Ability of an Upright-Supine Test to Differentiate Skew Deviation From Other Vertical Strabismus Causes

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Objective: To determine the sensitivity and specificity of a new upright-supine test to differentiate skew deviation from trochlear nerve palsy and other causes of vertical strabismus in a large number of patients.

Methods: The study consisted of 125 consecutive patients who sought treatment from January 1, 2008, through December 31, 2010, for vertical strabismus of various causes: skew deviation (25 patients), trochlear nerve palsy (58 patients), restrictive causes (14 patients), and other causes (eg, myasthenia gravis and childhood strabismus) (28 patients). Twenty healthy participants served as controls. The deviation was measured by the prism and alternate cover test using a near target at ⅓ m in both the upright and supine positions. A vertical strabismus that decreased by 50% or more from the upright to supine position constituted a positive test result.

Results: The upright-supine test result was positive in 20 of 25 patients with skew deviation (sensitivity, 80%) but negative in all patients with trochlear nerve palsy, restrictive, or other causes (specificity, 100%).

Conclusions: The upright-supine test is highly specific for differentiating skew deviation from other causes of vertical strabismus. This test could be added as a fourth step after the 3-step test, and if the result is positive, neuroimaging should be considered if indicated clinically.

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SKEW DEVIATION IS VERTICAL strabismus caused by a supranuclear lesion[1-9] that disrupts the vestibulo-ocular reflex projections from the utricles in the inner ears to ocular motor nuclei (ie, the utriculo-ocular reflex).[6,7,10-13] It is typically caused by damage to the brainstem, cerebellum, or peripheral vestibular system (ie, the inner ear and its afferent projections).[4,7,11,14-17] Because the utricles lie roughly in the horizontal plane when the head is in the upright position, they normally detect static positions (tilts) of the head. In a previous study,[5] it has been observed that the magnitude of vertical misalignment and ocular torsion in skew deviation is dependent on head position; it decreased substantially when patients changed from an upright to a supine position. Conversely, in patients with trochlear nerve palsy, the vertical strabismus and ocular torsion changed minimally between these 2 positions.[5] On the basis of this observation, we sought to devise a simple, new bedside upright-supine test to differentiate skew deviation from trochlear nerve palsy and other causes of vertical strabismus and to determine the sensitivity and specificity of this test in a large number of patients. Preliminary results were presented in a workshop and its published proceedings.[18]

METHODS

STUDY PARTICIPANTS

The medical records of all adult (≥18 years of age) and pediatric (<18 years of age) patients who sought treatment for vertical strabismus at the University Health Network–Toronto Western Hospital, The Hospital for Sick Children, and private offices in Toronto, Ontario, Canada, from January 1, 2008, through December 31, 2010, were reviewed. The patients' clinical history, ophthalmic and neurologic findings, and test results (eg, tests for myasthenia gravis, thyroid ophthalmopathy, or other orbital diseases) were recorded.

Skew deviation was diagnosed in patients who fulfilled all the following clinical criteria: (1) a vertical misalignment that is comitant, incomitant, or alternating (ie, positive or negative 3-step test result[19]) with or without head tilt posture or fundus torsion[4]; (2) no deficiency of depression in adduction; (3) presence of associated symptoms and signs suggestive of brainstem or cerebellum involvement;

