Alder Hey Children's NHS Foundation Trust

Guidelines on Diagnosis and Management of Idiopathic Intracranial Hypertension (IIH) in children

Introduction

Idiopathic intracranial hypertension (IIH) is a rare neurological disorder in children and is characterized by raised intracranial pressure (ICP) in the absence of intracranial pathologies like brain parenchymal lesion, vascular malformations, hydrocephalus or central nervous system (CNS) infection. The diagnosis is usually confirmed by high opening pressure of cerebrospinal fluid (CSF) by CSF manometry with exclusion of secondary causes of intracranial hypertension. If not treated properly, it may lead to severe visual dysfunction.[1]

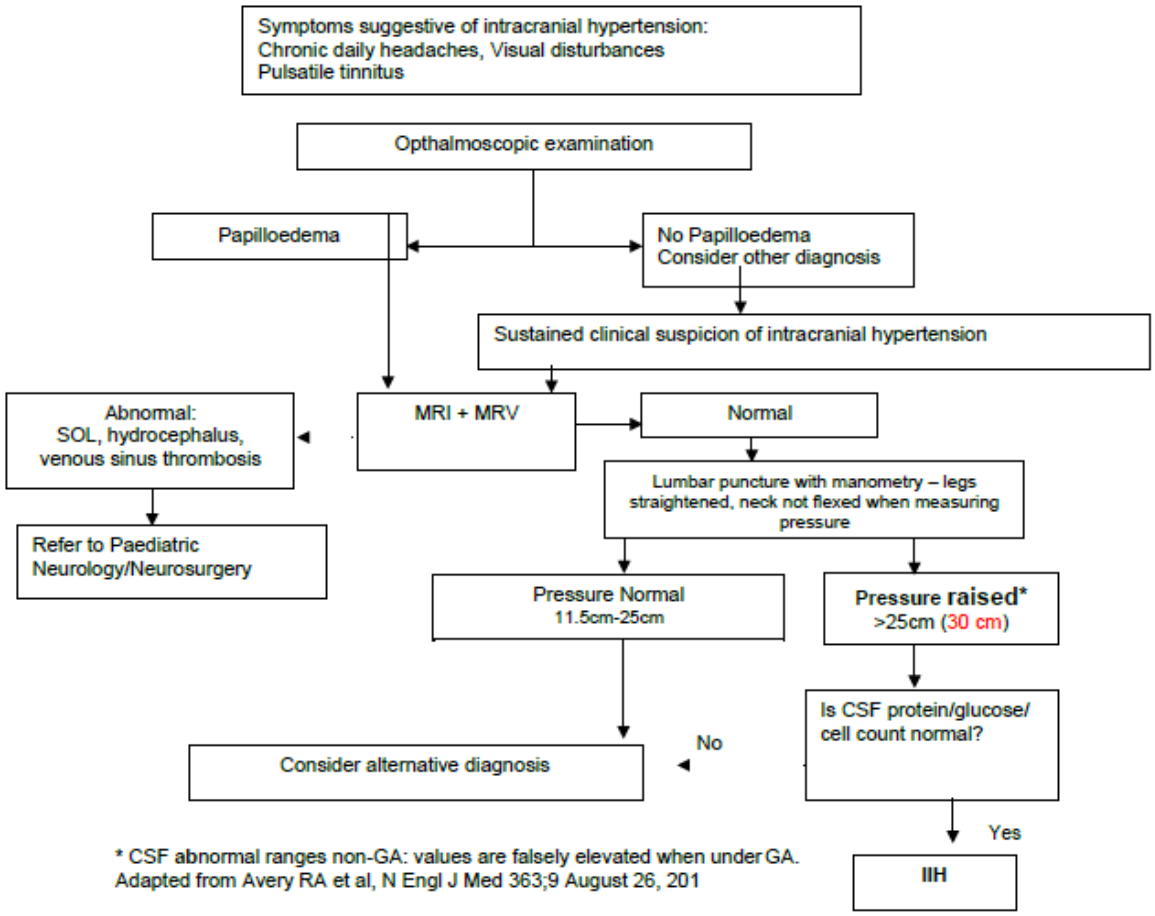
Pathogenesis

The exact pathogenesis of IIH is not known. IIH can occur in all age groups, in both genders and both obese and non-obese individuals. It is more frequently recognised in the paediatric population.

Current data suggest that intracranial hypertension in prepubertal children is more likely to be secondary than idiopathic in nature.

