Asymmetric Hearing During Development: The Aural Preference Syndrome and Treatment Options

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Deafness affects ~2 in 1000 children and is one of the most common congenital impairments. Permanent hearing loss can be treated by fitting hearing aids. More severe to profound deafness is an indication for cochlear implantation. Although newborn hearing screening programs have increased the identification of asymmetric hearing loss, parents and caregivers of children with single-sided deafness are often hesitant to pursue therapy for the deaf ear. Delayed intervention has consequences for recovery of hearing. It has long been reported that asymmetric hearing loss/single-sided deafness compromises speech and language development and educational outcomes in children. Recent studies in animal models of deafness and in children consistently show evidence of an “aural preference syndrome” in which single-sided deafness in early childhood reorganizes the developing auditory pathways toward the hearing ear, with weaker central representation of the deaf ear. Delayed therapy consequently compromises benefit for the deaf ear, with slow rates of improvement measured over time. Therefore, asymmetric hearing needs early identification and intervention. Providing early effective stimulation in both ears through appropriate fitting of auditory prostheses, including hearing aids and cochlear implants, within a sensitive period in development has a cardinal role for securing the function of the impaired ear and for restoring binaural/spatial hearing. The impacts of asymmetric hearing loss on the developing auditory system and on spoken language development have often been underestimated. Thus, the traditional minimalist approach to clinical management aimed at 1 functional ear should be modified on the basis of current evidence.

Deafness is one of the most common congenital impairments.\textsuperscript{1,2} Newborn hearing screening programs, implemented in many countries, have decreased the age at diagnosis of hearing loss. When hearing loss occurs in only 1 ear, the screening result may be overlooked or dismissed as unimportant, particularly when hearing in the opposite ear is normal (unilateral or single-sided deafness). The consequence will be a failure to intervene until long after major developmental effects have set in, which causes significant negative clinical implications. Screening programs will also miss children who acquire deafness in 1 ear from infection, trauma, or worsening of preexisting hearing loss.\textsuperscript{3–6} Acquired unilateral deafness can go unidentified until educational, social, or other impairments push families and caregivers to seek medical consult. Because the prevalence of permanent unilateral hearing loss in neonates is reported to vary from 0.45 to 2.7 in 1000,\textsuperscript{7,8} and estimates in school-aged children range from 30 to 56 in 1000,\textsuperscript{9,10} awareness of medical
professionals, and especially of pediatricians, to this hearing disorder is of crucial importance.

Asymmetric hearing loss can also be established in children who have profound hearing loss in both ears by treating only 1 side. Since the appearance of cochlear implants (CIs) in clinical medicine, this therapy for profound deafness has become very effective.11 Of the >100 000 children who presently use CIs worldwide,11 the majority have bilateral deafness but are only implanted in 1 ear12; they are, in effect, children with asymmetric hearing loss.

In this State-of-the-Art Review, we present evidence from basic and applied neuroscience, audiology, and otology that points to the existence of an impairment of the central representation of the poorer hearing ear if developmental asymmetric hearing is left untreated for years. First, we review the current state of the problem as viewed in the clinic. Next, we consider the background from well-controlled animal models, in which investigations have ranged from defined areas of the brain to individual neurons. A review of evidence from human brain imaging and behavioral studies complement the picture by highlighting effects of single-sided hearing in children. The combined data support our contention that a preference for 1 ear is established biologically, functionally, and subjectively from asymmetric hearing in early development. This “aural preference syndrome” requires rapid diagnosis and intervention.

CURRENT STATE OF THE PROBLEM

One ear alone carries only limited information regarding locations of sound sources. Without this information, hearing is degraded in adverse listening conditions. Some rooms pose particular problems because acoustic sound waves easily bounce between the walls, floor, and ceiling, adding reflections that are difficult to distinguish from the original sound. Other situations are challenging because >1 sound source is present. Many people could be speaking at a time such as in a typical cocktail party.13,14 For children, common complex listening environments include classrooms, playgrounds, and school hallways where they spend much of their daily life. These can be more spatially dynamic than the “cocktail party” example because both the listener and his/her peers tend to be on the move.