Table. Clinical and MRI Findings in Patients With Skew Deviation

Patient No.	Hypertropia (Upright), PD	Hypertropia (Supine), PD	Change in Hypertropia <5%	MRI Findings	Clinical Features (in Addition to Skew Deviation)
1	9 LHT	12 LHT	33[a]	Pilocytic astrocytoma in midbrain tegmentum	Vertical gaze palsy, bilateral ptosis
2	5 RHT	2 RHT	–60	Hemosiderin deposits in brainstem, intraventricular hemorrhage, and periventricular leukomalacia	Ataxia, cerebral palsy
3	5 RHT	5 RHT	0[a]	Left paramedian midbrain infarct extending into thalamus	Vertical gaze palsy, facial nerve palsy, ataxia
4	6 RHT	3 RHT	–50	Pineal cyst	Vertical gaze palsy, bilateral abduction deficit
5	5 RHT	No HT	–100	Pilocytic astrocytoma in midbrain tegmentum	Vertical gaze palsy, convergence-retraction nystagmus, convergence insufficiency, light-near dissociation of pupils
6	12 RHT	No HT	–100	Pilocytic astrocytoma in left middle cerebral peduncle extending to left medulla	Gaze-evoked nystagmus, ataxia
7	10 RHT	2 RHT	–80	Left cerebellar hemispheric hemorrhage extending into mesial aspect of right cerebellar hemisphere	Hypometric saccades, saccadic pursuit, gaze-evoked nystagmus, head tremor, ataxia
8	4 LHT	No HT	–100	Hemosiderin deposits in left pons	Left internuclear ophthalmoplegia
9	8 RHT	4 RHT	–50	Hemorrhage in right dorsal midbrain and right cerebellum after a car crash	Vertical gaze palsy
10	7 LHT	No HT	–100	Medulloblastoma involving cerebellum and medulla bilaterally	Facial nerve palsy, ataxia
11	2 LHT	2 LHT	0[a]	Pilocytic astrocytoma involving cerebellum and medulla bilaterally	Gaze-evoked nystagmus, facial nerve palsy, ataxia, alternating skew deviation on lateral gaze
12	3 RHT	No HT	–100	Left cerebellar hemorrhage from arteriovenous malformation	Gaze-evoked nystagmus, ataxia
13	8 LHT	1 LHT	–88	Left clival chordoma	Right-sided weakness and spasticity, ataxia
14	2 LHT	No HT	–100	Delayed hemorrhage in pons and medulla after combined radiation and chemotherapy for acute lymphoblastic lymphoma	Ataxia, facial nerve palsy
15	2 LHT	No HT	–100	Bilateral cerebellar degeneration	Ataxia
16	5 RHT	1 RHT	–80	Demyelination involving cerebellar peduncles and brainstem	Gaze-evoked nystagmus, ataxia
17	2 RHT	1 RHT	–50	Astrocytoma involving left medulla and left middle cerebellar peduncle	Ataxia
18	12 LHT	6 LHT	–50	Fourth ventricular ependymoma involving medulla and right pons	Ataxia
19	8 RHT	4 RHT	–50	Right thalamic infarct	Ataxia
20	12 LHT	No HT	–100	Fourth ventricular medulloblastoma involving cerebellum	Ataxia
21	8 RHT	8 RHT	0[a]	Infarct in right thalamus, midbrain, and right cerebellar hemisphere	Ataxia
22	18 RHT	8 RHT	–56	Infarct in left pons and thalamus	Left-sided weakness and numbness
23	3 RHT	2 RHT	–33[a]	Left cerebellar arteriovenous malformation with vasogenic edema in the midbrain	Vertical gaze palsy, ataxia
24	16 LHT	5 LHT	–69	Hemorrhage in right thalamus extending to pons and midbrain bilaterally	Vertical gaze palsy, convergence-retraction nystagmus, light-near dissociation of pupils
25	5 RHT	No HT	–100	Demyelination involving brainstem	Bilateral internuclear ophthalmoplegia

Abbreviations: LHT, left hypertropia; MRI, magnetic resonance imaging; PD, prism diopters; RHT, right hypertropia.
[a] Negative upright-supine test result.

and (4) presence of a lesion in the posterior fossa, as confirmed by magnetic resonance imaging (MRI). Twenty-five patients (14 adults and 11 children) were identified. Their mean (SD) age was 26.3 (19.5) years (range, 4-65 years). Eleven were female. The underlying causes included neoplasm (9 patients), hemorrhage (7 patients), infarct (4 patients), demyelination (2 patients), intraparenchymal edema (1 patient), pineal cyst (1 patient), and cerebellar degeneration (1 patient). Their detailed clinical and MRI findings are given in the **Table**. Two (patients 7 and 12) of the 25 patients with skew deviation had a positive 3-step test result. Both of them had acute onset of vertical diplopia, ataxia, and other neurologic symptoms as a result of a hemorrhage in the cerebellum. None of the 25 patients in the current series had a nystagmus in the primary position.