Studies also suggest that IIH is infrequent in children less than 10 years of age and extremely rare in children less than 3 years old.

Section 1: Diagnostic algorithm



Please note: If the lumbar puncture with opening pressure is performed under a general anaesthetic ensure that the end tidal pCO2 is normal before and during the procedure and that the values are recorded.

Section 2: Diagnostic criteria and symptoms

A

IIH symptoms

- Headache (increasingly severe and frequent) (76-94%)
- Visual obscuration's (darkening of the vision) (68-72%)
- Pulsatile tinnitus (52-61%)
- Back pain (53%)
- Dizziness (52%)
- Neck pain (42%)
- Blurred vision (32%)
- Cognitive disturbance (20%)
- Radicular pain (19%)
- Diplopia (typically horizontal) (18%)

B

IIH Diagnostic criteria

A. Papilloedema
B. Normal neurological examination (except sixth cranial nerve palsy)
C. Neuroimaging: normal brain parenchyma (no hydrocephalus, mass, structural lesion or meningeal enhancement). Venous thrombosis excluded in all.
D. Normal CSF constituents
E. Elevated lumbar puncture pressure ≥ 25cmCSF

C

IIH without Papilloedema (IIHWOP) Diagnostic criteria

Presence of criteria B-E for IIH plus:

- Unilateral or bilateral sixth cranial nerve palsy

Suggestion of possible IIHWOP if:

Presence of criteria B-E for IIH plus:

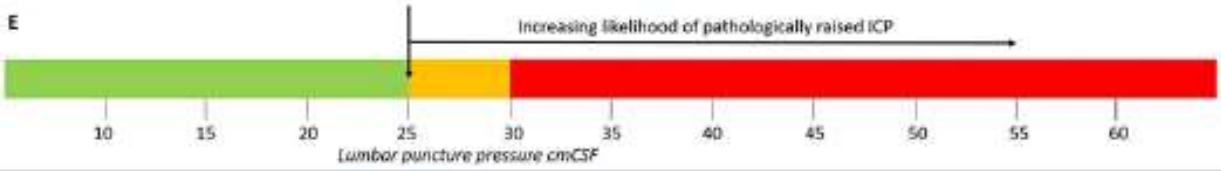
- 3 neuroimaging finding suggestive of raised intracranial pressure
  - Empty sella
  - Flattening of posterior aspect of the globe
  - Distention of the perioptic subarachnoid space ± a tortuous optic nerve
  - Transverse venous sinus stenosis

