Classification of Human Senile Cataractous Change by the American Cooperative Cataract Research Group (CCRG) Method

I. Instrumentation and Technique

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The American Cooperative Cataract Research Group (CCRG) has adopted a system of classifying human cataractous changes that is based on separate and independent photographic documentation of opacification and nuclear color. This system has been extremely useful to the laboratory scientist who wishes to know the significance of associations between laboratory data and the extent or type of cataractous change. It has been applied to the analysis of nearly 2500 cataracts since 1976. This study presents the details of the instrumentation and technique of this new system and the results of classifying 2231 intracapsularly-extracted cataracts. Invest Ophthalmol Vis Sci 24:424-431, 1983

Classification of human cataractous change may be defined as the description and organized grouping of discrete features of lens opacities. This has been done in the past by clinicians desiring a qualitative record of the course of cataract formation in individual patients. However, the descriptive terms and the organizational guidelines employed varied from clinician to clinician and from country to country. In fact, many clinicians failed to note the individual features of a cataract and relied on the term "senile" cataract to describe a process that, if sufficiently advanced, led only to cataract extraction or blindness. Investing more effort in describing cataracts had no dividend, since all anatomical types of cataract eventually were removed if the patient wished to have improved vision.

However, the expansion of our understanding of the lens, which has occurred in the past 40 years, has indicated that anatomical, biochemical, and biophysical differences among different cataracts can be measured. It was in response to this burgeoning understanding of lens metabolism that a system for classifying the features of human cataracts was proposed in 1978 and adopted by the American Cooperative Cataract Research Group (CCRG) in 1980. This system assumes that there are four identifiable zones (subcapsular, cortical, supranuclear, and nuclear) of cataractous change and that there is a definable anatomical, biochemical, physiologic, or biophysical identity for each zone of opacification. By systematically identifying and grouping features of many cataracts and then by analyzing these same cataracts in the laboratory, it is hoped that a correlation between anatomy and laboratory science can be made with the resultant elucidation of mechanisms of cataract formation. Other systems of classifying cataractous change have been proposed and have enjoyed widespread application in Europe. However, the above systems employ a qualitative measure or estimate of nuclear color (yellow-brown-black) as a measure of the severity of cataract formation. This has occurred in spite of Pirie's restriction in her original paper to use nuclear color solely as a measure of insoluble lens protein. No one has shown that there is a direct relationship between color and severity of cataract formation. In fact, Pirie states that there is

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“no close correlation between color and age of the person from whom the lens was extracted,” in spite of the well-documented increase in the severity of cataract with age. Clearly, an alternative approach was needed, and in 1978 a system for independently describing nuclear color and cataract features was proposed.1 It is the purpose of this manuscript and others to follow to describe in detail our experience at the Massachusetts Eye and Ear Infirmary with this system since its implementation in 1976. With the refinement of this basic system of cataract classification, we may proceed with confidence to develop a similar “extended” in vivo system of classification using slit-lamp biomicroscopy as proposed in 1978.1

Purposes of the American CCRG Cataract Classification Effort

1. To semiquantitatively describe the extent of subcapsular, cortical, and supranuclear opacification and the relative intensity of nuclear opacification and sclerosis (coloring through yellow to brown and black) in human cataractous lenses immediately after intraocular cataract extraction.

2. To create a permanent set of stereoscopic, color, 35 mm transparencies of cataracts that are used in classifying cataracts and that can be recalled and reviewed if revision of the system of classification is indicated.

3. To create a classification protocol that, while documenting most of the anatomical complexities of cataractous change, is still amenable to simplification and application to small groups of cataracts.

4. To document the extent of cortical, subcapsular, and supranuclear opacification with measurable (as opposed to ranked or ordinal) variables. The intensity of nuclear cataract formation in the present CCRG system is a ranked or ordinal variable.

5. To computerize the classification system so as to enable rapid data entry, management, and analysis. This has been accomplished with the PROPHET system and will be described in Part II of this series.

6. To apply biostatistical techniques for rapid correlation of clinical, laboratory, and classification data, and to illustrate the application of these techniques with analyses of cataractous change as a function of age, sex, visual acuity, and the presence or absence of diabetes mellitus.

