Principles and Practice of Clinical Electrophysiology of Vision

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Standard for Clinical Electroretinography

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INTRODUCTION

Michael F. Marmor

The electroretinographic (ERG) protocol and technical specifications which follow represent an international Standard that describes a set of basic responses that should be recorded wherever and whenever an ERG is performed (Fig 36–1). Since ERGs obtained in this manner are comparable in waveform and amplitude, use of the Standard responses ensures that clinical and research data can be shared and evaluated by the same criteria anywhere and anytime.

The Standard should serve several purposes. It proposes a set of basic responses that will become recognizable and comparable anywhere. It defines minimum capabilities (and recommends higher ones) for instrumentation, and hopefully will serve to stimulate manufacturers to improve their products. It will lead to the development of normative values for ERG parameters that can be used anywhere. It will stimulate more accurate data recording and dissemination of information. However, it will work only if everyone adheres to it. All readers are strongly urged to use the Standard responses as the core of their routine recording system and protocol, and journal editors and granting agencies should consider requiring the use of Standard responses in research work and publications.

One may reasonably ask why ERG Standardization has been so long in coming, given the obvious benefits to medicine and science. When the International Society for Clinical Electroretinography (ISCERG) was founded, its by-laws[1] stated that the work of the Society should include "establishing norms for instrumentation, recording, procedure and measurement in clinical electroretinography." The first ISCERG Symposium in 1961 was devoted to Standardization and H. van der Tweel summarized the proposals in a brief report.[2] ERG technology was still evolving, however, and little more was done until 1981 when ISCEV (ISCERG was renamed the International Society for Clinical Electrophysiology of Vision) and the International Council of Ophthalmology published (again with the guidance of van der Tweel) a more comprehensive report on instrumentation and procedures.[3] This document described equipment and parameters that *needed* to be standardized, but stopped short of defining the conditions for a basic set of responses. In 1987 the National Retinitis Pigmentosa Foundation initiated a program to accelerate the process of ERG standardization and asked the author to convene a meeting of United States ophthalmologists to write a working draft of a Standard. This document served as the stimulus to establish an International Committee composed of Marmor (representing the RP Foundation), G.B. Arden (representing the International Council of Ophthalmology and ISCEV), S.E. Nilsson and E. Zrenner (both representing ISCEV). This