Unilateral peripheral trochlear nerve palsy was diagnosed in patients who fulfilled all of the following clinical criteria[19-21]: (1) deficient depression of the hypertropic eye in adduction; (2) incomitant hypertropia that increased with adduction of the hypertropic eye and with head tilt toward the hypertropic eye, with or without excyclotorsion (ie, positive 3-step test result); (3) absence of any other neurologic symptoms and signs; and (4) absence of any intracranial lesion on MRI. Fifty-eight patients (47 adults and 11 children) were included. Their mean (SD) age was 39.3 (19.5) years (range, 4-77 years). Twenty-three were female.

Restrictive strabismus was diagnosed based on a positive forced duction test result. In addition, all patients exhibited a compressed pattern of motility in the affected eye that did not obey the muscle sequelae of paralytic strabismus on the Hess/Lees chart.

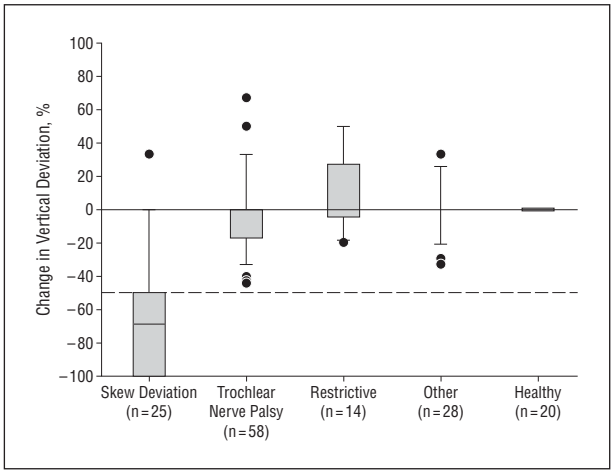

Figure. Percentage changes in vertical deviation from the upright to supine position for each group. A positive percentage change indicates an *increase* in vertical deviation from the upright to supine position, whereas a negative percentage change indicates a *decrease* in vertical deviation from the upright to supine position. The horizontal dashed line represents the *50% decrease threshold* used to define a positive upright-supine test result. The bottom and top of the box indicate the 25th and 75th percentiles, respectively, and the band near the middle of the box indicates the 50th percentile or the median (the median and 75th percentile in the trochlear nerve palsy group, the median in the restrictive group, and the median and 25th and 75th percentiles in the healthy groups are 0%). The error bars indicate the 10th and 90th percentiles (in the skew deviation group, the 25th and 10th percentiles are –100% and the 90th percentile is 0%). Black circles indicate outliers.

Fourteen patients (10 adults and 4 children) were identified in this category, including those with scleral buckle that caused muscle or soft-tissue entrapment (5 patients), orbital fracture with muscle entrapment in the fracture site (4 patients), Graves disease (3 patients), and Brown syndrome (superior oblique tendon sheath syndrome; 2 patients). The mean (SD) age was 46.7 (26.3) years (range, 7-81 years). Five were female.

The other causes of vertical strabismus included conditions that were not attributable to any of these diagnoses. Twenty-eight patients (10 adults and 18 children) were identified, including those with myasthenia gravis (2 patients), oculomotor nerve palsy (1 patient), strabismus after cataract surgery (1 patient), monocular elevation deficit (1 patient), and vertical strabismus that occurred in the context of typical childhood strabismus (23 patients; eg, inferior oblique muscle overaction, dissociated vertical deviation, partially accommodative esotropia, and intermittent exotropia). The mean (SD) age was 20.9 (21.3) years (range, 4-81 years). Eighteen were female.

Twenty healthy individuals (mean [SD] age, 33.9 [18.4] years; age range, 4-70 years; 10 female), without any vestibular, neurologic, or eye diseases, served as controls. The research protocol was approved by the research ethics boards of the University Health Network and The Hospital for Sick Children and adhered to the tenets of the Declaration of Helsinki.

MEASUREMENT OF VERTICAL DEVIATION

The magnitude of vertical strabismus was measured by the prism and alternate cover test. While sitting upright with the head erect (participants were not allowed to adopt their usual abnormal head posture, if present), the participant fixated on a single-letter optotype (12-point font size) located ⅓ m away in the midsagittal plane at eye level. Prisms of increasing power were placed over the deviated eye while the cover alternated between the eyes. The highest prism strength where no refixation movement occurred was recorded in prism diopters (PD). The test was repeated with the participant in a supine position.