7. To analyze the relative strengths and weaknesses of this classification system.

Materials and Methods

The techniques for proper acquisition, photography, and storage of human cataracts have been described in detail.1,10 Only key features or important revisions are described here.

Acquisition, Storage, and Transport of Cataracts

The lens should be irrigated carefully off the cryo-probe with sterile, room-temperature BSS (Alcon Pharmaceuticals, Fort Worth, TX) into a small beaker. Photography should be completed as rapidly as possible, since storage of cataracts in any solution for more than an hour alters the appearance of the cataract. Storage in a small (3.0 cc) glass, moist chamber at 4°C for 4 hrs will not alter the appearance (classification) of the cataract.10 Simply pouring off the BSS or normal saline from the small glass vial and then capping the vial will create a satisfactory moist chamber. Lenses may be transported safely on ice to the lab in these vials.

Photographic Equipment and Technique

The film is Kodak Ektachrome Professional Film, ASA 200. A black plastic cuff is attached to the operating microscope objective lens to eliminate reflections from the circular fluorescent lamps. If the apparatus is used in the operating suite, a plexiglass and aluminum enclosure for the lamp and ballast may be a required safety feature.

In addition to the views specified previously,1 simultaneously side and frontal views are obtained with a mirrored 45° prism (Fig. 1) apparatus.

The cataract is immersed in normal saline and with the overhead room lights shielded or turned off, the magnification dial set at 16X, the following photographs are obtained under conditions specified in Table 1.

Information on age, sex, preoperative visual acuity, primary and secondary diagnoses, current medications, etc, are entered on a 5" × 7" printed card (Figs. 2a, b).

Classification Protocol

The terms used to identify the individual features of a cataract are defined below and illustrated diagrammatically in Figure 3.

I (Immature): An immature cataract is one in which the opacity does not totally obscure all anatomical regions of the lens (Fig. 4a).

M (Mature): A mature lens has no recognizable normal anatomical zone. These are usually obliterated by a totally degenerated cortex. However, in contrast to a hypermature cataract, the antero-posterior dimension of the lens is not increased (Fig. 4b).
Fig. 1. Mirrored prism apparatus. A 2-inch watch glass or plastic petri dish is painted with flat black enamel paint. A 45° prism mirrored on the longest side, a 1.0 cm x 0.3 cm disc and a small ruler are mounted on the base of the dish. Two views of the lens are obtained simultaneously.

H (Hypermature): A hypermature cataract is a mature cataract that has undergone swelling with a marked increase in the antero-posterior thickness (Fig. 4c).

CXA (Anterior Cortex): The central anterior cortex is divided into four quadrants. This zone exists between the supranuclear and subcapsular zones. The extent of quadrantic opacification is expressed by subscripts 1-4 (Fig. 5a).

CXE (Equatorial Cortex): These opaque zones involve the lens cortex and extend out to the lens capsule. The extent of opacification is expressed by the number of quadrants involved (Figs. 7a, b).

CXP (Posterior Cortex): Similar to CXA but in the posterior cortex (Fig. 5c).

SCA (Subcapsular Anterior): A thin shell of opacity just beneath the anterior capsule in the anterior half of the lens (Fig. 6a). The extent of opacification is estimated by comparing the opaque zone to the number of concentric circles, the largest representing the equatorial circle of the lens. The percent of the total area involved is estimated by the circles and added to the symbol as a subscript (eg, SCA1).

SCP (Subcapsular Posterior): Similar to SCA but applied to the posterior half of the lens (Fig. 6b).

SN (Supranuclear): This zone of opacity is found between the cortical and nuclear zones. It has been called "lamellar" or "zonular" opacity in other systems of classification. As with CXE opacification, its extent is described by the number of quadrants involved (Figs. 7a, b).

N (Nuclear): The nuclear opacity is characterized by its density, not its extent. The density is judged in the slit beam view by the degree to which the beam transmitted through and viewed on the black surface behind the lens is obliterated. A subscript 1 indicates only a faint blur to the image, 2 represents more blur, 3 represents near obliteration of the image, and 4 indicates complete invisibility of the image. The ruler, incorporated in the frontal and prism views allows quantitation of the extent of nuclear haze if such is desirable (Figs. 8a-d).

