
X-ray spectrometry appears to be a reliable and safe method for noninvasive detection and measurement of metals in the eye for clinical and experimental purposes. Preliminary results in rabbits show that the dissolution of small copper intraocular foreign bodies can be detected shortly after their implantation. The dissolution was measured repeatedly and described as a function of time. It is hoped that this method can supply data regarding the nature and the extent of dissociation of intraocular foreign bodies, thus supplementing methods which can give information regarding only their presence and location.

The decision whether to attempt the often hazardous operation of nonmagnetic intraocular foreign body (IOFB) extraction should depend on the presence or absence of metallosis since nonmagnetic, nondissociating IOFB's are not necessarily harmful and need not be extracted. Available methods of IOFB investigations, such as ophthalmoscopy, roentgenography, and ultrasonography, provide data regarding only the presence and location of the IOFB. Ophthalmoscopy, biomicroscopy, and electroretinography supply only indirect and delayed evidence of IOFB dissociation. A method for direct measurement of the concentration of metals in the eye is thus clearly desirable in order to provide the clinician with early and direct evidence of metallosis and thus with a clear indication for operating to extract a nonmagnetic IOFB.

In this communication a noninvasive, safe, and repeatable method for monitoring the content of metals in eyes, in vivo, is described. The application of the method to preliminary animal experiments is given.

Method and material. The principle involved in our method is based on the fact that metals can be detected, and their concentration evaluated, by the measurement of the x-ray fluorescence.\(^1\), \(^2\)

The block diagram given in Fig. 1 demonstrates the essential features of the system. This method was used for noninvasive measurement of the corneal copper concentration in cases of Wilson's disease.\(^3\)

The vitreous is irradiated through the sclera by an x-ray beam of 2 by 4 mm. cross section. The incident radiation is absorbed by the various elements present in the eye, which subsequently emit their characteristic x-ray radiation, termed fluorescence. This radiation is detected by a solid state detector. The intensity of the radiation as a function of energy is displayed as a fluorescence spectrum in which each element is represented by a peak at a definite position (Fig. 2). Elements with atomic numbers ranging from 26 to 30 (iron, cobalt, nickel, copper, and zinc) can be detected in rabbits' eyes at concentrations below one part per million (p.p.m.). Elements with atomic numbers between 17 and 26 can also be detected, although the threshold concentration for their detection is higher. Since the fluorescence is strongly absorbed by the ocular tissues, chemical elements can be detected only when they are present near the ocular wall. The metallic IOFB itself can be detected only if it lies within a few millimeters from the sclera and is hit directly by the incident radiation. The fluorescence signal of a given element is a measure of its overall content in the ocular wall and vitreous. The accurate concentration of the elements in the different ocular tissues cannot at present be determined, since they probably are not homogeneously distributed. For clinical and experimental purposes, however, the differences in the signal between the two eyes of an individual, or its variation in time, is sufficient for evaluation of pathologic content. The copper signal is compared with a signal obtained from homogeneous solutions of copper and is given in concentration units (p.p.m.), thus supplying an evaluation of the mean copper concentration in the ocular tissues.

In the following report we describe the results of preliminary animal experiments using this method. We focused our attention on copper, which is relatively common in eye injuries, nonmagnetic, and very toxic. A pure sterile copper wire weighing approximately 3 mg. (0.5 mm. diameter, 2.0 mm. length) was inserted through the pars plana into the right eye of each of eight rabbits. It was left in the vitreous in two rabbits (rabbits 1 and 2) and implanted in the retina at the posterior pole in the other six eyes. In the first five animals a pure sterile platinum wire of the same dimensions was similarly implanted in the fellow eye. Platinum was used as a control since it has no known tissue toxicity. The copper content of these eyes was measured repeatedly in vivo in the equatorial nasal region, not overlying the IOFB. The radiation per measurement was 10 rad.

Results. The copper signals obtained during the 20 days following implantation are shown in Figs. 3 and 4. The error of the system was measured by nine repeated measurements of a healthy rabbit's eye and the one standard deviation was found to be 0.13 p.p.m. The standard deviation determined by 14 repeated measurements in an injured rabbit's eye containing a platinum IOFB was 0.16 p.p.m. The latter, higher value was chosen as the working estimation of the error of the system. The vertical bars in the
Fig. 1. Block diagram of measuring system.