STATISTICAL ANALYSIS

The primary outcome measure was the percentage change in deviation measured from the upright to supine position. The percentage changes for all 5 groups were compared using analyses of variance. Significant effect was analyzed further using post hoc Tukey honestly significant difference tests. All statistical analyses were performed using the SAS statistical software, version 9.2 (SAS Institute Inc, Cary, North Carolina). The significance level was set at $P<.05$.

On the basis of the results of a previous study,[5] a positive upright-supine test result was defined as a 50% or greater *decrease* in the vertical deviation measured from the upright to supine position. *Sensitivity* of the upright-supine test was calculated by dividing the number of patients with skew deviation who exhibited a positive result by the total number of patients with skew deviation. *Specificity* was calculated by dividing the number of patients with vertical strabismus other than skew deviation (ie, trochlear nerve palsy, restrictive strabismus, and other causes combined) who exhibited a negative result by the total number of patients with vertical strabismus other than skew deviation.

RESULTS

The **Figure** shows the percentage change in vertical deviation from the upright to supine position for each group. A positive percentage change indicated an *increase* in vertical deviation from the upright to supine position, whereas a negative percentage change indicated a *decrease* in vertical deviation from the upright to supine position. The mean (SD) changes in vertical deviation were –63.3% (39.0%) in skew deviation, –2.8% (21.5%) in trochlear nerve palsy, 8.4% (23.0%) in restrictive strabismus, –0.6% (15.5%) in other causes of vertical strabismus, and 0% in healthy controls (analysis of variance, $P<.001$). Post hoc Tukey honestly significant difference tests revealed that patients with skew deviation exhibited a significantly different mean percentage change in vertical deviation when compared with each of the other groups ($P<.001$). No significant differences were found among patients with trochlear nerve palsy, patients with restrictive strabismus, patients with other causes of vertical strabismus, and healthy controls.

In patients with skew deviation, the deviation disappeared completely (ie, 100% decrease) in 9 of 25 patients (36.0%) and decreased 50% or more but less than 100% in 11 of 25 patients (44.0%) when changing from the upright to supine position. The mean (SD) decrease in vertical deviation for these 20 patients with a positive upright-supine test result was –79.1% (22.1%). Of the remaining 5 patients with skew deviation who had a negative upright-supine test result, 3 had no change (1 had a right hypertropia of 5 PD, 1 had a left hypertropia of 2 PD, and 1 had a right hypertropia of 8 PD), 1 had a 33% decrease of right hypertropia from 3 PD upright to 2 PD supine, and 1 had a 33% *increase* of left hypertropia from 9 PD upright to 12 PD supine. Four of these 5 patients had a lesion that involved the midbrain (1 had a pilocytic astrocytoma with vertical gaze palsy and bilateral ptosis; 1 had a midbrain infarct with vertical gaze palsy, facial nerve palsy, and ataxia; 1 had a lacunar infarct in the thalamus, midbrain, and cerebellar hemisphere with ataxia; and 1 had a cerebellar arteriovenous malformation and vasogenic edema in the mid-

brain with vertical gaze palsy and ataxia). The fifth patient had an alternating skew deviation caused by a pilocytic astrocytoma that involved the cerebellum and medulla bilaterally. This patient also had gaze-evoked nystagmus, facial nerve palsy, and ataxia.

Overall, 20 of 25 patients with skew deviation had a positive upright-supine test result (ie, ≥50% *decrease* in the vertical deviation measured from the upright to supine position), giving the test a sensitivity of 80%. All patients with trochlear nerve palsy, restrictive strabismus, or other causes of vertical strabismus had a negative test result, giving the test a specificity of 100%. All healthy controls had a negative test result.