NS (Nuclear Sclerosis): The color of the nucleus of the excised lens as seen against a white background is rated on a scale from 1-8 (Table 2) (Figs. 9a-h).

Table 1. Exposure and lighting data for human cataract classification.

<table>
<thead>
<tr>
<th>Lens orientation</th>
<th>Exposure time (sec)</th>
<th>Ring lights</th>
<th>Slit beam</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Anterior surface up (AR) (with ruler)</td>
<td>0.5</td>
<td>On</td>
<td>Off</td>
</tr>
<tr>
<td>2. Anterior surface up (S) (with slit beam)</td>
<td>0.5</td>
<td>On</td>
<td>On</td>
</tr>
<tr>
<td>3. Posterior surface up (P)</td>
<td>0.5</td>
<td>On</td>
<td>Off</td>
</tr>
<tr>
<td>4. Anterior surface up with white background (W)</td>
<td>0.25</td>
<td>On</td>
<td>Off</td>
</tr>
<tr>
<td>5. Anterior surface up (prism apparatus) with focus on lens (M,)</td>
<td>0.5</td>
<td>On</td>
<td>Off</td>
</tr>
<tr>
<td>6. Anterior surface up (prism apparatus) with focus on prism image (M)</td>
<td>0.5</td>
<td>On</td>
<td>Off</td>
</tr>
</tbody>
</table>
Classification Protocol

One may classify a cataract while viewing it during photography and then check the accuracy of the classification with the photos, or one may wait to classify the cataract until the photos are ready. A viewer from Asahi Pentax (Asahi Optical Co., Ltd., Japan) is used to see the stereo images. A much faster technique employs slides mounted in a Kodak carousel and projected on a translucent plastic screen placed between the viewer and the projector. By diverging one's gaze, it is possible to see the image in stereo without using a stereo viewer.

Fig. 3. Diagrammatic representation of the separate zones of opacification in human senile cataract: equatorial cortical opacity (CXE), anterior cortical opacity (CXA), posterior cortical opacity (CXP), anterior subcapsular cataract (SCA), posterior subcapsular cataract (SCP), supranuclear opacity (SN), and nuclear opacity (N).
Left side: Fig. 4. Top. Three major classes: a, immature; b, mature cataract viewed in prism apparatus mirror; and c, hypermature cataract viewed as in b. Fig. 5. Center. Cortical opacification: a, anterior cortical opacity (CXA); b, equatorial cortical opacity (CXE); and c, posterior cortical opacity (CXP). Stereo pairs. Fig. 6. Bottom. Subcapsular opacification: a, anterior subcapsular opacification (SCA); b, posterior subcapsular opacification (SCP) viewed with posterior lens surface up. Stereo pairs. Right side: Fig. 7. Top. Supranuclear opacification: a, four quadrants of SN involvement (SN4); b, scattered SN opacification equivalent to SN3 if all opacified area were contiguous. Stereo pairs. Fig. 8. Center. Nuclear opacification: a, N1, only slight obliteration of slit image in the central region; b, N2, moderate obliteration of slit image; c, N3, marked obliteration; and d, N4, total obliteration of slit image in central lens. Fig. 9. Bottom. Composite photograph of different degrees of nuclear sclerosis: a, colorless; b, very pale yellow; c, pale yellow; d, yellow; e, dark yellow; f, very dark yellow; g, brown; and h, black.
For certain studies in which there may be an association between a laboratory measurement and the volume of lens involved, it may be more appropriate to express the extent of opacification in terms of a volume. In Table 3, the volume of each quadrant of CXA, CXE, CXP has been estimated by using elliptical geometry in the following manner:

\[ V_L = \frac{2}{3}\pi a^2b \quad \text{L = entire lens} \]
\[ V_N = \frac{2}{3}\pi (a')^2(b') \quad \text{N = nucleus} \]
\[ V_C = V_L - V_N \quad \text{C = cortex} \]

A, b = long, short radii, respectively.

