

Lecture 24 – Amblyopia

(Steinman Chapter 9; Adlers 9th Edition Chapter 24)

AMBLYOPIA

Amblyopia is a condition in which the patient has poor vision due to *incomplete development of the visual system*. It is caused by some kind of deprivation during the sensitive period. Amblyopia is diagnosed by the presence of a subnormal best-corrected visual acuity, with *no sign of ocular disease or damage to the visual system*. **Amblyopia is usually found in just one eye, but in some cases a patient may be amblyopic in both eyes.**

Normal visual development requires **good image quality** on both retinas and **good correlation** between the images **during the sensitive period**. With this in mind, amblyopia may be classified according to the type of visual deprivation that led to the amblyopia.

Tychsen (Adler's Ch. 24) recognizes three categories of deprivation that may cause amblyopia:

- pattern deprivation (light but no image)
- optical defocus (poor image quality)
- strabismus (poor correlation)

For each of these, the severity of any resulting amblyopia depends on the:

- magnitude of the deprivation
- time of onset (earlier is worse)
- duration of the deprivation

Pattern deprivation

Among the three types of deprivation, pattern deprivation is the most severe. **(Steinman refers to this as stimulus deprivation amblyopia.)** The most common cause is an infantile cataract that scatters light and prevents formation of an image on the retina. Light reaches the retina, but all spatial detail (high and low spatial frequencies) is lost. **This could also be caused by conditions such as congenital ptosis, or a corneal opacity.**

Quoting from Tychsen (Adler's Ch. 24, p. 830)

Pattern deprivation in the first 3 postnatal months produces profound and permanent reductions in spatial acuity, typically to the level of legal blindness. Deprivation during this period is highly correlated with later development of sensory deprivation nystagmus ...Deprivation in the human before the age of 30 months for a period of at least 3 months leads to a visual acuity of less than 20/200. Deprivation commencing between the ages of 30 months and 8 years differs only in that vision is reduced at a slower rate and is more likely to respond to subsequent occlusion therapy. Clinical reports over the last decade have shown that if surgery and optical correction are performed in the first 3 months of life, good visual acuity can be preserved (e.g., acuity of 20/50 or better) even in the face of dense cataracts. Delay of surgery beyond the third postnatal month greatly decreases the probability that acuity will be better than 20/200 and greatly increases the risk of sensory deprivation nystagmus.

Research has established three basic requirements for successful treatment and prevention of amblyopia, in cases of **pattern deprivation**:

- surgery before the age of 4 months
- optical correction, and
- reverse occlusion **(of the non-deprived eye)** 75-90% of the time.

Optical defocus

Optical defocus is less damaging to visual development than complete pattern deprivation because defocus removes high spatial frequencies (fine detail, sharp edges, etc.) from the retina image, but low

spatial frequencies (large shapes) remain. Spherical defocus causes a general amblyopia but high astigmatism can cause a *meridional amblyopia*.

The most common cause of this kind of amblyopia is anisometropia, and except in the case of very high myopia, the more hyperopic eye is usually the one that becomes amblyopic. The degree of amblyopia is related to the age of onset, duration before correction and amount of optical blur. Again, referring to Tychsens,

The prevalence of amblyopia increases with increasing amounts of anisometropia. Studies of anisometropic patients found an amblyopia prevalence of 100% in hyperopes with 4.0 diopters of anisometropia and myopes with 6.0 diopters of anisometropia. The prevalence was still 50% for hyperopes with 2.5 diopters and myopes with 4.0 diopters.

Steinman refers to two kinds of amblyopia within this category.

- *Anisometropic amblyopia* - significantly different refractive errors between the two eyes, as discussed above.
- *Refractive or isometropic amblyopia* - a large, nearly equal uncorrected refractive error in both eyes. For example both eyes may be extremely myopic (-9 diopters or more) or hyperopic. In this case, the patient might develop a bilateral amblyopia.

The best way to prevent this kind of amblyopia is to correct the refractive error as early as possible. Reverse occlusion also helps to treat unequal visual acuities. A large scale study of over 3,000 children by Atkinson showed that among children with more than +2.50 diopters of hyperopia or astigmatism, 75% became amblyopic without treatment, but among those who were corrected, only 23% developed amblyopia (Tychsens, p. 831).

Steinman points out that, it may be better not to fully correct the refractive error of a small child. On average, most young eyes are hyperopic, but by a process called **emmetropization**, the visual system senses the hyperopic blur and **causes the eye to grow and develop** toward emmetropia. If we completely correct the blur, it may disrupt the natural emmetropization process, and leave the child with a large refractive error. It maybe advantageous therefore, to under-correct hyperopic refractive errors.

Strabismic amblyopia

Strabismus can lead to amblyopia since the eyes receive *uncorrelated retinal images*. This hinders development of binocular neurons beginning in area V1. Rivalry between the input of the two eyes usually leads to suppression, which can then interfere with the development of synaptic connections from the deviating eye. The result is arrested development of visual function (including visual acuity) and amblyopia.