COMMENT

In this investigation, we found that skew deviation is the only condition in which the vertical misalignment *decreased by at least 50%* when the patients changed from an upright to a supine position. All other vertical strabismus, including trochlear nerve palsy, restrictive strabismus, oculomotor nerve palsy, myasthenia gravis, and vertical strabismus that occurred in the context of typical childhood strabismus, had a negative upright-supine test result. However, only 2 patients had myasthenia gravis, which is known to mimic nearly all other ocular motility disorders. Therefore, the test may not be 100% specific in all clinical populations. In addition, the study is limited because the examiners were not masked. Nevertheless, the high specificity of the upright-supine test in the current series of patients suggests that this test holds promise as an additional diagnostic step to aid the differentiation of skew deviation from other causes of vertical strabismus.

What is the physiologic basis of this new upright-supine test? Skew deviation has been attributed to an asymmetric disruption of the utriculo-ocular pathway.[6,7,10-13] The utriculo-ocular pathway originates from the otolithic receptors of the utricle in the inner ear, which project to the vestibular nuclei. The second-order neurons in the vestibular nuclei, in turn, project to the oculomotor and trochlear nuclei either directly via the brainstem (ie, a disynaptic pathway)[22,23] or indirectly via the cerebellum (ie, polysynaptic pathways).[24,25] Hence, skew deviation can occur at a variety of sites where damages cause an imbalance in the utriculo-ocular pathway. These damages include lesions in the *peripheral* vestibular organ or its nerve[2,26-28] and *central* lesions within the posterior fossa that involve the vestibular nuclei (eg, in the lateral medullary syndrome),[17,29] pons,[13,30] midbrain,[15,31-34] diencephalon,[35,36] or cerebellum.[7,37]

Normally, with the head upright, the utricles lie roughly in an earth-horizontal plane. When the head changes from an upright to a supine position during the upright-supine test, the orientation of the utricles changes from earth-horizontal to earth-vertical. This new orientation of the utricles with respect to absolute earth-vertical (gravity) may lead to a saturation or reduction in the overall afferent activities of the utriculo-ocular reflex such that any imbalance of utricular (otolithic) input is minimized. This, in turn, may lead to a reduction of vertical misalignment in skew deviation in the supine position. Conversely, in isolated unilateral peripheral trochlear nerve palsy and other causes of vertical strabismus, the utriculo-ocular pathway remains intact. Thus, the magnitude of vertical deviation does not change significantly between the upright and supine positions. We observed a few patients with trochlear nerve palsy who had a larger amount of change in vertical deviation between positions (ie, the 4 outliers in the Figure) that could not be readily explained. Nevertheless, none of them had a *decrease* in vertical strabismus that was 50% or greater between positions, an observation found exclusively in patients with skew deviation. Therefore, a 50% or greater *decrease* in vertical strabismus between positions appears to be a specific criterion to differentiate skew deviation from all other causes of vertical strabismus.

We found that 5 patients with skew deviation had a negative upright-supine test result. Interestingly, 4 of these 5 patients had a lesion affecting the midbrain. We speculate that their vertical strabismus may have resulted from a combination of skew deviation and nuclear-fascicular trochlear nerve palsy, which may explain why the upright-supine test result was negative.

Clinical differentiation between skew deviation and trochlear nerve palsy is important because the treatment of patients with these conditions is different. Trochlear nerve palsy is typically diagnosed with the 3-step test.[19] In contrast, the vertical strabismus in skew deviation may be comitant or incomitant, and in some cases, it may even be alternating on lateral gaze (ie, bilateral abducting hypertropia).[16,31,38] It may mimic trochlear nerve palsy during the 3-step test with increased hypertropia on contralateral gaze and with ipsilateral head tilt; however, it may also increase on ipsilateral gaze or with contralateral head tilt, or it may remain unchanged with gaze direction or head tilt.[39,40] Conversely, a long-standing trochlear nerve palsy with spread of comitance may simulate a comitant skew deviation. In addition, in both conditions, the head is usually tilted toward the side of the hypotropic eye, although the head tilt in trochlear nerve palsy is a *compensatory* mechanism to minimize diplopia, whereas that in skew deviation is part of the *pathologic* process seen in ocular tilt reaction.[1-4] Furthermore, because both conditions may result from brain trauma or from lesions in the posterior fossa,[41] differentiating skew deviation from trochlear nerve palsy can be challenging.

