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The Pupil as Indicator of a Cranial Vault Under Pressure: On Sir William Macewen contributions

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We do not despair until the pupil ceases to contract (Cheyne 1812) [1].

The history of the dilated pupil (fixed to changes in ambient and direct light) is not widely known [2]. Recognition of the significance of anisocoria and the association between intracranial pressure and change in one or both pupils was slow to develop. We now know that new anisocoria has a potential clinical significance, and its detection has greatly increased after the introduction of the pupillometer—for better or worse. A physiological asymmetry of the pupils of $\leq$0.5 mm, found in about 20% of healthy people, has been well recognized, but when does it reach significance? When nursing staff in modern neurointensive care units detect an asymmetry, they call on attending physicians to come at the bedside, which invariably leads to repeating a computed tomography scan of the brain. Its importance was taught to generations of neurologists and neurosurgeons.

When did we come to realize that pupil size was significant? We are not the first to ask. Wide pupil(s) are one of the oldest recorded neurologic signs of acute brain injury. Galen had noted that the iris could change in size. Although he did not understand the reflex arc, he nevertheless observed that the contralateral pupil dilated when the opposite eyelid was shut. Galen, whose physiologic interpretation of the brain involved spirits, attributed this reaction to a substance he called the "breath of vision" or "pneuma," which came from the brain into the eye via the optic nerves. Yet, until the nineteenth century, no writer commented on pupillary changes occurring in association with a mass lesion.

Best remembered for Cheyne-Stokes respiration, John Cheyne (1777–1836) recorded the contraction and dilatation of the pupil in a case of acute brain injury in 1812, noting that "great changes may be observed in the state of the different functions in the course of every attack of apoplexy. Our prognostic is formed accordingly as the vital functions are more or less disordered" [1]. In many case examples, he observed either contracted or dilated pupils without mentioning anisocoria or a comparison between left and right. He became most concerned when the pupil became fixed to light. He also concluded that, "with any return of sensibility our hopes rise, and with the diminution of it they are destroyed."

The neurosurgical pioneer Sir William Macewen already noted at the end of the nineteenth century that "[Pupil changes] are still regarded by some, as curious, interesting, but erratic phenomena, far too variable to be depended upon, and without any connecting thread upon which these conditions, as seen in a variety of diseases, could be strung" [3]. Once we had a better understanding of the anatomy of the brain stem and recognized that areas in the brainstem controlling consciousness were anatomically adjacent to the fibers controlling the pupillary responses, the pupillary light reflex became a useful indicator of presence and location of brain and brainstem injury and diseases causing coma.

Pupil Theory

Macewan's classic article from 1887 provided the best description of pupillary changes and is full of detailed observations (Fig. 1) [3]. In one patient, he astutely observes four periods, each with a "peculiar pupillary condition." The first period involves severe intracranial pressure, "in which the brain function was for the most part suspended"; the pupils at this stage were widely

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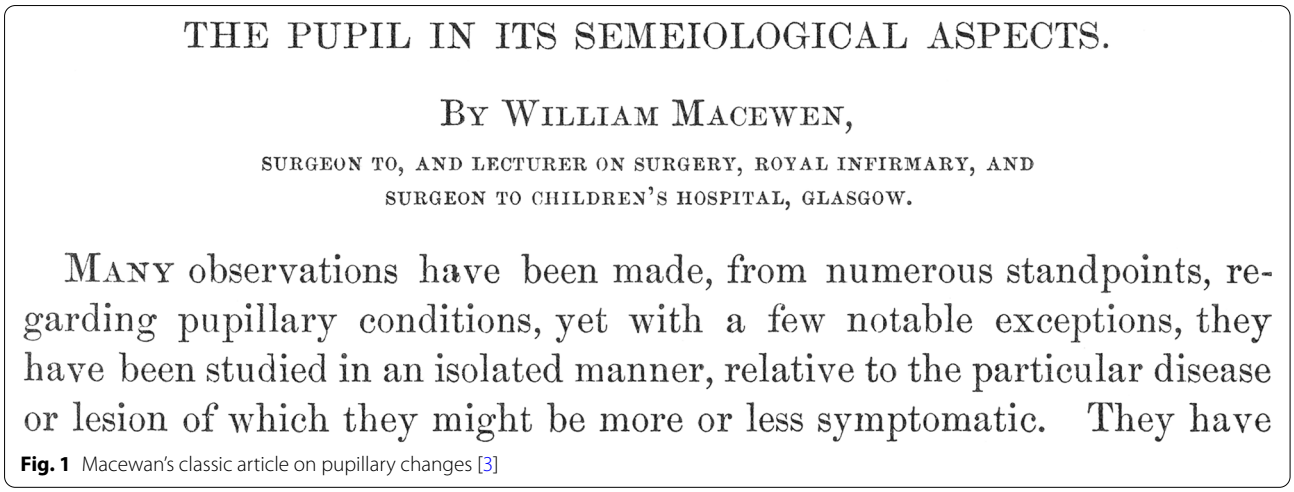

THE PUPIL IN ITS SEMEIOLOGICAL ASPECTS.

