LETTERS TO THE EDITOR

Differential diagnosis of iridocorneal endothelial syndrome and posterior polymorphous endothelial dystrophy

EDITOR,—In the paper by Laganowski *et al*[1] the point is made strongly that endothelial specular photomicroscopy (ESP) 'by revealing ICE cells and distinguishing between ICE-bergs and PPD vesicles, will always provide a definitive diagnosis even in uncertain cases and thus promote accurate management of patients and their families'. Their own cases reflect the consistent unilaterality of iridocorneal endothelial (ICE) syndrome and the usual bilaterality of posterior polymorphous dystrophy (PPD). The authors describe unilaterality in four out of 19 vesicular types, none out of two of the diffuse, and 14 out of 23 of the band type. Taken at face value this might suggest that there could be a large percentage of people with unilateral PPD disease that could be mistaken for the consistently unilateral ICE syndrome. On the other hand, the band type of PPD is so characteristic in its pattern that it does not share a similar slit-lamp picture with any ICE syndrome patient. Once these patients have been taken from the unilateral cases, then there is only one strictly unilateral case out of the 44 patients in whom a possible confusion could exist. Examination of this patient's relatives would almost certainly show typical PPD findings which would confirm the diagnosis without the need for expensive instrumentation such as specular microscopy.

In addition, Laganowski *et al* assert that subtotal ICE plus syndrome has a characteristic circumscribed nest of abnormal endothelial cells which is pathognomonic of ICE and not seen in PPD. Figure 11 in the paper by Hirst and Waring,[2] bears a remarkable resemblance to Figure 2 of Laganowski *et al*.[1] The patient described by Hirst and Waring[2] came from a family of patients with posterior polymorphous endothelial dystrophy in which histology confirmed the diagnosis in one of the family members. As Laganowski *et al* contend 'while the two conditions may conceivably co-exist in the same eye or in different members of the same family, the ICE syndrome and PPD are distinct entities,' the only explanation for our case would be that the two diseases are co-existing in the same family, or perhaps it is more likely that the findings of Laganowski *et al* are not pathognomonic of the subtotal ICE plus syndrome. Similar findings to these seen in Figure 2 were seen in a further 11 patients with the geographic type of posterior polymorphous endothelial dystrophy in the original study by Hirst and Waring.[2] Since that time, examination of further patients has confirmed these abnormal cells occurring in typical, familial posterior polymorphous endothelial dystrophy.

In the first line of the discussion, it is suggested that Hirst and Waring reported the simultaneous occurrence of ICE syndrome and PPD in an individual or separately in different members of a family.[2] We have not reported this. Perhaps the confusion was in the similar cell findings in some of our patients with geographic PPD and their patients with subtotal ICE plus. This finding is not ours alone as the similarity of cells as seen in Figure 2 of Laganowski *et al*[1] is also illustrated in Bourne's paper.[3] He highlights the difficulty in differentiating between these two conditions if the family history is negative and examination of family members provides no additional patient involvement.

Contrary to the statement that histopathological studies are based only on decompensated corneas and that they reveal differences in Descemet's membrane which makes a relationship between ICE and PPD highly unlikely, there are some similarities histopathologically in the conditions particularly relating to intermediate filament staining as described by Rodrigues *et al*[4] and Hirst *et al*.[5] This is *not* to suggest that these are one and the same disease, or that they even occur in the same patient population: rather, as dicussed in Hirst,[6] it is possible that in the progressive geographic PPD, and the ICE syndrome a final common pathway of epithelialisation of the anterior segment takes place. The pathology bears an uncanny resemblance to iatrogenically produced epithelial downgrowth.

I would caution readers against assuming that the progressive form of PPD and ICE syndrome can necessarily be differentiated by specular microscopy. There is much still to be understood about these two diseases, and perhaps the future may show that they are actually variants of one disease which might explain the confusing picture resulting from different researchers' findings.

