

## Review Article

# Chronic Headache in Children with Meningism is caused by Autoimmune Inflammation of Dura Mater

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## Abstract

Tension headache is a common clinical diagnosis in children suffering from chronic headache, but little known about this condition. We conducted clinical observation of 6100 patients (ages 5-18, citizens of Israel), suffering from "Tension Headache" and found meningeal symptoms and the whole complex of Meningism in 97% of them. This led us to conclusion that chronic headache in children is a result of damage caused to brain membranes (Dura Mater). Next step was to look for the root cause of the brain membranes damage and we found it to be Streptococcal infection (80% of cases), Epstein–Barr virus (10% of cases), Helicobacter Pylori (2% of cases) and head trauma (8% of cases).

## INTRODUCTION

This study is based on 25 years of our experience in this field.

In pediatric neurology, up to these days exists the term "chronic headache", which includes two major subtypes: migraine and tension headache [1]. Tension headache is a common clinical diagnosis in children suffering from chronic headache, but little known about this condition - there is no significant data on etiology, pathological process, nor localization. The definition of "tension headache" was taken from the field of adult neurology, with same definitions and same mythology.

According to medical statistics [2], 20%-50% of children ages 5 to 18 years old, complain on headaches. Even nowadays, children with "normal" neurological evaluation, no pathological findings on CT and MRI, nor anamnestic findings suggesting migraine, fall under "Tension Headache" definition, and condition attributed to stress and psychological conditions. Tension headache then, treated with antidepressants. Clinical practice that included questioning the parents showed, that the use of antidepressants does not provide expected benefits and the children continue to suffer from headache, in some cases even severe. According to the parents, examinations by psychologists and psychiatrists showed that the children do not suffer from any psychological conditions.

The term "Tension headache" was introduced in pediatric neurology in "The International Classification of Headache Disorders". Pediatricians well know that children are not "small adults" but completely different organisms. Therefore, in 21<sup>st</sup> century exists a pediatric illness, in which except the headache, nothing is known about.

One of the most important parts of neurological diagnosis is thorough examination of the patient to determine patient's neurologic status. In neurological guidelines, before the existence of imaging techniques, there were no additional tools to examine brain function, therefore the diagnosis was established solely on clinical picture. From 1995 to 2020 we performed a clinical observation of 6100 patients suffering from headache. In multiple studies we conducted, our goal was to determine causes of chronic headache in children. Results of these studies showed that in 97% of the patients, who had been diagnosed with "Tension Headache", were present meningeal symptoms and the whole complex of Meningism. Therefore, it led us to conclusion that chronic headache in children is a result of damage caused to brain membranes.

It is important to emphasize that the hard part of the brain membrane (dura mater), contains the highest concentration of pain receptors in the human body, while these receptors are absent in the brain tissue (white and gray matter). Also it is important to distinguish Meningism from Meningitis, which is out of scope in this study. We do not expect inflammatory cells in cases of Meningism.

Therefore, the outcomes of our study prove that the diagnosis of "Tension Headache" does not exist in pediatric neurology, instead there is Meningism syndrome which develops as a result of dura mater damage mostly caused by microorganisms. We were the first to study this subject and up until our discovery this fact did not appear in any medical literature.

Another point to emphasize, that MRI was performed on 414 children (without previous CT evaluation). MRI showed

thickening of dura mater in 263 patients. This data confirms that pathology of dura mater is a cause of meningism as a part of pachi-meningism. We state, that correct clinical and laboratory work up can exclude the need for performing imaging modalities, such as brain CT or MRI.

Meningism [3-5], is a term describing reaction of brain membranes (Dura) to trauma, inflammation or infection, presenting with symptoms of headache and meningeal symptoms, but without clinical picture of meningitis. The most important aspect is the lack of findings in CSF (cerebrospinal fluid), even when LP (Lumbar puncture) is performed.

Meningeal symptoms in patients previously diagnosed with “Tension Headache” include:

- Nuchal rigidity
- Kernig’s sign
- Brudzinski’s sign (upper)
- Brudzinski’s sign (middle)
- Tripod sign
- Guillain’s sign
- Facial sign

In addition, under flexure of head forward, pain appearance in

- Occiput
- Neck
- Epigastrium
- Back
- Chest

During our work we identified four major diseases that showed up as the cause of headache with meningeal syndrome:

## **STREPTOCOCCAL INFECTION**

The most common cause of chronic headache was found to be Streptococcal infection (80%) [6,7]. Streptococcus belongs to opportunistic pathogens (gram positive microorganism) existing as normal flora in human body. As any other opportunistic infections, it causes no symptoms in immunocompetent patients, but when immune status is being altered, Streptococcus may cause range of clinical diseases.