In Table 4, our experiences in collecting and classifying lenses during the past five years is found. The steady improvement in yield of usable lenses and photographs is evident. This was achieved by having a member of our laboratory present in the operating room at least 4–6 hrs/day and by establishing good rapport with operating room nurses and ophthalmic surgeons.

Table 3. Approximate volume of quadrants of CXE, CXA, and CXP opacification

<table>
<thead>
<tr>
<th>Number of quadrants</th>
<th>CXE</th>
<th>CXA</th>
<th>CXP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent total cortical volume</td>
<td>18.5</td>
<td>4.3</td>
<td>2.1</td>
</tr>
<tr>
<td>Cumulative percent of total cortical volume</td>
<td>18.5</td>
<td>37</td>
<td>55.5</td>
</tr>
</tbody>
</table>

Results

The most striking finding was the paucity of pure cataract types: 500/2231 (22.41%). The largest group of pure cataracts was the nuclear group (214/2231 = 9.59%). In 1476/2231 (66.16%) lenses, the cataract was a compound opacity involving more than one region in the opacity. It was clear that a study of single region (pure) cataracts, except for the nuclear cataract, would be almost impossible due to the scarcity of these forms. The largest group (17.03%) of mixed cataracts is one in which the subcapsular, cortical, supranuclear, and nuclear regions are involved. It is the great preponderance of mixed cataracts that forces the scientist to deal with the statistical and scientific complexities inherent in their study. There is no simple way of avoiding them.

Consistency of Classification Techniques

To test the consistency of the classifier (Dr. Chylack) and to detect the weaknesses in the CCRG system, a subset of this large group was created so that in 82 lenses, there were represented the same proportion of simple and compound cataracts as in the total population. All cataracts in the subset were classified; after 48 hours and a mixup of the sequence of photographs, the lenses were reclassified by the same classifier who did not have access to the classification data recorded during the first time. The two sets of classification data were compared and errors analyzed:

1. In 82/82 cases, there was correspondence between the choice of H, M, and I designations. This choice can be made with 100% confidence.
2. In 4/82 cases, CXP or CXA opacities were later classified as SCP or SCA respectively. This is a trivial difference, because all SCP opacities are to some degree cortical in location. The distinction between SCP and CXP is based on the depth of cortical involvement, and frequently the photos do not allow accurate delineation of depth. More important is the knowledge that one should not look for biochemical/physiological differences between these nearly indistinguishable types of lens opacity.
3. Of 44 cases of either SCA or SCP opacities, there were only eight examples (three SCA, five SCP) in which the areas of opacity did not correspond exactly.

Table 2. Codes for NS (Nuclear Sclerosis)

<table>
<thead>
<tr>
<th>Subscript</th>
<th>Color</th>
<th>Code</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Colorless</td>
<td>c</td>
</tr>
<tr>
<td>2</td>
<td>Very pale yellow</td>
<td>vpy</td>
</tr>
<tr>
<td>3</td>
<td>Pale yellow</td>
<td>py</td>
</tr>
<tr>
<td>4</td>
<td>Yellow</td>
<td>y</td>
</tr>
<tr>
<td>5</td>
<td>Dark yellow</td>
<td>dy</td>
</tr>
<tr>
<td>6</td>
<td>Very dark yellow</td>
<td>vdy</td>
</tr>
<tr>
<td>7</td>
<td>Brown</td>
<td>br</td>
</tr>
<tr>
<td>8</td>
<td>Black</td>
<td>bl</td>
</tr>
</tbody>
</table>

These results also indicate that studies, which heretofore allocated all lenses into nuclear or cortical groups, probably oversimplified their analyses and obtained misleading or incorrect conclusions.
Table 4. Summary of disposition of 3722 cataractous lenses obtained at the Massachusetts Eye and Ear Infirmary from 1977 to 1981