By William Macewen,

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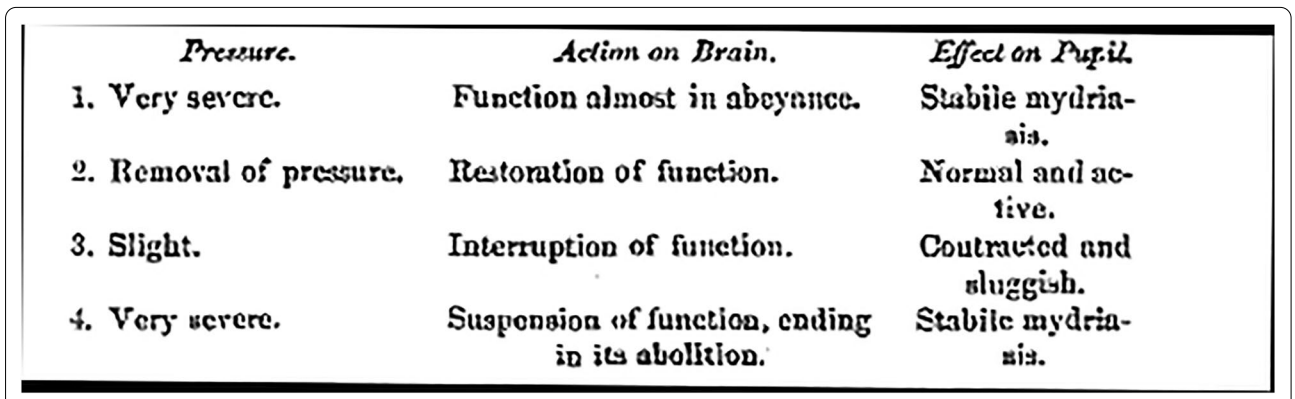
Many observations have been made, from numerous standpoints, regarding pupillary conditions, yet with a few notable exceptions, they have been studied in an isolated manner, relative to the particular disease or lesion of which they might be more or less symptomatic. They have

Fig. 1 Macewan's classic article on pupillary changes [3]

dilated and fixed. Relief of the intracranial pressure ushered in the second period, in which compression of the brain disappeared and the patient regained consciousness (blood apparently "escaped from the interior of the skull"). The pupils then became normal, responding to changes in light exposure ("This state was the immediate sequence of the relief of the pressure on the brain by the escape of the pent-up blood"). In the third period, there was renewed cerebral pressure as a direct result of the reaccumulation of blood within the skull and, consequently, pressure on the brain, due to the formation of a clot in the aperture in the fractured ethmoid. The patient at this stage would become drowsy. The pupils gradually lost their activity, becoming very sluggish and contracted. A stage of severe intracranial pressure ensued during the fourth period, marked by all the symptoms of cerebral compression and accompanied by widely dilated and fixed pupils. This lasted until death. Macewen showed it in a tabulated form (Fig. 2).

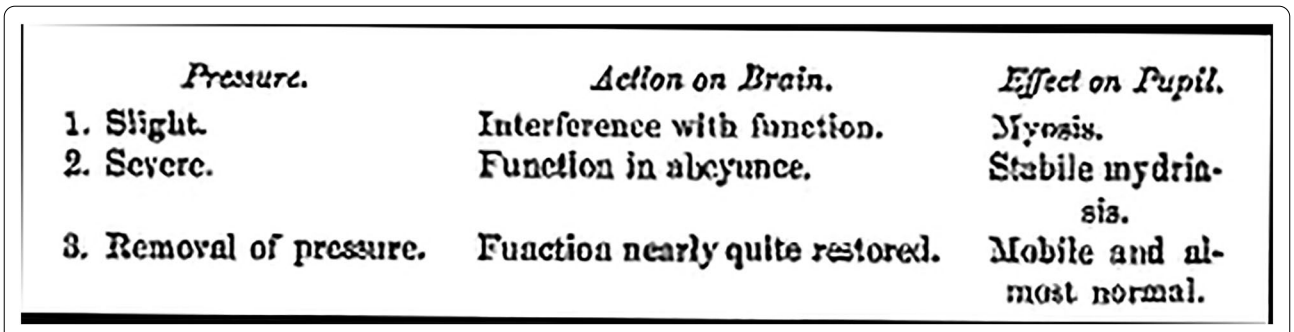
In a case of tuberculous meningitis, the patient unleashed "a hydrocephalic cry" (high pitched, or a flat melody and the occurrence of biphonation), which was followed by miosis worsening to mydriasis from increasing pressure. After the ventricles were punctured ("spinal fluid escaped in a jet"), the pupils became smaller and light reflex returned but stayed sluggish (Fig. 3). He further described (1) both pupils dilated and fixed from large unilateral lesions; (2) one pupil dilated and fixed, the other contracted, accompanied by lesions on both hemispheres; (3) one pupil dilated and fixed, the other normal; and (4) a pupil contracted on only one side. He observed that hemorrhage into the pons causes "strongly contracted pupils; but when it is more extensive, involving the gray matter beneath the aqueduct of Sylvius, a state of stabile mydriasis is induced."

