Fourth nerve palsy:
Historical review and study of 215 inpatients

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Article abstract—A review of inpatient trochlear nerve pareses diagnosed over 23 years revealed head trauma as the principal cause, with surgical injury, inflammation, and brain tumors seen occasionally. Ischemic (microvascular) neuropathies were rare. About one-half of the patients (52%) had no other neuro-ophthalmologic signs, but only 5% were truly isolated, without other neurologic or ophthalmologic signs or symptoms. Fourth nerve palsies are underdiagnosed on hospital services, where stuporous patients encounter unsuspecting physicians.

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Galen overlooked the trochlear nerve and failed to include it among his seven cranial nerves.[1] Vesalius, in 1543, in perhaps his least accurate work, illustrated seven cranial nerves at the base of the brain, including an idiosyncratic trochlear nerve apparently arising from the temporal lobe.[2] In contrast, the elegant 16th-century drawings of Eustachius[3] show a realistic fourth nerve emerging from behind the pontomesencephalic junction. By 1664, Willis had expanded the cranial nerve count to 10 and accurately illustrated (with Christopher Wren) and described the fourth nerve[4]:

"The fourth conjugation of nerves hath a diverse origine from all the rest, for whereas most of the others proceed from the foot or fides of the oblong marrow, this hath its root in the top of it behind the round protuberances, called Nates and Testes. . . . We call these nerves the Pathetick nerves of the eyes . . . the proper office of these is to move the eyes pathetically, according to the force of the passions and instinct of nature."

The name "pathetick" referred to an alleged ability to express passion, but any emotions relayed solely by the fourth nerve must have been subtle. (Anatomists of antiquity, who envisioned nates [buttocks], testes, and mamillary bodies at the base of the brain, may have been preternaturally susceptible to passion.)

The modern classification of twelve cranial nerves was established by Soemmerring[5] in 1778, but, curiously, Charles Bell in 1802 portrayed only nine pair.[6] His clearly defined fourth pair of cranial nerves was now, less romantically, called the trochleares. (In French, they remain "pathétique.")

One of the soundest early discussions of damage to the trochlear nerve is found in Dixon's *Diseases of the Eye* (1860, 2nd ed). He states[7] that isolated palsies are rare, require cooperation of the patient for diagnosis, and may accompany catastrophic brain injury or pass away without residual. Intorsion of the eye on downward gaze is noted as a sign of fourth nerve action in the presence of third nerve paralysis.

Soelberg Wells[8] (1878) was more typical of 19th-century ophthalmology textbook authors in relegating discussion of eye movements to a few pages in the back of the book. The accepted causes of diplopia—cold drafts, rheumatism, and syphilis—were discussed; proven treatments such as strychnine and faradization (if galvanization didn't succeed) were recommended, and "when all other remedies have failed to effect a cure, it may be necessary to have recourse to operative interference. . . ."[8]

For once, Gowers (1888) was of little help, writing[9] that "the symptom of paralysis of the fourth nerve is paralysis of the superior oblique, which has been already described." Osler[10] (1892) acquitted himself only slightly better, stating that the course of the fourth nerve made it "liable to be compressed by tumors, by aneurism or in the exudation of basilar meningitis. Its nucleus in the upper part of the fourth ventricle may be involved by tumors or undergo degeneration with the other ocular nuclei." Refreshingly, he dismissed contemporary treatments.

The multivolume *Twentieth Century Practice of Medicine*[11] (1897) contained this startling confession: "Isolated disease of the fourth nerve is extremely rare. I know of no instance of it." A few years later, a more modern note was sounded by Posey and Spiller[12] (1906): "Isolated trochlear paralysis is most often due to syphilis, tabes, meningitis, sometimes to traumatism (especially injuries about the trochea). It is seldom the result of diphtheria, influenza, or pons lesions, and is very rarely caused by multiple sclerosis."

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Even in 1916, only five lines of Ball's 911-page ophthalmology text[13] were devoted to affections of the fourth nerve: "Trochlear paralysis is seldom found alone. It is usually caused by syphilis, tabes, multiple sclerosis, and meningitis at the base of the brain, and by pressure in the valve of Vieussens."

