Pediatric Rheumatology

COMMENTARY

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Reducing the risk of visual disability for children with juvenile idiopathic arthritis uveitis through disease surveillance: past and future challenges

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Abstract

Childhood blindness significantly impacts development, education, employment, and mental health, creating burden for families and society. Between 8% and 30% of children with Juvenile Idiopathic Arthritis (JIA) develop a potentially blinding chronic inflammatory eye disease, uveitis (JIAU). Alongside the use of disease-modifying agents and anti-TNF immunomodulators, JIAU surveillance has helped to reduce the risk of JIAU related blindness.

Inconsistent guidance on JIAU surveillance has previously been a hindrance to care delivery and access for professional and families. The Multinational Interdisciplinary Working Group for Uveitis in Childhood (MIWGUC) has brought some much-needed standardisation to JIA surveillance, developing a consensus-based screening proposal which simplifies the protocol, supporting implementation amongst non-specialists, and ensuring that children at risk receive the timely eye examination necessary to avoid life-changing visual disability. In this commentary on the MIWGUC surveillance proposal, we also address the implementation of such surveillance. A global shortage of ophthalmologists threatens the sustainability of these surveillance programs. Innovative approaches could be imaging-based detection. The accessibility of Optical Coherence Tomography (OCT) imaging may make OCT a feasible future option for community-based surveillance, reducing the burden on ophthalmologists, and on patients and their families.

Main text

Childhood blindness irrevocably changes a young person's life trajectory [1]It brings developmental, educational and employment challenges, and the risk of poorer general and mental health [2] Children with visual impairment typically have other disorders or impairments [3] resulting in an accumulation of risk, challenge, and burden.

One in every 1000 children have Juvenile Idiopathic Arthritis (JIA), and between 8 and 30% of children with JIA have an associated uveitis (JIAU) [4–6] JIAU related blindness is becoming uncommon, with recent reassuring reports of good visual outcomes [7], although one

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in three children have some degree of visual loss, and the remainder may remain at risk of further sight loss throughout their life course [7–9]. Good visual outcomes in JIAU have been hard won, through the earlier use of disease modifying agents [10] the introduction of 'blockbuster' anti- tumour necrosis factor monoclonal antibodies (biological agents), like adalimumab [11] and the introduction of whole population interventions: surveillance programmes for children at risk.

Children with JIAU have mostly "white uveitis" and may not experience or notice symptoms of active disease. Visual changes may only be apparent to a child or to the parent of a young child once there is advanced visual loss in both eyes A programme of regular scheduled eye examinations undertaken by a trained professional can ensure timely detection of JIAU, thus preventing childhood visual impairment [12] Until relatively recently, there was a wide variation in guidance and practice of JIA uveitis surveillance [5, 13] Such variation is an obstacle to the successful implementation of screening or surveillance programmes, leading to confusion amongst health care professionals and families, and increasing the risk of either over-surveillance, with a resultant burden on families and health care services, or under-surveillance, preventing the timely diagnosis which is the aim of such a programme. Attempts by supranational groups, such as the Multinational Interdisciplinary Working Group for Uveitis in Childhood (MIWGUC), to standardise uveitis surveillance [14] should support health care professionals in delivering appropriate care to children in need. The MIWGUC recommendations remove the need for the knowledge of the child's JIA category, ANA positivity or treatment status when scheduling surveillance visits. This results in guidance which, when compared to other recommendations in use, can be more easily implemented by local eye care professionals, particularly in those settings where limited information on non-ocular disease state is available.

The components of a programme of ongoing disease surveillance include the eligibility criteria for entrance into the programme ('who to test?'), the timing of the ongoing examinations ('when to test?') and determining which testing procedures should be used for surveillance ('how to test?').

Who to test?

In recognition of the higher prevalence of uveitis amongst children with oligoarticular, polyarticular, enthesitis-related and psoriatic JIA, those children form the population in need of regular testing [5, 12–14] There is, however, differential risk within those populations, which may be child specific (e.g., younger age at JIA onset being a strong predictor of JIAU) [4, 5, 9, 15–18] or treatment specific. For example, children whose disease is well controlled with a disease modifying anti-rheumatic drug (DMARD), such as methotrexate or adalimumab, are less likely to develop uveitis, but this is not yet reflected in JIAU surveillance schedules. There are concerns about the long-term effectiveness of adalimumab, as some patients may experience a loss of response over time. This would necessitate continued vigilance for uveitis for children whose JIA was in apparent long-term drug-controlled disease remission [17, 19].

