PHAKOCHRONOLOGY*†

THE STUDY OF DATING STRUCTURAL CHANGES IN THE LENS

BY

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PHAKOCHRONOLOGY‡ is the science of determining the time of events that affect the crystalline lens during its lifetime. In this study the lens is considered to be a sensitometer and a chronograph recording and dating structural changes caused by local and systemic disturbances. While the term phakochronology is new, some of the underlying phenomena are well known to ophthalmologists. I am concerned herein with developing methods for dating structural changes in the lens.

The Lens as a Sensitometer and a Chronograph

The avascular lens depends on the surrounding aqueous medium to maintain its integrity. Alterations in the composition of the aqueous milieu as a result of hyperglycaemia, galactosaemia, and other metabolic, endocrine, and nutritional disorders frequently produce opacities and other structural changes in the lens. Moreover, sunlight, trauma, and radiation may cause direct injury to the cells of the lens and are not mediated by the aqueous medium (Bellows, 1944). All these disturbances are registered in the lens as if it were a sensitometer.

Not only is the lens a sensitometer, but it may also be regarded as a chronograph which dates the disturbance. The singular, regular, and predictable growth pattern of the lens is a factor which lends it the properties of a chronograph. Since the old lens fibres are incorporated in the lens and not desquamated as in other epithelial tissues, the ophthalmologist can observe structural changes that have occurred in the lens from its incipient stage to its death. Fibre layers form throughout life adding 7 microns of thickness to the anterior cortex each year (Huggert, 1946). This accretion permits dating events in the lens just as the dendrologist dates environmental influences by observing tree-rings. In addition to counting luminous bands, the ophthalmologist can verify the date by measuring the depth of an opacity.

Biomicroscopy with a Mercury-Vapour Light

Biomicroscopy with a mercury-vapour lamp§ discloses fine delicate bands called elementary stripes which are hardly visible with the incandescent lamp. Ordinarily only three or four elementary stripes are seen because the older ones merge with the anterior and posterior zones of disjunction. Goldmann, who first described them, reported that a new elementary stripe forms every 2 to 3 years.

* Received for publication July 3, 1967.

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‡ Phakochronology (Greek: phakos = lens, chronos = time).

§ H 85A3/μν G.E.

The reasons for increased visibility with the mercury light are unclear. The greater intrinsic brightness of the mercury lamp and the interference phenomenon may be factors. Because the blue band is so near the toe of the sensibility curve that it may be disregarded, and the yellow and green bands are close together (between the D and E of the Fraunhofer lines), the mercury light may be regarded as being almost monochromatic. The increased visibility of the elementary lines can be explained by the properties of a monochromatic light, according to Copeland (1967). A monochromatic light improves resolution and discrimination by reducing the hyperchromatic state in the eye of the observer and the eye being observed; it decreases the residual chromatic aberration of the microscope; and it produces a harder image than that obtained with an incandescent light.

Nature of Alternating Light and Dark Bands

Alternating light and dark bands occur not only in the lens but also in the tree, beet, tooth, and elsewhere (Fig. 1). Many ophthalmologists believe the alternating luminous and dark zones represent differences in the specific gravity producing corresponding variations in the refractive indices. However, if the cause were merely the compressing force of the newly formed fibres over the older fibres, the density should increase uniformly from the outer layers to the centre rather than alternating zones of increased and decreased densities.

FIG. 1.—Growth rings in different organisms.

Several hypotheses and observations may be considered:

- (1) Alternating zones are stress lines. Light coming from stress lines will pass through polaroid lenses placed perpendicularly to each other. When the luminous zones are viewed [with the slit lamp] through polaroid lenses placed perpendicularly to each other, they are invisible; therefore stress is not a factor. Supporting this view are observations made in a 20-year-old male, who was first seen at the age of 5 years, after he had suffered a blunt blow to the right eye. Although he developed paralytic mydriasis and paralysis of accommodation, the luminous and dark zones in the injured and normal eye were similar 15 years later.
- (2) Alternating zones result from nutritional, metabolic, or endocrine influences. Goldmann (1937) suggested that zones of discontinuity in animals represent temporary growth inhibitions; however, these bands appear in every man, regardless of geography, diet, or economic level, thus nullifying nutrition as a factor. Furthermore, no known counterpart in biennial nutritional, endocrine, or metabolic activities exists.
- (3) Alternating lines are an optical phenomenon. Such lines would then correspond to the multiple reflections observed in a negative meniscus or myopic lens.