Bielschowsky (1935) placed the diagnosis of trochlear nerve paralysis on a rational basis.[14] He emphasized that superior oblique weakness was the most common cause of vertical diplopia, pointed out (as had others before him) that patients typically tilt their head away from the affected side, and introduced his head-tilt test based on the observation that head tilts contralateral to the damaged fourth nerve decrease and ipsilateral head tilts magnify the diplopia of superior oblique palsy.

And yet, one of the principal studies[15] of cranial nerve injury in World War II found isolated fourth nerve paresis in only one of 1,800 patients with blunt head injury, illustrating the persisting difficulty in diagnosing trochlear nerve palsy. Following the war, interest in corrective muscle surgery, as well as an increase in road carnage, produced an upsurge of interest in fourth nerve palsies. Over the past 35 years, a progressive increase in the proportion of trochlear pareses reported from the Mayo Clinic[16] suggests continuing improvement in the ability to recognize fourth nerve palsies.

Trochlear nerve paralysis is usually diagnosed in the ophthalmologist's office. Of all the cranial nerves, only the nervus terminalis (cranial nerve zero)[17] is less familiar to neurologists and neurosurgeons. Many articles on fourth nerve pareses are penned by strabismologists to emphasize surgical treatments. The following study analyzes a contrasting group of neurologic inpatients with trochlear nerve palsies.

Patients. Patients personally examined on the neurosurgery and neurology wards of the Los Angeles County/University of Southern California Medical Center and Rancho Los Amigos Hospital (rehabilitation) during the past 23 years form the basis of this study.

The diagnosis of (acute) superior oblique weakness was based on the presence of vertical diplopia maximal when the affected (higher) eye is turned down and in. Alternate cover testing was useful in identifying the hypertropic eye in those few confused patients who could not participate in bedside diplopia field testing.

Gravity-dependent findings of a positive Bielschowsky head-tilt test and spontaneous head tilts were sought as soon as patients could sit. Excyclotropia was diagnosed by funduscopy. The three-step test[18] was occasionally useful in confirming that the superior oblique was the affected muscle. Bilateral trochlear pareses were diagnosed by demonstrating alternating adduction hypertropia on right and left downgaze, "V" pattern esotropia, and severe excyclotropia. When possible, eye movements were photographed and Lancaster diplopia fields and Maddox double-rod tests were performed.

Patients with immobile globes associated with cavernous sinus lesions were considered to exhibit fourth nerve paralysis as were cooperative patients with complete third nerve palsies who failed to show intorsion on maximum downward gaze. Alternating adduction hypertropia accompanying pretectal lesions was assumed to represent alternating skew deviation rather than bilateral trochlear nerve palsies.

Patients with orbital trauma and those with myopathic or neuromuscular causes of superior oblique muscle weakness were excluded. Close follow-up, rather than edrophonium testing, was relied upon to uncover myasthenia gravis presenting with isolated superior oblique weakness. No such cases occurred among 149 myasthenic patients with ocular involvement seen during the same period.

Table 1. Etiology of trochlear nerve paresis in 215 inpatients

Causes	Unilateral		Bilateral		Total
	Isolated*	Accompanied	Isolated*	Accompanied	
Trauma					113
Automobile	23	11	10	0	44
Motorcycle	8	8	5	1	22
Assault–blunt	9	1	2	1	13
Assault–penetrating	2	4	1	0	7
Pedestrian	8	1	1	1	11
Falls	8	1	0	0	9
Bicycle	3	1	0	0	4
Sports	1	1	0	1	3
Surgery	2	27	1	0	30
Inflammation					30
Meningitis	0	12	0	4	16
Mucormycosis	0	3	0	0	3
Cysticercosis	1	0	10	0	11
Tumor	0	14	0	0	14
Vascular/older	8	0	0	0	8
Spontaneous/youth	1	6	0	0	7
Brainstem strokes	2	2	0	0	4
Congenital	2	1	0	0	3
Other	3	2	0	1	6
Total	81	95	30	9	215

* No other eye signs.

Results. Patient ages ranged from 9 to 83, with an average of 34 years. Women composed 29% of the group. Trochlear nerve involvement was right-sided in 41%, left-sided in 40%, and bilateral in 19%.

