

# Primary versus Secondary Headache in Children: A Frequent Diagnostic Challenge in Clinical Routine

Timo Roser<sup>1,\*</sup> Michaela Bonfert<sup>1,\*</sup> Friedrich Ebinger<sup>2,3</sup> Markus Blankenburg<sup>4</sup> Birgit Ertl-Wagner<sup>5</sup>  
Florian Heinen<sup>1</sup>

<sup>1</sup>Department of Paediatric Neurology and Developmental Medicine, Hauner Children's Hospital, University of Munich, Munich, Germany

<sup>2</sup>Department of Paediatrics, St. Vincenz Hospital Paderborn, Paderborn, Germany

<sup>3</sup>Department of Paediatrics, Ruprecht-Karls-University Heidelberg, Heidelberg, Germany

<sup>4</sup>Department of Neuropaediatrics, Olgahospital, Stuttgart, Germany

<sup>5</sup>Institute of Clinical Radiology, Klinikum Grosshadern, Medical Faculty, Ludwig-Maximilians-University Munich, Munich, Germany

**Address for correspondence and reprint requests** Timo Roser, MD, Department of Paediatric Neurology and Developmental Medicine, Hauner Children's Hospital, University of Munich, Lindwurmstrasse 4, 80337 Munich (e-mail: timo.rosler@med.uni-muenchen.de).

\*Timo Roser and Michaela Bonfert share the first authorship.

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## Abstract

A sensitive and specific triage of patients with primary or secondary headache is a major concern in evaluating pediatric headache patients. History and physical examination are the major tools for differentiating primary headache disorders from symptomatic headaches caused by defined pathologies. If the criteria of the International Headache Society for a primary headache disorder are met, no further investigations are necessary. However, physicians should be familiar with subtle signs in history and physical examination that raise suspicion of intracranial pathology. These features, also named “red flags” and “relatively red flags,” are outlined in detail in this review. Any red flag should prompt neuroimaging. In case of relatively red flags, a more restrained approach can be appropriate depending on the individual setting. Excessive concerns of patients and parents regarding an underlying pathology can constitute an indication for neuroimaging. Offering neuroimaging implicates the important issues of incidental findings and of “false reassurance.” These risks should be discussed with patients and parents before the investigation. In any pediatric headache patient, regular clinical reevaluations should be warranted, even if neuroimaging is normal. The value of clinical follow-up examinations for a reasonable and reliable assessment of the patients cannot be overestimated.

## Keywords

- ▶ pediatrics
- ▶ children
- ▶ adolescents
- ▶ primary headache disorder
- ▶ secondary headache
- ▶ symptomatic headache
- ▶ diagnostics
- ▶ red flags
- ▶ neuroimaging

## Introduction

Headaches are among the most frequent health complaints in children and adolescents.<sup>1</sup> An unknown number of patients just bear the pain without seeking medical advice. However, a considerable proportion of affected patients present to primary care providers or even to pediatric

emergency departments depending on the acuity and severity of symptoms.<sup>2</sup> The vast majority of pediatric headaches can be classified as either primary (e.g., migraine, tension-type headache, mixed-type headaches, and numerous less common primary headache disorders) or as secondary due to non-life-threatening diseases, such as upper

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**Table 1** Intracranial pathologies causing symptomatic headache

- Infection
- Neoplasia
- Cyst/rupture of cyst
- Hemorrhage
- Stroke
- Cerebrovenous thrombosis
- Subdural effusion
- Arterial dissection
- Benign intracranial hypertension

airway infection, influenza, sinusitis, or mild head trauma. However, in a small portion (0.4 to 4%) of patients acute or chronic headache is the presenting symptom of a hazardous intracranial disease (► **Table 1**).<sup>2,3</sup>

When a serious intracranial condition, such as a primary brain tumor, already is far advanced, the diagnostic decision making is usually not demanding due to the severity of symptoms. However, establishing an early diagnosis can be a major challenge for the primary care or emergency department pediatrician. The diagnosis of primary headache is usually readily made when certain criteria of the International Headache Society (IHS) are fulfilled (► **Tables 2–4**).<sup>4</sup> Though, in pediatric patients, it can be difficult to establish a definitive diagnosis at the time of the first office visit. The uncertainty during the process of establishing the diagnosis may strain the patient, the parents/caretakers, and the physician and in turn may lead to unnecessary overinvestigation and/or overprotection of the affected child. Hence, primary care providers should be familiar with subtle signs and symptoms of intracranial pathology to identify affected patients, establish an early diagnosis, and thus ascertain an optimal outcome for the individual patient. In our review article we focus on important aspects of history and physical examination that are relevant for optimally triaging pediatric headache patients. Moreover, we outline important indications for neuroimaging as well as points to consider in prompting this investigation in pediatric headache patients.