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1 Laganowski H, Sherrard ES, Kerr-Muir MG, Buckley RJ. Distinguishing features of the iridocorneal endothelial syndrome and posterior polymorphous dystrophy: value of endothelial specular microscopy. *Br J Ophthalmol* 1991; 75: 212–6.
2 Hirst LW, Waring GO. Clinical specular microscopy of posterior polymorphous endothelial dystrophy. *Am J Ophthalmol* 1983; **95**: 143–55.
3 Bourne WM. Primary corneal endotheliopathies (letter). *Am J Ophthalmol* 1983; **95**: 852–3.
4 Rodrigues MM, Sun TT, Krachmer J, Newsome DA. Epithelialization of the corneal endothelium in posterior polymorphous dystrophy. *Invest Ophthalmol Vis Sci* 1980; **19**: 832.
5 Hirst LW, Green WR, Luckenbach M, de la Cruz Z, Stark WJ. Epithelial characteristics of the endothelium in chandler's syndrome. *Invest Ophthalmol Vis Sci* 1983; **24**: 603–11.
6 Hirst LW. Congenital anterior segment epithelialisation. *Aust J Ophthalmol* 1983; **11**: 209–13.

Reply

EDITOR,—We thank Dr Hirst for his comments on our paper.[1] The purpose of our study was to determine whether the specular microscopical features of the ICE syndrome and PPD were unique to each condition and could be used to establish a definitive diagnosis in cases which apparently have features of both. We, therefore, chose patients with features of unequivocal ICE or PPD on slit-lamp examination.

We acknowledge that the majority of ICE and PPD cases can be distinguished clinically at the slit-lamp. In some cases, however, confusion and misdiagnosis occur and our paper confirms that such errors in diagnosis and classification can be overcome by examining the corneal endothelium by wide field contact specular microscopy, a non-invasive, painless outpatient technique.

We assert that 'ICE cells', which give rise to the hammered silver appearance on slit-lamp examination and appear as a negative of normal endothelial cells with the specular microscope, are pathognomonic of the ICE syndrome. In some cases of 'subtotal ICE plus' these cells may appear as an isolated feature in the remaining endothelium. We agree that Figure 11 in the paper by Hirst and Waring,[2] resembles our Figure 2 of 'subtotal ICE plus'. We contend that their Figure 11 shows classic ICE cells well demarcated from endothelium and is, therefore, a case of 'subtotal ICE plus'. That this patient's relatives have posterior polymorphous dystrophy (PPD) would not lead us to change our diagnosis since we believe that the diagnosis of ICE or PPD can only be based on the clinical signs of the eye in question (providing, as this study has demonstrated, the condition has distinguishing features) and that ICE and PPD could co-exist in different members of the same family in the same eye.

Dr Hirst's histological report is from a relative of the case shown in his Figure 11. To extrapolate histological data from one family member with PPD to explain different physical signs in another member is scientifically unacceptable. Furthermore, this corneal button was not examined preoperatively by specular microscopy. The only currently practical means of deriving unequivocal evidence to distinguish ICE and PPD is to examine the endothelium from an affected eye with precise cell to cell correlation of specular photomicrographs with light and electron micrographs.

With regard to PPD, we disagree that examination of the relatives 'would almost certainly show typical PPD findings which would confirm the diagnosis.' Moreover, in Hirst and Waring's paper,[2] the majority of relatives of patients with PPD showed no abnormality.

We also disagree with his statement that ICE is 'consistently unilateral'; six of our 80 patients with ICE syndrome have typical ICE cells bilaterally. We do agree, however, given the advanced pathology of corneal buttons removed at penetrating keratoplasty, that the histopathology may well represent a common pathway of cellular response and therefore be a poor discriminator of the primary diagnosis.

We are sure that Dr Hirst would agree that the present enigma of ICE/PDD will only be resolved by close collaboration between clinician and pathologist, and preferably by building detailed correlative databases as a multicentre activity.

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1 Laganowski HC, Sherrard ES, Kerr-Muir MG, Buckley RJ. Distinguishing features of the iridocorneal endothelial syndrome and posterior polymorphous dystrophy: value of endothelial specular microscopy. *Br J Ophthalmol* 1991; 75: 212–6.
2 Hirst LW, Waring GO. Clinical specular microscopy of posterior polymorphous endothelial dystrophy. *Am J Ophthalmol* 1983: **9**: 143–55.