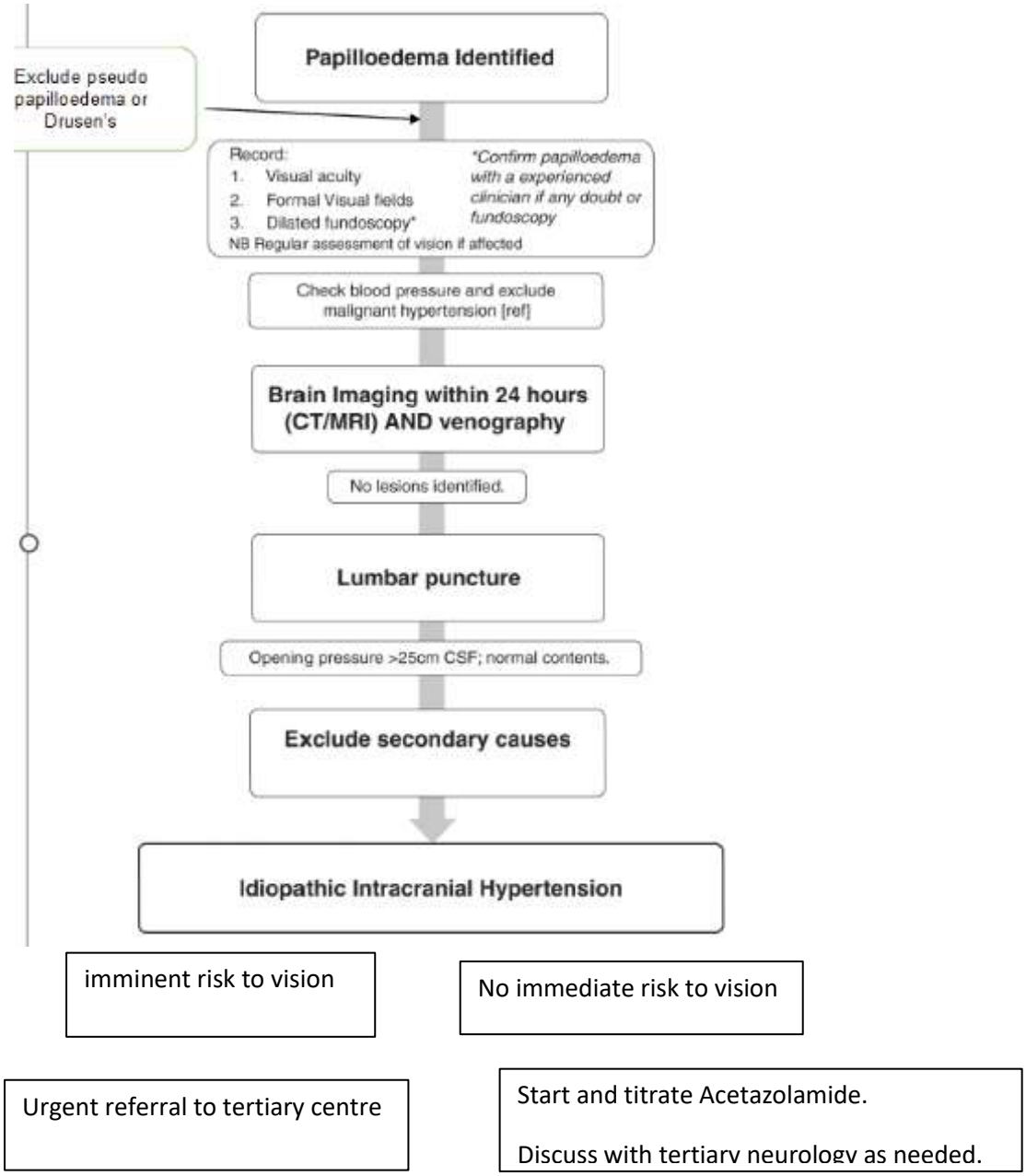
D

Headache attributed to IIH (ICHD-3b)

A. Any headache fulfilling criterion C
B. IIH has been diagnosed with lumbar puncture pressure ≥ 25cmCSF
C. Evidence of causation demonstrated by at least 2 of:
   A. Headache developed in temporal relation to IIH
   B. Headache relieved by reducing ICP
   C. Headache exacerbated in temporal relationship to increased ICP
D. Headache not accounted for by another ICHD-3 diagnosis

E





Investigations

1. Blood investigations

FBC, U&E, LFT, Bone profile, plasma glucose, TFT, PTH , Vitamin D level and cortisol to exclude secondary causes.

2. **Neuroimaging**

Brain MRI + MRV is indicated to rule out any evidence of hydrocephalus, intraparenchymal lesions, or abnormal meningeal enhancement[12] & cerebral venous sinus thrombosis.

3**. Lumbar Puncture**

Ideally, the test must be performed without sedation and preferred positioning is the lateral decubitus position. Measurement of the opening pressure should be done and Cerebrospinal fluid (CSF) should be removed (“therapeutic tap”) and sent for microscopy and culture, Glucose (with matched serum sample) and Protein. Interpreting lumbar puncture opening pressure (LPOP) results in the paediatric population is difficult due to the lack of any large-scale normative data. If done under anaesthesia also document the end tidal CO2 which should ideally be normal before Lumbar puncture and throughout the procedure.

Table 1

Patient Category	CSF Opening Pressure	Comments
Child 1-18yrs	20cm H20	Normal
Child 1-18yrs	20-25cm H20	Abnormal if papilloedema present
Obese child <18yrs	≥28cm H20	Abnormal
Sedated child <18yrs	≥ 28cm H20	Abnormal
Non-obese, non-sedated child	≥25cm H20	Abnormal

If initial workup suggests possible IIH, urgent ophthalmologic evaluations is mandatory to assess visual acuity, visual fields (age seven and over), colour vision, spontaneous venous pulsations, papilledema (and Frissen grading) and ocular Computer Tomogram (OCT) if available.

Other testing to rule out secondary causes should be guided by the history, examination and other investigations.

Patient management: treatment and follow-up

Goals of treatment:

1) To relieve symptoms

2) To preserve vision.

