

**Date published/posted: October 17, 2007**

## **Treatment of Amblyopia in Children**

### **Clinical Questions**

P (population/problem)	In children with amblyopia
I (intervention)	does patching
C (comparison)	compared to atropine
O (outcome)	improve visual acuity at 6 months?
P (population/problem)	In children with amblyopia
I (intervention)	does patching 6 or more hours per day
C (comparison)	compared to patching 2 hours per day
O (outcome)	improve visual acuity at 6 months?
P (population/problem)	In children with amblyopia
I (intervention)	does atropine
C (comparison)	compared to patching
O (outcome)	improve initial acceptability of treatment for amblyopia?

### **Target Population**

Children with amblyopia (see disease definition in Discussion section)

### **Recommendation:**

It is recommended that children with amblyopia be treated with:

- 1) optimum refractive correction (glasses) (*Wallace 2007 [3a], Stewart 2004a [3b]*)

**AND**

- 2) either

- occlusion by patching the sound eye (*Holmes 2003b [2a], PEDIG 2003c [2a], Repka 2003 [2a], PEDIG 2002 [2a]*)

**OR**

- penalization using atropine sulfate 1% in the sound eye (*PEDIG 2003b [2a], PEDIG 2002 [2a]*).

Occlusion or penalization may be used concurrently with glasses, or after no further improvement in visual acuity is achieved by glasses alone (*Wallace 2007 [3a], Stewart 2004a [3b]*).

The recommended dose of atropine or patching is a range (*Stewart 2007 [4b]*). Initial dose ranges are:

- atropine: 1 drop per day, from 2 to 7 days per week
- patching: from 2 to 6 hours per day,

Increasingly more severe amblyopia indicates increasingly more aggressive initial dose (*Holmes 2003b [2a]*).

Also, increasing the dose is appropriate if there is no improvement (*PEDIG 2003c [2a]*).

Additional recommended treatment options that are in current trials, or have not been well-studied, include:

- Bangerter foils of graded densities on the glasses lens of the sound eye; foils allow binocularity and may be weaned in density as the vision improves
- addition of plano lens to atropine therapy
- when and if to wean from occlusion therapy
- the addition of one hour per day of near work during patching.

Follow-up is recommended every 4 to 8 weeks, frequency depending on patient-specific criteria (see Discussion section), in order to assess improvement and adjust therapy as needed. Consider even more frequent follow-up in infants and young children (*Stewart 2004b [3b]*).

## Health Benefits, Side Effects and Risks

### Any effective treatment of amblyopia

Successful treatment of amblyopia in childhood results in life-long benefits. One study measured more than \$2000 per quality-adjusted life-year (QALY) gained (*Membreño 2002 [1a]*).

### Treatment with atropine or patching

Children are at increased risk for accidents when vision is impaired in the sound eye (*Local Consensus [5]*). Precipitation of or an increase in the magnitude of strabismus, diplopia, and occlusion-induced amblyopia has been reported, and can be prevented or reversed by adjustment of regimen at the recommended follow up visits (*Holmes 2003b [2a]*, *AAO 2002 [5]*).

### Atropine

Facial flushing has been reported with treatment of amblyopia with atropine (*PEDIG 2002 [2a]*). Other potential systemic effects, such as tachycardia, may be of concern for infants less than one year of age; for children with cardiac conditions, a consult with their cardiologist may prevent adverse effects (*AAO 2002 [5]*, *Local Consensus [5]*).

Instruction on safe methods of eye drop administration for families of children on atropine may prevent injury, especially in children with neck vertebrae instability, including children with Down syndrome who are at greater risk for atlantoaxial instability (*Nucci 1996 [5]*, *Local Consensus [5]*).

### Patching

Skin irritation has been reported with use of patches (*PEDIG 2002 [2a]*). Latex-free patches are available for latex-allergic individuals.

## Discussion:

Disease definition: Amblyopia is reduced best corrected visual acuity as a result of defective central visual processing. It is a disorder of visual development that is caused by an optical, physical, or ocular alignment defect during early childhood (*AAO 2002 [5]*).

Many options for treatment of amblyopia are available to families and clinicians, and decisions about treatment method, intensity, and duration will need to be considered in the context of the individual patient (*Stewart 2007 [4b]*).