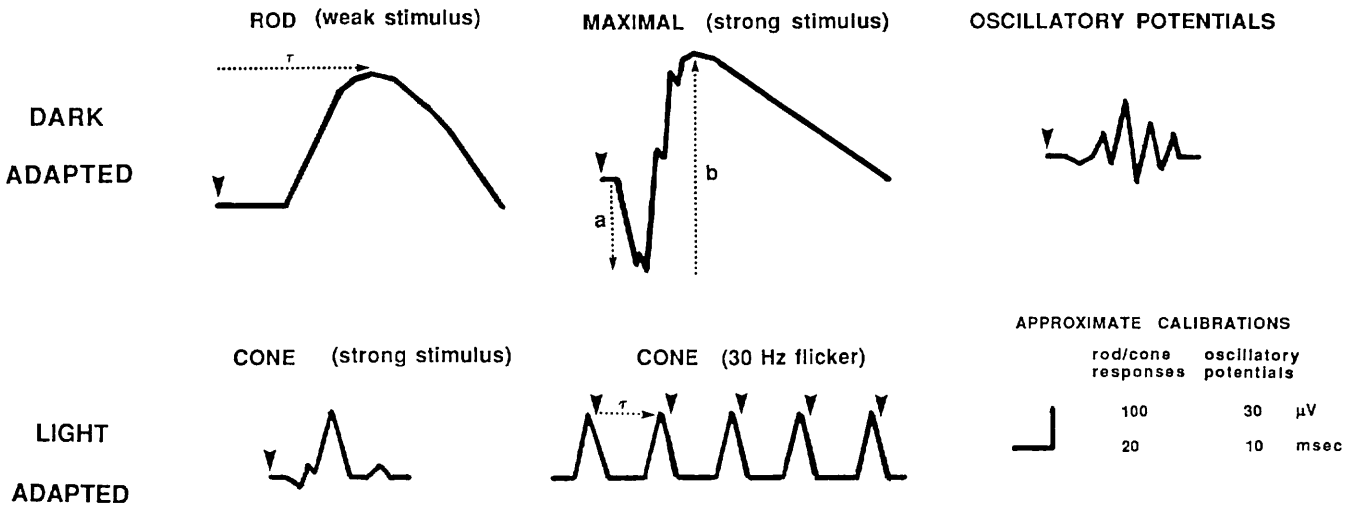

FIG 36–1.
Diagram of the five basic ERG responses defined by the Standard. These waveforms are exemplary only, and are not intended to indicate minimum, maximum or even average values. *Dotted arrows* show the measurement of time-to-peak (τ, implicit time), a-wave and b-wave.

committee refined the Standard, and in conjunction with international consultants and input from the ISCEV membership the final Standard was approved.

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OFFICIAL STANDARD*

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(International Standardization Committee)

Full-field electroretinography (ERG) is a widely used ocular electrophysiologic test, and a basic protocol should be standardized so that certain responses will be recorded comparably throughout the world. We propose standards for five commonly obtained responses:

1. A maximal response in the dark-adapted eye
2. A response developed by the rods (in the dark-adapted eye)
3. Oscillatory potentials
4. A response developed by the cones
5. Responses obtained to a rapidly repeated stimulus (flicker)

While this document is intended as a guide to practice and will assist in interpretation of ERGs, we recognize that there are many additional techniques and protocols that certain laboratories may choose to use. The standard describes simple technical procedures that allow reproducible ERGs to be recorded under a few defined conditions. Different procedures can provide equivalent ERG responses. It is incumbent on users of alternative techniques to demonstrate that their procedures do in fact produce signals that are equivalent in basic *waveform, amplitude,* and *physiologic significance* to the standard.

Our intention is that the standard method and responses be used widely, but not to the exclusion of other responses or additional tests that individual laboratories may choose or continue to use. We also recognize that the investigation of certain eye conditions may not require all five of the standard responses. In addition, specialized types of ERG (eg, focal ERG, early receptor potential, pattern ERG, bright-flash ERG, prolonged-flash ERG, and DC recording) are not covered by the standard.

These Standards have been officially endorsed by the International Society for the Clinical Electrophysiology of Vision and the National Retinitis Pigmentosa Foundation Fighting Blindness. They originally appeared in Archives of Ophthalmology, *1989; 107:816–819, and are reprinted with permission of the* Archives of Ophthalmology *and the American Medical Association.*

Because of the rapid rate of change of ERG techniques, these standards will be reviewed every 4 years. We have made recommendations that commercial recording equipment have the capability to record ERGs under conditions that are outside the present standard but that are nevertheless either widely used or likely to be needed in the future. Note that this document is not a safety standard and does not mandate particular procedures for individual patients.

The organization of this report is as follows:

- Basic technology
  - Light diffusion
  - Electrodes
  - Light sources
  - Light adjustment and calibration
  - Electronic recording equipment
- Clinical protocol
  - Preparation of the patient
  - ERG measurement and reporting
- Description of the five standard responses
  - Rod response
  - Maximal response
  - Oscillatory potential
  - Single-flash cone response
  - Flicker response

BASIC TECHNOLOGY

Light Diffusion

We believe strongly that full-field (Ganzfeld) dome stimulation should be used. With focal flashes, the area of retinal illumination is not uniform, and its extent is unknown (although focal flashes may be used for certain specialized ERG tests). Ocular diffusers (e.g., 100-D or opalescent contact lenses) are also less desirable since there is no way to accurately measure the illumination produced by such devices.

Electrodes

Recording Electrodes

Corneal contact lens electrodes are recommended for basic full-field recording; they should have an optical opening as large as possible and incorporate a device to hold the lids apart. The corneal surface should be protected during use with a nonirritating and nonallergenic ionic conductive solution that is relatively nonviscous (e.g., ≤0.5% methylcellulose). Skin electrodes and other types of corneal electrodes (wicks, fibers, foils, etc.) are less stable than corneal electrodes and may not be comparable for ERG amplitude and waveform measurements.