Treatment is indicated when there is raised intracranial pressure, any visual loss or risk to vision, moderate to severe papilledema, or persistent headache[15]. In general, the selection of medical, surgical or combined treatment depends on the severity of the visual symptoms and signs and in the majority of cases medical treatment is the first choice; if it fails or if the visual function is deteriorating, surgical intervention is indicated[1].

1. **Lifestyle Modification**

Lifestyle modification such as weight reduction, especially in overweight patients was found to be beneficial.[16] (aim for six to seven percent weight loss)

2. **Pharmacologic treatment/ Medical treatment**

Treatment should aim at lowering ICP, relieve symptoms, and preserve visual function. Pharmacological Management is indicated if raised ICP is confirmed by lumbar puncture and secondary causes have been ruled out.

Carbonic anhydrase inhibitors have been shown to decrease ICP. Acetazolamide is the most commonly used carbonic anhydrase inhibitor[4].

Furosemide is usually reserved for cases, in which acetazolamide is not tolerated due to its minimal effect on lowering ICP or significant side effects experienced on Acetazolamide.

Note: Beware of dehydration in individuals affected by severe raised intracranial pressure.

Topiramate is an antiepileptic drug with the secondary effect of inhibiting carbonic anhydrase. It might be potentially used as an add on to acetazolamide in obese patients. Weight reduction as well as the reduction of the CSF formation is the possible mechanism of action.

Note: Monitor blood gases and electrolytes on introduction and titration of carbonic anhydrase inhibitors

The role of corticosteroids has not been proven. A short course of high-dose corticosteroids might be considered in situations of elevated ICP with papilloedema associated with acute vision loss[25] in the rare situation when rapid access to neurosurgical services to facilitate CSF drainage (for example lumbar drain) is not available in a timely manner.

Acute visual deterioration requires urgent referral to Alder Hey Children's Hospital (Neurology, Ophthalmology)

Table 2- Drug Dosage

Medication	Dose	Side Effects	Monitoring	Comments
Acetazolamide (250mg tablets) First line drug	Day 1 - 62.5mg TDS Day 2 – 125mg TDS Day 3 – 187.5mg TDS D4 – 250mg TDS Then titrate up slowly if needed to 375mg TDS. Doses of 500mg TDS can be tried but are often not tolerated in our experience. In practice starting at a lower dose and slower titration is more likely to be tolerated. Starting dose not to exceed the BNFC recommended starting dose)	GI upset, paraesthesia of lips, fingers and toes, metabolic acidosis, nephrolithiasis Rapid titration is associated with side effects of pins/needles, nausea, vomiting and non-compliance	Monitor plasma electrolytes, pH, bicarbonate after 5-7 days, then after 4 weeks unless dose changes or concerns regarding side effects. Do ultrasound kidneys to look for nephrocalcinosis, if used for more than 6 months.	**Initial starting dose not to exceed 8mg/kg TDS)** Please be aware that the dosage needs to be calculated based on ideal weight to avoid overdosing.
Furosemide Second line drug (in practice in our experience rarely used)	1-2mg/kg/day with or without Acetazolamide	Metabolic alkalosis, Hyponatraemia, Hypokalaemia, Hypotension, Hyperglycaemia	Monitor Electrolytes May need potassium supplements	Additive effect with Acetazolamide Consult with Paediatric Neurologist
Topiramate (usually not first line treatment)	1.5-3mg/kg/day in two divided doses, the dose should increase by a maximum of 25mg/ week. Maximum dose 200mg per day [4].	Paraesthesia Drowsiness Kidney stones Lethargy Contraindicated in Pregnancy and liver failure		In an open-label study in adults, topiramate was as effective as acetazolamide with the added benefit of reducing weight.[29]

3. **Removal of CSF at the time of diagnosis**

Lumbar Puncture is performed both as diagnostic and therapeutically. If opening pressure is high, CSF is drained to attain normal pressure as per table1. At a time 5ml of CSF is drained and pressure is rechecked and drained accordingly. Reduce the CSF opening pressure by about 30% of the opening pressure but not lower than 20 cm H2O.

Ideally, the procedure should be carried out without any sedation, under topical and local anaesthesia. The use of Entonox and General Anaesthesia can alter the CSF pressures. When performed under GA, end-tidal C02 must be monitored and maintained in normal range. End-tidal CO2 should be recorded in the notes along with the opening pressures.

4. **Serial lumbar puncture** – This is not recommended routinely. LP should be reserved for initial diagnostic purposes and subsequently performed only when needed to assess CSF pressure in response to treatment if persistently

symptomatic and or if no improvement of papilledema after discussion with tertiary neurologist.

