News Report

第59回日本臨床眼科学会より　10月10日・北海道厚生年金会館

The 59th Congress of Clinical Ophthalmology of Japan

第24回ドライアイ研究会

世話人　関西ろうさい病院眼科部長 渡辺 仁氏

眼が乾く，疲れるなどを主訴とするドライアイはこれまで“愁訴”的な扱いを受けてきた。しかし，近年の研究から眼の乾きが角結膜上皮を障害し，視力にも影響を与えることが明らかとなり，ドライアイを“疾患”として積極的に治療する必要性が高まっている。

1990年に発足したドライアイ研究会では，ドライアイ研究の促進に加え，診断・治療の重要性が正しく認識されるべく活動を行っている。ここでは，専門別研究会として行われた第24回ドライアイ研究会の概要を紹介する。

【特集1】

ドライアイNEW!!

座長　京都府立医科大学視覚機能再生外科学教授 木下 茂氏

国際基準確立への第一歩 ドライアイの定義を提案

ドライアイへの関心が世界的に高まっている今日，その定義と診断基準の統一に向けて大きな一歩が踏み出されたことが，慶應義塾大学眼科学講師のMurat Dogru氏より報告された。近年，ドライアイをめぐる状況は大きく変化し，その臨床的重要性が高まっている。こうした動向に伴い，ドライアイの定義，診断基準について，国際的な統一が強く求められるようになり，2004年11月15～17日に世界ドライアイワークショップ（DEWS）の開催が実現した。DEWSにはドライアイおよび角膜研究の専門家が世界中から集まり，涙液，眼表面および自覚症状の3つの部会に分かれて，最近10年間のドライアイに関する全論文をレビュー，討議を重ねた。

その最終報告では「ドライアイとはさまざまな要因による涙液および角結膜上皮の慢性疾患であり，眼不快感や視覚障害を伴う」とするドライアイの定義が提案された。さらに，定義や新しい診断基準の応用性，種々の検査法の感度や特異性を調べるために大規模多施設共同研究の必要性が強調された。Murat氏は2008年3月末まで予定されているDEWSの活動への支援を訴え，報告を終えた。

眼表面におけるムチンの発現コントロールがドライアイ治療のかぎ

ドライアイの発症要因のうち，最近特に注目されているのが眼表面のムチンの変化である。関西ろうさい病院眼科部長の渡辺 仁氏は，ムチン発現のコントロールはドライアイ治療法の新たな展開につながることを指摘した。

ムチンは親水性の高分子の糖蛋白であり，眼表面においては涙液の保持，外界からのバリア機能など，眼表面を正常に保つための重要な役割を担っている。近年，分子生物学的アプローチにより，ヒトの眼表面には膜貫通型ムチンであるMUC1，MUC4，MUC16および分泌型ムチンであるMUC5ACが発現していることが明らかになった（図1）。さらにドライアイにおいては，膜型ムチンの発現が低下していることもわかっている。したがって，ドライアイによる角結膜上皮障

ドライアイ研究会主催
後援：TFOS／日本DEWS

ドライアイ研究会

ハーバード大学眼科デボラ・シャンバーグ先生来日記念公開講座

世界のドライアイアップデート2006

日　　時：2月13日(月) 18:00～19:30

会　　場：六本木ヒルズクラブ　裏面に会場地図があります
東京都港区六本木6-10-1 六本木ヒルズ森タワー50階

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Program

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坪田 一男
2. 世界におけるドライアイ診療および研究の現状
デボラ・シャンバーグ
訳：村戸ドール 慶大眼科
3. ドライアイNew！ ドライアイで視力は下がる！
坪田 一男
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デボラ・シャンバーグ、坪田 一男 ほか
5. 質疑応答
6. クロージングリマークス

Debra Ann Schaumberg, O.D., M.P.H, Sc.D
ハーバード大学眼科講師

イリノイ大学にてODを取得後、ジョンズホプキンス大学眼科、ハーバード大学眼科にて勤務リサーチフェローとして勤務。角膜疾患であるドライアイにおいて眼科領域のみならず、体の他の疾患との関連の研究など独自の研究の視点で注目を集める。この講義では、世界的な環境の変化、人々の生活スタイルの変化により、世界におけるドライアイ診察および研究がどのように進んでいるのかを中心にお話いたします。

□主催者を代表して‥

Kazuo Tsubota, M.D.
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このたび、アメリカを代表する角膜の専門家の１人であるハーバード大学のデボラ・シャンバーグ先生が来日されたのを記念して、このような講座を企画いたしました。ドライアイ研究会では、昨年「ドライアイで視力は下がる!」という新しいデータを発表し、今年はドライアイ診断基準委員会を中心に日本発の新しい診断基準の作成が完成する予定です。ドライアイは、眼科の角膜疾患の中で、潜在的な患者数の増加が見込まれる大きな疾患の1つですが、正しい診断と治療のできる眼科専門医は多くありません。世界レベルで討議される、ドライアイの新しい情報をお伝えする講座にご期待ください。

Changing Trends in the Definition and Diagnosis of Dry Eyes

MURAT DOGRU, MD, MICHAEL E. STERN, PHD, JANINE A. SMITH, MD, GARY N. FOULKS, MD, MICHAEL A. LEMP, MD, AND KAZUO TSUBOTA, MD

ONE OF THE PROBLEMS IN DEALING WITH DRY EYES is the lack of a precise definition. Until recently, the term *dry eye* implied tear volume deficiency, which is associated mainly with Sjögren syndrome.[1] The National Eye Institute/Industry Workshop on Clinical Trials in Dry Eyes in 1993 to 1994 sought to provide consensus definitions to assist in clinical trial development and communication and reported a global definition of dry eye: "Dry eye is a disorder of the *tear film* because of tear deficiency or excessive tear evaporation which causes damage to the interpalpebral *ocular surface* and is associated with *symptoms* of ocular discomfort."