**Table 2** Diagnostic criteria of the International Headache Society for pediatric migraine without aura<sup>4</sup>

- A ≥ 5 attacks fulfilling criteria B to D<sup>a</sup>
- B Headache attack lasting 1–72 h
- C Headache has at least 2 of the following 4 features:
  - (1) Bilateral or unilateral (frontal/temporal) location
  - (2) Pulsating quality
  - (3) Moderate to severe intensity
  - (4) Aggravated by routine physical activity
- D At least one of the following accompanies headache:
  - (1) Nausea and/or vomiting
  - (2) Photophobia and phonophobia (may be inferred from patient’s behavior)
- E Headache is not attributed to another disorder

<sup>a</sup>If < 5 typical attacks are reported, diagnosis is coded as “probable migraine.” If attacks occur on 15 days a month for > 3 months, diagnosis is coded as “chronic migraine.”

**Table 3** Diagnostic criteria of the International Headache Society for typical aura with pediatric migraine headache<sup>4</sup>

- A ≥ 2 attacks fulfilling criteria B to D
- B Aura consisting of at least one of the following features, but no motor weakness<sup>a</sup>:
  - (1) Fully reversible visual symptoms including positive features (e.g., flickering lights, spots, or lines) and/or negative features (e.g., loss of vision)
  - (2) Fully reversible sensory symptoms including positive features (e.g., pins and needles) and/or negative features (e.g., numbness)
  - (3) Fully reversible dysphasic speech disturbance
- C At least 2 of the following 3 features characterize the aura:
  - (1) Homonymous visual symptoms (additional loss or blurring of central vision may be associated) and/or unilateral sensory symptoms
  - (2) At least one aura symptom develops gradually over ≥ 5 min and/or different aura symptoms occur in succession over ≥ 5 min
  - (3) Each symptom lasts ≥ 5 and ≤ 60 min
- D Headache fulfilling criteria B-D for “migraine without aura” (► **Table 2**) begins during the aura or follows aura within 60 minutes<sup>b</sup>
- E Aura symptoms are not attributed to another disorder

<sup>a</sup>If aura includes motor weakness, diagnosis is coded as “familial or sporadic hemiplegic migraine.”

<sup>b</sup>If headache does not fulfill criteria for migraine without aura, diagnosis is coded as “typical aura with non-migraine headache.” If headache occurs neither during aura nor after aura within 60 minutes, diagnosis is coded as “typical aura without headache.”

## History

Generally, the diagnosis of migraine and tension-type headache is obvious when a patient’s history fits the appropriate criteria of the IHS (► **Tables 2–4**).<sup>4</sup> Nevertheless, in addition to

**Table 4** Diagnostic criteria of the International Headache Society for tension-type headache (TTH)<sup>4</sup>

- A Infrequent TTH: ≥ 10 episodes on < 1 day per month on average (< 12 days per year) ...  
Frequent TTH: ≥ 10 episodes on ≥ 1 but < 15 days per month for ≥ 3 months (≥ 12 days and < 180 days per year) ...  
Chronic TTH<sup>a</sup>: headache on ≥ 15 days per month on average for > 3 months (≥ 180 days per year) ...  
fulfilling criteria B–D<sup>b</sup>
- B Headache lasting 30 min to 7 days
- C Headache has at least 2 of the following 4 features:
  - (1) Bilateral location
  - (2) Pressing/tightening (nonpulsating) quality
  - (3) Mild or moderate intensity
  - (4) Not aggravated by routine physical activity
- D Both of the following:
  - (1) No nausea or vomiting (anorexia may occur)
  - (2) No more than one of photophobia or phonophobia
- E Headache is not attributed to another disorder

<sup>a</sup>To differentiate chronic TTH to chronic migraine and medication-overuse headache, some minor changes in criteria D and E have been established (for details see<sup>4</sup>).

<sup>b</sup>If all but one criteria A–D are fulfilled, diagnosis is coded as “probable TTH.”