Hearing from 2 ears (binaural) allows precise localization of sound sources. Time and level differences between the ears are initially detected and evaluated in the auditory brainstem and midbrain.13 The listener uses these cues to separate and distinguish between sound sources in space, thereby improving the signal-to-noise ratio for complex sounds (binaural unmasking) and separating original sounds from their reflections (precedence effect).15 Additional benefits of binaural hearing are that the ear closer to the sound source can receive up to 20 dB louder input than the other ear, providing an advantage for speech comprehension (better ear or head shadow effect) and an improvement in hearing sensitivity by ~3 to 10 dB, which provides increased accessibility to sound (binaural summation/redundancy effect or diotic benefit). Although the pinna (outer ear) can provide some localization ability from 1 ear alone by using spectral cues,16,17 it is less precise than with binaural hearing and works best if the sound is broadband (containing many frequencies) and is familiar to the listener.

Without normal binaural hearing, individuals with asymmetric hearing loss have impaired sound localization abilities, particularly in the hemifield of the impaired ear,18 and compromised speech understanding in noise.19,20 Deficits in the development of speech, language, and cognition are well recognized in children with unilateral deafness,21–28 with reports of increased effects for right-eared impairments.19,29,30 A recent large-cohort study indicated lower mean vocabulary, verbal IQ, full-scale IQ, and oral language scores in children with unilateral hearing loss compared with normal-hearing sibling controls.20 These children have high risks of educational problems, including repeating at least 1 grade and/or receiving individualized educational assistance.31–36 Moreover, behavioral problems are more prevalent.37 Individuals with asymmetric hearing loss perceive themselves to have significant handicaps38 and exhibit reduced quality-of-life scores compared with normal-hearing peers.39 Importantly, these issues are not captured by a typical clinical hearing test (audiogram), which measures sensitivity to sound in a quiet situation.

AUDITORY PROSTHESSES PRESENTLY USED TO AID ASYMMETRIC HEARING LOSS

To date, treatment approaches for unilateral hearing loss range from “watchful waiting” to hearing rehabilitation by means of a variety of hearing devices, as shown in Fig 1, depending on the child’s age, degree and type of hearing loss, and listening environment. These devices include the following: a CI (Fig 1A), a hearing aid (Fig 1B), a bone-anchored hearing aid (RAHA) (Fig 1C), and a personal assistive listening device (Fig 1D).

The most common auditory prosthetic is the hearing aid, which primarily amplifies sound so that it is audible to the impaired ear (Fig 1B). Although fitting a hearing aid to the ear with hearing loss has the potential of providing bilateral stimulation, evidence for effectiveness is limited to small groups40 and is predominantly based
Auditory prostheses worn by children. A, CIs are indicated for ears with severe-to-profound deafness. Candidacy for cochlear implantation in children involves a comprehensive assessment of the child, including radiologic assessment of the cochlea and auditory nerve, medical suitability for surgery, confirmation that hearing aids do not provide adequate benefit, realistic expectations of the child/family, and enrollment in an appropriate educational/therapy program. The external equipment is shown. The ear-worn piece includes a microphone to pick up sound and a sound processor that analyzes the sound for frequency and intensity over time. This information is sent to the internal equipment through FM signals via the round transmitting coil, which sits on the child’s head. It stays in place with a magnet that is attracted to another magnet in the internal device. The internal device delivers electrical pulses to stimulate the auditory nerve. B, A hearing aid is shown as worn on a child’s head. Sounds are picked up by a microphone and amplified by gains specific to the child’s hearing loss. The amplified sounds are sent via a tube into an earmold (here in blue) to the child’s ear. For high-gain hearing aids, the earmold must seal sounds in the ear to avoid feedback (whistling caused by a leak of amplified sounds back into the hearing aid microphone). C, A BAHA is shown. The internal device vibrates the skull to stimulate fluid movement in the cochlea. Acoustic sound is picked up by a microphone on the external equipment and sent to the internal device through a direct connection (percutaneous abutment) or magnetic connection as in the device shown. The device can also be secured by a soft band of elastic placed around the head. D, Two parts of an FM system are shown. The equipment shown on the desk contains a microphone to be worn by a speaker (ie, a teacher) attached to a transmitter. The sound is transmitted by FM signal to a receiver worn by the child in his better hearing ear (enlarged insert). The sound is sent to the ear via a tube connected to an earmold. Little amplification is required, and thus the earmold is not sealed and allows other sounds to enter the ear.