Factors influencing the decisions include:

- the likelihood of compliance with the selected therapy and dose (*Stewart 2007 [2b]*)
- more aggressive therapy may get quicker results, though not necessarily better end results (*PEDIG 2003c [2a]*, *Stewart 2007 [2b]*)
- as little as one hour per day may be effective in some children (*Stewart 2005 [3b]*)
- some cases are easily treated, others are more resistant; the causes of these differences are not understood, though compliance may be a confounder
- when equal visual acuity between eyes is achieved, tapering treatment compared to immediate cessation of treatment may reduce the risk of recidivism
- younger ages appear to be more treatable, but many older children also benefit; compliance in the teen years may be a confounder (*Stewart 2007 [2b]*, *PEDIG 2004 [3a]*)
- there is a risk of reversal of visual acuity in the sound eye, particularly with:
  - more aggressive therapy,
  - when therapy has been continued after visual acuity between eyes is achieved, or
  - when a plano lens has been added to atropine therapy (*PEDIG 2003b [2a]*)
- systemic effects of atropine may be a concern in infants less than one year of age (*AAO 2002 [5]*)
- in children with high myopia, atropine use alone does not sufficiently penalize vision to be an effective treatment.

## PEDIG Trial Notes:

**Note 1:** A large randomized controlled trial (RCT) of children age 3 years to less than 7 years with moderate amblyopia found that improvement in visual acuity in the amblyopic eye after 6 months of treatment was equivalent in patients whose sound eye was treated either by atropine or by patching at least 6 hours per day. There was no difference based on patient characteristics of age, gender, cause of amblyopia, depth of amblyopia, previous treatment, refractive error in the sound eye, or initial patching regimen of 6 or 10 hours per day (PEDIG 2003b [2a], PEDIG 2003a [2a], PEDIG 2002 [2a]). Children less than 3 years of age have not been studied.

**Note 2:** A questionnaire to measure acceptability of atropine and patching interventions was administered after five weeks of treatment to parents of participants enrolled in the RCT described in Note 1. Both interventions were well tolerated by the child and family, though atropine received more favorable scores on all three subscores (Holmes 2003a [2a], Cole 2001 [2b]).


**Note 3:** A large RCT of children age 3 years to less than 7 years with moderate amblyopia found that improvement in visual acuity in the amblyopic eye at 6 months was equivalent for eyes treated either by patching 2 hours or 6 hours per day (Repka 2003 [2a]). Children less than 3 years of age have not been studied.













**Note 4:** A large RCT of children age 3 years to less than 7 years with severe amblyopia found that improvement in visual acuity in the amblyopic eye after 4 months of treatment was equivalent in patients whose sound eye was treated either by 6 hours of prescribed daily patching or full-time waking hours prescribed patching (Holmes 2003b [2a]) Children less than 3 years of age have not been studied.

**Note 5:** A Cochrane search found no trials which evaluated treatments for amblyopia caused by stimulus deprivation (Hatt 2006 [1a]).

**Note 6:** A large RCT of children age 3 years to less than 10 years with moderate bilateral refractive amblyopia found that improvement in visual acuity in the amblyopic eye after 1 year of treatment with spectacles correction achieved binocular visual acuity of 20/25 or better in 73% of children (Wallace 2007 [3a]).

## References/citations

**Note:** When using the electronic version of this document,  indicates a hyperlink to the PubMed abstract. A hyperlink following this symbol goes to the article PDF when the user is within the CCHMC network.