Reference Electrodes

Reference electrodes may be incorporated into the contact lens–speculum assembly to make contact with the conjunctiva ("bipolar electrodes"). Otherwise, skin electrodes can be placed centrally on the forehead or near each orbital rim as a reference for the corresponding eye. Other positions may not be equivalent.

Ground Electrodes

A separate skin electrode should be attached to an indifferent point and connected to ground. Typical locations are on the forehead or ear.

Skin Electrode Characteristics

Skin electrodes used for reference or ground should have 10-kΩ or less resistance measured at 30 to 200 Hz when applied. The skin should be prepared by cleaning and the use of suitable conductive paste to ensure good electrical connection.

Electrode Stability

Whatever corneal and reference electrode system is used, the baseline voltage in the absence of light stimulation should be stable. Some electrode systems may need to be made of nonpolarizable material to achieve this stability.

Electrode Cleaning

Recording the ERG exposes corneal electrodes to tears and skin electrodes to blood if there has been any abrasion of the skin surface. We advise that electrodes be suitably cleaned after each use to prevent the transmission of possible infectious agents. The cleaning protocol should follow current standards for devices that contact skin and tears.

Light Sources

Stimulus Duration

The standard is based upon stimuli of duration considerably shorter than the integration time of any photoreceptor. Thus, the light stimulus should consist of flashes having a maximum duration of 5 ms.*

**Prolonged-flash ERGs are currently used for studying slow potentials and off-responses that are outside the scope of the Standard. We recognize that one can adjust the intensities of long flashes to produce response amplitudes equivalent to those produced by brief flashes; thus Standard ERG responses can be obtained from such longer stimuli. However, this procedure requires careful comparison of "V/log I" curves and particular care to avoid interference from off-responses and signal attenuation by light adaptation (i.e., the interstimulus interval must be appropriately lengthened). The verification of equivalence to the Standard ERG is recommended only for laboratories with special needs.*

Short flash durations may be obtained from gas discharge tubes, from stroboscopes, and potentially from other devices.

Stimulus Wavelength

The stroboscopic flash tubes in use have a color temperature near 7,000 K and should be used with domes or diffusers that are visibly white. Colored filters are used by some laboratories to enhance the separation of rod and cone responses, but this is not part of the Standard.*

Stimulus Strength

A Standard system is defined as one that produces a stimulus strength (in luminance · time) at the surface of the Ganzfeld bowl of at least 1.5 to 3.0 cd · m^{-2} · sec (note that these are photometric units and that 3.43 cd · m^{-2} = 1 fL).† A flash of this strength will be called the "Standard flash" (SF).

Background Illumination

In addition to producing flashes, the stimulator must be capable of producing a steady and even background luminance of at least 17 to 34 cd · m^{-2} (5 to 10 fL) across the full field. For this Standard, a white background is used, but we recognize that colored backgrounds may also be used.

Light Adjustment and Calibration

Adjustment of Stimulus and Background Intensity

Methods of modifying both the stimulus and background intensity must be provided. We recommend that a Standard system be capable of attenuating flash strength from the SF over a range of at least 3 log units, either continuously or in steps of no more than 0.25 log units. The method of attenuation should not change the wavelength composition of the light. The background luminance needs sufficient adjustability to calibrate and recalibrate the intensity to the levels specified below under "Single-Flash Cone Response." It is preferable that the color temperature of the background not alter with intensity. We recognize that the stimulus and background requirements for a full range of ERG testing are both more extensive and more stringent, and we recommend that equipment manufacturers exceed the minimum standard.*

Stimulus and Background Calibration

The stimulus strength (in luminance · time) produced by each flash on the surface of the Ganzfeld bowl must be documented by the user or manufacturer, ideally with an integrating photometer (luminance meter) placed at the location of the eye. The light output per flash of most stroboscopes varies with the flash repetition rate; therefore separate calibrations will need to be made for single and repetitive stimuli. The photometer must record the luminance of the Ganzfeld bowl's surface, must meet international standards for photometric measurements based on the photopic luminous efficiency function (photopic luminosity curve), and must be capable of recording the total output of very brief flashes. The committee recommends that in the future, manufacturers of stimulators provide a suitable photometer as part of the equipment. Background luminance may be measured with the same instrument in a nonintegrating mode.