An option that should be considered for unilateral severe-to-profound hearing loss is a CI (Fig 1A), as performed in adults whose single-sided deafness was accompanied by intractable tinnitus. The use of CIs in individuals with single-sided deafness is supported by significant improvements in speech understanding in noise, localization ability, and subjective hearing benefits in adults (meta-analysis). Preliminary data on 3 children (aged 4, 10, and 11 years old) with noncongenital unilateral hearing loss after cochlear implantation provide evidence for binaural benefits.

An alternate solution is to send sound from the ear with severe-to-profound hearing loss to the better hearing ear by contralateral routing of signal (CROS) hearing aids. BAHAs have also been provided on the side of the impaired ear as an alternative to CROS hearing aids. Sounds from the impaired side are converted by the BAHA into skull vibrations that stimulate the opposite, better functioning cochlea. The use of BAHAs in children with profound unilateral hearing loss remains controversial, despite better speech understanding in background noise and significant improvements in quality of life. It is important to remember that any therapeutic approach that bypasses the impaired ear, such as the CROS aid and BAHA, will leave it untreated.

There are other assistive listening devices to help the child with asymmetric hearing loss. Frequency modulated (FM) technology has long been effectively used for increasing the signal-to-noise ratio in individuals with hearing impairments to hear from a distance, in noise, and in reverberant environments. FM systems transmit the input from a microphone worn by a speaker,
puberty. If the single-sided deafness was adjustable before, but not after, exhibited a postoperative dichotic ear patients with unilateral atresia implanted ear. Similarly, children who receive the second implant ear are significantly poorer than the outcomes with the first implanted ear. The difference in performance increases as the delay between implantation lengths and gains are particularly slow in children who receive the second implant after puberty. Similarly, patients with unilateral atresia exhibited a postoperative dichotic ear advantage in the nonatretic ear that was adjustable before, but not after, puberty. If the single-sided deafness occurs during adulthood, asymmetric performance after treating the deaf ear is not prominent. In a large study involving 2251 individuals with postlingual deafness, the implanted ear was not a predictive factor for outcomes: results were similar whether the ear with longer or shorter duration of deafness was implanted. This outcome difference between sequential bilateral implantation in adults and children provides evidence for a developmentally sensitive period for reorganization promoted by asymmetric hearing.

Long periods of asymmetric hearing in development also affect measures of binaural hearing after bilateral implantation. Whereas adults who became deaf after childhood perceive changes in both interaural level and timing cues, the latter cues are not detected either by children implanted sequentially or by adults whose deafness was present at birth. Nonetheless, both adults and children benefit from using bilateral over unilateral implants due to the reduction in the head shadow effect and binaural summation. Reducing the interimplant delay in children appears to improve sound localization and speech perception in noise, providing evidence for the importance of bilateral input during early auditory development.

**ASYMMETRIC HEARING LOSS IN EARLY DEVELOPMENT**

Clinical studies show that the use of a congenitally deaf ear may be limited later in life even when the other ear has early access to sound. In children who are bilaterally implanted in sequential procedures, outcomes of speech perception using the second-implant ear are significantly poorer than the outcomes with the first implanted ear. The difference in performance increases as the delay between implantation lengths and gains are particularly slow in children who receive the second implant after puberty. Similarly, patients with unilateral atresia exhibited a postoperative dichotic ear advantage in the nonatretic ear that was adjustable before, but not after, puberty. If the single-sided deafness occurs during adulthood, asymmetric performance after treating the deaf ear is not prominent. In a large study involving 2251 individuals with postlingual deafness, the implanted ear was not a predictive factor for outcomes: results were similar whether the ear with longer or shorter duration of deafness was implanted. This outcome difference between sequential bilateral implantation in adults and children provides evidence for a developmentally sensitive period for reorganization promoted by asymmetric hearing.

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**PHYSIOLOGY AND PATHOPHYSIOLOGY OF UNILATERAL HEARING**

The mammalian brain is immature at birth and can be manipulated by changes to the input it receives during development. The human auditory system continues to develop after birth, with auditory areas of the cerebral cortex requiring more than a decade of life to reach maturity. The circuitry for binaural processing is inborn and functional soon after hearing onset, but is sensitive to manipulation of hearing with sometimes lifelong consequences (reviewed in refs 13 and 78).

