# Recent Trends in Diagnosis and Treatment of Multifocal Choroidopathies

Essay

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وأنزل الله عليك
الكتاب والحكمة
وعلّمك ما لم تكن
تعلم وكان فضل
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*Hadeer Ahmed El-Sherbiny*

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## List of Abbreviations

| | |
|---|---|
| **AMD** | Age related macular degeneration |
| **AAV** | Adeno associated virus |
| **AGEs** | Advanced glucation end product |
| **AMN** | Acute macular neuroretinopathy |
| **APMPPE** | Acute posterior multifocal placoid pigment epitheliopathy |
| **ARPE** | Acute retinal pigment epitheliitis |
| **AZOOR** | Acute zonal occult outer retinopathy |
| **BM** | Bruch's membrane |
| **BRMs** | Biological response modifiers |
| **CME** | Cystoid macular oedema |
| **CNV** | Choroidal neovascularization |
| **CsA** | cyclosporine A |
| **CSC** | Central serous chorioretinopathy |
| **CSR** | Central serous chorioretinopathy |
| **DNA** | Deoxyribo nucleic acid |
| **DSF** | Diffuse subretinal fibrosis syndrome |
| **DUSN** | Diffuse unilateral subacute neuroretinitis |
| **DUSU** | Diffuse unilateral subacute neuroretinitis |
| **EOG** | Electro-oculogram |
| **ERG** | Electroretinograms |
| **ERM** | Epiretinal membrane |
| **FA** | Fluorescein angiography |
| **HLA** | Human leukocyte antigen |
| **ICG** | Indocyanin green |

## List of Abbreviations

| | |
|---|---|
| **IL** | Interleukin |
| **IOP** | Intraocular pressure |
| **LD** | Lyme disease |
| **LP** | Laser photocoagulation |
| **LP** | Laser photocoagulation |
| **MCP** | Multifocal choroiditis and panuveitis |
| **MEWDS** | Multiple evanescent white dot syndrome |
| **mfERG** | Multifocal ERG |
| **MMF** | Mycophenolate mofetil |
| **OCT** | Optical coherence tomography |
| **OHS** | Ocular histoplasmosis syndrome |
| **PAS** | Peripheral anterior synechiae |
| **PDT** | Photodynamic therapy |
| **PDT-V** | Photodynamic therapy with verteporfin |
| **PIC** | Punctate inner choroidopathy |
| **PXE** | Pseudo xanthomae lasticum |
| **RD** | Retinal detachment |
| **RNV** | Retinal neovascularization |
| **RP** | Retinitis pigmentosa |
| **RPC** | Relentless placoid chorioretinitis |
| **RPE** | Retinal pigment epithelium |
| **RUV** | Retinal neovascularization |
| **SFU** | Subretinal fibrosis and uveitis syndrome |
| **SO** | Sympathetic ophthalmia |
| **TB** | Tuberclosis |

## List of Abbreviations

| | |
|---|---|
| **TGF** | Transforming growth factor |
| **TNF** | Tumor necrosis faction |
| **TNF-a** | Tumor necrosis factor-a |
| **t-PA** | Tissue plasminogen activator |
| **VA** | Visual acutiy |
| **VEGF** | Vascular endothelial growth factor |
| **VKH** | Vogt–Koyanagi–Harada |

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# INTRODUCTION

***Multifocal Choroidopathies*** or white dot syndromes are a group of rare disorders involving a primary pathologic process occurring at or near the level of the retinal pigment epithelium (RPE) with or without choriocapillaris involvement**.** ***[1]***

The white dot syndromes consist of the predominantly noninfectious ocular syndromes including multiple evanescent white dot syndrome (MEWDS), acute posterior multifocal placoid pigment epitheliopathy (APMPPE), Birdshot retinochoroidopathy, Serpiginous choroiditis, multifocal choroiditis and panuveitis (MCP), punctate inner choroidopathy (PIC), subretinal fibrosis and uveitis syndrome (SFU), acute retinal pigment epithelitis (ARPE), acute zonal occult outer retinopathy (AZOOR), acute macular neuroretinopathy (AMN), relentless placoid chorioretinitis (RPC) and unifocal helioid choroiditis**.** ***[2]***