Fig. 2. X-ray fluorescence spectrum of rabbit 3, 12 days after implantation of a copper IOFB.

figures represent the 2 S.D. range, i.e., that which includes 95 per cent of cases. The dissolution reached a meaningful value within 1 to 7 days (mean, 3.5 days) after implantation. In all eight rabbits we found a natural background signal of copper equivalent to a concentration of 1 p.p.m. The two test eyes (rabbits 1 and 2) in which the copper IOFB was placed in the vitreous showed a brief, small rise of the copper content in response to the implantation of the IOFB (Fig. 3). The six eyes in which the copper IOFB was implanted into the retina showed three types of responses: (1) rabbits 3 and 5 (Fig. 3) developed copper responses of 3 to 4 p.p.m. with a later decline; (2) rabbits 4 and 8 (Figs. 3 and 4) showed a gradual increase in copper response up to 7 and 11.5 p.p.m., respectively, at the end of the experiments; and (3) rabbits 6 and 7 (Fig. 4) showed an initial, abrupt rise in copper content, up to 2.1 and 6 p.p.m., respectively, during the first day after implantation. Within 5 to 7 days the inflammation subsided and the copper content declined. It later increased, however, until the end of the experiment. None of the control eyes showed any change in the copper content. In all the cases except two, the reaction of the eye was restricted to the region adjacent to the IOFB. In rabbits 6 and 8 a mild endophthalmitis appeared at the end of the follow-up.

Discussion. The main feature of the present results is the early detection of the dissolution after an average of 3.5 days following implantation. In no case was a severe reaction sustained by the eye before the detection of the dissolution. The changes in copper concentration were not the result of the surgical trauma of implantation since the control eyes with platinum IOFB did not show any significant change. Taking into account (as described in reference 2) the ab-
Absorption of the fluorescence by the sclera, the mean vitreous concentration is estimated to be about 10 p.p.m. This estimated concentration agrees well with the results obtained on aspirated vitreous samples. Although atomic absorption spectroscopy is more accurate than x-ray excitation spectroscopy, a method based on the aspiration of the vitreous is, of course, clinically impractical. Attempts have been made to overcome these limitations by in vitro measurements of copper in the aqueous humor of eyes containing copper IOFB in the posterior segment. This approach to the problem has inherent limitations: the copper concentration in the aqueous does not correspond well with that in the vitreous and is late in appearance. Anterior chamber tapping is not entirely free of risks and cannot be repeatedly used for follow-up.

Each of the test animals showed a different pattern of response to the presence of the IOFB in terms of the magnitude of the ocular copper content as well as the time interval between implantation and the development of a meaningful signal. The relatively low copper signals in rabbits 1 and 2 may have resulted from the fact that the IOFB did not touch the retina, a position in midvitreous apparently leading to a low-grade reaction. The differing copper contents in the other six eyes, however, cannot be explained by the known factors which affect the development of chalcosis, i.e., the composition of the IOFB, its surface area, and its location in the eye. These factors were identical in all animals. Neither can these differences be explained by variations in the concentration within the vitreous as a function of the distance from the IOFB, since all measurements were performed by directing the x-ray beam at a fixed point on the nasal sclera and the IOFB was implanted in all eyes at almost the same location in the posterior pole. The differences in copper content between the test animals must therefore represent different individual responses to the presence of a copper IOFB, a known clinical and experimental observation.

Presently available methods for IOFB examinations, such as roentgenography and ultrasonography, supply only data regarding the presence and location of an IOFB. Other methods such as electroretinography (ERG) give only delayed and indirect indications about the damage caused to the eye by the penetration and retention of the IOFB. None of these methods can diagnose the nature of the dissociating IOFB and measure the extent of this dissociation. Data about these parameters supplied directly and noninvasively by x-ray spectrometry may be important in reaching a decision whether or not to undertake the often hazardous operation of nonmagnetic IOFB extraction. X-ray spectrometry as a clinical tool has the advantage that it does not require paracentesis, surgery, or any handling of the eye. It is repeatable and sufficiently sensitive. In order to establish the clinical utility of the method, further
Fig. 4. Variation of copper signal with time in test eyes containing copper IOFB (●) and control eyes with IOFB (•) of rabbits 6 to 8.

The authors wish to thank Professor H. Zauberman, Head of the Ophthalmology Department, Hadassah University Hospital, for his continuous interest and generous help throughout all the phases of this work. We would like to thank Mr. A. Yitschak and Miss H. Gnesin of the Eye Pathology Laboratory, Hadassah University Hospital, for technical assistance.

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Key words: intraocular foreign bodies, copper, chalcosis, metallosis, x-ray spectrometry.

REFERENCES