

# Postinfectious syndromes

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## Essentials

- Postinfectious syndrome (or postinfectious state) refers to symptoms triggered by or associated with an infection and occurring after it.
- Such symptoms may vary from quite mild to severe or life-threatening symptoms that must be identified and treated (e.g. Guillain–Barré syndrome).
- The symptoms may affect various organ systems (central and peripheral nervous system, musculoskeletal system, gastrointestinal or respiratory tract or the heart) and not necessarily the organ system where the preceding infection occurred.
- Diagnosis is based on the clinical picture and supported by laboratory tests and imaging. Normal levels of inflammatory markers do not exclude a postinfectious syndrome.
- Symptoms are often mild, and if so, it is sufficient to identify the patient's state, give symptomatic treatment, as necessary, monitor the situation and explain it to the patient.

## Underlying mechanisms and frequency

- The mechanisms underlying the various syndromes vary and are poorly known.
- The term 'postinfectious syndrome' has also been used to describe symptoms occurring after vaccination [1].
  - New scientific knowledge has been recently acquired concerning the pathogenetic mechanism of narcolepsy [26].
  - Special attention is being paid on the safety of the COVID-19 vaccines that are based on new technology. The pathogenetic mechanism of the newly discovered thrombosis with thrombocytopenia syndrome (TTS) is being investigated [27].
- Various causes of postinfectious symptoms have been suggested, such as:
  - an inflammatory reaction triggered by the infection
  - tissue destruction caused by inflammation
  - underlying chronic infection (for instance, in Chlamydia-induced reactive arthritis)
    - STD-causing *Chlamydia trachomatis* is often asymptomatic. Asymptomatic chlamydia infection may be found when an infection that has triggered reactive arthritis (ReA) is being investigated. In acute ReA, a 3-month treatment with lymecycline has shown efficacy in acute chlamydia-induced ReA in a randomized placebo-controlled trial. This suggests that chlamydia persists as a chronic infection in ReA [2].
    - Further support to this pathogenetic mechanism behind uroarthritis is supported by a study in which a favourable treatment response has been obtained also in chronic ReA with a 6-month combined antimicrobial treatment targeting chlamydia (using a combination of [doxycycline/azithromycin](#) and [rifampicin](#)) [3].
    - Microbes causing enteroarthritis (salmonella, yersinia, campylobacter) may cause ReA, but there is no confirmation on their ability to persist as a latent, chronic infection [2]. They may also cause a bacteremic/septic clinical picture, campylobacter as an example [4] [29].
  - failed immune response or failed response to treatment
  - other cause, unknown as yet.
- The patient may be genetically predisposed to the syndrome (e.g. the HLA B27 allele in reactive arthritis).
- There is no scientific evidence of the frequency of such syndromes in relation to the number of infections. The frequency of individual syndromes varies (reactive arthritis is rather common, many other syndromes quite rare).

# The main postinfectious syndromes

## Guillain-Barré syndrome

- A rare progressive, ascending radiculitis affecting primarily the motor system and starting from the lower limbs, in most cases preceded by a respiratory tract infection, gastroenteritis or vaccination or other manipulation of the immune system [1]. See .
  - May proceed to paralysis of cranial nerves or life-threatening respiratory paralysis.
  - Microbes identified as triggering the syndrome include *Campylobacter* (most common), cytomegalovirus, Epstein-Barr virus, *Mycoplasma pneumoniae*, *Haemophilus influenzae*.
- Symptomatic supportive treatment and immunotherapy (plasmapheresis or intravenous immunoglobulin; if both are necessary, plasmapheresis first) can be used.

## Other neurological syndromes

- Postinfectious neurological syndromes (PINS) affect either the central nervous system (postinfectious encephalitis, encephalomyelitis or myelitis) or both the central and peripheral nervous systems (postinfectious encephalomyelorradiculitis or myelorradiculoneuritis).
  - Diseases such as infectious encephalitis, vasculitis or MS should be considered in the differential diagnosis [7].
  - Treatment depends on the syndrome and the preceding infection.
  - The syndromes may recur.
- An example of these syndromes is encephalitis after chickenpox in children, occurring 2 to 4 weeks after the primary infection. [Aciclovir](#) is used to treat it.