***The etiology*** of the white dot syndromes is unknown. Most of the diseases subsumed under the white dot syndromes share an association with systemic infectious diseases, such as viral infections, toxoplasmosis, or tuberculosis. In many cases, an intensive medical and infectious workup is indicated **.[3]**

Others have suggested an autoimmune/inflammatory pathogenesis arising among individuals with common non-disease-specific genetics, triggered by some exogenous agents. Although they have similarities, the white dot syndromes can be differentiated clinically based on their variable lesion morphology and evolution, distinct natural histories, and angiographic behavior***. [4]***

Many different genetic mutations are involved, in different combinations and to varying degrees. Some genetic factors, such as HLA(Human Leukocytic Antigen)-A29 have strong association with birdshot retinochoroidopathy, others as HLA-DR2 and HLA-B7 has elevated prevalence in the patients of APMPPE.**[5]**

***Common presenting symptoms*** include photopsia, blurred vision, nyctalopia, floaters, and field loss contiguous with a blind spot. In many cases, a prodromal viral syndrome can be identified. Bilateral involvement, albeit asymmetrically (with the exception of MEWDS), is the rule. Other than patients with birdshot retinochoroidopathy and serpiginous choroidopathy, the majority of individuals are younger than 50 years of age. A female predominance is more commonly observed in patients with MEWDS, birdshot retino-choroidopathy, MCP, PIC, and AZOOR***. [3]***

The inflammatory chorioretinopathies, or white dot syndromes, are a heterogeneous group of inflammatory

disorders with overlapping clinical features that share the common presence of discrete, multiple, well-circumscribed yellow-white lesions at the level of the retina, outer retina, RPE, choriocapillaris, and choroid during some phases of their disease course. ***[6]***

***Their differential diagnosis*** includes systemic and ocular infectious entities such as tuberculosis, syphilis, diffuse unilateral subacute neuroretinitis (DUSN), Lyme disease and ocular histoplasmosis syndrome (OHS), as well as noninfectious entities such as central serous chorioretinopathy (CSC), sarcoidosis, sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) syndrome, idiopathic uveal effusion syndrome and intraocular lymphoma. ***[7]***

Although some of these disorders are self-limited and have good visual outcomes, others are associated with serious retinal and choroidal sequelae and can result in visual loss. This has important implications with respect to disease-specific indications for treatment and predictions of the ultimate visual prognosis. ***[8]***

The aim of ocular inflammatory treatment is to prevent visual loss, discomfort and ocular morbidity. Understanding the pathogenesis and progression of uveitis is important for targeted therapies with greater efficacy and less side effects for the most cases of ocular inflammatory diseases. ***[9]***

There are different treatment modalities for this wide group of diseases, including medical treatment in form of corticosteroids, immunosuppressive drugs, anti VEGF (vascular endothelial growth factor) drugs, laser photocoagulation (LP), photodynamic therapy (PDT), and surgical treatment**.**

The recent modalities include tissue plasminogen activator, maculoplasty, retinal pigment epithelium replacement therapy and gene therapy**.** ***[4]***

# ANATOMY OF THE CHOROID

Choroid is a thin but highly vascular membrane lining the inner surface of sclera. It extends from anteriorly ora serrata to the optic nerve posteriorly. It has a rough outer surface which is attached to sclera at the optic nerve and at the exit of the vortex veins. The smooth inner surface of choroid is attached to the retinal pigmented epithelium (RPE). Choroid becomes continuous with pia and arachnoid at the optic nerve. The choroid is qualitatively assessed with fluorescein angiography and even better with ICG angiography that explores the choroidal vasculature and the different originating pathologies. The quantitative assessment is yet clinically performed with OCT, Choroid normally ranges from 287±74.2 to 345±111μ depending on the instrument, the OCTtechnic, of the delineation of the choroidal limit, thickness is highest at macula 500- 1000 μm. Choroidal thickness increases in intraocular inflammation. The smooth configuration of choroid can be observed ophthalmoscopically in choroidal detachment. ***[10]***

**Microscopic structure of choroid:**

Choroid is composed predominantly of blood vessels surrounded by melanocytes, nerves and connective tissue. Choroid can be divided into the following layers histologically: