Pupillary 'dilatation lag' in Horner's syndrome

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When a patient has a minor ptosis and miosis it is often hard to be sure that it is a case of Horner's syndrome. This diagnostic problem may be resolved by a careful review of the patient's medical history and an examination for further clinical signs (Tables I and II). In cases in which additional clinical signs are absent and the history is of little help, further evidence to confirm or refute the diagnosis of Horner's syndrome may be sought by pharmacological or physiological testing.

Pharmacological testing

Horner's syndrome results from disruption of the ipsilateral sympathetic pathway. This may occur at any site between the diencephalon and the sympathetic end-organs (Karplus and Kreidl, 1910; Jaffe, 1950; Carmel, 1968; Walsh and Hoyt, 1969). Locally applied cocaine eye drops (2 to 10 per cent) will fail to produce pupillary dilatation if any part of the sympathetic pathway is disrupted, while topical hydroxyamphetamine will fail to cause pupillary dilatation if the postganglionic pathway is disrupted. Locally applied epinephrine or phenylephrine will classically demonstrate adrenergic supersensitivity in postganglionic lesions. The pharmacological rationale, method, and clinical interpretation of these various tests are described in the literature (Thompson and Mensher, 1971; Thompson, 1974; Grimson and Thompson, 1975) and need not be reviewed here.

Physiological testing

The dynamics of pupillary movement in Horner's syndrome are well known (Carmel, 1968; Löwenstein and Friedman, 1942; Löwenstein and Loewenfeld, 1950; Riley and Moyer, 1970, 1971) and have been described in detail using both cinematographic and electronic pupillography. The main features of unilateral Horner's syndrome are:

1. A miosis compared with the normal eye, the degree of anisocoria being greater in darkness than in light.
2. 'Dilatation lag', a slow and delayed dilatation in darkness because of the lack of the active radial pull of the dilator muscle.
3. Reduction in the degree of psychosensory dilatation compared with the normal pupil.

All of these features could be expected from sympathetic pupillomotor denervation, and they can be clearly seen on pupillographic tracings of unilateral Horner's syndrome (Fig. 1).

A Horner's anisocoria can be hard to distinguish from a 'simple' anisocoria, since in both there is

Table I *Clinical signs of Horner's syndrome*

Ptosis
Miosis
'Upside-down ptosis' of the lower lid
Narrowed palpebral fissure
Conjunctival congestion
Facial or body anhidrosis
Heterochromia iridis, in congenital cases

Table II *Clinical situations associated with Horner's syndrome*

Contralateral hypoaesthesia of the body*
Brachial plexus palsy†
Pancoast's syndrome†
Facial pain‡
Anhidrosis of face and neck†
Loss of sweating on entire half of body*
Flushing or blanching of face and neck†
No loss of sweating, except perhaps in supraorbital area‡
Thyroidectomy scar and hoarseness†
Vertigo*
Cervical osteoarthritis†
Thoracic surgery†
Syringomyelia*

Each of these clinical situations also has localization value:

- *Central neuron
- †Preganglionic neuron
- ‡Postganglionic neuron

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FIG. 1 Pupillogram of unilateral Horner's syndrome. Note characteristic fluctuations in anisocoria: A, more anisocoria in darkness than in light; B, sudden increase in anisocoria after psychosensory stimulus, due to sympathetic discharge to innervated dilator muscle; C, transiently increased anisocoria after lights have gone out, due to 'dilatation lag' of the Horner's pupil

FIG. 2 Pupillogram of 'simple' anisocoria*. Note that there is more anisocoria in darkness than light (A), just as in Horner's syndrome. Unlike Horner's syndrome psychosensory stimulus causes both pupils to dilate (B), and there is no 'dilatation lag' of smaller pupil so that there is no transient increase in anisocoria during first few seconds of darkness (C)

*'Simple' anisocoria is sometimes called 'physiological' anisocoria because it has no known clinical significance. Löwenstein, in a personal communication, suggested the term 'central' anisocoria because the peripheral innervation of the iris muscles could be shown to be intact in these cases. He preferred not to call it physiological anisocoria because it seemed to change from time to time, sometimes within a few hours. We have tried to avoid this term because of possible confusion with 'central Horner's syndrome'. Charles (1970) observed it to come and go and has associated 'simple' anisocoria with fatigue

more pupillary inequality in darkness than in light (see Fig. 2).

The two characteristic pupillographic features of Horner's syndrome—namely, failure of psychosensory dilatation, and dilatation lag in darkness—are closely related: they are both the direct result of denervation of the dilator muscle and either of them can be clinically useful. Dilatation lag in darkness is the more consistently reproducible because psychosensory dilatation is complicated by the patient's fright response to the stimulus. Some stolid subjects remain unruffled by the sudden noise, and little further anisocoria is produced. The so-called 'cilio-spinal reflex' is, of course, nothing more than a psychosensory reflex dilatation of the pupil (Reeves and Posner, 1969; Duke-Elder and Scott, 1971) and is subject to the same variability.

