

TO MAKE
THE PFAPA SYNDROME
MORE FAMILIAR



questions & answers

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1. What does the acronym PFAPA stand for?

PFAPA stands for Periodic Fever, Aphthous, Pharyngitis and Adenitis. These are the symptoms related to this syndrome. In Polish the acronym would be OGAZP, it does not sound very well, so we can stand by the English acronym PFAPA.

2. What is PFAPA syndrome?

The patients suffer from the recurrence of the high fever episodes lasting for a couple of days. The illness usually starts between the age of one and five. Despite its chronic character, it is mild and does not lead to any complications. In most of the cases it recedes as the patient grows up, but it can also last for up to ten years.

3. How often does it occur?

The frequency of PFAPA syndrome is unknown. It has been being recognized in Poland for only fifteen years. The number of patients with this recognition has been recently growing significantly, especially during the last couple of years. It is surely related to the increase of the doctors knowledge of this illness specifics.

4. What causes the illness?

While the illness has been described for the first time in 1987, its exact causes remain unknown. It is considered as a an autoinflammatory illness. Recurrent or chronic excessive activation of the immune system is characteristic for this kind of illnesses. The immune system inflames independently, without any adequate cause, e.g. viral or bacterial infection. This activation is manifested by the high fever and an inflammation of the mucous membrane, tonsils, adenoids or lymph nodes. The inflammatory reaction is being automatically suppressed after a couple of days. There aren't any known infectious factors causing the recurrence.

5. Is PFAPA an autoimmune illness?

PFAPA is an autoinflammatory illness. Autoinflammation and autoimmunity are not the same thing, despite the immune system abnormal activity being characteristic for both these phenomena. The system starts attacking its own organism, becomes autoaggressive. In the cases of autoimmune illnesses we can identify the antibodies acting against their own tissues, e.g. thyroid or liver, causing the illness symptoms. In the cases of autoinflammatory illnesses these antibodies aren't being identified and the inflammatory reaction is unspecific and systemic, so it is not directed at any specific body organ.

6. Is PFAPA an immunodeficiency?

In the cases of PFAPA patient's immunity is not decreased. As the immune system does not work properly – it is excessively responsive – we consider it as one of the immune system disorders.



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7. Is PFAPA an hereditary illness?

The genetic foundations of PFAPA are not currently known. The syndrome cannot be inherited as the other genetic disorders can be. But there are described cases of PFAPA occurring at the members of the same family. Usually the interview with any of the parents was showing that they were suffering from the PFAPA syndrome in the childhood.

8. Is PFAPA infectious?

Absolutely not. It is not the kind of illness you can get infected with, neither between its recurrent episodes nor during the symptoms manifestation period.

9. What are PFAPA symptoms?

At the time of the syndrome recurrence there is the high fever at every patient, usually higher than 39 degrees, lasting for about three to five days. Another symptoms are the inflammation of the side tonsils, that are enlarged, reddened, carnosus and often covered by the different sizes of coatings, while enlarged lymph nodes are detectable at the submandibular area and on the neck. The ulcers of different sizes are appearing on the cheeks and lips mucosae. The tongue is often reddened or coated. During the high fever periods the child is weakened, loses the appetite, may complain because of the legs, head and stomach pains. The general symptoms are similar to the influenza. Sometimes the motions are loose, but it is never a kind of acute, watery diarrhoea.

10. How does the child feel like between the recurrent episodes?

Between the recurrent episodes the children don't complain about any ailments and do not manifest any worrying symptoms during the medical examination. Their physical (increase of the body height and weight) and psychomotor development should be proper.

11. Is the course of illness the same in every child's case?

While the symptoms are similar, the recurrence is different for each patient. The recurrent episodes specifics and intensity may differ as the child grows up. The length of high fever and related symptoms periods may be also different.

12. How frequent are PFAPA recurrent episodes?

The frequency of the recurrent episodes is very specific for this syndrome. They often occur frequently every three or four weeks so the parents are even able to predict the exact time of the next episode. But they may also occur more frequently, e.g. every week or less frequently, e.g. every eight weekes or may not be frequent at all. In some cases for unknown reasons the recurrent episodes usually start at the weekends.



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13. Are the longer symptomless periods possible?