When to test?

The timing of testing within a surveillance schedule has, in the past, been determined by the differential risk of developing uveitis, with 'high risk' patients (those early in their disease course, of female gender, with high antinuclear antibody titres, or those who have early disease onset) [19, 20] being seen every 3 to 4 months, and other children undergo checks every 6–12 month. However, if the aim of a surveillance programme is indeed *timely* detection [14] then, arguably every child at risk should undergo examination at a time which would prevent the avoidance of structural complications should uveitis become active between tests. A 3–4 month time window has been suggested as a 'safe' interim period for all children undergoing uveitis surveillance, irrespective of their individualised risk of disease [12]. Exit from a surveillance programme is determined either by the absence of disease risk (i.e. time from diagnosis) or the absence of the need for surveillance for disease detection (i.e. when the child or young person is thought able to note the signs of new disease). For example, the MIWGUC surveillance programme advises that examinations continue through childhood up to the age of 18 years, whilst the United Kingdom surveillance programme suggests that surveillance ends around the 12th birthday (or at one year from diagnosis for those aged 11 years or more) with families asked to continue with the regular optician checks advised for all children irrespective of JIA diagnosis [14].

How to test?

The long accepted answer to the question 'How to test?' has been, for children at risk of JIAU, face to face ophthalmic examination undertaken by a specialist with the training and expertise necessary to exclude the presence of inflammation. During this examination, the child's anterior ocular chamber is examined (usually by an ophthalmologist) using slit lamp biomicroscopy.

A key obstacle to successful implementation of uveitis surveillance programmes is the growing shortfall in eye health care professionals [21–23]. As this worsening resource scarcity, may result in a loss of the ground gained in the fight against JIAU associated blindness,

