

Ataxic hemiparesis

To the Editor: The recent paper on ataxic hemiparesis syndrome contained two errors: 1. Drs. Sakai, Murakami, and Ito claimed that theirs was the first case of this syndrome studied by CT. Two other cases have been reported.^{2,3} 2. They stated that Fisher⁴ described four pathologically examined cases, but he described only three.

There have been different opinions about the site of the lesion responsible for the "ataxic hemiparesis syndrome" ("homolateral ataxia and crural paresis"). Fisher and Cole⁵ described several cases in 1965, one with pathologic examination; although there were multiple lesions, the syndrome was attributed to one in the superior part of the posterior limb of the contralateral internal capsule. In 1978, Fisher⁴ reported 3 autopsied cases, all three with lesions at the junction of the third and medial segments of the contralateral basis pontis; he attributed the ataxic cerebellar disorder to the pontine nuclei lesion and concluded that "this study has furnished the solution to an old neurologic problem—the site of the lesion responsible for ipsilateral, pyramidal, and cerebellar signs." In 1980, Perman and Racy² reported a case with CT evidence of a lesion in the posterior limb of the contralateral internal capsule, similar to the one in the case of Fisher and Cole.⁵ Bendheim and Berg³ described CT evidence of a lesion in the contralateral rostral midbrain, and Sakai et al¹ reported a lesion in the contralateral basis pontis disclosed by CT.

The problem of the site of the lesion responsible for "ataxic hemiparesis" is not yet solved. It can be said that the lesion is contralateral to the clinical signs and that it is located in an area that extends in a rostrocaudal direction from the posterior limb of the internal capsule to the middle segment of the pons.

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References

1. Sakai T, Murakami S, Ito K. Ataxic hemiparesis with trigeminal weakness. *Neurology (Ny)* 1981;31:635-6.
2. Perman GP, Racy A. Homolateral ataxia and crural paresis: case report. *Neurology (Ny)* 1980;30:1013-5.
3. Bendheim PE, Berg BO. Ataxic hemiparesis from a midbrain mass. *Ann Neurol* 1981;9:405-7.
4. Fisher CM. Ataxic hemiparesis: a pathologic study. *Arch Neurol* 1978;35:126-8.
5. Fisher CM, Cole M. Homolateral ataxia and crural paresis: a vascular syndrome. *J Neurol Neurosurg Psychiatry* 1965;28:48-55.

Reply from the Authors: We thank Dr. Canetti-Nakson for his comments, and we would like to answer as follows. We believe it is important to consider the original paper when a new idea is proposed. One concept of "ataxic hemiparesis"¹ allows uncertainty because when one sees

a patient with pure hemiparesis after a stroke, the misdiagnosis of "ataxic hemiparesis" may be made because of hemiparesis and clumsiness of limb which may resemble ataxia. "Ataxic hemiparesis" must be limited to cases of lacunar stroke because of the diagnostic and therapeutic implications; patients with "ataxic hemiparesis" have an excellent prognosis. Anticoagulant therapy and angiography are not indicated, as shown by Fisher's cases.

Therefore, it does not seem appropriate to use the term "ataxic hemiparesis" in cases of brain tumor in demyelinating diseases that show the combination of ipsilateral pyramidal signs and cerebellar-like ataxia; "ipsilateral pyramidal and cerebellar signs" would be preferable.

Answer to comment 1. Perman and Racy reported "homolateral ataxia and crural paresis" and CT demonstrated the responsible lesion in the superior portion of the posterior limb of the internal capsule and thalamus, but not in the upper pons.² Fisher reported that infarcts at sites other than the upper pons do not cause the same combination of signs.¹ In addition, sensory loss in the case of Perman and Racy differed from Fisher's original report.

Bendheim and Berg reported "ataxic hemiparesis from a midbrain mass."³ However, their case was not cerebrovascular disease, but a mass lesion associated with leukemia.

Answer to comment 2. Fisher included within "ataxic hemiparesis" a fourth case, which had been reported as the "dysarthria-clumsy hand syndrome" in 1967.¹

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References

1. Fisher CM. Ataxic hemiparesis: a pathologic study. *Arch Neurol* 1978;35:126-8.
2. Perman GP, Racy A. Homolateral ataxia and crural paresis: case report. *Neurology (Ny)* 1980;30:1013-5.
3. Bendheim PE, Berg BO. Ataxic hemiparesis from a midbrain mass. *Ann Neurol* 1981;9:405-7.
4. Fisher CM. A lacunar stroke: the dysarthria-clumsy hand syndrome. *Neurology (Minneapolis)* 1967;17:614-7.