In some cases the longer intervals between the recurrent episodes are being observed during the summer time (e.g. three months). The recurrent episodes occur in the longer intervals in the syndrome remission period, usually between the age of eight and ten.

14. How the PFAPA syndrome is being diagnosed?

The explicit diagnosis of PFAPA is very difficult as there are no tests able to confirm it. So the searching symptoms analysis, planned observation and exclusion of the other illnesses manifesting similar symptoms are crucial here. This is why the most of the necessary examinations give the positive results. Firstly it is important to show the increase of inflammatory state indicators, examining the child's blood during the recurrent episode (blood morphology with the smear, erythrocyte sedimentation rate, CRP test), as well as their later normalization, through the follow-up tests during the good health period. So it is impossible to avoid subjecting the children to multiple blood drawing from the veins, but we must take care that in every case it is absolutely necessary as the children stress related to the veins punctures should be possibly minimized.

15. Is every child submitted to the same additional examinations?

The basic laboratory examinations are being conducted in every case with the similar pattern. Except the morphology, ESR, CRP or procalcitonin tests, the tonsils smears are necessary, as well as the general examination and urine culture are. The other examinations are being chosen individually for every patient, depending on the manifested symptoms. Some tests may be performed only in the hospital, e.g. blood culture, but sometimes they are necessary for the proper diagnosis. Each patient requires exact stomatologist and laryngologist assesment, often connected with the third (throat) tonsil size assesment, so called videofiberoscopy. One of the tests we perform expecting the proper result is ECHO, the ultrasonographic heart examination.

16. Does PFAPA diagnostics require hospital conditions?

The most of the tests may be performed on an outpatient basis. But in fact the children, especially the youngest ones, require the hospitalization, especially during the first recurrent high fever episodes with unknown etiology. Sometimes the hospitalization is necessary for the later observation and monitoring patient's state without antibiotics usage, what is impossible at home because of the parents' concerns. Patient's admission to the hospital simplifies the in-depth interview with his or her parents, as it sometimes takes several minutes. It is also useful when we want to analyse the child's medical record and, later, to present the further diagnostics and treatment plans to the parents. It is significantly more difficult during the short visits on an outpatient basis.



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17. Which illnesses may be similar to PFAPA syndrome?

The illness recurrence is very similar to the tonsils inflammation, commonly known as tonsillitis, that may be caused by the viruses or bacteria. There is often the infectious mononucleosis suspicion, and, with the massive ulcers, the herpetic oral cavity inflammation is being recognized. In the cases of poorly manifested oral cavity symptoms the only visible symptom is the high fever so the list of the possible recognitions is quite long, e.g. three day fever, urine system infection or even sepsis.

18. Can we easily see the difference between PFAPA recurrence and an infectious illness?

Unfortunately, it is often very difficult. The clinical symptoms, medical tests aberrations and additional tests, e.g. blood morphology, ESR or CRP, may suggest the infection. Procalcitonin assesment may be very useful as it increases significantly during bacterial infections while its increase in the case of PFAPA recurrence is insignificant. Unfortunately this test is not performed regularly in every laboratory. We perform the tonsils smear for the bacteriology test, a regular culture (the results are known after three days) or the quick streptococcus test. If we can't see any infection localization in the physical examination, we examine the urine (it's always a general test and a culture), sometimes we perform blood culture (three times) or imaging, what means the chest radiography or abdominal cavity ultrasonography.

19. What may happen if we don't recognize the infection properly and don't use the antibiotics?

The most of children infections connected with the high fever is caused by different viruses and the antibiotics usage is absolutely unnecessary. We should avoid using them if the bacterial infection is not confirmed or highly probable. In the case of tonsils inflammation the antibiotics usage is necessary if it is caused by the streptococcus pyogenes bacteria (group A).

20. How can we treat PFAPA recurrence?

There is no one specific way of PFAPA syndrome treatment. We use the medicines fighting the symptoms, like an antipyretic medicines, avoiding an unnecessary antibiotic usage. Using one steroids dose in the form of the medicine named Encorton on the first day of the high fever is very effective way of fighting the recurrence. Encorton causes fast suppression of the inflammatory state while it does not prevent the manifestation of another recurrent episodes.



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21. Are antipyretic medicines being used in the standard doses?

