# PATTERNS OF INTRAOCULAR INFLAMMATION IN CHILDREN

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## SUMMARY

*Aim:* To report on the causes of uveitis in children and young adults and their effects on visual functions.

*Materials and Methods:* Two hundred and seventy six patients, 18 years old or younger, with uveitis were included in this study. The intraocular inflammation (uveitis) was classified according to anatomical site of ocular involvement and the most probable etiological factor. The final diagnosis was based on clinical manifestations and the results of specific laboratory investigations.

*Results:* Bilateral intraocular inflammation was observed in 70.3% of the cases and 29.7% had either the left or the right eye involved. The symptomatology was relatively mild in most cases despite the fact that the visual acuity was markedly affected. An associated systemic disease was detected in 40.2% of the cases classified as non-infectious. Of this group, juvenile rheumatoid arthritis was the most common single systemic associated cause detected in 41 children. In 110 children (59.8%), the uveitis was strictly confined to the eyes with 70 of these (25.4% of the total group) classified as idiopathic.

Parasites were the most common infectious-associated cause for the uveitis followed by viruses and bacteria.

*Conclusion:* Uveitis is highly prevalent among children. In children, symptomatology of the intraocular inflammation may be very mild. However, visual acuity is markedly reduced leading to amblyopia in the young children. Early detection and treatment is therefore of utmost importance.

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## RÉSUMÉ

*But:* Rapporter les causes d'uvéite chez les enfants et jeunes adultes et leurs effets sur les fonctions visuelles.

*Matériel et méthodes:* Les auteurs ont inclus dans cette étude 276 patients âgés de 18 ans ou moins présentant une uvéite. L'inflammation intra-oculaire (uvéite) a été classée selon le site anatomique de l'atteinte oculaire et le facteur étiologique le plus probable. Le diagnostic final a été basé sur les manifestations cliniques et les résultats d'examens de laboratoire spécifiques.

Résultats: Une inflammation intra-oculaire bilatérale a été observée dans 70.3 % des cas et 29.7 % presentaient une atteinte soit de l'oeil droit ou gauche. La symptomatologie était relativement peu prononcée dans la plupart des cas en dépit du fait que l'atteinte visuelle était atteinte de façon marquée. Une maladie systémique associée a été détectée dans 40.2 % des cas classés comme non-infectieux. Dans ce groupe l'arthrite juvénile rhumatoide était la cause systémique associée unique la plus fréquemment détectée chez 41 enfants. Chez 110 enfants (59.8 %) l'uvéite était strictement limitée aux deux yeux, dont 70 (25.4 % du groupe entier) étaient classés comme idiopathiques. Les parasites étaient la cause infectieuse la plus fréquente de l'uvéite, suivis par les virus et les bactéries.

*Conclusion:* L'uvéite est hautement prévalente chez les enfants. Chez les enfants la symptomatologie de l'infection intra-oculaire peut être très prononcée. L'acuité visuelle est cependant réduite de façon marquée, entrainant une amblyopie chez les jeunes enfants. Le dépistage et le traitement rapide sont donc d'importance primordiale.

### KEYWORDS:

uveitis, intraocular inflammation, juvenile rheumatoid arthritis, pediatric.

### MOTS-CLÉS:

uvéite, inflammation intra-oculaire, arthrite juvénile rhumatoide, pédiatrie

## INTRODUCTION

Intraocular inflammation affecting mostly the uveal tract (uveitis) occurring in childhood has been reported at a much lower incidence than in adults.<sup>16</sup> Children with uveitis comprised 2.2% to 10.6% of the total number of uveitis patients examined and followed in specialized adult clinics.<sup>4,10,18,19,23</sup>

A marked variability in the incidence and /or prevalence of the different uveitis entities has been observed.<sup>15,23-25,29</sup> Regional and genetic factors along with a heightened awareness of previously unsuspected entities have markedly influenced these variable incidences.<sup>7,25,29</sup> In children, juvenile rheumatoid arthritis (JRA) has been reported as the accompanying systemic manifestation in 81% of children with uveitis<sup>17</sup> and in 95% of children with anterior uveitis.<sup>21</sup>

We report herein our observations based on the examination of 276 children less than 18 years old with uveitis diagnosed and treated in our clinic during a period of 10 years.

## MATERIAL AND METHODS

**Patients:** Eight hundred and twenty one consecutive patients with uveitis were diagnosed in the Immuno-Ophthalmology Service from March 1989 to February 1999. The 821 patients included 276 patients 18 years old or younger.

**Clinical Examination:** History of possible systemic disease and ocular manifestation were carefully reviewed with the patients and parents. All patients, including the preverbal children, underwent a complete ocular examination during their first visit in our clinic.<sup>1</sup> In a few complicated cases, IOP assessment, fundus examination and refraction data were obtained under general anesthesia.

Ocular movement abnormalities, the presence or absence of strabismus and the binocular functions were also assessed.