5. **Surgery**

Surgical procedures, such as optic nerve sheath fenestration (ONSF) and CSF shunting is reserved for cases of acute, significant or progressive visual impairment or intractable headache despite medical treatment[4].

6. **Emergency management**

Neurosurgical consultation for CSF shunting may be required if there is sudden deterioration of visual function.

Timely referral to and discussion with tertiary neurology is recommended for all children/ adolescents affected by confirmed raised intracranial pressure.

Indications for Paediatric Neurology referral:

1. Presence of visual deficit and or worsening of the same despite LP & acetazolamide.
2. Headaches not responding to LP & acetazolamide.
3. Diagnostic uncertainty

Indications for Paediatric Neurosurgical input:

1. Younger children with severe papilloedema where visual assessment is difficult.
2. Progressive visual failure despite maximal medical treatment.
3. Severe visual failure at presentation or accelerated clinical course.

Follow up

- Children should have regular ophthalmology follow up including visual fields, acuity, colour vision and presence/absence of papilloedema.
- After initiation of acetazolamide arrange paediatric follow up in one week with bloods as advised and then 4-6 weekly as clinically indicated.
- First Ophthalmology follow up 2 weeks and further follow up 4-6 weekly (or with Opthalmology as deemed appropriate by Opthamologist).
- Repeat LPs :
  A) If clinically improving and papilloedema is resolving and tolerating acetazolamide would not generally need repeat LP.
  B) If symptoms and or papilloedema not improving or worsening would need repeat Lumbar puncture. If opening pressure is still elevated please discuss with neurology (for optimising medical management).
  C) If there are acute visual concerns, urgent discussion with neurology team.

- Weight reduction measures should be advised to the children and families as per local programmes.

Table 4 Consensus of follow-up intervals for patients with idiopathic intracranial hypertension (IIH) based on their papilloedema grade and their visual field status

Papilloedema grade	Visual field status: Normal	Affected but improving	Affected but stable	Affected but worsening
Atrophic			4–6 months	Within 4 weeks
Mild	6 months	3–6 months	3–4 months	Within 4 weeks
Moderate	3–4 months	1–3 months	1–3 months	Within 2 weeks
Severe		1–3 months	Within 4 weeks	With 1 week

Note: Once papillodema has resolved, visual monitoring within the hospital services may no longer be required. However, caution in those patients who were asymptomatic at presentation, as they will likely be asymptomatic if a recurrence occurs and longer term follow-up, may need to be considered.

Prognosis

With early diagnosis and treatment, most children with mild to moderate visual field defects will have complete resolution of their symptoms[4]. Permanent visual loss or blindness is the most serious morbidity and is mainly related to the severity of papilledema at presentation. High risk groups for irreversible visual loss include black population, male gender, and morbidly obese, anaemic patient with fulminant IIH[22]. Permanent loss of visual acuity has been reported in up to 10% of the patients and visual field loss persists in up to 17 % of the patients[23].

Summary

The diagnosis of IIH in a Paediatric patient is becoming more common. Understanding of this condition, diagnosis, and its treatment have largely been based on data obtained in the adult population. There is now increasing evidence that Paediatric IIH is quite different from the adult disease. An increased understanding of this disease in children has led to more specific diagnostic and treatment guidelines that will aid the clinician in management.

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28. Fifteen-minute consultation: the child with idiopathic intracranial hypertension
29. Mohamed O E Babiker1, Manish Prasad2, Stewart MacLeod1, Gabriel Chow3, William P Whitehouse3,4

Appendix 1

Table 3. Reported risk factors for secondary intracranial hypertension[1]

Medications	Infections	Medical conditions
Amiodarone Cyclosporine Nalidixicacid Nitrofurantoin Oral contraceptive pills Steroids therapy Tetracycline Vitamin A analogues Lithium Penicillin Phenytoin Sulphonamides	Coxsackie B encephalitis HIV Infectious mononucleosis Lyme disease Malaria Poliomyelitis Prior meningitis Syphilis	Adrenal insufficiency Chiari malformation Chronic anaemia Congestive heart failure Craniosynostosis Cushing's disease Guillain-Barre syndrome Hydrocephalus Leukaemia Polycystic ovary syndrome Renal failure Superior sagittal sinus thrombosis Systemic lupus erythematosus Traumatic brain injury Trisomy 21 Vitamin D deficiency

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