Disease processes and terminology cannot be determined by opinion polls but have to be based on objective facts: The "white dots" case

The imperative need for evidence-based medicine has never been more evident than in the modern era of medical science, where the accuracy of diagnosis and treatment significantly impacts patient outcomes. A notable example highlighting the evolution of medical understanding through scientific evidence is the refinement of diagnostic criteria across various medical fields, underscoring the shift from consensus-based to evidence-based approaches. This evolution emphasizes the critical role of rigorous, evidence-based analysis in overcoming the limitations of traditional, opinion-based practices, ensuring that medical classifications and diagnoses are grounded in verifiable research and clinical data.[1]

In 1995, an opinion article was at the origin of the term "white dots" grouping a number of unrelated conditions.[2] We know now that the hypothesis trying to link these conditions was incorrect. These entities were lumped together solely on the basis of a similar fundus picture, "white dots," which, contrary to what was claimed, do not have a "similar pathological process." No attempt was made to go beyond the clinical appearance and analyze the different mechanisms of these amalgamated, in fact not so similar diseases, with angiographic methods that were already available at the time.

Remarkably, this terminology swiftly gained acceptance, linking physiopathologically diverse choroidal diseases such as multiple evanescent white dot syndrome (MEWDS), acute posterior multifocal placoid pigment epitheliopathy (APMPPE), and multifocal choroiditis (MFC) on one side and birdshot retinochoroiditis (BRC) and Vogt–Koyanagi–Harada disease (VKH) on the other side that were thrown into a potpourri basket without justification, together with completely unrelated conditions such as diffuse unilateral subacute neuroretinitis.

The ophthalmological community rushed into accepting a concept without a real basis and the question is why did that happen? A possible explanation is that newly described diseases such as MEWDS, MFC, and BRC were puzzling the clinicians. Therefore, having even an improper framework within which to classify the diseases was somewhat reassuring, even though there was no practical gain to justify such a useless terminology. Nevertheless, textbooks promptly adopted the terminology, some of which included almost every posterior uveitis with one of them citing 25 conditions within the white dot syndrome (WDS) group.

An ongoing problem in medicine is that once a faulty concept or belief is largely diffused, it is practically impossible to eliminate it. It sticks in a way that it is repeated over and over again without questioning its validity or soundness.

In the early years of this century, the rationale and usefulness of the concept of WDS were starting to be questioned by demonstrating its misconception and irrelevance with physiopathological angiographic arguments. With the advent of indocyanine green angiography (ICGA), available since the early 1990 ties, the choroid could be precisely investigated and it became possible to analyze the choroidal inflammatory conditions according to their mechanisms and not simply according to their clinical aspect.[3] A precise terminology including the disease process in its denominations could replace the inappropriate and descriptive "white dot" term and reclassify these conditions meaningfully.

It is now clear that noninfectious choroiditis has to be subdivided into those diseases that principally involve the choriocapillaris and those principally involving the choroidal stroma.[4] Moreover, recent advances in multimodal imaging modalities, including enhanced-depth optical coherence tomography, have provided additional insights into these different entities. The combination of these imaging studies has revolutionized the understanding of the temporal sequence and provided precise anatomical involvement of these different entities.[5] This has implications for their precise diagnosis and management options.

Choriocapillaris entities are due to inflammatory choriocapillaris nonperfusion well identified by ICGA that shows nonperfusion of varying severity at the origin of diverse diseases. They range from benign, mostly reversible non or hypoperfusion conditions such as MEWDS to diseases with gradually more severe choriocapillaris involvement, such as MFC, APMPPE, and serpiginous choroiditis. For these diseases, the name of choriocapillaritis is perfectly adequate as it relates to the disease mechanism.[6]

On the other hand, ICGA semiology characterized also precisely choroiditis involving the choroidal stroma in the form of inflammatory foci appearing as hypofluorescent dark dots (HDDs) which develop within the stroma and, hence, should be called stromal choroiditis, an adequate term which again accurately reflects the disease process.[7] Among the entities included in this group, the more frequently occurring conditions are BRC and VKH as well as sympathetic ophthalmia.