Fourth nerve palsy was the sole neuro-ophthalmologic sign in 52%, but only 5% had no other neurologic or ophthalmologic signs or symptoms. Other ocular motor nerve palsies, occurring in 26%, consisted of third nerve involvement in eight patients, sixth in five, and both third and sixth in forty-four. The optic nerve was damaged in 23 patients, the fifth nerve in 19, and the seventh in fourteen. Five patients had Horner's syndrome, six had pupillary light-near dissociation, six had papilledema, and five had homonymous hemianopia. Nystagmus was observed in 12 patients (upbeat in four, downbeat in two, torsional in two, and horizontal-only in four), two had rhythmic oculopalatal myoclonus, and one had internuclear ophthalmoplegia. Functional signs of monocular diplopia and convergence spasm were present in one patient each.

Trauma, causative in more than one-half of patients, produced 90 (51%) of the unilateral and 23 (59%) of the bilateral fourth nerve palsies (table 1). Automobile accidents were most common, but a variety of injuries were represented (table 1). A single

Table 2. Reported etiology of fourth nerve palsy

Series	No. cases	Trauma	Tumor	Ischemia	Congenital	Unknown	Other
Mayo[16]	578	29%	5%	18%	0%	32%	16%
Albany[19]	82	34	1	2	—	59	4
Barcelona[21]	84	31	1	37	11	7	13
Miami[22]	33	39	18	21	0	6	15
Montreal[20]	52	31	23	4	29	8	6
Boston[23]	22	22	10	7	5	36	20
Los Angeles (present)	215	52	8	4	1	0	34

patient gave a history of double vision beginning 1 week after being assaulted; otherwise, all patients experienced diplopia as soon as their state of consciousness allowed. Iatrogenic trauma associated with neurosurgical procedures was another frequent source of injury (30 patients). In 18 cases, the operation involved tumors, usually arising from the clivus-petrous ridge or in the cavernous sinus; 13 procedures were for aneurysms, most commonly at the basilar tip. In one instance, balloon obliteration of a cavernous aneurysm by radiologists produced a fourth nerve palsy. Usually, the trochlear nerve was divided intentionally to provide adequate surgical exposure; less commonly, such damage was unsuspected during the procedure and became manifest in the postoperative period.

Infectious causes included meningitis (acute bacterial, 4; tuberculous, 4; herpes zoster, 3; and others, 5), rhino-orbital-cerebral mucormycosis (3), and cysticercosis (11). In 10 of the patients with cysticercosis, bilateral trochlear palsies resulted from a large cyst lodging in the caudal aqueduct, stretching the fourth nerve fascicles.

All patients with tumors had multiple neuro-ophthalmologic signs. No one tumor type predominated: pituitary apoplexy and lymphoma each occurred three times; upper brainstem gliomas were seen twice; and medulloblastoma, metastasis, nasopharyngeal carcinoma, chordoma, enchondroma, and epidermoid (with associated meningitis) each occurred once.

Eight middle-aged or older patients in the "vascular" group developed spontaneous, self-limited palsies in the presence of diabetes (3 patients) and other vascular risk factors (5). Of the seven youthful patients whose palsies were spontaneous and self-limited, four had painful cavernous sinus syndromes suggesting granulomatous cavernous sinusitis (Tolosa-Hunt syndrome) and three had isolated pareses. Brainstem strokes were divided between infarcts (2) and hemorrhages (2). Both upper brainstem hematomas occurred in young individuals, one in association with a cavernous angioma and the other with a presumed vascular malformation. Three patients had congenital fourth nerve pareses as documented by consistent head tilts in old photographs. Other causes consisted of undiagnosed intrinsic brainstem disease in three patients, cavernous aneurysms in two (one with rupture, producing a carotid-cavernous fistula), and midbrain sarcoidosis in one patient. Most cases had a clear-cut etiology; the few with uncertain origins could be partially classified and were included in the "spontaneous" and "other" categories rather than as "unknown."

Etiologic diagnosis is relatively easy in an inner-city setting such as ours where severe trauma is common and tumors and infections are usually far advanced at presentation. On the other hand, adequate follow-up is difficult; a minority of the patients return to clinic, most have no telephone and many no fixed address. At best, we could establish that 35 patients (16%) had complete resolution of their trochlear nerve pareses.