**Laboratory Tests:** Complete blood count (CBC), sedimentation rate (ESR), C-reactive protein (CRP), urine culture, kidney and liver function tests were performed in all cases. According to the clinical observations and the results of these

routine preliminary examinations, a tailored more arduous battery of tests was designed for each case as necessary.<sup>13</sup>

**Classification of uveitis:** The type of intraocular inflammation (uveitis) was classified according to the anatomical site of the major inflammatory manifestations and the most probable etiological factors involved in this reaction.<sup>5,13</sup> The intraocular inflammation was further subdivided to whether the disease was strictly ocular or associated with a systemic disease.<sup>2,11</sup> Systemic disease associations were determined according to established sets of criteria.<sup>3,6,29</sup>

## RESULTS

Of the 276 patients 18 years old or younger, 49.6% were boys and 50.4% were girls. Inflammation in one eye was detected in 29.7% of the children. An equal involvement of the left or the right eye was found in these cases.

Many of these children were referred because they failed a routine visual acuity screening in school. In 80 children (29.0% of all cases), there were no symptoms despite the active intraocular inflammation and the poor vision on presentation.

The cause of the intraocular inflammation was infectious in 92 (33.3%) of the cases while a non-infectious etiology was made in 66.7%, including 25.4% classified as "idiopathic.

In 18 children, 19.6% of the infectious group, a bacterial or chlamydial infection was the cause for the uveitis. Viruses were responsible for the uveitis in 30.4% of the infectious etiologies. Parasites comprised 50% of all infectious cases and were the cause for the uveitis in 16.7% of the 276 children.

JRA was diagnosed in 41 children, an incidence of 55.4% of the non-infectious etiologies associated with systemic disease but an incidence of only 14.9% of the 276 children with uveitis. Ocular Behçet's disease was diagnosed in 13 children, 17.6% of 74 children with associated systemic disease, 7.1% of 184 children with uveitis of non-infectious origin and 4.7% of the 276 children with uveitis. Other systemic diseases were implicated at a much lower incidence.

## DISCUSSION

A higher proportion of girls has been reported previously in children with uveitis.<sup>21</sup> In our group of 276 children however, 137 were boys and 139 were girls.

An intraocular inflammation strictly confined to the anterior segment was observed only in 13.4% of the patients. This figure is lower than most estimates reported for adult series<sup>9,15,24,29</sup> and much lower than the figures published for children with uveitis<sup>12,16,20,27,28</sup> These discrepancies may derive from our definition of anterior uveitis.

When analyzing the causes of uveitis according to etiological factors, only 25.4% of our cases were classified as idiopathic, a very low incidence compared to the findings of other authors and our own observations in adults.<sup>29</sup>

This achievement was probably due to the tailored methodological diagnostic approach<sup>2,11</sup> and the fact that most of our patients were evaluated before the initiation of any systemic treatment.

The incidence of JRA as a single specific diagnosis is as high as 55.4% within the group of children with a non-infectious systemic disease-associated etiology but only 14.9% of the entire cohort of 276 children with uveitis. An incidence of JRA associated uveitis, around 15% of all children with uveitis, is most probably a more realistic figure than the very high incidence of 40 to 95% as reported by others.<sup>1,1,2,17, 21,25</sup>

Toxoplasmosis was considered as the etiological factor for the uveitis in 43.5% of the cases due to parasitic infestation, 21.7% of the infectious causes and 7.2% of all cases. Despite the fact that toxoplasmosis was an important cause for the uveitis in our series, its incidence is far lower than that reported by others.<sup>14,19,22,23</sup> Toxocara and other visceral larvae migrans were important triggering factors for the uveitis, being the cause for the intraocular inflammation in 28.3% of the infectious causes and in 9.4% of all causes.

Viral infection as the cause for uveitis in our group of children was detected in 28 (10.0%) of all cases. Most of these suffered from anterior uveitis complicated by herpetic keratitis. Five children had CMV-associated ocular disease. All of these children were after bone marrow transplantation. Unlike the high incidence of HIV associated uveitis observed by others,<sup>8,15,26</sup> none of our 276 children suffered from uveitis-associated HIV disease. This finding illustrates best the possible discrepancies which may occur when patients from different countries and/or different cultures are compared.

The visual acuity was markedly affected on presentation in most cases. Only 12.0% of the children complained of decreased vision and being the cause for referral. On the other hand, 80 out of the 276 children (29%) had no ocular symptomatology and were referred because of poor vision detected on routine screening in kindergarten or school. Detection of the intraocular inflammation in these cases had been delayed and influenced the prognosis for visual recovery and treatment of the amblyopia especially in the younger children.

Thus, uveitis occurring in childhood should be handled very carefully as its consequences may lead to severe sequelae. Most importantly, symptomatology and external signs of uveitis may be mild and are probably underestimated. Therefore, attempts to achieve early diagnosis and aggressive treatment including surgery are mandatory in order to circumvene the evolving amblyogenic processes and prevent the loss of vision in these affected children.