Fisher syndrome in childhood

To the Editor: The paper of Becker et al¹ on Fisher syndrome in children was informative but it invites comments. First, they seem to be unaware of our CT demonstration of a midbrain lesion in a child with ataxia, ophthalmoplegia, and hyporeflexia.² Indeed the possibility of a central mechanism underlying the syndrome had already been raised by others.^{3,4}

Second, despite their reference to the possibility of central mechanisms the authors seem unable to divorce themselves from traditional views of the pathogenesis of the Guillain-Barré syndrome in general or the Fisher syndrome in particular. I believe this is a mistake if

there is a possibility of anterograde disorder in a peripheral nerve after injury of its centrally-located perikaryon. The following clinical observations therefore argue for central lesions in infectious polyneuritis: entirely or predominantly motor disorders; predominantly distal or proximal motor manifestations in different patients; paucity (or absence) of autonomic symptoms and the usual preservation of sphincter functions; more rapid recovery in most patients than expected for axonal regeneration; demonstration of central lesion in Fisher syndrome;^{2,5} genuine Babinski response in otherwise "typical" Guillain-Barré syndrome (personal observations); and optic neuritis (i.e., involvement of the central nervous system) in infectious polyneuritis.⁶

Regarding the pupil in Fisher syndrome,^{1,4} as Becker et al observed, both components of the Holmes-Adie syndrome are seen in some patients with Fisher syndrome.^{2,4} Whereas the currently accepted "ganglionic" notion of the Holmes-Adie pupils is clearly irrelevant in relation to the coexisting hyporeflexia, a strategically located midbrain lesion (figure) could explain that association (i.e., interrupting the descending facilitator

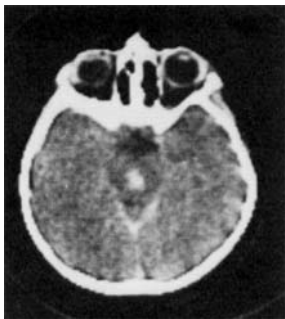


Figure. Orbital projection. Enhancement at the edge of incisural notch is evident. Quadrigeminal plate, quadrigeminal plate cistern, and the interpeduncular cistern are easily identifiable. A definite enhancing lesion is seen in the midbrain tegmentum at midline with an EMI number of 66 units.

fibers to the spinal cord²). On the other hand a midbrain lesion could (by transynaptic neuronal degeneration) affect the ciliary ganglion,^{7,8} but leave the hyporeflexia unexplained.

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References

1. Becker WJ, Watters GW, Humphreys P. Fisher syndrome in childhood. *Neurology (Ny)* 1981;31:555-60.
2. Derakhshan I, Lotfi J, Kaufman B. Ophthalmoplegia, ataxia, and hyporeflexia (Fisher syndrome) with a midbrain lesion demonstrated by CT scanning. *Eur Neurol* 1979;18:361-6.
3. Collard M, Mathe JF, Guihenneur P, Coquilat G, Eber AM, Ruth D. Syndrome de Fisher: Origine peripherique ou centrale. *Rev Neurol* 1978;134:325-39.
4. Keane J. Tonic pupils with acute ophthalmoplegic polyneuritis. *Ann Neurol* 1977;2:393-6.
5. Littlewood R, Bajada S. Successful plasmapheresis in the Miller-Fisher syndrome. *Br Med J* 1981;283:778.
6. Behan PO, Lessell S, Roche M. Optic neuritis in the Landry-Guillain-Barre-Strohl syndrome. *Br J Ophthalmol* 1976; 60:58-9.
7. Lowenfeld I, Thompson HS. The tonic pupil: a re-evaluation. *Am J Ophthalmol* 1976;63:46-87.
8. Harriman DFG. Pathological aspects of Adie's syndrome. *Adv Ophthalmol* 1970;23:55-73.

To the Editor: I had the opportunity to read the article entitled "Fisher syndrome in childhood" by Becker et al which appeared in the May 1981 issue.

In the introduction to this paper the authors note that only 11 documented cases of Fisher syndrome have been reported in children under the age of 15.

I'd like to call your readers' attention to another case report of this syndrome which appeared in the *Cleveland Clinic Quarterly* vol. 45, No. 2 Summer 1978:27-52. It was written by Drs. Price, O'Connor, and Rothner and was entitled "Acute ophthalmoplegia, ataxia, and areflexia (Fisher syndrome) in childhood."

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Reply from the Authors: The child reported by Price et al with Fisher syndrome had evidence of concomitant infection with infectious mononucleosis, one of the infections that may be associated with this syndrome. We regret having omitted this reference. We thank Dr. Tomsak for bringing it to our attention.