1. **AAO:** Pediatric Ophthalmology Panel, Amblyopia. *American Academy of Ophthalmology*: 25 p., 2002, [5]   
[http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthAAO2002Amblyopia.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthAAO2002Amblyopia.pdf).
2. **Cole, S. R. et al.:** The Amblyopia Treatment Index. *Journal of AAPOS: American Association for Pediatric Ophthalmology & Strabismus*, 5(4): 250-4, 2001, [2b]   
[http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthCole2001.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthCole2001.pdf).
3. **Hatt, S.; Antonio-Santos, A.; Powell, C.; and Vedula, S. S.:** Interventions for stimulus deprivation amblyopia. *Cochrane Database of Systematic Reviews*, 3: CD005136, 2006, [1a]   
[http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthHatt2006.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthHatt2006.pdf).
4. **Holmes, J. M. et al.:** Impact of patching and atropine treatment on the child and family in the amblyopia treatment study. *Arch Ophthalmol*, 121(11): 1625-32, 2003a, [2a]   
[http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthHolmes2003ArchOphth.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthHolmes2003ArchOphth.pdf).
5. **Holmes, J. M. et al.:** A randomized trial of prescribed patching regimens for treatment of severe amblyopia in children. *Ophthalmology*, 110(11): 2075-87, 2003b, [2a]   
[http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthHolmes2003Ophth.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthHolmes2003Ophth.pdf).
6. **Local Consensus:** During recommendation development timeframe. [5] .
7. **Membreno, J. H.; Brown, M. M.; Brown, G. C.; Sharma, S.; and Beauchamp, G. R.:** A cost-utility analysis of therapy for amblyopia. *Ophthalmology*, 109(12): 2265-71, 2002, [1a]   
[http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthMembreno2002.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthMembreno2002.pdf).
8. **Nucci, P.; de Pellegrin, M.; and Brancato, R.:** Atlantoaxial dislocation related to instilling eyedrops in a patient with Down's syndrome. *American Journal of Ophthalmology*, 122(6): 908-10, 1996, [5] .
9. **PEDIG:** A comparison of atropine and patching treatments for moderate amblyopia by patient age, cause of amblyopia, depth of amblyopia, and other factors. *Ophthalmology*, 110(8): 1632-7; discussion 1637-8, 2003a, [2a]   
[http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthPEDIG2003.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthPEDIG2003.pdf).
10. **PEDIG:** The course of moderate amblyopia treated with atropine in children: experience of the amblyopia treatment study. *Am J Ophthalmol*, 136(4): 630-9, 2003b, [2a]   
[http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthPEDIG2003AJAtropine.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthPEDIG2003AJAtropine.pdf).
11. **PEDIG:** The course of moderate amblyopia treated with patching in children: experience of the amblyopia treatment study. *Am J Ophthalmol*, 136(4): 620-9, 2003c, [2a]   
[http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthPEDIG2003AJ06-HrPatching.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthPEDIG2003AJ06-HrPatching.pdf).
12. **PEDIG:** A prospective, pilot study of treatment of amblyopia in children 10 to <18 years old. *Am J Ophthalmol*, 137(3): 581-3, 2004, [3a]   
[http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthPEDIG2004.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthPEDIG2004.pdf).

13. **PEDIG:** A randomized trial of atropine vs. patching for treatment of moderate amblyopia in children. *Arch Ophthalmol*, 120(3): 268-78, 2002, [2a] [http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthPEDIG2002.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthPEDIG2002.pdf).
14. **Repka, M. X. et al.:** A randomized trial of patching regimens for treatment of moderate amblyopia in children. *Arch Ophthalmol*, 121(5): 603-11, 2003, [2a] [http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthRepka2003.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthRepka2003.pdf).
15. **Stewart, C. E.; Fielder, A. R.; Stephens, D. A.; and Moseley, M. J.:** Treatment of unilateral amblyopia: factors influencing visual outcome. *Investigative Ophthalmology & Visual Science*, 46(9): 3152-60, 2005, [3b] [http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthStewart2005.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthStewart2005.pdf).
16. **Stewart, C. E.; Moseley, M. J.; Fielder, A. R.; Stephens, D. A.; and Cooperative, M.:** Refractive adaptation in amblyopia: quantification of effect and implications for practice. *British Journal of Ophthalmology*, 88(12): 1552-6, 2004a, [3b] [http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthStewart2004BIO.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthStewart2004BIO.pdf).
17. **Stewart, C. E.; Moseley, M. J.; Stephens, D. A.; and Fielder, A. R.:** Treatment dose-response in amblyopia therapy: the Monitored Occlusion Treatment of Amblyopia Study (MOTAS). *Investigative Ophthalmology & Visual Science*, 45(9): 3048-54, 2004b, [3b] [http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthStewart2004IOVS.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthStewart2004IOVS.pdf).
18. **Stewart, C. E.; Stephens, D. A.; Fielder, A. R.; and Moseley, M. J.:** Objectively monitored patching regimens for treatment of amblyopia: randomised trial. *BMJ*, online(Sep 13), 2007, [2b] <http://www.bmj.com/cgi/reprint/bmj.39301.460150.55v1?maxtoshow=&HITS=10&RESULTSFORMAT=&fulltext=objectively-monitored-patching&searchid=1&FIRSTINDEX=0&resourcetype=HWCIT>.
19. **Stewart, C. E.; Stephens, D. A.; Fielder, A. R.; Moseley, M. J.; and Cooperative, M.:** Modeling dose-response in amblyopia: toward a child-specific treatment plan. *Investigative Ophthalmology & Visual Science*, 48(6): 2589-94, 2007, [4b] [http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthStewart2007IOVS.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthStewart2007IOVS.pdf).
20. **Wallace, D. K. et al.:** Treatment of bilateral refractive amblyopia in children three to less than 10 years of age. *Am J Ophthalmol*, 144(4): 487-496, 2007, [3a] [http://groups/p2/EBC\\_Files/Articles\\_Cited\\_in\\_EPIC\\_Ophth/OphthWallace2007.pdf](http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthWallace2007.pdf).