Fundus examination may be useful to differentiate between the 2 conditions. The fundus is usually excyclotorted in the hypertropic eye in trochlear nerve palsy, but it is usually incyclotorted in the hypertropic eye (excyclotorted in the hypotropic eye) in skew deviation.[11,42,43] However, objective assessment of fundus torsion requires pupillary dilation and indirect ophthalmoscopy, which may not be readily available or feasible for nonophthalmologists, including neurologists and orthoptists. It is also difficult to assess fundus torsion in uncooperative patients.

Most patients with skew deviation exhibit other neurologic signs that would prompt their physicians to perform neuroimaging. However, subtle neurologic signs may sometimes be missed by general ophthalmologists and orthoptists, and brain MRI may not always be readily available. Some patients with skew deviation may have an iso-

lated vertical strabismus and a positive 3-step test result without any detectable neurologic signs. In the present study, we encountered 2 patients with acute onset of vertical deviation as a result of cerebellar hemorrhage who exhibited a positive 3-step test result that mimicked a trochlear nerve palsy, but they had a positive upright-supine test result that suggested skew deviation. The upright-supine test is thus an additional test that would be useful to alert physicians to rule out skew deviation even if the patients have typical features of trochlear nerve palsy. The test is simple and quick to perform by covering each eye alternately while patients fixate a near target at ⅓ m (eg, using a near vision card at patients' arm length) in both the upright and supine position, with or without the use of prisms. Unlike fundus torsion, this test does not require pupillary dilation or indirect ophthalmoscopy. In some instances, we have also performed the upright-supine test by tilting the patient's head backward while the patient sat upright (so that the head's anteroposterior axis and thus the plane of the utricles were aligned with the earth-vertical axis). We found the same results whether the vertical strabismus measurement was performed with the whole body or the head only in a supine position.

In the present study, we only included patients with neurologic signs to establish an unequivocal diagnosis of skew deviation. It would be interesting to investigate whether the upright-supine test would be useful in a more clinically relevant and challenging scenario—one in which a patient has an isolated vertical strabismus, a positive 3-step test result, and an absence of neurologic signs. A prospective study is currently under way to evaluate the added value of the upright-supine test beyond the classic 3-step test in this challenging scenario. This prospective study will also investigate the overall sensitivity and specificity of the *combined* use of the 3-step test, fundus torsion, and upright-supine test to differentiate skew deviation from trochlear nerve palsy.

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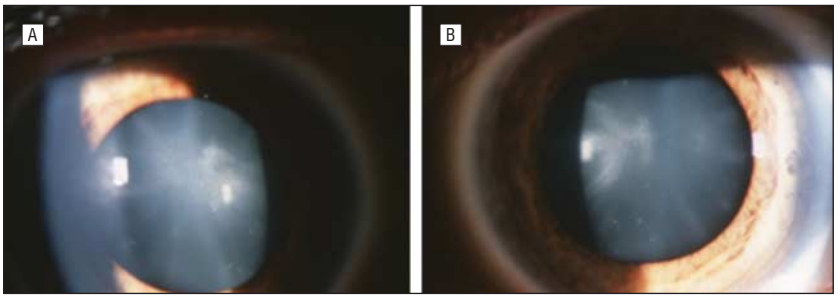
REFERENCES