### REFERENCES

- BENEZRA D. and ROSE L. Intraocular versus contact lenses for the correction of aphakia in unilateral congenital and developmental cataract. Eur J Implant Refract Surg. 1990; 2:303-307.
- (2) BENEZRA D. Posterior uveitis. In: "Ocular Inflammation. Basic and Clinical Concepts".
  (D. BenEzra ed), Martin Dunitz publishers, London 1999 pp. 239-266.
- (3) BENEZRA D. Ocular Behçet's disease. In: Developments in Ophthalmology Vol. 31 "Uveitis Update" (BenEzra D ed.), S. Karger AG Basel publishers, 1999; 31: 109-117.
- (4) BLEGVAD O. Iridocyclitis and diseases of the joints in children, Acta Ophthalmol 1941; 19: 219-236.
- (5) BLOCH-MICHEL E. NUSSENBLATT RB. International Study Group recommendations for the evaluation of intraocular inflammatory disease. Am J Ophthalmol 1987; 103: 234-235.

- (6) BREWER E.J. Jr., BASS J., BAUM J., CASSI-DY J.T., FINK C., JACOBS J., HANSON V., LE-VINSON JE., SCHALLER J., STILLMAN JS. – Current proposed revision of JRA criteria. Arthritis Rheum. 1977; 20: 195-199.
- (7) BREWERTON D.A. HL-A27 and acute anterior uveitis. Ann Rheum Dis 1975; 34 (suppl 1): 33-35.
- (8) CASSOUX N., BODAGHI B., LEHOANG P. European experience with HIV and the eye. Oph-thalmol Clin North Am 1997; 10: 105-116.
- (9) DARREL R.W., WEGENER H.P., KURLAND L.T. – Epidemiology of uveitis. Incidence and prevalence in a small urban community. Arch Ophthalmol. 1962; 68: 502-505.
- (10) DAVID M. Endogenous uveitis in children; associated band shaped keratopathy and rheumatoid arthritis. Arch Ophthalmol. 1953; 50: 443-454.
- (11) DICK A.D., FORRESTER J.V. Immune tests of diagnostic and management value in uveitis. In: "Ocular Inflammation. Basic and Clinical Concepts". (D. BenEzra ed) Martin Dunitz publishers, London, 1999. pp. 61-70.
- (12) DOLLFUS H. Eye involvement in children's rheumatic diseases. Baillere's Clin Rheumatol. 1998; 5: 197-202.
- (13) FORRESTER J.V., OKADA A.A., BENEZRA D., OHNO S. (eds). – Posterior Segment Intraocular Inflammation Guidelines. Kugler publications, The Hague, 1998 pp. 4-24.
- (14) GILES C.L. Uveitis in childhood. III. Posterior Ann Ophthalmol 1989; 21: 23-28.
- (15) HENDERLY D.E., GENSTLER A.J., SMITH R.E., RAO N.A. – Changing patterns of uveitis. Am J Ophthalmol 1987; 103: 131-136.
- (16) KANSKI J.J. Juvenile arthritis and uveitis. Surv Ophthalmol. 1990; 34: 253-267.
- (17) KANSKI J.J., SHUN-SHIN GA. Systemic uveitis syndromes in childhood: An analysis of 340 cases. Ophthalmology 1984; 91: 1247-1252.
- (18) KIMURA S.J., HOGAN M.J. Uveitis in children: analysis of 274 cases, Trans Am Ophthalmol Soc. 1964; 62: 173-192.
- (19) KIMURA S.J., HOGAN M.J., THYGESON P. Uveitis in children. Arch Ophthalmol. 1954; 51: 80-88.
- (20) KOTANIEMI K., KAIPIAINEN-SEPPANEN O., SAVOLAINEN A., KARMA A. – A population-

based study on uveitis in juvenile rheumatoid arthritis. Clin Exp Rheumatol 1999; 17: 119-122.

- (21) O'BRIEN J.M., ALBERT D.M. Therapeutic approaches for ophthalmic problems in juvenile arthritis. Rheumatol Dis Clin N Amer. 1989; 15: 413-422.
- (22) OKADA A.A., FOSTER C.S. Posterior uveitis in the pediatric population. Int Ophthalmol Clin 1992; 32: 121-152.
- (23) PERKINS E.S. Patterns of uveitis in children. Br J Ophthalmol. 1966; 50:169-185.
- (24) PERKINS E.S., FOLK J. Uveitis in London and Iowa. Ophthalmologica 1984; 189: 36-42.
- (25) ROTHOVA A., BUITENHUIS H.J., MEENKEN C., BRINKMAN C.J., LINSSEN A., ALBERTS C., LUYENDIJK L., KIJLSTRA A. – Uveitis and systemic disease. Br J Ophthalmol. 1992; 76: 137-141.
- (26) ROSBERGER D.F., HEINEMANN M.H., FRIED-BERG D.N., HOLLAND G.N. – Uveitis associated with human deficiency virus infection. Am J Ophthalmol 1998; 125: 301-305.
- (27) SOYLU M., OZDEMIR G., ANLI A. Pediatric uveitis in southern Turkey. Oc Immunol Inflam 1997; 5: 197-202.
- (28) TUGAL-TUTKUN I., HAVRLIKOVA K., POWER W.J., FOSTER CS. – Changing patterns in uveitis of childhood. Ophthalmology 1996; 103: 375-383.
- (29) WEINER A., BENEZRA D. Clinical patterns and associated conditions in chronic uveitis. Am J Ophthalmol. 1991; 112: 151-158.

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