Streptococcus Pyogenes, is an important pathogen responsible for variety of diseases, including erysipelas, scarlet fever, bronchitis, pneumonia, abscesses, sepsis and many more.

The source of infection may be infected, clinically ill person or asymptomatic carrier (less common). Infections in children may appear in several ways:

- a. Entrance through damaged skin in close contact with ill person or by using common objects (toys, tools, tableware, etc.)
- b. Air - droplets (aerosol) – coughing, speaking...

Besides, the risk of Streptococcal infections significantly

increases during alterations in protective barriers of organism (chronic illness, immune suppression, hypothermia).

In order to determine the severity of the infection and to eliminate complications, blood tests and microbiologic tests should be conducted. These include cultures from sputum, throat and skin.

Streptococcal infection, past and present, can be diagnosed by ASLO (Antistreptolysin-O), or ASOT (Antistreptolysin-O-Titer). When streptococci enter the body, they produce the chemical component Streptolysin-O, which is used by the microorganism to destroy blood cells. “O” in this term means that this compound is rapidly degenerates on exposure to Oxygen. Human immune system immediately responds to Streptolysin-O by producing antibodies to block it. These antibodies called Antistreptolysin-O.

It is determined, that ASLO levels in the blood do not increase simultaneously with onset of streptococcal disease, but only 1 – 3 weeks later.

In our study 80% of patients with chronic headache had higher than normal ASLO levels (normal levels up to 200 IU/ml), which led us to conclusion that these children suffered from streptococcal infection. In these 80% of the patients ASLO levels were 200 – 1790 IU/ml.

Mainstream therapy for Streptococcal infections is based on Penicillin (Rafapen, Pen-Rafa...).

## **PANDAS**

In 1994 Dr. Swedo and her colleagues described a new medical condition and highlighted that in diseases, such as tics disorders, Turret’s syndrome, and some other conditions, there is presence of streptococcal autoimmune response with ASLO levels above normal [8]. This medical condition was named as PANDAS (Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infection).

Initially, PANDAS was considered as a condition related to Rheumatic Fever and especially Chorea; it was supported by relation to infections caused by Beta Hemolytic Streptococci Group A and relatively successful antirheumatic therapy. This led to assumption that PANDAS is a result of autoimmune reaction, in which antibodies produced by immune system attack nervous system cells.

Clinical – Diagnostical Complex of PANDAS is similar with symptoms of Rheumatic Chorea – one of the well-known forms of Rheumatic Fever. Development of PANDAS is characteristic for prepubertal children (chorea is more common in children 5 – 8 years of age). The disease is acute in onset and progression. Clinical picture for both, chorea and PANDAS, is diverse, but features of obsessive-compulsive disorders are common. One of the most common features of PANDAS include obsessive disorders, that appears with certain periodicity (average duration of the symptoms last about 12 – 15 weeks) and significantly impair patient’s life quality.

Diagnostic criteria for PANDAS:

1. Presence of obsessive-compulsive disorder and/or tics disorder.

2. Symptoms in children from 3 years old to pubertal age.
3. Disease is characterized by relapses, with sudden onset or exacerbation of the symptoms.
4. Exacerbation is associated with Streptococcal infection, means elevated ASLO levels.
5. Relation to neurological changes: chorea-like movements.

We would like to emphasize, that in our observation, most of children with PANDAS were also complaining about headaches, and neurological evaluation showed signs of meningism.

For treatment of PANDAS a prolonged course of antibiotic therapy is recommended.

## EPSTEIN-BARR VIRUS (EBV)

We discovered that chronic headache with signs of meningism can also be caused by EBV (subgroup of Herpes viruses). In our study we detected it in 10% of our patients with headache.