The paracetamol based medicines are the most commonly used ones, acting antipyretically and analgetically. These are so called unsteroid anti-inflammatory medicines: ibuprofen with an additional anti-inflammatory acting. Medicines dosage in the case of PFAPA treatment is not much different than dosing them in the other illnesses cases. But it is necessary to determine together with the doctor what doses are the most effective while still safe for the child. This dosage should be determined according to not only the patient's age but also to his or her body weight. The doses that are too small or taken not frequently enough may be inefficient. On the other hand it is easy to overdose the medicines in the case of the child suffering from intensive high fever. Paracetamol is a safe medicine but its overdose may also cause serious liver damage. The overdose is much more probable for the dehydrated child, so it's important to take care that the patient is being provided with enough liquids during the high fever periods. The patients observation indicates that the paracetamol is the most efficient medicine in the PFAPA cases. It is often necessary to use both ibuprofen and paracetamol to efficiently fight the high fever. Additionally airing the rooms, avoiding the overheating of the child and using the cooling compresses and baths (one degree colder than the child's body temperature) are also useful.

22. Is it safe to use the steroids in the cases of PFAPA?

The steroids (Encorton) are only used once at the PFAPA recurrence. Using one or two (or even three or four) doses of steroids in a month causes no undesired consequences. It doesn't affect child's growth, body weight increase or his or her immunity. Even if the one-time steroids dose is given in the case of 'real' infection it will not cause its more serious character or any later complications.

23. Can the children suffering from PFAPA experience the febrile seizures?

The risk of febrile seizures for children with PFAPA is the same as for any other children. The treatment is also similar and should be determined after the medical examination and eventual additional tests. It is worth to remember that in the periods of high fever the chills are quite common, sometimes mistaken by the parents for the febrile seizures.

24. Can we implement the treatment that will cause the entire symptoms suppression?

If we perform the entire tonsillectomy surgical procedure the symptoms will be entirely suppressed. But we will not achieve this effect if the tonsils will be removed only partially. The third tonsil removal is not necessary but it is recommended, especially if it is enlarged.



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25. Is the tonsils overgrowth the reason to remove them in the PFAPA cases?

No, the children with PFAPA syndrome have not usually got the overgrown tonsils, sometimes these tonsils are even surprisingly small, taking into account their recurrent inflammations. The fact that the tonsils are not overgrown should not be the reason for resignation from their removal. The tonsils are probably the tissue where the inflammatory reaction starts and where the inflammatory starts develops. The tonsils removal causes the symptoms suppression.

26. Does tonsillectomy affect the children's immunity, especially for the younger ones'?

The tonsils removal does not affect the children's immunity, regardless of their age. The tonsils, formed and visible behind the palatal arches, are only the small part of the lymphoid tissue in the oral cavity and throat area. Even their entire removal will not cause the worse protection against the infections. It is not true that the lack of tonsils may cause the infection to go down the respiratory system, e.g. to the lungs or bronchus. The tonsils that are overgrown or not working properly (like in the PFAPA cases) may cause more harm than good.

27. Is the tonsils removal necessary in the PFAPA cases?

The PFAPA syndrome tends to decrease as the child grows older, without causing any complications. So it is possible to adopt the waiting approach and only fight the symptoms. This kind of treatment is considered for the patients with mild recurrent episodes. In the most cases, if the recurrence lasts for several years and affects children's normal activity, e.g. causing school absence or the symptoms are very strong, the surgery procedure may be necessary.

28. Is it possible that the symptoms still appear despite tonsillectomy?

Only in the ten to fifteen percent of cases the recurrent episodes will be still observed but their character will probably be milder. The lack of remission after the tonsillectomy will indicate the direction of extended diagnostics, e.g. toward genetic autoinflammatory illnesses.

29. Are the children with PFAPA syndrome more vulnerable to infections?

The children suffering from PFAPA are not more infections-prone. On the contrary, they are less likely to catch the infections than their peers.



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30. Are there any contraindications against the immunization of the children with PFAPA syndrome?

There are absolutely no contraindications against the immunization. They have no impact on the syndrome. We also suggest to realize all the recommended vaccinations so the child with recurrent high fever episodes can have the guaranteed protection against the dangerous infections like sepsis meningitis, invasive pneumococcal disease or varicella. The vaccinations should be, if possible, realized between the PFAPA recurrent episodes.