Dilatation lag of the Horner's pupil was mentioned by Riley and Moyer as a sensitive pupillographic indicator of denervation of the dilator muscle (Riley and Moyer, 1970), and we too have found dilatation lag to be useful in diagnosing Horner's syndrome by pupillography. This paper is an effort to extend the usefulness of this sign from the pupillographic laboratory into the ophthalmologist's office by means of flash Polaroid photography.

Flash photography

Clinical pupillography in normal subjects shows that after a short light stimulus, the pupils will return to their original darkness diameter in about 12 to 15 s with about 90 per cent of this dilatation occurring during the first 5 to 6 s. Horner's pupils, after a light stimulus, return to their original darkness diameters in about 25 s, and reach approximately 90 per cent of their final diameter within the first 10 to 12 s. Figs 1 and 2 show that in a photograph taken 10–12 s after the lights go out both pupils would be at approximately their original darkness diameters. Furthermore, it can clearly be seen from the pupillograms that the maximum separation between normal and Horner's pupils on dark dilatation occurs after 4–5 s of darkness. This separation is an expression of the 'dilatation lag' which is typical and diagnostic of Horner's syndrome.

Flash Polaroid photographs, taken at the right moments, will separate Horner's syndrome from 'simple' anisocoria. Photographs should first be taken in bright light, then in darkness 4–5 s after the lights have gone out, and lastly in darkness 10–12 s after the lights have gone out (Fig. 3).

Methods

Between July 1974 and February 1975, we examined 23 patients with a clinically apparent anisocoria which was greater in darkness than in light. Photographs were taken using the CU-5 Polaroid close-up camera with 80 per cent of the ring flash covered. Fixation was at a distance of 2 m. Three photographs were taken: the first in room light with added penlight stimulus unilaterally, the second in darkness, 4–5 s after cessation of light stimulus, and the third in darkness, 10–12 s after cessation of light stimulus.

No specific psychosensory stimuli were added. The camera was adjusted to give slight overexposure which made the measurement of pupillary diameter easier. All photographs were measured at the conclusion of the project using a Peak Scale Loupe Magnifier with a magnification of approximately $\times 3$ and a built-in graticule. All measurements were made randomly by a technician skilled in pupil measurement. Measurements were taken in the vertical pupillary meridian whenever

FIG. 3 Fluctuating anisocoria of Horner's syndrome demonstrated by flash photography

Both Horner's and 'simple' anisocoria will tend to show greater anisocoria after 10–12 s of darkness than in light; but Horner's pupil is obviously not as large at 4–5 s of darkness as it is after 10–12 s. This is not true of normal pupils or of pupils showing 'simple' anisocoria. Notice greater anisocoria at 4–5 s of darkness than at 10–12 s of darkness in Horner's syndrome.

There is an advantage in taking the 4–5 s darkness picture before the 10–12 s picture since plunging the patient into darkness will have greater psychosensory effect on first occasion than on any other occasion. This will tend to further accentuate transient anisocoria seen in Horner's syndrome at 4–5 s of darkness.

A psychosensory stimulus such as a firm hand clasp (Redlich phenomenon), Jendrassik manoeuvre, or sudden noise (Duke-Elder and Scott, 1971) just after lights go out will similarly tend to increase anisocoria at 4–5 s by causing psychosensory dilatation of normal pupil

possible to minimize errors caused by ocular divergence. Many measurements were randomly repeated and the measuring error was consistently in the region of ± 0.1 mm. The anisocoria present in each of the three situations was then calculated.

The patients were next classified as cases of Horner's syndrome or 'simple' anisocoria on the basis of:

1. Their earlier clinical examination.
2. Pupillography.
3. Pharmacological testing.

Criteria for inclusion in either group required confirmatory findings in at least two of these parameters with no contradictory findings (Table III).

Finally, the mean anisocoria for each group in each of the three situations was calculated, standard deviations were computed, and the groups statistically compared.

Results

It so happened that the patients with 'simple' anisocoria and the patients with Horner's syndrome had a similar degree of anisocoria. When judged in light and in darkness (10–12 s after cessation of light stimulus) there was no significant difference ($P > 0.25$ by comparison Student's t test in each case). There was, however, a highly significant difference in the degree of anisocoria between the two groups after 4–5 s of darkness ($0.005 > P > 0.001$ by comparison t test).