Recalibration

Light output from the dome may vary with time from changes in the flash tube, the tube power source, the background light bulbs, the attenuation systems, the paint in the dome, etc. This may be especially critical for background illumination provided by incandescent sources. Responsibility for electronic stability and warnings about sources of instability should rest with the manufacturers of the equipment; however, at present this cannot be presumed. The frequency with which recalibration of flashes and backgrounds is required will vary from system to system and could be as high as weekly for some units. Self-calibrating units are to be encouraged.

**Chromatic stimuli offer certain advantages in the separation of cone and rod responses, but the calibration of colored stimuli and the relation of the responses produced to the Standard ERG requires special procedures. We recommend that white flashes be employed for the Standard responses in addition to other stimuli that may be used.*

†This measurement can in practice be made with inexpensive light meters that integrate the flash output over time (see the section "Light Adjustment and Calibration"). Technically, the Standard describes a source that delivers at the cornea the same number of quanta during the period of its flash as would be produced in 1 second by the Ganzfeld bowl when continuously illuminated by a source that produces a luminance of 1.5 to 3.0 cd · m^{-2}. Units: cd = candela; fL = foot Lambert.

**We recommend that the flash source of commercial instruments be capable of generating strengths 1 log unit above the SF and be attenuable through 6 log units below the SF. Regardless of whether attenuation is achieved by filters or electronic means, we strongly recommend that commercial units incorporate a means of inserting additional colored and neutral-density filters to meet a variety of individual (and unforseen) needs. We also suggest that background luminance be adjustable to perform electro-oculography with the same equipment. Commercial units should also allow the insertion of colored and neutral filters into the background illumination system to meet a variety of needs.*

Electronic Recording Equipment

Amplification and Display Systems

We recommend that the band pass of the amplifier and preamplifiers include the range of 0.3 to 300 Hz and be adjustable for OP recordings and special requirements. We advise that the input impedance of the preamplifiers be at least 1 MΩ. Amplifiers should generally be ac coupled and capable of handling offset potentials that may be produced by the electrodes.*

Display System

We strongly recommend that the equipment that provides the final record be able to represent, without attenuation, the full amplifier band pass. Good resolution can be achieved with oscilloscopes or computer-aided systems, but not with direct pen recorders. With the computer-aided systems, it is important that responses be displayed promptly so that the operator can continuously monitor stability and make adjustments during the test procedure.

Patient Isolation

We recommend that the amplifiers be electrically isolated from the patient according to the current standards for safety of biological recording systems used clinically.

CLINICAL PROTOCOL

Preparation of the Patient

Pupillary Dilatation

We recommend that pupils be maximally dilated for all ERG recordings in this Standard and that pupil size be noted when dilatation is, for any reason, less than maximal.

Initial Dark Adaptation

Dark adaptation for at least 20 minutes is required to achieve a relatively stable physiological condition and relatively maximal scotopic responses. The ERG recording electrodes can be inserted under dim red light at the end of this period to minimize corneal irritation from the electrodes.

Pre-exposure to Light

We advise that fluorescein angiography or fundus photography be avoided before ERG testing, but if these examinations have been performed, a period of dark adaptation of 1 hour is needed. It is usually preferable to record scotopic responses to weak flashes before the mixed and cone responses to more intense flashes to minimize light adaptation and to reduce the time that the patient wears the contact lens electrode.

Fixation

A fixation point is useful but not essential. Some patients will not be able to see it, and the Ganzfeld dome minimizes the need for accurate fixation. In the absence of fixation, patients can be instructed to look straight ahead and keep their eyes steady.