Despite these advances, being accepted by more and more clinicians,[8-10] WDS continued to be used and persisted, underscoring the difficulty to modify entrenched terminology. Indeed, it is quasi-impossible to eliminate such ingrained notions despite their obviously erroneous and useless character. It should be noted here that choriocapillaris had been described well before the arrival of WDS thanks to the careful observation and obvious conclusions of some astute clinicians and should have been taken into account at the time the terminology WDS was proposed.[11-13]

In an article published in 2022, we appealed explicitly to abandon this term for the reasons repeated here.[14] This article was the culmination of several articles published in the last two decades[15-17] castigating the use of WDS which was starting to pay off (the term was abandoned in the new edition of a major ophthalmology textbook). Recently, the unfortunate decision to reinstate the term was taken by a uveitis interest group, allegedly to better explain the different entities composing the group.

As many organisms before, this attempt wants to base its project by sending out a questionnaire (the International Uveitis Study Group (IUSG) white dot survey) asking for the responders' opinions on several diseases and their mechanisms. The reliance on opinion polls to guide disease classification is problematic, as it reinforces existing biases rather than advancing our understanding based on new objective evidence. This approach risks to perpetuate inadequate and misleading terminology. Indeed, disease processes are not determined by opinion polls but by objective facts. Moreover, such surveys are invariably biased, either by groups of influence or in this case by the fact that a significant number of persons who take the survey do not perform ICGA, a crucial element in this situation. Furthermore, the fact of multiplying the participants in the poll will not help, only giving the group a false sense of legitimacy.

Many examples have shown that this kind of approach, based on polls, consensus decisions, or expression of opinions turns out very often to be counterproductive, with inappropriate or even wrong recommendations because biased toward the group of interest which convened the meeting. The result is often a step backward which may take years to be rectified.

We will cite only two examples which illustrate the dangers of such approaches that, as a consequence, take the entire medical community hostage, as their, often inadequate and erroneous, conclusions become the "official" guidelines.

In 2006, a set of diagnostic criteria of BRC was published as the result of a "consensus workshop" held in Los Angeles.[18] These criteria have since been revised and corrected because of the many shortcomings they contained.[19] They were subdivided into required and supportive findings. They did not take into account ICGA, one of the most important diagnostic tests. Depigmented "birdshot lesions" were a required criterion. We know by now that birdshot lesions are not required any longer for diagnosis, as diagnostic HDDs on ICGA appear well before the "birdshot lesions." HLA-A29 antigen was categorized as supportive but not required, yet HLA-A29 is not only a supportive but a required criterium as the positivity rate is close to 100% if the appropriate laboratory test is used. Retinal vasculitis was largely ignored in these diagnostic criteria and merely considered a supportive element of BRC, illustrating the minor importance attributed to this feature in the past. Furthermore, keratic precipitates were listed as an exclusion criterion, which is also incorrect.[20] These inappropriate, partially erroneous criteria hampered the correct appraisal of BRC for many years.[19]

In 2001, the "revised VKH diagnostic criteria" were published as a result of a consensus workshop held at Lake Arrowhead in San Bernardino, California.[21] The criteria aimed to classify VKH as complete, incomplete, and probable diseases. The proposed system was flawed, however, because it mixed acute and chronic signs and the complete form thus could never technically be diagnosed according to these criteria. Hundreds of irrelevant studies were conducted only to demonstrate that the criteria did not allow to diagnose what was called the complete form.[22] These criteria not only contributed little to the management of VKH but also hampered a correct approach to the disease that must be subdivided into the acute form on the one hand and the chronic form on the other with according precise diagnostic criteria for each form.[23]

As illustrated by the diagnostic criteria for BRC and VKH, the history of consensus-driven criteria demonstrates the limitations and potential pitfalls of relying on collective opinion rather than rigorous, evidence-based analysis. These experiences underscore the importance of a critical and informed disease classification and diagnosis approach.

Apart from the fact that such opinion polls do not generally give useful results precisely because based on opinions and not on objective facts, the deleterious consequence of reusing the term WDS in the recent project cited above is that it perpetuates the use of an inadequate and useless term and obscures an objective and reasoned approach to this issue.

The endeavor to delineate and systematize clinical entities reflects a laudable commitment to enhancing our understanding and management of diseases. However, such an attempt should aim at a progressive approach rather than an approach perpetuating an old term, WDS that should absolutely be abandoned for the reasons given hereabove. The project could have gone beyond this terminology, acknowledging our field's growth, and use the more appropriate terminology characterizing these diseases, namely that of noninfectious choroiditis, which would have constituted a progressive attitude. This evolution in terminology is crucial for the continued refinement of diagnosis and treatment strategies. By embracing a more precise and evidence-based lexicon, we can better classify and understand the diverse conditions previously grouped under this broad umbrella (WDS), facilitating targeted investigations and interventions that benefit patient care.

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