EBV infection usually appears in early childhood or teen ages. Some antibodies related to EBV remain to the rest of the life [9]. Source of infection may be infected individual. EBV has low infectious potential. Transmission occurs by the way of air-drops, but most common by sputum (as indicated by commonly used other name of this disease – Kissing Disease / Mononucleosis). Virus can also be transmitted by blood transfusion. Virus is expelled into environment for 18 months after primary infection (as proven by samples from nasopharynx). In patients recovered from EBV it still can be found in nasopharyngeal samples in 15 – 25% of cases.

The virus may cause variety of symptoms/diseases:

- Infectious mononucleosis
- Lymphogranulomatosis (Hodgkin's disease)
- Hepatitis
- Herpes – like lesions of skin and mucosal surfaces
- Herpangina
- Chronic fatigue syndrome (common for many types of hidden infections) [10].

Infectious mononucleosis is the most common form of hidden EBV infection. Virus has the ability to selectively damage lymphoid and reticular tissues, clinically present as lymphadenopathy and hepatosplenomegaly. In many cases the disease is asymptomatic or with only mild non-specific symptoms. Antibodies to EBV found in 50 – 80% of adults. Prolong existence of virus in the body, in form of hidden infection, increases the risk of chronic mononucleosis, and in turn increases the risk of disease exacerbation in immunosuppressed or immunocompromised states. Secondary/opportunistic infections (streptococci, staphylococci), are playing role in pathogenesis of Infectious Mononucleosis.

Incubation period lasts 4 – 15 days (most common about a week), and usually acute on onset. On 2<sup>nd</sup> – 4<sup>th</sup> day of infection chorea and other symptoms of general "intoxication" reach the pick. Initial stages of the disease characterized by general

weakness, headache, myalgia and arthralgia; shortly later painful swallowing occurs. Usually body temperature rises to 38 – 40 degrees Celsius, it sometimes has wave-like pattern and may last for 1 – 3 weeks or longer. Contrary, in many, disease symptoms may be sub febrile, with body temperature of 37–37.5°C.

Chronic mononucleosis is a disease caused by EBV. Prolonged existence of the virus in the body not always asymptomatic. Symptoms and clinical features may vary significantly. Almost all the patients complain of general weakness, headache, early fatigue, insomnia, myalgia, some have fever, lymphadenopathy, pneumonia, pharyngitis, nausea, abdominal pain, diarrhea and vomiting. Not all patients have hepatosplenomegaly. Some patients have viral exanthemas, most common in form of herpes-like lesions: oral in 26%, genital in 38%. In blood test leucopenia and thrombocytopenia are characteristic, but these findings are non-specific, because they appear in wide variety of other chronic infectious diseases.

Diagnosis of EBV is based on characteristic symptoms of silent infection. Blood test evaluation playing a major role in diagnosis. Characteristic feature on blood work include elevated lymphocytes levels (15% above upper limit normal) and presence of atypical mononuclear cells (higher than 10% of the all leukocytes). Specific methods allow to confirm reactivation of silent infection. This reaction is positive in 100% of the patients. Antibodies to EBV appear in the blood after 3 – 6 weeks following primary infection (in 100% of patients) and remain for life.

In mild EBV disease it is possible to treat by vitamins and symptomatic therapy alone.

For treatment of chronic headache caused by EBV, multiteam involvement may be necessary, including pediatric neurologist, infectious diseases specialist, immunologist, pediatrician, etc. Parents of the child should be aware and informed that headaches caused by EBV infection may last for long period of time and reoccur in immunodeficient states, caused by other factors. In medical literature we did not find recommendations regarding chronic headache caused by EBV infection. We are the first to describe headaches caused by EBV infection.

It is important to emphasize, that EBV is "related" to CMV (Cytomegalovirus) and both may coexist at the same time. A child has a very low risk to develop serious complications, even in coinfection by both these viruses. Besides, CMV, after primary infection, usually provides immunity. CMV infection may be dangerous only if appears during pregnancy, because it may cause damage to multiple systems in fetus.

## HELICOBACTER PYLORI

Helicobacter Pylori [11] (HP) is a gram-negative, helically-shaped, microaerophilic bacterium. It was first discovered in 1875 by German scientists, but relation between HP and gastritis was established only in 1983 by Australian scientists Robin Warren and Barry Marshall.

Interesting fact – for 23 years these scientists tried to convince scientific world about their theory of pathogenic features of HP, including deliberate self-infection of B. Marshall that caused him to develop gastritis. Their discovery revolutionized the approach

to gastritis and gastric ulcers, and they were awarded a Nobel price at 2005.