**Evidence for an Aural Preference Syndrome**

When unilateral deafness occurs in early development, the hearing ear becomes overrepresented in the auditory system. Novel auditory projections from the hearing ear are formed when experimental lesions are induced in animals near birth but do not occur in adult animals. Moderate unilateral hearing loss leads to similar, although less extensive, reorganization. The consequences for the opposite deaf ear remained unexplored until CIs entered the scene. In congenitally deaf white cats, CI stimulation revealed that complete (binaural) deafness reduces what has been termed the normal “aural preference” in the auditory cortices for the contralateral ear. As shown in Fig 2A, electrodes placed in the primary auditory cortex of a hearing cat reveal larger and faster responses to contralateral than ipsilateral ear stimulation. The wiring pattern of the afferent auditory system can explain this finding, in part, because the majority of fibers cross contralaterally at the brainstem. Congenital deafness changes this normal pattern; in bilateral deafness, the normal contralateral aural preference was reduced. (Fig 2B). In unilateral deafness, on the other hand, both cortical hemispheres showed larger and faster responses from the hearing ear (Fig 2B and D). In unilateral deafness, the other ear is “weaker” (less well represented in the auditory system). The early onset of unilateral hearing thus puts the deaf ear into a significant disadvantage for competition for cortical resources. These effects decreased with increasing age of onset of single-sided hearing, signaling an early sensitive period for unilaterally driven reorganization. Importantly, the responses for the deaf ear were not completely eliminated in the feline brain; this finding significantly differs from effects of monocular deprivation in which projections from the sighted eye extensively take over neurons originally responsive to the deprived eye or both eyes. In the case of unilateral deafness, even some (although substantially weakened) extraction of binaural cues was preserved at the cellular level, suggesting that the reorganized aural preference is not permanent and can potentially be reversed. This is why the term “aural dominance,” originally proposed for aural cortical representation in the auditory
Supporting evidence for a developmental change toward abnormal cortical aural preference is available in humans with asymmetric hearing who did not receive treatment. Various imaging techniques have been used, including electroencephalography and functional MRI. A number of studies documented a stronger than normal representation of the hearing ear at the cortex ipsilateral to the hearing ear in adult onset of single-sided deafness. This change resulted in a more symmetric activation of both auditory cortices from the hearing ear. The differences from normal were larger when the loss occurred in the right ear compared with the left ear. More extensive effects, including recruitment of additional cortical areas/networks, were observed in children with unilateral hearing loss, in line with the increasing effects found in younger cats and the language, cognitive, and educational challenges these children are reported to have (discussed in “Current State of the Problem” section above).

Further support for abnormal aural preference comes from children who receive bilateral CIs sequentially. Although expected cortical electrophysiologic responses were measured from the first implanted ear, responses from the second, later-implanted ear remained abnormal. The developing auditory brainstem, the first point of binaural integration in the ascending pathways, is already affected. Brainstem responses rapidly change over the first year of unilateral CI use in children with early-onset deafness. When the opposite (second) ear was implanted after this period (>1.5 years), the brainstem responses from this ear remained abnormally prolonged despite up to 3 years of bilateral implant use. By contrast, bilateral implantation with minimal or no delay in early development promoted symmetric maturation of the responses for both ears. Cortical responses of sequentially implanted children revealed a reduction in normal contralateral aural preference, consistent with the animal studies.

