Aims: To describe an unusual endophthalmitis-like reaction after an intravitreal injection of triamcinolone acetonide in four patients.

Methods: Retrospective case series.

Results: Four patients are reported with an endophthalmitis-like reaction following an intravitreal injection of triamcinolone acetonide. There was a dense vitreous haze with severe reduction of fundus view in all cases. One case was treated as an infectious endophthalmitis but the vitreous tap showed no evidence of an endophthalmitis and no bacterial or fungal growth in culture. In all four cases, the vitreous haze cleared without specific treatment. The anterior chamber remained quiet in all cases but one, which was examined 30 minutes after the injection, and there was no periorbital inflammation or pain.

Conclusion: Pseudo-endophthalmitis after an intravitreal injection of triamcinolone acetonide seems to be a distinct clinical entity that may resolve without specific treatment.
there was an area of central atrophy with no evidence of exudation or scarring. Intraocular pressure remained within normal limits at all times.

Case 2
An 87 year old female patient presented with visual acuity 6/18 in both eyes. Ophthalmological examination and fundus fluorescein angiography showed geographic atrophy in the right eye and a minimally classic choroidal neovascular membrane in the left eye. Triamcinolone acetonide 4 mg was injected intravitreally as described above. One week later visual acuity had dropped to 2/60 and there was a diffuse vitreous haze obscuring any view of the fundus. There were no inflammatory signs in the anterior chamber and the patient did not report any discomfort. The intraocular pressure was 25 mm Hg. No biopsy was taken, no specific treatment was started, and the vitreous cleared gradually. After 10 weeks the visual acuity had increased to 6/60 and intraocular pressures returned to normal. Three months after the injection, the vitreous was entirely clear and the visual acuity had increased to 6/45. The decline in visual acuity from the pre-injection level was felt to be consistent with the subretinal neovascularisation.

Case 3
A 77 year old male patient presented to his ophthalmologist with exudative age related macular degeneration of the right eye. He was referred to a retinal specialist but lost central vision of his right eye completely within 3 weeks, because of an unusually aggressive process. One year later he presented with visual complaints in his left eye. Best corrected visual acuity was counting fingers in the right eye and 6/9 in the left. Fundus fluorescein angiography showed a small classic choroidal neovascular membrane within 50 µm of the centre of the left macula. Because of the extremely aggressive course of the disease in the fellow eye, a combined treatment with intravitreal triamcinolone and photodynamic therapy was proposed to the patient. Triamcinolone acetonide 4 mg was injected intravitreally as described above and photodynamic therapy was planned for 2 days later. Two days after the injection, visual acuity had dropped to 2/30 at 1 metre. The slit lamp examination showed punctuate keratopathy and 2+ cells (or particles) in the anterior chamber. In the vitreous there was a diffuse haze as well as 4+ cells or particles. The visual acuity had dropped to counting fingers at 25 cm and there was a very poor view of the fundus.

Two days later the anterior chamber had cleared but there was still a diffuse haze and the visual acuity was only counting fingers at 2 metres. Two weeks after treatment the vitreous haze had cleared and the visual acuity was back to 6/30.

DISCUSSION
These four cases of an acute episode of marked anterior vitreous haze after an injection of triamcinolone share several common features. In all cases, impaired vision was noted immediately or very soon after the injection. Examination of the anterior vitreous revealed heavy particulate infiltration precluding a view of the retina. No patient reported any pain or swelling, and the anterior chamber remained quiet in all cases but one where the examination was performed immediately after the procedure. The vitreous haze cleared gradually over the ensuing weeks, without specific treatment in the second, third, and fourth cases, and without any other apparent adverse events.
At this stage, the cause of this acute vitreous haze remains uncertain. The clinical picture has some features of an infectious endophthalmitis, but the lack of pain, swelling, and anterior segment reaction, coupled with the spontaneous resolution without antibiotic therapy are not consistent with an infectious process. Possibly the true course of the infection was masked by the intravitreal steroid, but this seems unlikely without antibiotic cover. The one case that was tapped was culture negative. An acute reaction to the vehicle of the drug is theoretically possible (the vehicle contains 6.9 mg sodium chloride for isotonicity, 15 mg benzyl alcohol as a preservative, 7.5 mg carmellose sodium, and 0.4 mg polysorbate 80), but judging from the analysis of the vitreous tap in case 1, a true inflammatory reaction (immune or infectious) seems unlikely. Furthermore, triamcinolone was originally chosen as a candidate steroid for intraocular injection because the vehicle seemed to be well tolerated by rabbit eyes. It is perhaps pertinent that in all four cases the triamcinolone seemed to be dispersed throughout the vitreous rather than forming the discrete mass that is usually observed after the injection. We found that jamming of the triamcinolone in the needle upon injection was not uncommon before we switched from a 30 gauge to a 27 gauge needle. It is possible that there was partial jamming of the crystalline steroid in the barrel of the needle as the injection was given, resulting in spraying of the drug into the vitreous at a high velocity causing in a type of suspension. In that case the observed particulate matter might be particles of triamcinolone. This possibility is consistent with the immediacy of the loss of vision after the injection which was reported by all four patients, and which one would not expect with an inflammatory reaction which would begin 2 or 3 days later. Consistent with this possibility also are the findings from the vitreous tap performed on the first patient where there were a large number of small triamcinolone crystals but very few inflammatory cells in the smear (Fig 2).

The true incidence of acute vitreous haze after an intravitreal injection of triamcinolone is unknown. The four cases described are drawn from a sample of around 600 injections at the Sydney Eye Hospital and in the private practice of one of the authors over the past 8 years. Remarkably, none of first three patients described were sufficiently concerned about their problem to contact their doctor before their scheduled post-injection check and the fourth patient was examined only because of post-injection irritation of the eye, so it is possible that less severe manifestations of the phenomenon have gone undetected. In our randomised clinical trial of intravitreal triamcinolone for exudative age related macular degeneration, none of the 75 patients receiving the injection exhibited acute vitreous haze at the formal 1 week post-injection study examination.

It is important to note that this paper neither recommends nor supports the use of intravitreal triamcinolone for any condition until adequate data are available from properly designed clinical studies. Investigators performing these studies need to be aware, however, that acute vitreous haze is an uncommon event after an intravitreal injection of triamcinolone, that it does not appear to be associated with other serious adverse events, and that it may resolve spontaneously without treatment. Naturally, one has to bear in mind that the clinical picture and course of a true infectious endophthalmitis may be altered in the presence of steroids in the vitreous and that any deviation from the relatively benign course exhibited by the four cases presented would need to be treated aggressively as an infectious endophthalmitis.