1. Rabinovitch HE, Sharpe JA, Sylvester TO. The ocular tilt reaction: a paroxysmal dyskinesia associated with elliptical nystagmus. *Arch Ophthalmol.* 1977;95(8):1395-1398.
2. Halmagyi GM, Gresty MA, Gibson WPR. Ocular tilt reaction with peripheral vestibular lesion. *Ann Neurol.* 1979;6(1):80-83.
3. Zackon DH, Sharpe JA. The ocular tilt reaction and skew deviation. In: Sharpe JA, Barber HO, eds. *Vestibulo-Ocular Reflex and Vertigo.* New York, NY: Raven Press; 1993:129-140.
4. Brodsky MC, Donahue SP, Vaphiades M, Brandt T. Skew deviation revisited. *Surv Ophthalmol.* 2006;51(2):105-128.
5. Parulekar MV, Dai S, Buncic JR, Wong AM. Head position-dependent changes in ocular torsion and vertical misalignment in skew deviation. *Arch Ophthalmol.* 2008;126(7):899-905.
6. Schlenker M, Mirabella G, Goltz HC, Kessler P, Blakeman AW, Wong AM. The linear vestibulo-ocular reflex in patients with skew deviation. *Invest Ophthalmol Vis Sci.* 2009;50(1):168-174.
7. Wong AM, Sharpe JA. Cerebellar skew deviation and the torsional vestibulooocular reflex. *Neurology.* 2005;65(3):412-419.
8. Chandrakumar M, Blakeman A, Goltz HC, Sharpe JA, Wong AM. Static ocular counterroll in patients with skew deviation. *Neurology.* 2011;77(7):638-644.
9. Wong AM. *Eye Movement Disorders.* New York, NY: Oxford University Press; 2008.
10. Westheimer G, Blair SM. The ocular tilt reaction: a brainstem oculomotor routine. *Invest Ophthalmol.* 1975;14(11):833-839.
11. Brandt T, Dieterich M. Skew deviation with ocular torsion: a vestibular brainstem sign of topographic diagnostic value. *Ann Neurol.* 1993;33(5):528-534.
12. Dieterich M, Brandt T. Ocular torsion and tilt of subjective visual vertical are sensitive brainstem signs. *Ann Neurol.* 1993;33(3):292-299.
13. Zwergal A, Cnyrim C, Arbusow V, et al. Unilateral INO is associated with ocular tilt reaction in pontomesencephalic lesions: INO plus. *Neurology.* 2008;71(8):590-593.
14. Smith JL, David NJ, Klintworth G. Skew deviation. *Neurology.* 1964;14:96-105.
15. Keane JR. Ocular skew deviation: analysis of 100 cases. *Arch Neurol.* 1975;32(3):185-190.
16. Moster ML, Schatz NJ, Savino PJ, Benes S, Bosley TM, Sergott RC. Alternating skew on lateral gaze (bilateral abducting hypertropia). *Ann Neurol.* 1988;23(2):190-192.
17. Morrow MJ, Sharpe JA. Torsional nystagmus in the lateral medullary syndrome. *Ann Neurol.* 1988;24(3):390-398.
18. Wong AM. Understanding skew deviation and a new clinical test to differentiate it from trochlear nerve palsy. *J AAPOS.* 2010;14(1):61-67.
19. Parks MM. Isolated cyclovertical muscle palsy. *Arch Ophthalmol.* 1958;60(6):1027-1035.
20. Ellis FD, Helveston EM. Superior oblique palsy: diagnosis and classification. *Int Ophthalmol Clin.* 1976;16(3):127-135.
21. Flanders M, Draper J. Superior oblique palsy: diagnosis and treatment. *Can J Ophthalmol.* 1990;25(1):17-24.
22. Uchino Y, Ikegami H, Sasaki M, Endo K, Imagawa M, Isu N. Monosynaptic and disynaptic connections in the utriculo-ocular reflex arc of the cat. *J Neurophysiol.* 1994;71(3):950-958.
23. Uchino Y, Sasaki M, Sato H, Imagawa M, Suwa H, Isu N. Utriculoocular reflex arc of the cat. *J Neurophysiol.* 1996;76(3):1896-1903.
24. Büttner-Ennever JA. A review of otolith pathways to brainstem and cerebellum. *Ann N Y Acad Sci.* 1999;871:51-64.
25. Angelaki DE. Eyes on target: what neurons must do for the vestibuloocular reflex during linear motion. *J Neurophysiol.* 2004;92(1):20-35.
26. Ng D, Fouladvand M, Lalwani AK. Skew deviation after intratympanic gentamicin therapy. *Laryngoscope.* 2011;121(3):492-494.
27. Riordan-Eva P, Harcourt JP, Faldon M, Brookes GB, Gresty MA. Skew deviation following vestibular nerve surgery. *Ann Neurol.* 1997;41(1):94-99.
28. Safran AB, Vibert D, Issoua D, Häusler R. Skew deviation after vestibular neuritis. *Am J Ophthalmol.* 1994;118(2):238-245.
29. Dieterich M, Brandt T. Wallenberg's syndrome: lateropulsion, cyclorotation, and subjective visual vertical in thirty-six patients. *Ann Neurol.* 1992;31(4):399-408.
30. Choi SY, Kim DH, Lee JH, Kim J. Jerky hemi-seesaw nystagmus and head tilt reaction combined with internuclear ophthalmoplegia from a pontine infarction. *J Clin Neurosci.* 2009;16(3):456-458.
31. Keane JR. Alternating skew deviation: 47 patients. *Neurology.* 1985;35(5):725-728.
32. Brandt T, Dieterich M. Pathological eye-head coordination in roll: tonic ocular tilt reaction in mesencephalic and medullary lesions. *Brain.* 1987;110(pt 3):649-666.
33. Halmagyi GM, Brandt T, Dieterich M, Curthoys IS, Stark RJ, Hoyt WF. Tonic contraversive ocular tilt reaction due to unilateral meso-diencephalic lesion. *Neurology.* 1990;40(10):1503-1509.
34. Brandt T, Dieterich M. Two types of ocular tilt reactions: the 'ascending' pontomedullary VOR-OTR and the 'descending' mesencephalic integrator-OTR. *Neuroophthalmology.* 1998;19:83-92.