**FIGURE 2**
Summary of the results of cortical responsiveness from binaural hearing, binaurally congenitally deaf, and single-sided hearing cats, obtained by microelectrode mappings (>100 recording positions) of cortical local field potentials in the primary auditory cortex (field A1) evoked by CI stimulation. Shown are maximum positive amplitudes as a function of recording position. A, In a hearing control, similar to acoustic stimulation, electrical stimulation at the contralateral ear results in larger responses and shorter latencies (color denotes onset latency) compared with ipsilateral stimulation. Consequently, there is an aural preference for the contralateral ear: B, In a single-sided hearing cat if the hearing ear is the ipsilateral ear, the aural preference reverses: ipsilateral responses become larger and appear earlier (color). C, Summary of the binaural cats. Normal-hearing cats show a contralateral aural preference. In binaurally deaf cats, the contralateral aural preference is weakened but not reversed. D, In unilaterally hearing cats, aural preference reverses at the ipsilateral hemisphere to the hearing ear and stronger responses are observed for the hearing ear in both hemispheres. Rudimentary responsiveness for the deaf ear is, however, preserved. Thus, a “stronger” and a “weaker” ear effect results. Data and figures were modified from refs 91 and 90, respectively.
Importantly, this abnormal asymmetry was not found in children who received bilateral implants with <1.5 years of interimplant delay (short delay or simultaneous bilateral implantation). Protection against aural preference to 1 ear thus requires bilateral input during development.

The change in aural preference from the contralateral ear to preference for the hearing ear in both cats and children⁹¹,¹²² may reflect differential reorganization of inhibition and excitation in both hemispheres, i.e., hemisphere-specific reorganizations.⁸⁴–⁸⁶,⁹⁰,¹²³ Because of the earlier development of inhibitory synapses,¹²⁴,¹²⁵ there is a shorter sensitive period for the change in aural preference at the hemisphere ipsilateral to the hearing ear⁹¹ and a longer sensitive period for the hemisphere contralateral to the hearing ear.⁹⁰ In other words, single-sided deafness leads to an asymmetric brain that shows distinct adaptations at the 2 hemispheres,⁹⁰ which both result in boosting responses from the hearing ear. Stronger representation of the hearing ear in developmental single-sided deafness will lead to a biased input to higher-order cortical areas and cognition. Behaviorally, it is likely further aggravated by subjective factors such as an attentional bias toward the better-represented ear. In this context, the aim of treating asymmetric hearing loss is to prevent this reorganization.

**IMPORTANT FACTORS FOR A NEW TREATMENT OF ASYMMETRIC HEARING LOSS**

Single-sided hearing, due to reorganization toward the hearing ear, likely protects from hearing and language deficits associated with the completely deaf brain (reviewed in refs 126 and 127), including immature cortical circuits, cross-modal reorganization, and reduced plasticity (reviewed in refs 78 and 128). Initial acquisition of speech and language by children with single-sided deafness has made the hearing loss difficult to identify in the absence of neonatal hearing screening programs and has also fueled arguments against treatment. Yet, by the time challenges in spatial hearing and listening in noise have been found, these children often are school-aged,²¹,¹²⁹ long after many of the changes reviewed above have already occurred. The increased age/duration of deafness will thus limit the potential benefits of hearing aids, as already reported,¹³⁰ or of CIs. Treatment is thus important and cannot be delayed.

Despite the increased representation of the hearing ear in the brain, the representation of the deaf ear does not vanish completely (Fig 2). Moreover, residual sensitivity for binaural cues persists in cochlear-implanted humans,¹²⁰ in experimental animals with asymmetric hearing,⁷⁷,⁸⁷ and in congenital deafness.⁷⁵,⁹⁴ Thus, even in the worst condition (early onset, long duration of single-sided deafness), there is some hope for stimulating hearing in the deaf ear and establishing binaural hearing, with demonstrable benefits already realized.⁶⁴–⁶⁶,⁶⁸–⁷⁰,¹³¹–¹³⁴ On the other hand, these skills remain abnormal, reflecting persistent reorganization after single-sided hearing. Without focused training, 3 to 4 years of bilateral implant use was not sufficient to reduce the preference of the first-implanted ear.