**Table 5** Key points of headache-specific history

Acute headache	Additional features in recurrent headache
<ul style="list-style-type: none"> <li>• Time of onset</li> <li>• Duration</li> <li>• Localization</li> <li>• Quality</li> <li>• Intensity</li> <li>• Premonitory symptoms</li> <li>• Aura</li> <li>• Associated vegetative symptoms</li> <li>• Impairment of daily routine</li> <li>• Ameliorating factors</li> <li>• Aggravating factors</li> <li>• Triggering factors</li> <li>• Factors possibly associated to onset</li> <li>• Efficacy of medications taken</li> </ul>	<ul style="list-style-type: none"> <li>• Number of headache types</li> <li>• Frequency</li> <li>• Sequence of typical episode</li> <li>• Impairment of quality of life</li> </ul>

a thorough headache-specific history (►Table 5), which should include taking a family history for headache disorders, an orienting general medical history should be gathered in all pediatric headache patients. When taking the history, several

aspects should not be missed and should be specifically noted (►Table 6). The red flags are alerting as patients reporting one or more of these red flags are at high risk for an underlying intracranial disease. Relatively red flags constitute suspicious features that have to be taken seriously, when deciding further proceedings.<sup>2,5-10</sup> Nevertheless, such listings and classifications always constitute a theoretical approach. Physicians should trust their clinical intuition in judging the patient’s individual situation more than strictly ticking off a checklist.

**Physical Examination**

In any patient presenting with headache, the physical examination needs to include a complete neurologic examination with a thorough assessment of mental state, cranial nerves (including visual acuity, field of vision, ocular movements, pupillary responses, and funduscopy), reflexes, and coordination. In addition, blood pressure, weight, and head circumference should be collected. If the primary care pediatrician does not feel fully confident in assessing the papillae by funduscopy, referral to an ophthalmologist is required.<sup>10</sup> However, this referral should not delay further diagnostic decision making if an increase in intracranial pressure is clinically suspected. On the other hand, absence of papilloedema does not exclude raised intracranial pressure. When

**Table 6** Red and relatively red flag features in history of pediatric headache patients

Red flags (high-risk features)	Relatively red flags (suspicious features)
<b>Character of headache</b>	
<ul style="list-style-type: none"> <li>• Sudden severe headache</li> <li>• Recent onset of severe headache (specified to up to 4 weeks by some authors)</li> <li>• Occipital headache</li> <li>• Cluster headache</li> <li>• Early morning headache</li> <li>• Pain that wakes the child from sleep or occurs on waking</li> <li>• Worsening of headache in recumbency and/or during straining, coughing, and/or other forms of Valsalva maneuver</li> <li>• Change of the character of headache in patients diagnosed with primary headache</li> </ul>	<ul style="list-style-type: none"> <li>• Increase in frequency and intensity of headache over time</li> <li>• High intensity of headache</li> <li>• Continuous headache</li> <li>• Constrictive headache</li> <li>• Diffuse headache</li> <li>• Inability of the patient to characterize the headache</li> </ul>
<b>Specific findings in history (“headache +”)</b>	
<ul style="list-style-type: none"> <li>• (Morning/fasting) nausea or vomiting (not associated with typical migraine)</li> <li>• Neurologic dysfunction (other than typical aura associated with migraine)</li> <li>• Confusion, disorientation</li> <li>• Seizure(s)</li> <li>• Changes of behavior and/or personality</li> <li>• Cognitive decline</li> <li>• Polyuria, polydipsia</li> </ul>	<ul style="list-style-type: none"> <li>• Impaired psychomotor development</li> <li>• Antecedent systemic or localized head/neck infection (e.g., middle ear infection, sinusitis)</li> <li>• Prior head trauma</li> <li>• Medication and their side effects (e.g., contraceptives in female adolescents)</li> <li>• Comorbidity (e.g., malignancy, hypercoagulopathy, sickle cell disease, hypertension, immunodeficiency, neurofibromatosis, arteriovenous malformation, congenital heart disease)</li> <li>• Negative family history of primary headache disorders (especially migraine)</li> <li>• Young age of the patient (by some authors specified to preschool age or younger)</li> </ul>

performing the physical examination, several signs should not be missed, because these red flags are often encountered in patients suffering from symptomatic headache caused by intracranial pathology (► **Table 7**).<sup>2,7-10</sup>