ERG Measurements and Recording

Measurement of the ERG

Both amplitude and implicit time should be measured for selected ERG signals. For practical purposes the parameters most often measured are the cone, the rod, and the maximal b-wave amplitudes and the cone or flicker b-wave time to peak. According to current convention, the a-wave amplitude is measured from baseline to a-wave trough, the b-wave amplitude from a-wave trough to b-wave peak, and the b-wave time-to-peak from flash onset to the peak of the wave.

Normal Values

We recommend that each laboratory establish or confirm normal values for its own equipment and patient population and that all ERG reporting (whether for local records, publication, or even for nonstandard responses) include normal values and the *limits of normal.* Some manufacturers may choose to distribute norms for their standard protocols. An effort is underway to establish worldwide norms.

Reporting the ERG

Standardization of ERG reporting is critical to the goal of having comparable data worldwide. We recommend that reports or communications of ERG data include a representative waveform of each of the standard responses (if performed) displayed with amplitude and time calibrations and labeled with respect to stimulus parameters and the state of light or dark adaptation. The strength of stimulation (cd · m^{-2} · sec) and light adaptation (cd · m^{-2}) should be given in absolute values. *The reporting forms should indicate whether the recordings meet the international standard.* We recommend that the basic numerical measurements listed above be extracted from the data and listed along with the normal val-

**Direct current amplification can produce identical responses but is extremely difficult to use because of drift in the baseline and in offset potentials; we strongly advise AC recording except for laboratories with special requirements and expertise.*

ues and their variances (which must be provided on all reports).

SPECIFIC RESPONSES

"Rod Response"

We recommend that this be the first signal measured after dark adaptation since it is the most sensitive to light adaptation. The Standard stimulus is a dim white flash of strength 2.5 log units below the white SF (see above); we advise a minimum interval of 2 seconds between flashes. Blue is equally appropriate if equated to the white standard (see the footnote to "Stimulus Wavelength").

Maximal Response

This response is to be produced by the white SF in the dark-adapted eye. We recommend an interval of at least 5 seconds between stimuli. This response is normally produced by a combination of cone and rod systems.

Oscillatory Potentials

Oscillatory potentials (OPs) are obtained from the dark-adapted eye by using the same white SF. However, the high-pass filter must be reset to 75 to 100 Hz so that an overall band pass of 75 to 100 Hz on the low end and 300 Hz or above at the high end is achieved. Filters should attenuate sufficiently to achieve this result. Users should be aware of and test for artifacts (e.g., phase shifts or ringing) that may be produced by present-day filters. The OP response varies with the stimulus repetition rate and changes after the first stimulus. To standardize the response, we recommend that flashes be given 15 seconds apart and only the second or subsequent responses be retained or averaged.

Single-Flash "Cone Response"

We propose the white SF as the stimulus and advise that to achieve stable and reproducible cone responses, the rods be suppressed by a background with a luminance of 17 to 34 cd · m^{-2} (5 to 10 fL) measured at the surface of the Ganzfeld bowl. We recommend that the higher value of the background be chosen if the stimulus flash is at the upper end of the allowable SF range and that the lower background value be chosen if the flash stimulus is at the lower end of the range. The intention is that all Standard ERG recording systems have an identical intensity ratio between the SF and the rod-suppressing background, equivalent numerically to 3.0 (cd · m^{-2} · sec) divided by 34 (cd · m^{-2}). We recommend that patients light-adapt to the background luminance for 10 minutes before recording of the cone ERG since the cone responses may increase during this period.

Flicker Responses

These are to be obtained with SF stimuli, under the same rod-suppressing background illumination, after recording the single-flash cone response. Recording the flicker response in the light-adapted state reduces discomfort and allows the photopic adaptation to be standardized. We strongly advise that flashes be presented at a rate of 30 stimuli per second, and the first few responses should be discarded so that stable conditions are reached. Some flash tubes do not produce full output while flickering, and separate calibration or a change in neutral-density filtering may be needed to keep as closely as possible to the Standard.