**FIGURE 3**

A, EABR wave eV evoked by the CI-1 (right implant) and CI-2 (left implant) are at similar latencies to the BD in a child receiving both implants simultaneously. B, A period of unilateral CI use before bilateral cochlear implantation reduces wave eV latency evoked by CI-1 and the response from CI-2 remains delayed despite 2 years of bilateral CI use. The BD is delayed relative to the CI-1–evoked wave eV. C, CI-2–evoked wave eVs are significantly prolonged relative to CI-1 when the period of unilateral CI use exceeds 2 years. Plots were reprinted from ref 120, Fig 3. BD, binaural difference component; EABR, electrically evoked auditory brainstem response; eII, the second wave of the EABR; eIII, the third wave of the EABR; eV, the fifth wave of the EABR.
in the auditory cortices of children implanted sequentially with a long delay.\textsuperscript{122} Although these children learned to detect large changes in binaural timing cues after long periods of bilateral implant experience, they continued to judge input as coming from the side of their first implant more often than children receiving bilateral implants simultaneously.\textsuperscript{134} Furthermore, although speech perception was gained in the weaker ear, the progress was slow and did not match the stronger ear even after 5 to 9 years of implant use.\textsuperscript{58} Poor speech perception\textsuperscript{55} together with absent cortical binaural interaction\textsuperscript{135} in children receiving the second implant as adolescents suggest that there are continued difficulties in processing input from the second-treated ear. Overall, the data indicate that an early period of monaural hearing as brief as 1.5 years has long-lasting consequences.

**RECOMMENDATIONS FOR IDENTIFICATION AND TREATMENT OF ASYMMETRIC HEARING LOSS**

Combining the available evidence, we propose the existence of an "aural preference syndrome," characterized by a combination of following factors:

1. asymmetric hearing during development;
2. asymmetric speech understanding in each ear that is resistant to treatment (ie, persisting after compensation of the initial asymmetry); and
3. deficits in binaural hearing, including sound localization, resistant to therapy of the weaker ear.

Awareness of the problem is important. On the basis of recent evidence, a more aggressive approach to treating asymmetric hearing loss in children appears to be justified, with the following objectives:

1. early identification of hearing loss that is more pronounced in 1 ear than the other;
2. a reduction in asymmetric hearing by providing appropriate auditory prostheses* in each ear with limited delay; and

3. provision of auditory-based training to limit possible effects of “aural preference” for the stronger hearing ear.

**GAPS IN KNOWLEDGE**

The treatment of asymmetric hearing loss has traditionally occurred late or not at all. As this impairment becomes better recognized and more aggressively treated, we will be better able to define when aural preference becomes abnormal, to determine which treatment is most appropriate, and to delineate factors that contribute to the best outcomes of treatment. Timing of treatment will be essential and must consider both the age of the child and his/her hearing experience within the context of critical periods of development. More research on the mechanisms of plasticity and critical periods as well as the exact delineation of their limits in different species are required to understand the full potential for reversibility. For clinical purposes, further aspects require attention: Did the asymmetry of hearing exist after a period of bilateral deafness? Was the asymmetry experienced in early or later childhood and did the asymmetry progressively increase over time? Furthermore, how much asymmetry in hearing will lead to abnormal aural preference and can this condition be reversed during or after important stages of development? What minimal extend of the asymmetry may lead to aural preference? Finally, to what extent can the child’s hearing devices provide sufficiently symmetric hearing? For example, bimodal hearing (CI in 1 ear and a hearing aid in the other) provides benefits over unilateral listening but may not necessarily avoid or reverse asymmetric aural preference or provide accurate binaural cues.

The potential for reversing the preference for the stronger ear exists. After developmentally mild asymmetric hearing loss was restored in ferrets, localization training restored their spatial hearing abilities. Although long durations of bilateral implant use do improve some of the children’s ability to use both ears for listening, active training is likely necessary to overcome the significant developmental effects of previous unilateral hearing. Paradigms for training in children need to be developed. The treatment of asymmetric hearing loss must keep in mind that normal asymmetries between the ears do exist, with evidence in both normal-hearing and cochlear-implanted children of a “right ear advantage” for speech processing. Finally, the goal of establishing normally symmetric bilateral hearing in children is to promote binaural hearing. The use of independent devices and fitting paradigms that presently concentrate on the function of each device separately could be improved to provide more accurate binaural cues (eg, ref 147).

**SUMMARY: TREATMENT OF ASYMMETRIC HEARING LOSS**

On the basis of evidence of abnormal reorganization driven by single-sided hearing, a binaural simultaneous therapy should become the gold standard for early bilateral deafness. If asymmetric hearing has been identified, early restoration of hearing symmetry should be the goal with the use of appropriate auditory prostheses.

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*The specific auditory prosthesis appropriate to stimulate the impaired ear(s) will depend on the type and degree of hearing loss as reviewed above.

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Pediatrics; originally published online June 8, 2015;
DOI: 10.1542/peds.2014-3520

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