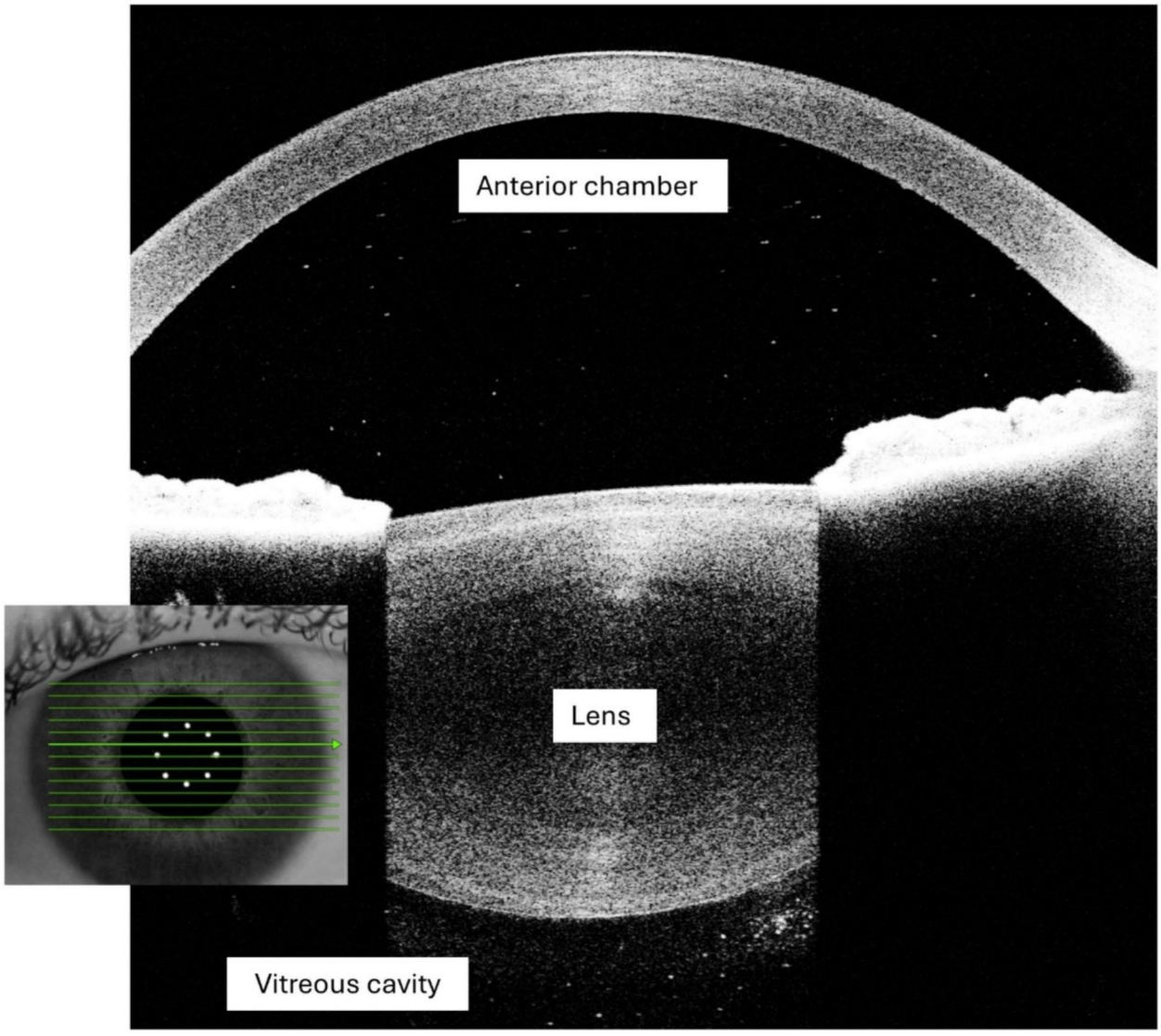

Fig. 1 Anterior segment optical coherence tomography image showing inflammatory leukocytes (hyperreflective particles) in the anterior chamber and 'spillover' cells in the anterior vitreous cavity

new detection and diagnostic approaches are needed to ensure continued care for children at risk.

Greater capacity for effective care delivery could be gained by harnessing resources currently available and accessible through community eye care centres, particularly Optical Coherence Tomography (OCT), a quick, easily learned, non-invasive and non-irradiating imaging modality which provides high resolution images of ocular structures (Fig. 1). Anterior segment OCT has been shown as a feasible, repeatable, sensitive and responsive metric for anterior uveitis in children and adults [24–26] As the evidence base on this modality grows, remote monitoring of children within surveillance programmes becomes possible, as does automation of image analysis, paving the way for resource effective care delivery. The wide accessibility of OCT machines (in contrast to the poor adoption of laser flare inferometers, which quantify ocular aqueous proteinaceous 'flare', another metric of ocular inflammation severity) [27] will support future implementation of imaging based JIAU surveillance. Future surveillance visits are likely to involve anterior segment OCT acquisition in the community, with images analysed immediately through algorithms embedded within the imaging platforms, or remotely at centralised reading centres, as is currently the case with adult imaging for diabetic retinopathy surveillance.

Conclusions

Effective surveillance for uveitis in JIA is essential to prevent visual disability. While current surveillance regimens vary according to care settings, reflecting interpretations of the evidence base and eye health resources within those settings, standardised timetables should support consistency and enhance care quality. In addition to providing supra-national standardisation, the MIWGUC proposal simplifies the screening protocol, so the screening ophthalmologist does not need disease specific knowledge about JIA class. Despite advances in JIA/JIAU treatment, regular ophthalmic examination remains crucial to catch the patient with active uveitis early before significant damage occurs, although it is likely that this examination becomes in long term imaging based. Integrated imaging and the adoption of uniform screening guidelines globally will be key to improving outcomes for children with JIA.

Abbreviations

AS	OCT-Anterior segment Optical coherence tomography
JIAU	Juvenile Idiopathic Arthritis related Uveitis
MIWGUC	Multinational Interdisciplinary Working Group for Uveitis in Childhood
SUN	Standardisation of Uveitis Nomenclature

Supplementary Information

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Supplementary Material 1

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Author contributions

Both authors contributed equally.

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Data availability

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Patient consent was gained for the use and publication of the illustrative clinical image, as part of the Imaging in Childhood Uveitis Study, approved by the NHS Health Research Authority (19/SC/0283).

Competing interests

The authors have no competing interests to declare.

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