TABLE OF EVIDENCE LEVELS											
DOMAIN OF CLINICAL QUESTION	TYPE OF STUDY / STUDY DESIGN										
	Systematic Review Meta-Analysis	RCT <sup>+</sup> CCT <sup>+</sup>	Cohort - Prospective	Cohort - Retrospective	Case - Control	Longitudinal	Cross - Sectional	Qualitative Descriptive (Psychometric)	Epidemiology Case Series	Economic Analysis Decision Analysis	Expert Opinion Case Reports
Treatment Therapy	1a*	2a	3a	4a	4a	4a	4a		4a	4a	5
	1b*	2b	3b	4b	4b	4b	4b		4b	4b	
Cost Analysis Decision Analysis		2a	3a							1a	5
		2b	3b							1b	
Meaning / KAP+	1a		3a				4a	2a			5
	1b		3b				4b	2b			
Harm	1a	2a	3a	4a	4a	4a			4a		5
	1b	2b	3b	4b	4b	4b			4b		
Guidelines	1a										5
	1b										

\*a = good quality study; b = lesser quality study; <sup>+</sup>KAB = Knowledge, Attitudes, and Beliefs  
 Unshaded boxes and bold level indicate an article with these quality levels are cited in the document.  
 Darkly shaded boxes indicate study design may not be appropriate or commonly used for the domain of the clinical question.

---

## Supporting information

### Group/team members

W. Walker Motley, MD, Pediatric Ophthalmology  
 Dean Bonsall, MD, Pediatric Ophthalmology  
 Constance West, MD, Pediatric Ophthalmology

#### Clinical Effectiveness Support

Eloise Clark, MPH, MBA, Facilitator  
 Robert Ochiai, MBA, Clinical Quality Consultant  
 Danette Stanko-Lopp, MA, MPH, Epidemiologist  
 Jennifer Russell, MHSA, Quality Improvement Consultant  
 Barbarie Hill, MLS, Pratt Library  
 Carol Tierney, RN, MSN, Education Specialist

### Search strategy

#### 1. Initial Search

##### OID DATABASES

- MEDLINE – OVID
- Cochrane Database for Systematic Reviews (CDSR) – OVID

##### OID SEARCH TERMS & MeSH TERMS

- amblyopia

##### OID FILTERS

- Children
- Human
- Guidelines, Systematic Reviews, and Meta-Analyses (1996 to present)

**Website search of all known ophthalmology related websites** – for guidelines related to amblyopia

2. **Additional articles** identified by clinicians, specifically RCTs published for the Pediatric Eye Disease Investigator Group (PEDIG)

3. **Additional articles** identified from references lists of reviewed articles

### Applicability issues

Outcomes that are planned to be measured include:

1. Of active unilateral amblyopic patients age 3 years or older  
 Percent who have best corrected visual acuity of 20/30 or better in the amblyopic eye
2. Of active amblyopic patients on patching or atropine therapy  
 Percent with an average therapy adherence score of excellent (3.5 or greater)

Complete operational definitions are on file.

### Note

**This Best Evidence Statement addresses only key points of care for the target population; it is not intended to be a comprehensive practice guideline. These recommendations result from review of literature and practices current at the time of their formulation. This Best Evidence Statement does not preclude using care modalities proven efficacious in studies published subsequent to the current revision of this document. This document is not intended to impose standards of care preventing selective variances from the recommendations to meet the specific and unique requirements of individual patients. Adherence to this Statement is voluntary. The clinician in light of the individual circumstances presented by the patient must make the ultimate judgment regarding the priority of any specific procedure.**

**Reviewed by** Clinical Effectiveness