### Value of History and Physical Examination

History and physical examination are highly sensitive for detecting an intracranial pathology and remain the most powerful diagnostic tools for the physician in a child presented with headache. Overall, the incidence of relevant intracranial pathologies in children with headaches is low (< 1 to 4%).<sup>11,12</sup> A normal neurologic examination has been demonstrated to highly correlate with the absence of relevant intracranial processes in several adult and pediatric studies.<sup>11-14</sup> Nevertheless, there are two important limitations concerning the physical examination. First, there is a high interindividual variation with regard to clinical experience, diagnostic accuracy, rating of findings and available time. A physical examination and its interpretation therefore remain a subjective matter. The conclusion “unremarkable examination” thus only translates to “not detected by the investigator” but does not indicate the absence of an abnormality with certainty. Second, neurologic symptoms can fluctuate in severity in the initial stages of an intracranial disease. A single normal neurologic examination cannot always exclude a symptomatic headache. In these instances, only a thorough history and regular clinical reevaluations can help to decide whether the patient will require further investigation at any point in time or not. Systematic clinical follow-up examinations constitute the most reliable measure in detecting patients in need of subsequent investigations. Moreover, the importance of taking the concerns of parents/caretakers seriously cannot be overemphasized, particularly if they describe their child to have changed in any way since the headache started. Specifically asking the parents/caretakers whether a visit was scheduled out of concern for a possible underlying condition or because the headache itself is tedious can add helpful information.

**Table 7** Red flag (high-risk) features in physical examination of pediatric headache patients

- Reduced general condition
- Impaired consciousness, mental state, behavior
- Increased head circumference
- Cranial bruits
- Cranial nerve palsies
- Abnormal ocular movements, squint, pathologic pupillary responses
- Visual field defects
- Papilloedema
- Focal neurologic deficits, even if only slight
- Change or worsening of fine and gross motor developmental skills
- Ataxia, gait abnormalities, impaired coordination
- Growth failure
- Precocious, delayed, or arrested puberty

### Counseling the Patients

Once the diagnosis of a primary headache disorder is made, both patients and parents/caretakers must be educated regarding specific features, prognosis, and treatment. When a symptomatic headache is considered, further diagnostic steps and their respective timing need to be discussed. If patients do not present red flags but the diagnosis of primary headache disorder is not ready to be made at the time of the first office visit, patients and parents/caretakers have to be thoroughly educated on any potentially alerting symptoms. The occurrence of red flags always calls for prompt reconsultation (also by telephone). Those patients reporting “relatively red flags” whose further investigation is postponed in the first instant should be additionally educated about the particular need for frequent reevaluation. Finally, the importance of regular clinical follow-up examinations should be discussed with all patients and parents. A continued assessment is indispensable in any pediatric headache patient. In this context, today's common doctor hopping constitutes an important issue. Reliable follow-up can only be warranted if the same physician (or team of physicians) is continuously responsible for the patient. This fact should be pointed out to the parents/caretakers.

### Neuroimaging

With the widespread availability of cross-sectional imaging modalities, neuroimaging methods, particularly magnetic resonance imaging (MRI), are increasingly used in the diagnostic evaluation of pediatric patients with headaches.<sup>15</sup> However, resources need to be used responsibly. Moreover, imaging can put an additional strain on the patient and the parents/caretakers. Indication guidelines for neuroimaging in headache patients are an ongoing matter of discussion.

In general, “routine” neuroimaging is not indicated in children with a typical long-standing recurrent primary headache consistent with the IHS criteria who do not report neurologic dysfunction and who do not show abnormal signs in the neurologic examination.<sup>12,16</sup> Headache patients with one or more of the following features should undergo imaging according to the currently available guidelines<sup>12,14,16</sup>:

- Recent onset of severe headache
- Incompatibility of headache character, associated symptoms, or time course with IHS criteria of primary headache
- Change of the headache pattern in a known headache patient
- Features in the patient's history that suggest neurologic dysfunction (other than typical aura associated with migraine)
- Any abnormal finding in the neurologic examination

In selected cases and based on individual decisions, neuroimaging can be indicated in the following situations<sup>8,14</sup>:

- Fear of patients and/or parents/caretakers regarding severe underlying diseases (e.g., brain tumor)
- History of brain tumor within the family
- Inability to thoroughly perform the physical examination due to incomppliance of the patient