31. Is any diet, e.g. gluten-free or dairy-free diet, efficient for the PFAPA syndrome?

There is no need to choose any kind of elimination diets in the cases of PFAPA. The illness has no allergic background and it is not any kind of food intolerance symptom, e.g. for gluten.

32. Should the immunomodulating agents be used?

The immune system of the children suffering from PFAPA is fully operational so it does not require any additional stimulation. There are even the contraindications as it may strengthen the recurring episodes.

33. Should the patient suffering from PFAPA take the diet supplements, e.g. the vitamins?

The proper diet provides the child all the necessary nutrients except the vitamin D3 as it should be supplemented. The vitamin D3 supplements should be given in the dosage adequate to the age and body weight for one year, excluding the period of extensive sun exposition period between 10 a.m. and 4 p.m. during the summer time (between May and August). The average dosage of vitamin D3 is between 400 and 500 units for a day, the dosage should be adequately increased for the obese children. With the proper supplementation there is no need to monitor the vitamin concentration in the blood. It is worth to underline, that the vitamin D3 supplementation is suggested for all the children, not only the ones suffering from the PFAPA syndrome.

34. Can the child with the PFAPA syndrome attend the nurseries or kindergartens?

There are no contraindications for these children to attend nurseries or kindergartens. They cause no threat for other children as PFAPA is not an infectious illness. The child with PFAPA is not more vulnerable to catching the infections from the peers either.



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35. Can the child suffering from the PFAPA syndrome take part in the sports and swimming pool connected activities?

The patients should be active without any specific restrictions. Obviously, the physical effort is not desired during the periods of recurrent high fever episodes, until the high fever recedes.

36. Can the high fever cause any complications, e.g. neural system damage?

Even if the fever is higher than 39 degrees it makes no damage to the tissues and organs. It is just the manifestation of the inflammatory state inside the organism, where the thermoregulation center in the brain (in the hypothalamus) has been „set to the higher temperature” by the cytokines (the small inflammatory state proteins circulating in the blood).

37. Is the high fever an enemy or an ally for the child?

The high fever should be considered as our ally. It is the warning signal, sometimes the only one, that there is some illness in the organism. Sometimes the warm forehead helps us to notice the sore throat or some other infection. The organism sets the higher temperature to make some of the immune processes more efficient. But the long lasting high fever can also cause many undesired effects, e.g. the bad mood, increased metabolism, increased need for fluids and fastened heartbeat. This is why we try to lower the body temperature to the below 38 degrees level. It is important to remember about providing the patient with the proper liquids quantity.

38. Can the pyralgin be used for the children suffering from the high fever unresponsive to ibuprofen and paracetamol?

Pyralgin or metamizole is not the medicine registered for the children treatment. It is very efficient in the high fever suppression, but not recommended for the children because of its possible toxicity. The pyralgin suppositories contain the metamizole dose adequate for the adults. The suppositories are the form impossible to divide because of the uneven dispersion of the medicine in their mass. So it is recommended to use the pyralgin only in the emergency cases.

39. How long does it take to diagnose the PFAPA syndrome?

The parents suspecting PFAPA must be patient. There is no simple test to conduct, the diagnosis is based on the searching observation and performing several planned additional examinations. The entire process takes at least a couple of months, sometimes even longer. This is why it is so important that the parents should be precisely informed about the specifics of the illness, the diagnosis and treatment methods and the lack of compli-



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cations for this syndrome. The individual diagnostic stages cannot be hastened, as it is necessary to observe the consecutive recurrent high fever episodes, recurring every few weeks.

40. Are the cases of urticaria or other skin rashes being observed in the course of PFAPA?

Usually no skin changes are being observed at the patients suffering from PFAPA. The skin rash may be caused by an infection, e.g. scarlet fever or monucleosis. If the urticaria or other skin changes occur together with the recurrent high fever episodes, the autoinflammatory illnesses other than PFAPA should be considered in the diagnostic process. One of these illnesses is the cold induced urticaria. So it is important to observe whether the urticaria and high fever symptoms do not recede in the reaction to the cold temperature exposition.



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