We thank Drs. Derakhshan, Lotfi, and Kaufman for drawing our attention to their interesting paper. The patient had features similar to patients accepted as having Fisher syndrome. The fact that the child had a lower facial weakness, hypoactive rather than absent stretch reflexes, and a Babinski sign, however, would not be accepted as typical of this entity. On the basis of the extraordinary CT scan findings the disorder she had was not Fisher syndrome as these authors agree. It seems reasonable to propose that the demonstrated CT midbrain lesion provides some support for the contention that a midbrain (central) lesion may be involved in patients with Fisher syndrome. On the other hand, a wealth of evidence suggests a peripheral rather than a central site for the pathological lesion in the Guillain-Barré syndrome.¹

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1. Asbury AK, Arnason BG, Adams RD. The inflammatory lesion in idiopathic polyneuritis: its role in pathogenesis. *Medicine* 1969;48:173-215.

Phenobarbital dosing in neonates and asphyxia

To the Editor: While Fischer et al¹ emphasize the wide interpatient variability in the disposition of phenobarbital in neonates, factors such as prenatal phenobarbital exposure, postnatal age, duration of phenobarbital therapy, and concurrent disease states were not evaluated for possible influence on phenobarbital clearance. Data

Table. Pharmacokinetic data for 18 neonates treated with phenobarbital

No.	Gestational age (wks)	Postnatal age (days)	V (L/kg)	Cl _B (ml/hg/h)
1	40	7	0.54	4.04
2	29	7	0.82	3.91
3	39	10	0.81	3.22
4	40	11	0.88	3.99
5	37	9	0.84	4.24
6	37	7	0.80	4.01
7	37	9	0.77	3.83
8	33	14	0.72	3.73
9	30	14	0.81	4.15
10	36	16	0.90	3.16
11	27	14	0.76	3.90
12	40	9	0.77	9.83
13	40	9	0.73	9.73
14	37	7	0.82	12.50
15	34	13	1.22	8.42
16	40	10	0.66	5.27
17	40	14	0.76	5.90
18	28	16	0.76	6.33

Patients 1 to 11 were asphyxiated and patients 12 to 18 were not asphyxiated.

from previous studies show that these factors confound the rate of phenobarbital elimination.^{2,3} We evaluated the possible association of neonatal asphyxia with phenobarbital disposition in 18 neonates with seizure disorders and our data suggest that asphyxia may account for substantial reduction in phenobarbital clearance.

Phenobarbital 15 mg per kilogram loading doses were given intravenously. Serum phenobarbital concentrations were determined two hours later by EMIT immunoassay. Daily maintenance doses of 2.5 to 5 mg per kilogram were selected and steady-state serum concentrations were checked at least weekly. The criteria for neonatal asphyxia included either: (1) an Apgar score at 1 or 15 minutes of 3 or less, (2) cardiac or respiratory arrest requiring resuscitation, (3) a Po₂ below 30 mm Hg documented on two consecutive blood gases while the neonate was receiving 100% oxygen, or (4) apnea lasting at least one minute and requiring bagging.

Pharmacokinetic calculations were performed to determine the apparent volume of distribution (V) and the apparent total body clearance (Cl_B) using the for-

mulas:

$$V = \frac{\text{loading dose}}{\text{2-hour phenobarbital concentration}}$$

$$Cl_B = \frac{\text{maintenance dose}}{\text{steady-state concentration} \times \text{dosing interval}}$$

The mean clearance values for asphyxiated and non-asphyxiated neonates were 3.83 (SD ± 0.35) and 8.28 (SD ± 2.61) ml per hour per kilogram, respectively (table). These mean clearances differed significantly ($p < 0.001$ using the unpaired t test). The mean total body clearance was 5.6 ml per hour per kilogram, similar to the 5.7 ml per hour per kilogram reported by Heimann and Gladtko⁴ and 6.4 ml per hour per kilogram reported by Fischer et al.¹ The mean V values did not differ in the asphyxiated and nonasphyxiated groups (0.79 L per kilogram and 0.82 L per kilogram). These values were also similar to those reported by others.^{1,3,4}

The reason for the reduced clearance in neonates who have been asphyxiated is unknown. Both liver and kidney are probably damaged by asphyxia so that drug elimination is reduced. Dosing guidelines should reflect the presence or absence of asphyxia. If the goal is to achieve a serum phenobarbital concentration of 20 mg per liter, asphyxiated neonates should receive 1.8 mg per kilogram per day and the dose for nonasphyxiated neonates should be 4.0 mg per kilogram per day.