Despite being one of the first physicians to describe a link between pressure and pupil, Macewen did not attempt to explain his observations. Holman and Scott were among the first to point out the clinical



Pressure.	*Action on Brain.*	*Effect on Pupil.*
1. Very severe.	Function almost in abeyance.	Stabile mydriasis.
2. Removal of pressure.	Restoration of function.	Normal and active.
3. Slight.	Interruption of function.	Contracted and sluggish.
4. Very severe.	Suspension of function, ending in its abolition.	Stabile mydriasis.

Fig. 2 Patient with increased pressure and changes in pupils [3]



Pressure.	*Action on Brain.*	*Effect on Pupil.*
1. Slight.	Interference with function.	Myosis.
2. Severe.	Function in abeyance.	Stabile mydriasis.
3. Removal of pressure.	Function nearly quite restored.	Mobile and almost normal.

Fig. 3 Changes in pupils after puncture of ventricles in acute hydrocephalus [3]

significance of pupillary enlargement, and they recommended surgical decompression on the side of the fixed pupil (they cited several cases in which this symptom was ignored with poor outcomes). The authors also noted that anisocoria of the pupils could be transitory but quickly followed by bilaterally widely dilated pupils. They further noted that "the mechanism of its appearance is not obvious, but it is assumed that the intracranial course of the third nerve, as it lies against the bony wall of the cranium, lends itself peculiarly well to compression from a pressure applied lateral and superior to it." The authors emphasized the utility of one-sided dilatation to localize the site of the injury and subsequent hemorrhage [4].

The potential significance of the pupil in monitoring brain swelling was first noted in a retrospective review by Shaw et al. [5]: "Not all of the patients were examined by neurologically oriented physicians, so that comparisons are not strictly possible." Ipsilateral pupillary dilation was the most commonly recorded finding (eight cases). In two other cases, ipsilateral constriction was followed by dilation of the pupil. Single cases had ipsilateral constriction, contralateral dilation, or bilateral pupillary dilation, respectively; only six patients who died during the first week were specifically noted to have normal pupils. In the patients dying after longer durations, they occasionally noted asymmetry of one or the other pupil. The authors asked whether an initial coma was the consequence of simultaneous ischemia of subcortical structures, such as the midbrain, through insufficiency of the posterior communicating and posterior cerebral arteries. They felt this was plausible: "superimposed on this early ischemia of the midbrain may later appear evidence of transtentorial herniation, which would make it difficult at autopsy to recognize the previous lesion." This proposal of ischemia rather than third nerve compression nearly disappeared in the literature until others resurrected it.

Our Interpretation Today

Currently, we know that a patient with an acute hemispheric mass will present early with a unilateral fixed dilated pupil, followed by bilateral fixed pupils. The shape of the pupil may change, become irregular, football shaped, or oval shaped. An oval pupil ipsilateral to the mass is most frequently seen but is transitory. It quickly becomes round, midsized, or dilated and fixed to light. Increased intracranial pressure commonly occurs with an oval-shaped pupil, but the opposite pupil retains its normal shape. Ropper was instrumental in pointing out that changes in the opposite pupil would refer to changes in the brainstem nuclei from brainstem compression and not from third nerve compression: "[the] neglected part of the examination of the comatose patient" [6]. The shape may be explained by differences in parasympathetic tone in various segments and thus could imply involvement of the midbrain rather than peripheral fibers: "Similarities between the evolution of pupillary changes on the 2 sides suggest sequential nerve compression by asymmetrically depressed posterior cerebral arteries" [6]. Before, many considered the presence of a unilaterally fixed pupil to be a result of an oculomotor lesion from direct compression, but other mechanisms could be compression of the midbrain oculomotor complex or traction of the oculomotor nerve against the clivus. There is insufficient proof of any of these theories, and clinicopathologic correlation is often unconvincing but it pointed out that detailed study of *both* pupils may teach us about mass effect and changes in the tentorial opening.

Pupillometers are now commonplace, but do miniscule changes matter? The reflex is difficult to detect with a wide pupil (e.g., a 0.5-mm reflex in a 5-mm diameter pupil is only a 10% reflex, whereas the same reflex in a 2-mm diameter pupil is a 40% reflex). Do we need to capitulate as clinicians and leave it all up to pupillometers? It worked for many of us for decades.

Macewen's quintessential (British pragmatic) ophthalmology on a shoestring should amuse us clinicians:

> *Many pupilometers have been invented…some of them being ingenious instruments. For practical purpose however, Hutchinson's idea of the disk of polished steel, with holes punched in it, or the simple narrow white card, having marked on it a series of black dots, measuring from one to nine millimetres, is sufficient. When in use it is placed close to the eye, and the dot which corresponds most to the size of the pupil is noted, and its exact size in millimetres is read off [3].*

Add the good old magnifying glass and you are all set.

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