Conclusions

Polaroid flash photographs taken in light, after 4–5 s of darkness, and after 10–12 s of darkness may be used clinically to demonstrate the presence

Table III *Pupillary measurements and basis for clinical subgrouping*

Age (yr)	Sex	Patient no.	Light stimulus			Darkness 4-5 s			Darkness 10-12 s			Diagnosis			
			Right eye	Left eye	Anisocoria	Right eye	Left eye	Anisocoria	Right eye	Left eye	Anisocoria	Clinical	Pharmacological	Pupillography	Result
46	Male	1	2.4	2.0	0.4	5.0	3.3	1.7	6.0	5.5	0.5	H	H	H	H
63	Male	2	2.8	2.3	0.5	5.9	4.7	1.2	6.5	5.9	0.6	H	H	H	H
27	Female	3	5.5*	5.0*	0.5	7.0*	5.6*	1.4	7.0*	5.9*	1.1	H	H	H	H
16	Female	6	3.7	3.3	0.4	6.5	4.8	1.7	6.8	5.8	1.0	H	—	H	H
19	Female	10	6.8	4.0	2.8	Inadequate photographs			7.3	6.1	1.2	H	H	H	H
13	Female	13	3.3	4.0	0.7	4.1	6.0	1.9	6.0	6.8	0.8	H	—	H	H
56	Male	14	2.8	3.4	0.6	4.2	6.2	2.0	5.2	6.1	0.9	H	—	H	H
33	Male	15	2.2*	2.3*	0.1	2.5*	3.4*	0.9	2.8*	3.5*	0.7	H	H	H	H
51	Male	17	2.8	3.1	0.3	4.4	5.0	0.6	4.9	5.0	0.1	H	H	?	H
	Male	19	2.8	3.8	1.0	6.0	6.5	0.5	6.4	6.8	0.4	?	H	H	H
75	Female	22	2.8	4.2	1.4	3.6	5.2	1.6	3.8	5.2	1.4	H	H	—	H
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25	Female	4	3.0	3.4	0.4	4.8	5.5	0.7	5.3	5.8	0.5	S	—	S	S
36	Female	5	2.0	2.3	0.3	3.4	4.0	0.6	3.8	4.6	0.8	S	S	S	S
67	Male	7	2.8	3.3	0.5	4.4	5.2	0.8	4.3	5.3	1.0	S	S	S	S
	Female	8	4.0	4.7	0.7	6.8	7.8	1.0	6.8	7.3	0.5	—	S	S	S
55	Female	9	3.4	3.0	0.4	5.0	4.5	0.5	5.5	5.0	0.5	S	S	S	S
53	Male	11	2.5	3.0	0.5	4.8	5.4	0.6	5.3	5.4	0.1	Inadequate classification			?
21	Female	12	3.9	3.4	0.5	6.5	6.4	0.1	6.5	6.3	0.2	S	—	S	S
18	Male	16	3.4	3.3	0.1	6.5	5.8	0.7	6.4	5.7	0.7	S	—	S	S
29	Female	18	3.7	4.0	0.3	6.9	6.9	0.0	6.8	7.0	0.2	S	S	—	S
32	Male	20	3.4	4.0	0.6	5.5	6.5	1.0	5.8	7.0	1.2	S	—	S	S
17	Female	21	3.2	3.9	0.7	6.0	6.7	0.7	6.8	7.0	0.2	S	S	—	S
1	Male	23	3.5	3.0	0.5	6.0	5.1	0.9	6.4	5.0	1.4	S	S	—	S

* = Measurements taken in the horizontal plane due to narrow palpebral fissure in one or more photographs

H = Horner's syndrome

S = 'Simple' anisocoria

? = Equivocal result

— = No clinical classification possible

Patient no. 10 was eliminated from the calculations because the photographs were of insufficient quality to allow accurate measurements to be made.

Patient no. 11 was eliminated because it was not possible to classify the patient unequivocally into one group

Sex ratios: Horner's group: 6 male : 5 female

'Simple' anisocoria group: 5 male : 7 female

Average age: Horner's group: 39.9

'Simple' anisocoria group: 32.2

of 'dilatation lag' in patients with anisocoria, and thus may be of use in making the clinical diagnosis of Horner's syndrome by physiological methods. The criteria for the recognition of 'dilatation lag' are:

1. Poor dilatation of the more miotic pupil at 4-5 s compared with the dilatation achieved after 10-12 s of darkness.
2. Increased anisocoria in darkness, more marked at 4-5 s than at 10-12 s.

Using the above criteria it is usually possible in a clinical situation to differentiate patients with Horner's syndrome from those showing 'simple' anisocoria. There are, however, occasions when the diagnosis is equivocal, but if the series of photographs is repeated with additional psychosensory stimuli the situation will frequently be clarified.

In our experience this procedure has proved to

be a useful clinical tool, and since the completion of the project, it has been used routinely in the differential diagnosis of anisocorias. On no occasion has the photographic result been at variance with either the clinical or pharmacological diagnosis.

Summary

1. Clinical examination will often fail to identify the presence of a unilateral Horner's syndrome.
2. Confirmation and localization of Horner's syndrome is of clinical prognostic value.
3. Cocaine testing provides confirmation of a Horner's syndrome, but it takes 45 min, is sometimes equivocal, and always delays the localizing hydroxyamphetamine test.
4. 'Dilatation lag' is a sensitive and physiological sign of Horner's syndrome, and can be demonstrated by simple Polaroid flash photographs.

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