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References

1. Fischer JH, Lockman LA, Zaske D, et al. Phenobarbital maintenance dose requirements in treating neonatal seizures. *Neurology (Ny)* 1981;31:1042-4.
2. Jalling B, Boreus LO, Kallberg N, et al. Disappearance from the newborn of circulating prenatally administered phenobarbital. *Eur J Clin Pharmacol* 1973;6:234-8.
3. Painter MJ, Pippenger C, MacDonald H, et al. Phenobarbital and diphenylhydantoin levels in neonates with seizures. *J Pediatr* 1978;92:315-9.
4. Heimann G, Gladtko E. Pharmacokinetics of phenobarbital in childhood. *Eur J Clin Pharmacol* 1977;12:305-10.

Reply from the Authors: The thoughtful comments on our paper¹ by Dr. Gal et al and their new data led

Table. Comparison of phenobarbital kinetics: Asphyxiated and nonasphyxiated infants

Patient no.	Gestational age (weeks)	Weight (gms)	Dose mg/kg	Kd (hr ⁻¹)	Half-life (hr)	TBC (ml/hr/kg)
Asphyxiated						
1	34	1900	14.7	0.0108	64.1	7.5
2	40	2780	14.4	0.0160	43.2	10.7
4	38	2280	13.2	0.0129	53.9	8.1
7	31	2330	12.9	0.0084	83.0	7.1
8	37	3040	16.5	0.0063	109.5	4.1
10	40	2540	15.7	0.0041	167.8	3.5
11	34	2000	15.9	0.0063	103.2	6.3
12	37	2250	20.0	0.0046	150.7	4.6
14	40	2330	19.7	0.0046	149.9	4.1
15	34	2390	20.1	0.0094	74.0	8.0
Mean (± SD)				0.0083 0.0038	86.4 45.2	6.4 2.2
Nonasphyxiated						
3	40	2820	15.1	0.0097	71.3	6.7
5	36	2040	13.8	0.0057	120.6	5.1
6	37	1810	13.8	0.0092	75.5	7.7
9	?	1220	14.8	0.0103	67.3	9.6
13	39	2340	21.4	0.0032	217.0	2.7
Mean (± SD)				0.0076 0.0027	110.34 56.7	6.4 2.3

us to review our raw data. Of our 15 patients, ten suffered from severe asphyxia due to respiratory distress syndrome, meconium aspiration, prolapsed cord, or other causes. As shown in the table, their disappearance rates, half-lives, and total body clearances of phenobarbital did not differ from the five infants who were not asphyxiated.

Contrary to Gal et al, Painter et al³ demonstrated only that duration of therapy influences disposition of phenobarbital in newborns; Jalling et al² studied disappearance of phenobarbital in infants who received phenobarbital transplacentally when their mothers were treated for complications of pregnancy.

The method of pharmacokinetic calculation used by Gal et al differs in important ways from ours. We determine volume of distribution by calculating the theoretical concentration at time zero from the disappearance rate after a single dose. Although their volume of distribution value does not differ from ours, it is calculated from a blood concentration arbitrarily obtained two hours after the loading dose. While calculation of clearance by their formula may allow estimation of an appropriate daily dose, it does not necessarily reflect clearance because no consideration is given to differences in gastrointestinal absorption, compartmentalization, or storage within the body.

Both their data and ours indicate that frequent determination of plasma blood levels is essential to maintain therapeutic blood concentrations of phenobarbital in these patients. Steady state is probably never achieved

because of rapid growth and continued maturation of enzymatic systems in the newborn infant. These factors make it even less appropriate to calculate clearance on the basis of daily dose requirements.

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References

1. Fischer JH, Lockman LA, Zaske D, et al. Phenobarbital maintenance dose requirements in treating neonatal seizures. *Neurology (Ny)* 1981;31:1042-4.
2. Jalling B, Boreus LO, Kallberg N, et al. Disappearance from the newborn of circulating prenatally administered phenobarbital. *Eur J Clin Pharmacol* 1973;6:234-8.
3. Painter MJ, Pippenger C, MacDonald H, et al. Phenobarbital and diphenylhydantoin levels in neonates with seizures. *J Pediatr* 1978;92:315-9.

Correction

In "Tourniquet-induced ischemia and somatosensory evoked potentials" by Thoru Yamada, Tatsuo Muroga, and Jun Kimura, December 1981, the illustrations for figure 3 (p. 1526) and figure 5 (p. 1527) should be reversed.

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Tourniquet-induced ischemia and somatosensory evoked potentials

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