Discussion. The diagnosis of trochlear palsy has been reviewed extensively in recent articles.[19,20] The relative youth and the male predominance of our patients are explained by the high frequency of trauma. Blunt head injury is the most common cause of unilateral, and especially bilateral, fourth nerve injury in all series (table 2). Our hospitals serve an inner-city, gang-dominated area, explaining the unusual number[7] of trochlear nerve injuries due to penetrating as well as blunt head trauma. Minor head trauma is occasionally reported to precipitate decompensation of a nerve already compromised by tumor compression.[24] Our trauma patients all sustained major head injury, and no underlying tumors were found. With one possible exception, delay in onset of diplopia after trauma represented depressed consciousness rather than late presentation of neuropathy. Although the third and sixth nerves are each injured more often than the fourth, the *percentage* of fourth nerve palsies due to trauma is three times that of the third or sixth cranial nerves at our hospital.[25]

Clinical conjecture,[22] supported by limited pathologic evidence[26] and recent imaging studies,[27] suggests that the trochlear nerve decussation is the usual site of bilateral fourth nerve injuries. CT reveals ambient cistern hemorrhage, a useful marker for dorsolateral midbrain contusion, in many cases of traumatic unilateral fourth nerve paresis. Less commonly, fractures adjacent to the cavernous sinus damage the fourth as well as the third and

sixth cranial nerves. In two of our patients, bullets came to rest in the inferior colliculus, resulting in permanent fourth nerve injury.[27] Surgery was a common cause of fourth nerve trauma in our group, and attempts to reanastomose the nerve at the conclusion of the neurosurgical procedure should be encouraged.[28] Certainly, nerves like the fourth and sixth, which innervate a single muscle, are a much more appealing target for restoration than the complex third nerve.

None of the fourth nerve palsies caused by tumors in our series was isolated, and such palsies are rarely reported.[22] There was no preferred site for involvement: tumors occurred along the entire course of the fourth nerve from the nucleus and fascicles to the cavernous sinus. Tumor surgery was more likely to cause trochlear nerve damage than the tumors themselves.

In our two patients with aneurysms, the location was intracavernous and other eye signs were present. However, of some eight reported cases of *subarachnoid* aneurysms causing fourth nerve palsies, there are two examples of large unruptured superior cerebellar artery aneurysms causing isolated trochlear nerve palsies.[29,30] Such cases are drawn from thousands of trochlear palsies and do not provide sufficient grounds to abandon the option of initial observation of patients with strongly presumed microvascular palsies (those due to intraneural vascular insufficiency in patients who are usually hypertensive or diabetic).

Inflammatory causes, consisting of meningitis, cavernous sinus mucormycosis, and cysticercal cysts in the aqueduct were relatively common in our series. Most of these patients did well except for the three fatal mucormycosis cases. Patients with diabetic/microvascular causes tend to be managed in ophthalmologists' offices or clinics and are underrepresented in our inpatient series (table 1).

Intramedullary involvement of the fourth nerve nuclei or fascicles occurred in only 10 of our cases. All had other signs and symptoms. Previously reported neighborhood signs were seen in one patient each: opposite Horner's syndrome[31] with infarction and opposite internuclear ophthalmoplegia[32] following surgery for a cavernous hemangioma. Rarely, fourth nerve palsy occurs as the predominant manifestation of a brainstem stroke.[33]

The best guide to prognosis is provided by the Mayo Clinic studies.[16,34] Overall, recovery of trochlear nerve deficits (in 53.5%) was at least as good as those of the other ocular motor nerves.[34] After combining the third, fourth, and sixth nerve data, microvascular causes had the best prognosis, with 72% recovery versus 57% clearing following head trauma. The severity of head trauma undoubtedly has a major effect upon recovery; major injuries will tend to produce irreversible nerve avulsions.[26] A series that included many patients with minor head trauma found 75% resolution[35]; another found 65% resolution in unilateral cases but only 25% when both fourth nerves were involved[36]; in a third group, none of 15 trauma patients had experienced recovery at the time of analysis.[20]

Fourth nerve pareses tend to be underdiagnosed on neurologic and neurosurgery services. Stringent bed utilization review procedures frequently result in discharge as soon as the patient becomes sufficiently alert to assist in the diagnosis. Follow-up in a convalescent or outpatient setting is particularly important for the diagnosis of traumatic fourth nerve palsies.

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