- (4) Alternating lines result from differing growth rates. Lens fibres developing in the rapid growth phase may differ in composition and density from those formed during the slower phase.
- (5) Lucid intervals in the lens represent clear fluid. If clear fluid separated the zones of increased density, it would facilitate changes in the shape of the lens during accommodation. That the clear intervals represent fluid between fibre layers has not, to my knowledge, been suggested previously. Although the usual histological procedures do not disclose the presence of clear fluid zones, special cryohistological techniques are now being employed to determine whether the lucid intervals consist of clear fluid.

Establishing Dates of Events

Chronological determination of a disturbance producing an opacity in the lens can be made either by using the visible luminous bands as units of measure or by measuring its distance from the lens capsule (Fig. 2).

FIG. 2.—Establishing dates of events in the lens by counting luminous bands or by measuring with a reticle (mercury light source).

Measurement by counting is feasible because luminous bands alternate with dark bands in a fixed chronological order. Thus any changes in the lens may be related to the chronological date of the nearest band. With the biomicroscope, past changes in the lens as well as progressive alterations and new developments can be observed and recorded (Fig. 3, opposite). The increased complexity of the suture system as it extends superficially, and the deepening colour of the nucleus of the ageing lens aid in dating events.

Various methods have been used by Lindstedt (1915), Vogt (1930–31), Goldmann (1937), and Huggert (1946) to measure depth within the lens. In this study measurements were made by replacing the right eyepiece of the slit lamp with one containing a reticle accurate to 0.1 mm. Then the distance of the alteration in the lens from the capsule is determined as follows:

FIG. 3.—Composite figure of a 60-year-old lens, showing method of dating lens changes by counting reflect bands.

Left to Right:

Opacities anterior to first elementary stripe, less than 2 to 3 years old.

Lamellar separations and water clefts anterior to band of disjunction, 10 years old.

Diabetic punctate opacities on anterior surface of senile nuclear band, formed at age of 20 years.

Dilacerata and coronary opacities between nuclear and foetal bands formed before the age of 10 years.

Floriform opacity lying on the posterior surface of the nuclear band caused by a blunt injury at the age of 20.

Cataracta complicata extending axially.

Water-clefts 3 to 10 years old shown above.

Opacity on inner surface of first posterior elementary stripe, 3 to 4 years old shown below.

The width is projected from the reticle on to the lens and the angle formed by the lines extending from the viewing lens and the mercury light is noted. The distance is calculated with the formula

$$D = \frac{W \tan \theta}{M_t C_e}$$

in which D(A—B) is the depth to be measured, W(B—C) is the projected width, $\tan \theta$ is the tangent of the angle; M_t (1.6) is the magnification of the microscope, and C_e (1.17) is the correction factor for the corneal curvature and index of refraction (Fig. 4).

FIG. 4.—Diagram showing method and formula for establishing dates of events by measuring distance.

A—B = D (distance)

B—C = W (projected width)

Formula for measuring distance

$$D = \frac{W \tan \theta}{M_t C_e}$$

To determine the date of alterations in the posterior cortex of the lens, their relationships to the posterior elementary stripes are noted and the corresponding anterior stripes are then measured as described. The measured distance is readily changed into time by using

Huggert's finding that the annual increment to the anterior cortex is 7 microns. Therefore if an opacity is 21 microns distant from the capsule, it is 3 years old.

Clinical Phakochronology

Over 500 patients were examined with a slit lamp specially equipped with the mercury vapour lamp. Special efforts were made to focus the opacities and structural alterations sharply in order to date them accurately. The dates of events were determined either by counting the elementary stripes to the alterations, or by measuring the linear distances from the anterior capsule to the alterations. Both methods were reliable for dating alterations within the preceding 10 years. Earlier disturbances were dated by relating them to the appropriate zone of discontinuity or Y sutures and to the foetal and embryonal nuclei.