In addition, visual deprivation, such as optical defocus, can hinder the development of normal oculomotor alignment and this can then lead to strabismus and further visual deprivation. **Accommodative esotropia is one example.**

Amblyopia is seen in about half of strabismic infants. Those who are not amblyopic have presumably learned to alternately fixate.

VISUAL ANOMALIES ASSOCIATED WITH AMBLYOPIA

Spatial Vision

Most patients with amblyopia have reduced contrast sensitivity, in addition to poor visual acuity. The visual anomaly can differ, however if the amblyopia is caused by strabismus or optical defocus. Strabismic amblyopes tend to have poor contrast sensitivity in the central visual field only, but normal peripheral contrast sensitivity. Optical-deprivation amblyopes, on the other hand, tend to have poor contrast sensitivity **across the entire** visual field.

Also, depending on the **magnitude of the defocus, optical-deprivation** amblyopes tend to have poor contrast sensitivity for high spatial frequencies only.

Luminance summation

In persons with normal binocularity, pupils are about 30% smaller with binocular viewing than with monocular viewing. This is an indication of summation of the input from the two eyes. In amblyopia, this effect is less pronounced, indicating a less complete summation of luminance input from the two eyes. Persons with poorer stereopsis appear to have less effective summation. The reduced summation is thought to be at the cortical level and not in the retina.

Pulfrich phenomenon

Some patients with amblyopia are able to appreciate the Pulfrich effect without using a ND filter. It appears that electrical signals are conducted at a slightly slower velocity in the geniculate or cortical neurons associated with the amblyopic eye.

Spatial distortions

Strabismic amblyopes also tend to have distorted space perception, as illustrated in **Steinman Fig. 9-8**. This causes objects to appear distorted and causes an abnormal sense of visual direction. This may be **the cause of the poorer-than-normal vernier acuity and the crowding effect, which seen in strabismic but not optical deprivation amblyopes.**

The **crowding effect** is described as difficulty reading a letter when it is surrounded by other letters or contours. For this reason, when testing visual acuity on amblyopes, you may measure a better visual acuity using isolated letters than if you use a single line or the entire chart. Also, when reading a row of letters, strabismic amblyopes can usually read the first and last letters more easily than the middle letters.

The space distortion is not seen in optical-deprivation amblyopes. In addition amblyopes have abnormal eye movements, poor motion perception, abnormal accommodation, and of course, reduced, or no stereopsis. **They may also have eccentric fixation, the topic of the next lecture. Quoting from Steinman (p. 286),**

Whatever the cause of these distortions, they cause the amblyopic eye to make erroneous judgments about the positions of objects in space. When spatial distortions are coupled with the typical erratic eye movements of amblyopies, strabismic amblyopes see the world with their amblyopic eye as a place where objects in particular parts of the visual field are constantly changing shape and position.

Normal visual function

Not all visual functions are decreased in amblyopic eyes. Optical-defocus deprivation and strabismic amblyopes usually have normal light perception (V-lambda functions), normal dark adaptation and normal color vision. These visual functions primarily depend on normal retinal development and occur early in life.

AMBLYOPIA THERAPY

In order to be effective, amblyopia therapy must be performed as early as possible within the sensitive period, which is thought to extend up to about age 8 or 9 in humans. In some individuals, treatment after age 9 may still help restore some visual function to the amblyopic eye. **Recall the case of "Stereo Sue."** She, fortunately was not amblyopic, but had an alternating strabismus and suppression that interfered with the development of normal binocular vision and stereopsis. In her case, she had good visual acuity in each eye and experienced a dramatic improvement in binocular vision after starting VT as an adult. **(Mention Saunya's recent case.)**

Steinman also mentions (p. 289) **the case of a meridional amblyope who was first corrected as an adult, and immediately noticed an improvement. The patients had "uncorrected high-monocular astigmatism**

treated with a balance lens his entire life, with no depth perception. After the patient's astigmatism was finally corrected, he stood up, looked down at his feet and remarked, "I'd never noticed my feet being above the floor like that before."

In general, amblyopia treatment should include both of the following.

- Optical correction to provide a high quality retinal image to the amblyopic eye.
- Reverse occlusion of the better eye.

The objective is to stimulate stronger synaptic connections in the visual cortex for neurons associated with the amblyopic eye, and give them a competitive edge by weakening input from the dominant eye.

If the patient has strabismus, it will also be necessary to restore correct ocular alignment if the patient is to recover normal binocular vision. In the accommodative esotrope, this is usually accomplished by the spectacle correction alone. Vision therapy may help to restore alignment. If these fail, surgery may also be needed.

Complete reverse occlusion may be accomplished by patching the better eye. Some doctors prefer partial occlusion, which may be accomplished using atropine to cycloplege the better eye. Another option is to degrade the better eye's image by putting semi-transparent tape over the spectacle lens of the better eye.