In medical literature we found only few cases describing headaches in patients with HP. These were mainly described as migraine headaches, somehow related to gastric ulcer [11,12]. We were the first to discover that 2% of the patients with signs of meningism, have been suffering from diseases caused by HP.

Diagnosis of HP

- Blood test for HP antigen
- Breath test (C13 urea breath test)

If HP found in a child with headache, it is possible to state with high degree of certainty that the headache is due to autoimmune meningism, caused by HP antigen. In our study we found that treatment resulted in resolution of headache and symptoms of meningism.

### PHYSICAL ACTIVITY AS A POSSIBLE CAUSE OF CHRONIC HEADACHE IN CHILDREN

Quite often (according our data, about 8%), chronic headache in children results from sport activities, specifically soccer, due to recurrent head traumas caused by headbutts used in this sport. These traumatic injuries cause damage to dura mater, which is the main source of pain receptors in the brain.

In these cases, the patient develops signs of meningism. Treatment of choice for these patients is bad rest (horizontal position 24 hours a day for 7 – 10 days), until full resolution of headaches. Possible to use analgesics for symptoms relief. Other sport activities may also contribute to development of headaches include martial arts, boxing and weightlifting. Headaches may also appear in children participating in dancing or gymnastics, but at lower probability.

### CONCLUSION

The data we collected from 6100 children allows to conclude that chronic headaches in children are not related at all to the “Tension Headache” diagnosis that doctors use for almost 100 years to describe headache in children and adults as psychological issues and treat with antidepressants.

Instead, the headache is a result of damage to dura mater, clinically present as meningism. Most often the cause is an autoimmune reaction involving dura mater caused by Streptococcal infection. Other causes appeared to be Epstein–Barr Virus, Helicobacter Pylori and head trauma related to physical activity.

We certainly hope that our discovery would change the attitude to chronic headaches experienced by 20-50% of

children. We found real causes of chronic headaches in children and we hope that child neurologists around the world would treat children according to our findings that gave positive results.

### CONFLICT OF INTEREST STATEMENT

The authors of this manuscript certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers’ bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript. No funding was received.

### REFERENCES

1. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 2nd edition. Cephalalgia. 2004; 24: 9-160.
2. Abu-Arafeh I, Razak S, Sivaraman B, Graham C. Prevalence of headache and migraine in children and adolescents: a systematic review of population-based studies. Dev Med Child Neurol. 2010; 52: 1088-1097.
3. Almazov I, Brand N. Meningeal symptoms of chronic headaches in children and adolescents—a new approach to diagnosis and treatment. European Journal of Neurology Supplement. 2003; 10.
4. Almazov I. Pachymeningitis: Possible pathogenic basis of chronic headaches in children. J Headache Pain. 2004; 5: 71.
5. Almazov I, Brand N. Meningismus is commonly overlooked finding in children and adolescents. J Child Neurology. 2006; 21: 423-425.
6. Almazov I, Burke M. Is Streptococcus a cause of Tension Type Headache in Children? Cephalalgia. 2007; 27: 629.
7. Almazov I, Burke M, Mosek A. Meningismus in children with chronic headache is most likely due to streptococcal infection. Med Hypotheses. 2014; 82: 490-492.
8. Susan E. Swedo, Henrietta L. Leonard, Marjorie Garvey et al. Pediatric Autoimmune Neuropsychiatric Disorders Associated With Streptococcal Infections: Clinical Description of the First 50 Cases. Am J Psychiatr. 1998; 155: 264-271.
9. Dunmire SK, Hogquist KA, Balfour HH. Infectious Mononucleosis. Curr Top Microbiol Immunol. 2015; 390: 211-240.
10. Lerner AM, Beqaj SH, Deeter RG, Fitzgerald JT. IgM serum antibodies to Epstein-Barr virus are uniquely present in a subset of patients with the chronic fatigue syndrome. In Vivo. 2004; 18: 101-106.
11. Bradbeer L, Thakkar S, Liu A, Nanan R. Childhood headache and H. pylori—a possible association. Aust Fam Physician. 2013; 42: 134-136.
12. Ciancarelli I, Di Massimo C, Tozzi-Ciancarelli MG, De Matteis G, Marini C, Carolei A. Helicobacter pylori infection and migraine. Cephalalgia. 2002; 22: 222-225.