35. Margolin E, Hanifan D, Berger MK, Ahmad OR, Trobe JD, Gebarski SS. Skew deviation as the initial manifestation of left paramedian thalamic infarction. *J Neuroophthalmol*. 2008;28(4):283-286.
36. Ortiz-Pérez S, Sánchez-Dalmau B, Molina J, Adán A, Candela S, Rumià J. Ocular tilt reaction as a delayed complication of deep brain stimulation for Parkinson disease. *J Neuroophthalmol*. 2009;29(4):286-288.
37. Kim HA, Lee H, Yi HA, Lee SR, Lee SY, Baloh RW. Pattern of otolith dysfunction in posterior inferior cerebellar artery territory cerebellar infarction. *J Neurol Sci*. 2009; 280(1-2):65-70.
38. Versino M, Hurko O, Zee DS. Disorders of binocular control of eye movements in patients with cerebellar dysfunction. *Brain*. 1996;119(pt 6):1933-1950.
39. Kushner BJ. Errors in the three-step test in the diagnosis of vertical strabismus. *Ophthalmology*. 1989;96(1):127-132.
40. Donahue SP, Lavin PJ, Hamed LM. Tonic ocular tilt reaction simulating a superior oblique palsy: diagnostic confusion with the 3-step test. *Arch Ophthalmol*. 1999; 117(3):347-352.
41. Brazis PW. Palsies of the trochlear nerve: diagnosis and localization—recent concepts. *Mayo Clin Proc*. 1993;68(5):501-509.
42. Brandt TH, Dieterich M. Different types of skew deviation. *J Neurol Neurosurg Psychiatry*. 1991;54(6):549-550.
43. Brandt T, Dieterich M. Vestibular syndromes in the roll plane: topographic diagnosis from brainstem to cortex. *Ann Neurol*. 1994;36(3):337-347.

Archives Web Quiz Winner

Congratulations to the winner of our July quiz, Arun Lakshmanan, MS, DNB, FRCS, MRCOphth, Department of Ophthalmology, Queens Medical Centre, Nottingham, England. The correct answer to our July challenge was cerebrotendinous xanthomatosis. For a complete discussion of this case, see the Small Case Series section in the August *Archives* (Monson DM, DeBarber AE, Bock CJ, et al. Cerebrotendinous xanthomatosis: a treatable disease with juvenile cataracts as a presenting sign. *Arch Ophthalmol*. 2011; 129[8]:1087-1088).



Be sure to visit the *Archives of Ophthalmology* Web site (http://www.archophthalmol.com) and try your hand at our Clinical Challenge Interactive Quiz. We invite visitors to make a diagnosis based on selected information from a case report or other feature scheduled to be published in the following month's print edition of the *Archives*. The first visitor to e-mail our Web editors with the correct answer will be recognized in the print journal and on our Web site and will also be able to choose one of the following books published by AMA Press: *Clinical Eye Atlas, Clinical Retina*, or *Users' Guides to the Medical Literature*.