## Reactive arthritis

- Multiple arthritis may be associated with mild fever and considerable elevation of ESR and CRP levels.
- The symptoms are not restricted to joints and may include insertional tendinitis, erythema nodosum, urethritis, conjunctivitis, iritis, carditis or balanitis .
- Symptoms may be prolonged and become chronic [15] [16]. If symptoms occur some time after acute reactive arthritis, elevated CRP or ESR levels are often no longer seen but radiologically observable tissue damage may develop gradually. In addition, axial spondylarthropathy may develop.
  - As many as 36% of patients with *Yersinia* arthritis develop radiologically detectable sacroiliitis within 10 years [15].
  - *Salmonella* arthritis becomes chronic in 16% of cases [16].
  - Fifteen per cent of patients with *Shigella* arthritis develop ankylosing spondylitis within 20 years [16].
  - In *Chlamydia* arthritis, the symptoms are due to underlying chronic infection [2] [3].
  - After a *Campylobacter* infection, prolonged joint symptoms may occur that do not fulfil the criteria of reactive arthritis [4] [5].
- Drugs such as [anti-inflammatory analgesics](#) and [sulfasalazine](#), [lymecycline](#) or [doxycycline](#) with both antimicrobial efficacy against *Chlamydia* [2] [3] and anti-inflammatory effects [17] [18] [19] have been used to treat reactive arthritis and prolonged forms of disease. **In chronic chlamydia-induced ReA, favourable evidence has been obtained on the use of combined antimicrobial treatment ([doxycycline/azithromycin](#) and [rifampicin](#)) [3].**
  - **Even though there is no research evidence, several guidelines suggest that all preceding infections capable of triggering ReA that are found would be treated with antimicrobials effective against the respective microbes. See more information on antimicrobial treatment of ReA-inducing infections (*campylobacter*, *yersinia*, *salmonella* and *chlamydia*) in the article [Reactive arthritis](#) .**
- Reactive arthritis; see
  - **The summary of product characteristics for [lymecycline](#) includes dosing advice on a 3-month treatment for chlamydia-induced ReA. Scientific evidence on the efficacy of long lymecycline therapy in chlamydia-induced ReA has been obtained from a placebo-controlled trial [2], unlike in enteroarthritis. Similar effects have not been shown with, for example, [doxycycline](#) [30]. Lymecycline has been shown to have also a MMP-mediated anti-inflammatory effect.**

- No consensus has been reached about symptoms associated with borreliosis [13] [14]. A Finnish multi-centre study recently showed that treatment of disseminated borreliosis can be carried out, instead of intravenous [ceftriaxone](#), also with oral doxycycline [31]. Doxycycline has been shown to have also a suppressing effect on MMP mediated inflammation [21]. The term PTLDS (post-treatment Lyme syndrome) refers to fatigue, myalgia, arthralgia and cognitive disturbance that still persist 6 months after antimicrobial therapy. The underlying mechanism is thought to be an inflammatory process [21].

## Glomerulonephritis

- Classic poststreptococcal glomerulonephritis (PSGN, see ) about 1 to 2 weeks after streptococcal pharyngitis or about 6 weeks after skin infection [9]
- The types of glomerulonephritis triggered by other microbes (e.g. staphylococci, Campylobacter) are called infection-related glomerulonephritis (IRGN) [9] [10].
  - IRGN has been considered to be associated with various upper respiratory, skin, pulmonary, cardiac, urinary, dental and bone infections.
  - IRGN may develop during the active infection already [9].
- Viral (e.g. hepatitis B or C, HIV, EBV, CMV, parvovirus [22]), fungal or parasitic infections (e.g. malaria) may trigger glomerulonephritis.
- Treatment consists of treatment of the infection and symptomatic treatment. Glucocorticoids are sometimes used for prolonged disease, see .

## Postinfectious irritable bowel syndrome

- This has most often been seen after Salmonella, Campylobacter or Shigella infections (in as many as 4 to 32% of cases [7] [8]) but may also occur after viral, protozoal or parasite infections.
- May occur after ordinary traveller's diarrhoea [23].
- Usually self-limited, but prolonged or chronic symptoms have been described.
- Genetic predisposing factors may partly explain why some persons have persisting intestinal symptoms after an acute infectious diarrhoea [24].
- The treatment is symptomatic.
- See also .

## Carditis, myocarditis

- Reactive arthritis may be associated with asymptomatic carditis or symptomatic perimyocarditis.
- Rheumatic fever following group A Streptococcus infections is nearly extinct in Finland.
- For diagnosis and treatment, see and

## Prolonged cough

- Prolonged cough is quite common after acute upper respiratory tract infections, occurring in as many as 50% of patients after *Mycoplasma pneumoniae* infection or whooping cough (*Bordetella pertussis* infection ) [11].
- The reasons are believed to be multiple [11].
- There is no evidence-based treatment available [12]. Various sources have suggested inhaled [ipratropium](#), inhaled glucocorticoid, oral glucocorticoid, [codeine](#), [dextromethorphan](#) and [montelukast](#) [25], for example.

## Long-term effects of COVID-19 ("long covid")

- On the 30th of January 2020, the WHO warned about a threat in the form of a new infectious disease. In March 2020, the disease had spread across the world as COVID-19 pandemic. See also .
- According to current knowledge, a large share of patients with COVID-19 go through an acute infection with a conventional recuperation period before being completely healed. It has been observed, however, that after the acute infection, some patients continue to have symptoms that have been assigned the term "long COVID" [32], but, from the medical viewpoint, the terminology is still unestablished and available knowledge insufficient.

- Several studies have been published on symptoms following a COVID-19 infection [33] [34]. After the acute COVID-19 disease, symptoms deriving from several different organs may occur. For the time being, no generally accepted, global definition exists for the symptoms following a COVID-19 infection, and neither is there precise information on how many patients have such symptoms after a COVID-19 infection.
- The pathogenetic mechanisms are not clear either. There is active research on the topic and therefore more knowledge accumulates.
- The WHO has recommended that the condition should be acknowledged and has developed a standardized form for reporting clinical information, in an attempt to reach a common understanding of the clinical description of the condition [35].

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