinins and fibrinolytic factors (5-7). Some other theories proposed are the type of antibiotic use and the rate of spirochetal clearance may also influence the reaction (8, 9). A simple model to illustrate this is shown below (Figure 1).

Clinical Manifestations

With exposure to antibiotics, initially patients may develop fever with rigors, then later defervesce and become diaphoretic. They may experience headache, malaise and myalgias (10). Additionally the signs and symptoms of the treated disease may worsen. Existing syphilitic lesions may become painful and rashes may become more inflamed. Patients may become hypertensive due to vasoconstriction in early treatment and then later become hypotensive and develop shock due to decreased peripheral resistance. In syphilis – related JHR, leukocytosis with an increase of neutrophils and decrease in lymphocytes has also been identified (11). Local swelling associated with the

reaction occurring in late syphilis can be dangerous if there is involvement in the coronary ostia, cranial nerves or larynx (12). The Jarisch-Herxheimer reaction is typically more severe in relapsing fever (borreliosis) and may include hypotension, a decrease in cardiac output, and lactic acidosis.

JHR in pregnant females may precipitate uterine contractions, preterm labor and/ or no fetal heart rate tracings especially in the second half of pregnancy. Women are counseled to report symptoms of labor or decreased fetal activity.

Differential Diagnosis

JHR is most commonly mistaken for a drug allergic reaction secondary to penicillin. Inappropriate discontinuation of antibiotic treatment can be fatal.

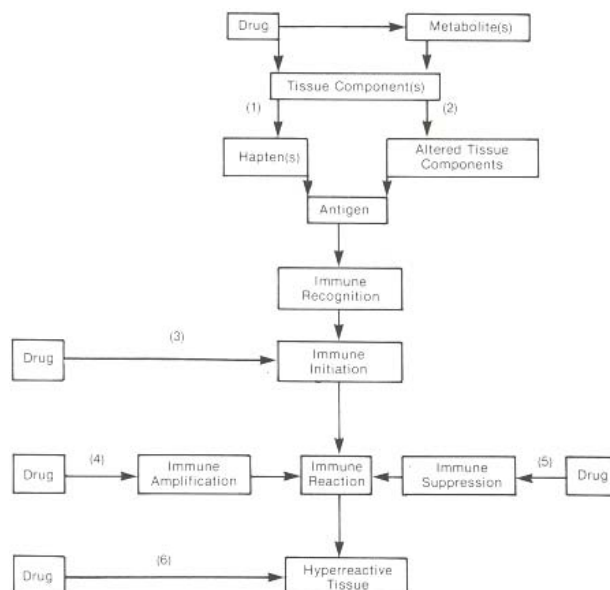
Treatment

Treatment of JHR is largely supportive (antipyretics, pain control and fluids). It can be prevented or treated with anti-inflammatory agent such as aspirin every 4 hours for a period of 24 to 48 hours. Steroids such as prednisone, has also been used to abort a reaction. One dose of 60 mg PO or IV should be given as adjunctive therapy to JHR patients with cardiovascular or symptomatic neurosyphilis and to pregnant patients to avoid catastrophic consequences (13).

Comments

JHR must be an expected occurrence when treating any patient with syphilis or other treponemal diseases. The signs and symptoms of JHR should be anticipated and providers should properly educate the patient on this phenomenon. Most importantly, it serves to remind practitioners that antibacterial therapy should be continued in these patients.

Figure 1



References

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