One of the major concerns in performing neuroimaging in patients with headaches is the occurrence of incidental findings. With the advent of MRI with ever higher spatial resolution, the incidence of detecting even minute incidental findings is increasing. The risk of detecting incidental findings has been reported to be as high as 20 to 40% in pediatric headache patients; this is of particular concern for patients who do not present red flag features.<sup>15,17</sup> The most commonly reported incidental findings without clinical significance are subtle focal areas of gliosis and other nonspecific white matter abnormalities.<sup>15</sup> However, these incidental findings can be a cause for major concern for patients, parents, and physicians. Reports of an incidental finding may further aggravate parental anxiety instead of causing relief and lead to unnecessary additional investigations (e.g., repeated neuroimaging). Therefore, patients and parents/caretakers should be informed about the risk of incidental findings before the investigation.

Another potential downside of neuroimaging constitutes a feeling of “false security” based on a normal report. As some patients may subsequently develop a structural lesion, regular clinical examinations should be continued even if imaging is normal. Other risks to be taken into account are allergic reactions to contrast media and (over-) sedation in younger children. To avoid inconsistencies, the communication of neuroimaging findings needs to be coordinated between the reporting radiologist and the referring pediatrician. In general, neuroimaging does not need to be repeated when there is no significant change in headache characteristics and physical examination over time.

MRI of the brain should be the imaging method of choice in children with headaches if at all possible. To exclude benign intracranial hypertension, an MR-based noninvasive measurement of intracranial pressure could be a promising, currently investigated alternative to lumbar puncture. However, the method is currently still investigational and only available in selected centers.<sup>18–20</sup> Thus, so far the lumbar puncture remains the investigation of choice to exclude benign intracranial hypertension. Computed tomography is decidedly inferior to MRI in regard to soft-tissue contrast and gray-to-white matter differentiation in the brain. Moreover, the radiation dose associated with head computed tomography in pediatric patients is a cause of major concern.<sup>21</sup> Cranial computed tomography in children with headaches should therefore be limited to emergency situations and to patients in whom MRI is not available or contraindicated (e.g., cardiac pacemakers). Dental braces are generally not a contraindication for MRI but may reduce the information due to artifacts. Other imaging modalities like radiographs of the skull, paranasal sinuses, and spine and ultrasound/duplex sonography of the neck vessels (e.g., to exclude dissection; however, T1-weighted MRI with fat suppression is more sensitive for this purpose) are reserved for selective indications and are usually not performed in the diagnostic evaluation of a headache patient.<sup>16</sup>

In our experience, most children with long-standing headaches undergo cranial MRI at some point either due to specific medical findings or for reassurance. We strongly recommend performing MRI of the neurocranium in patients with red flag

features in history or physical examination. In patients reporting relatively red flags, a more restrained approach with frequent clinical follow-ups can be appropriate depending on the individual setting. Regarding the age of patients, there is no lower limit that automatically warrants neuroimaging even if suspicious clinical features are absent. In our view, a particularly thorough physical examination as well as regular reevaluations are the most important and cost-effective monitoring tools also in young children, assuming the physician is experienced in evaluating preschool children. MRI of the brain should be considered when the affected patient or parents/caretakers cannot be reassured and express excessive concerns regarding an underlying pathology. In our experience, a normal MRI report allows these patients and parents to concentrate on pain therapy and prevents “overprotection” of the child as well as “doctor hopping.” Consistently, adult data demonstrate that worried patients cause less long-term medical costs if offered neuroimaging.<sup>22</sup>

## Conclusion

Headaches are a frequently encountered complaint in the pediatric population. Good clinical practice plays an important role in the diagnostic evaluation of these patients. History, including family history (especially for migraine), and physical examination are the most important tools to reach a correct clinical diagnosis of primary headache. Any suspicious or atypical feature needs to result in a more extended consultation. In case of the presence of red flags, prompt neuroimaging is warranted. In some patients with relatively red flags, postponement of further investigations can be appropriate. MRI of the brain is the imaging modality of choice to exclude intracranial pathologies. By offering neuroimaging the concerns of incidental findings and the feeling of “false security” should be taken into account. In all pediatric headache patients, regular clinical follow-up examinations should be ensured to warrant a continued assessment of the course of the condition. Overall, clinical monitoring constitutes the most reasonable and reliable measure in taking care of pediatric headache patients.

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