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Lenses collected</td>
<td>600</td>
<td>700</td>
<td>700</td>
<td>930</td>
<td>792</td>
<td>3722</td>
</tr>
<tr>
<td>Ruptured</td>
<td>30</td>
<td>29</td>
<td>19</td>
<td>0</td>
<td>0</td>
<td>78</td>
</tr>
<tr>
<td>Unsatisfactory photographs</td>
<td>32</td>
<td>39</td>
<td>25</td>
<td>2</td>
<td>0</td>
<td>98</td>
</tr>
<tr>
<td>No photographs</td>
<td>31</td>
<td>94</td>
<td>16</td>
<td>3</td>
<td>0</td>
<td>144</td>
</tr>
<tr>
<td>No photographs/no information</td>
<td>139</td>
<td>155</td>
<td>22</td>
<td>4</td>
<td>6</td>
<td>326</td>
</tr>
<tr>
<td>Clear lenses autopsy/eye bank</td>
<td>6</td>
<td>8</td>
<td>0</td>
<td>7</td>
<td>1</td>
<td>22</td>
</tr>
<tr>
<td>Total unclassified</td>
<td>238</td>
<td>325</td>
<td>82</td>
<td>16</td>
<td>7</td>
<td>668</td>
</tr>
<tr>
<td>Total classified</td>
<td>362</td>
<td>375</td>
<td>618</td>
<td>914</td>
<td>785</td>
<td>3054</td>
</tr>
</tbody>
</table>

Of these eight, four (1 SCA, three SCP) were examples of small opacities (SCA_{3,119}) that were noted in one but not the other reading.

4. In classifying supranuclear (SN) change, 35/37 cases corresponded exactly; in 2/37 cases, the extent of the opacity differed by one quadrant (ie, SN_{2} instead of SN_{1}).

5. In 65/66 cases with nuclear (N) opacification, the presence of a nuclear opacity was correctly noted. In the one case in which it was missed, it was an N_{1} cataract. In 2/66 cases, there was a difference of one unit in the N subscript.

6. In estimating the degree of nuclear sclerotic change (NS), there were 20/73 cases in which the NS subscript differed by one grade; 9/82 cases were either H or M, and in these, NS cannot be classified accurately. In no case did the estimate of NS differ by more than one grade.

These results suggest that this scheme can accurately and reproducibly describe zones of opacity and degree of NS in senile cataractous lenses. There are two weaknesses in the system that in no way limit its usefulness:

(1) It is difficult to distinguish consistently between SCA and CXA as well as SCP and CXP. Since this distinction is likely never to be sought, it is not a major problem in implementing this system.

(2) In correlating laboratory data with the degree of nuclear sclerosis, it may be advisable to condense the eight steps in the NS index into four.

Results obtained previously1 established the consistency of the photographic techniques, so that there should be no error introduced as a result of photographic inconsistency.

Discussion

The CCRG classification scheme has proven to be an extremely useful means of establishing meaningful correlations between laboratory data and cataract type. It has already been implemented in several studies2,6,7,10,13 and Parts II–V of this set of papers. It abandons nuclear color (sclerosis) as a measure of cataract formation; not only is it impossible to estimate accurately nuclear color under conditions optimal for viewing the cataract (black background), but it is impossible to see the cataract against a white background when nuclear color is most clearly appreciated. This has been demonstrated dramatically in Figures 9a–h in which one cannot see any opacity. Also, a biostatistical analysis (Part III) shows that the...
NS index is not useful in estimating the extent of opacification in pure or mixed cataracts. In spite of the popularity of systems of classification based on nuclear color, it must be recognized that reliance on nuclear color to classify cataractous change may yield misleading or incorrect correlations with epidemiologic or laboratory data. This precaution applies to systems of classification employing photography of lenses against a white, or black and white grid backgrounds.14

Duncan15 classified lenses after they had been frozen and refrozen. While the system may appear complex, it derives considerable strength and no real weaknesses from this complexity. In comparing populations of compound or mixed cataracts,15 it is quite easy to ascertain whether or not the degree, type, or mix of cataracts is different in each population. In Part II of this series, the techniques for simplifying the raw classification data are presented.

Although Dr. Chylack has done all of the cataract classification for the CCRG, the system has been learned and applied by others with excellent results. This system is currently being used by all members of the American Cooperative Cataract Research Group.

Acknowledgments

The authors would like to express our sincere appreciation to the surgeons and operating room nurses at the Massachusetts Eye and Ear Infirmary, without whose assistance these studies could not have been done.

References