Some doctors believe that it may be beneficial to stimulate the amblyopic eye with flashing lights or high contrast moving patterns, but other doctors disagree and consider this treatment ineffective.

NEUROANATOMIC ANOMALIES IN AMBLYOPIA

Animal studies have shown that visual deprivation causes observable anatomic changes and a loss of physiological function. The following main points summarize these discoveries.

- In optical defocus deprivation, most of the structural anomalies are seen in neurons of the parvocellular, rather than magnocellular system. Those are the neurons associated primarily with foveal vision and high spatial frequencies.
- In complete pattern deprivation, deficits are seen in both the parvo and magno systems.
- Neurons associated with the temporal hemi-retina (non-crossing fibers) are more severely affected by visual deprivation than those associated with the nasal hemi-retina.
- The neuronal atrophy associated with deprivation is not simply due to disuse, but is caused by competitive suppression.
- Anomalies in the visual pathways are more pronounced at higher-level neurons.
- Treatment is most effective at changing higher- rather than lower-level neurons.

Retinal and geniculate structural changes

Following pattern, defocus or strabismic deprivation, no anatomic or physiological anomalies of the retinal ganglion cells are apparent. The ERGs of amblyopic eyes are also normal. In contrast, you can expect the VER to be reduced in amblyopia.

In the LGN, some shrinkage of cells is seen in layers associated with the deprived eye. In the case of pattern deprivation, shrinkage is seen in both the parvo and magnocellular layers. This could be caused directly by deprivation, or it could be secondary to cortical atrophy. In optical defocus deprivation and strabismus, cell shrinkage is limited to the parvocellular layers

Primary visual cortex

Quoting from Tychsen (Adler's p. 835)

Pattern deprivation produced by monocular lid suture in the infant monkey causes a decrease in the width of the ocular dominance columns driven by the deprived eye. The change in width reflects the fact that cortical cells that should have been driven by the deprived eye shifted allegiance so that the overwhelming majority are driven by the dominant eye.

The reduction in ocular dominance column width is closely related to the degree of deprivation, and if corrected early enough, a normal column width can be restored. The correction must include reverse occlusion, and recovery is proportional to the amount of time occluded.

The critical period appears to be shorter for the initial levels of the primary visual cortex (layer IV), and longer for the higher-level neurons in levels II and III of V1.

Of the three kinds of deprivation, form deprivation is the most severe, followed by strabismus and then optical defocus deprivation. **Of course this depends on many factors, such as the time of onset, magnitude, and duration of the deprivation.**

Form deprivation >> strabismus >> optical blur

This is reflected in the changes in the ocular dominance columns and shows that complete decorrelation of retinal images **(caused by strabismus)** is a greater hindrance to binocular development than the competition between a clear and blurred image.

As with the LGN, the effects of optical defocus are limited to the parvocellular regions of the visual cortex. Those cells show a lower-than-normal sensitivity to high spatial frequency stimuli (**Adler's Fig. 24-67**).

In meridional amblyopia, neurons also show reduced sensitivity to high spatial frequency stimuli, but only if they are in the correct orientation. Little research has been done to study the effects of deprivation on the higher visual processing areas.

Tychsen (Adler's p. 837) emphasizes the importance of a similar, or competitive input from the two eyes, in order for the visual cortex to develop normal binocular function.

The neural mechanism for binocular suppression is usually explained along the lines proposed by Hebb in 1949. Hebb postulated that learning at any site in the central nervous system is proceeded by a process of synapse sustenance or elimination, which was in turn based on correlations in firing patterns between presynaptic and postsynaptic neurons. In the visual cortex, for example, right eye and left eye inputs converge on a binocular cell. The binocular cell will tend to be driven by the dominant eye. If the firing pattern of the nondominant eye repeatedly fails to correlate with the firing pattern of the binocular cell, the nondominant synapses are not sustained and wither away.

EPIDEMIOLOGY OF BINOCULAR ANOMALIES

According to Tychsen, up to age 40, amblyopia causes poor vision in more people than all ocular diseases or trauma combined.

The prevalence of amblyopia is about 5% in the US or about 15 million persons. Half of these people have a visual acuity of 20/80 or worse in the amblyopic eye. Strabismus also has an incidence of 4-7%, depending on the test conditions and type of strabismus.

Both strabismus and amblyopia are more common among low-birth-weight or premature infants (Table 1). These infants are particularly vulnerable to hypoxia, which can stunt growth and development of the visual cortex. In full term infants whose mothers smoke, abuse alcohol or drugs, the risk of strabismus and amblyopia is similar to that of premature babies.

Heredity may also contribute, since there is a 4-6 times greater prevalence of amblyopia and strabismus among children who had a parent with amblyopia and strabismus.

Table 1. Prevalence of strabismus by birth weight.

Birth weight (g)	Birth weight (lbs)	Prevalence (%)
3100+	7+	5
<2,500	<5.5	20
<1,500	<3.3	35