Clinical applications of phakochronology immediately come to mind. Cuneiform opacities, water clefts, and lamellar separation located deep in the cortex indicate that they have been present for a long time and are advancing little or not at all. On the other hand similar changes lying superficially indicate that they have formed recently and are therefore likely to progress more rapidly. In some patients seeking compensation for alleged drug-induced or traumatic cataracts, the stated time of symptom onset was verified by phakochronology; in others the events as related were at variance with the phakochronological measurements.

Case 1

Recent Changes in the Lens superimposed on an Old Traumatic Opacity

A 57-year-old man experienced visual impairment of the left eye which had progressed rapidly during the previous 6 months. The visual acuity in this eye had been poorer than in the right since a baseball injury at about age 20. A rosette-shaped opacity lay in the outer surface of the posterior senile nuclear band (Fig. 3). Anteriorly, lamellar separations, water clefts, and cuneiform opacities were present between the first and second elementary stripes. In the axial region, lamellar separations and water clefts were found only on the surface of the anterior elementary stripe, breaking the continuity of this band. The measured distance of the deepest located pre-senile or senile changes was 50 microns, or about 7 years. The most recent alterations, anterior to the first elementary band and measuring less than 15 microns, must have been formed in recent months.

Interpretation.—The poorer vision in the left eye dating from young manhood is adequately explained by the rosette-shaped opacity located on the external surface of the posterior senile nuclear band, formed about the 20th year. The pre-senile opacities began about 7 years before examination but did not disturb the patient until a few months before examination when they developed in the most recently formed lens fibres located in the axial region just anterior to the elementary stripe.

Case 2

Lens Opacities in a Diabetic Patient

A 41-year-old man stated that he had been diabetic for at least 18 years. The visual acuity in the left eye was reduced to 20/100; the right eye was blind. Severe diabetic retinopathy was present in both eyes. Slit-lamp examination of the left eye disclosed fine, white, flake-like opacities on the surface of the anterior senile nuclear band.

Interpretation.—Both the opacities and the anterior surface of the senile nuclear band were formed about 20 years ago in this patient. This agrees with his history of diabetes mellitus first detected 18 years previously. The dating in this instance depended entirely on the relationship of the opacities to the senile nuclear band, because linear measurements are unsatisfactory at this depth.

Case 3*Toxic Cataract*

A 44-year-old woman used triparanol for about one year and then developed skin and hair disturbances associated with diminished vision. The visual acuity was 20/80 in the right eye and 20/30 in the left. Examination of the right eye disclosed vacuoles in the equatorial region of the lens. Toward the axial region were numerous striate opacities, as well as anterior and posterior subcapsular opacities located immediately under the capsule. The changes were less advanced in the left eye.

Interpretation.—The location of the opacities in juxtaposition to the capsule indicates that they were of very recent origin and compatible with her history of impaired vision following the use of the drug.

Case 4*Triparanol Cataract Disproved*

A 67-year-old woman seen in April, 1966, attributed loss of vision to the use of triparanol in 1960. In November, 1966, lamellar separations, water clefts, and cuneiform opacities were observed in the first elementary line and the underlying lucid interval of the right eye. The projected width on the lens capsule was 0.05 mm. Similar changes were observed in the left eye. The visual acuity was 20/60 in the right eye, and 20/50 in the left. The distance from the lens capsule to the lens changes in the right eye as determined with the aforementioned formula was 21 microns or 3 years.

Interpretation.—Lamellar separations, water clefts, and cuneiform opacities in the right eye are characteristic of incipient senile cortical cataracts. In this patient, these changes measured 21 microns from the capsule and were only 3 years old. Therefore, the lens changes began to develop 2 or more years after the drug had been discontinued.

Summary

Phakochronology can establish the date of events occurring in the crystalline lens. Two means of dating structural changes in the lens are described: one is the actual counting of elementary stripes made more visible by using a slit lamp in conjunction with a mercury light; the second is measurement of the linear distance with a reticle in the eye-piece of the slit lamp, and the formula

$$D = \frac{W \tan \theta}{M_t C_e}$$

Several case histories illustrate the practical values of phakochronological determinations:

- (1) Recent changes in a lens superimposed on an old traumatic rosette-opacity;
- (2) Diabetic opacities found in a 41-year-old man, which had formed on the surface of the anterior senile nuclear band 20 years ago or about the time that he was found to have diabetes mellitus;
- (3) A toxic cataract of recent origin;
- (4) An alleged "triparanol-induced" cataract.

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