The 1994 workshop also provided a classification for dry eyes and descriptions of diagnostic testing procedures.[2] However, the past decade has witnessed the emergence of a new understanding of the inflammatory basis of some forms of dry eye disease that surrounds an alteration of the composition of the tear film. Additionally, new types of dry eyes with a neurogenic component (such as dry eyes that occur after LASIK procedures) recently have been recognized. These new entities would not be included in the 1994 workshop definition for dry eyes.[3–5]

Diagnostic dry eye definitions and protocols still vary widely around the world. For instance, symptoms are not included in the diagnostic criteria of dry eyes in Japan, where only decreased tear secretion and stability and positive ocular surface staining are considered essential for the diagnosis of dry eyes.[6] Yet, evaluation of the presence and nature of symptoms might represent early evidence of ocular surface distress and may be the best way to monitor the effect of any treatment as far as the quality of life of any given patient is concerned.

On that front, the use of a symptom questionnaire might be beneficial because it may allow the grading of symptoms and may be repeatable for comparison purposes before, during, and after any given treatment.[7] Currently, many questionnaires exist, but no single questionnaire is good for all purposes. At this time, there is also no consensus about which symptoms correlate most closely with dry eyes or about which symptom questionnaire or combination thereof should be used in the evaluation of dry eye disease.

Likewise, practices of evaluating the tear stability differ worldwide. Although some clinicians have access to noninvasive diagnostic technologies such as the tear scope and define tear stability with noninvasive techniques, most practitioners use the fluorescein staining of tears and measure the tear film break-up time invasively.[8] Even on that simple front, some clinicians use dye-impregnated strips, and other clinicians prefer one drop of dye delivered through commercially available vials or double vital staining with a mixture of fluorescein and lissamine green or Rose Bengal dyes that are delivered to the conjunctival sac by the aid of micropipettes. Each technique delivers different volumes of dye to the tear film and results in different measured stability values. The recent development of fluorescein break-up time measurement with the dry eye test method may provide a breakthrough that permits accuracy and repeatability by delivering a measured dose of fluorescein into the tear film and may provide a testing method that is practical in the office setting.[9]

In relation to assessment of tear quantity, the Schirmer test still remains the "gold standard" and it is commonly accepted that ≤5 mm of wetting denotes tear deficiency when the test is performed without anesthesia. A comparable diagnostic cut-off value has not been agreed on for the Schirmer test with anesthesia. Of many concerns that could be raised regarding the Schirmer test, an unresolved issue relates to the commonly accepted cut-off value because tear secretion is affected by age. There is still no consensus on age-adjusted cut-off values for Schirmer testing.[8]

Several studies on dry eyes appear in the literature each year with variations in diagnostic methods that are not measuring the same parameter, which makes the evaluation and comparison of results difficult to evaluate.

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It is clear that we also need new diagnostic markers of dry eye disease to make clinical diagnosis easier and to provide appropriate end points for clinical trials. It is important to understand where to place the new dry eye diagnostic technologies (such as improved tear osmolarity technology[10]) or biomarkers (such as adhesion molecules, inflammatory markers, cytokines, cytokeratins, or aquaporins), which have emerged as important over the past 10 years.[11,12] For instance, flow cytometry processing of conjunctival epithelial impression cytologic specimens has proved useful in the assessment of the ocular surface changes in Sjögren syndrome and may now be useful for large multicenter clinical trials.[13] The DR-1 tear film lipid layer interferometry appears to be a breakthrough development in the evaluation of tear stability and can assist in the analysis of the changes in thickness and the structure of the tear lipid layer.[14]

Likewise, a new tear stability analyses system that measures tear stability as a function of serial topographic indices that are measured at 1-second intervals during a 10-second period has demonstrated increases in the surface regularity index and the surface asymmetry index with reduced tear film stability in dry eyes of patients with Sjögren syndrome.[15] The focus of these new technologies seems to be shifting toward dynamic assessment of the tear film and dry eye conditions.

Taking into consideration the aforementioned discrepancies and variations in relation to definition and diagnosis of dry eyes and the changes that occurred over the past 10 years, it is time to organize another workshop. As an initial step, 47 recognized cornea and dry eye specialists who were chosen at random from the Association for Research in Vision and Ophthalmology membership database were sent a questionnaire to evaluate their current dry eye diagnostic practices, the details of which are given on the AMERICAN JOURNAL OF OPHTHALMOLOGY online site.

We think that such attempts will help in the evaluation of new diagnostic technologies and markers and in the determination of whether to include them into the realm of methods or tests that are ready for clinical prime time. Future dry eye workshops should also try to undertake the task of issuing briefing statements, an executive summary, a glossary of dry eye terminology, and guidelines for the interpretation of diagnostic data. We not only should examine methods of evaluating dry eye tests for clinical trials with Food and Drug Administration perspectives and guidelines but also make efforts to undertake the task of how to include symptoms in a revised definition of dry eyes and review of the data on existing symptom questionnaires that address the advantages and weaknesses of each instrument. New guidelines in relation to the use of the existing questionnaires for multiple purposes such as for case identification, the diagnosis of dry eye, and a description of change over time with treatment of dry eyes might provide invaluable assistance for future dry eye studies.

We anticipate that such efforts eventually will ensure that most dry eye practitioners and researchers are referring to well-described standards in relation to definition and diagnostics of dry eyes. Such efforts should be carried out more frequently and will pave the way to a better understanding of the pathogenesis of dry eyes and a better evaluation of specific treatment responses or at least to clarify the areas in which further prospective trials should be conducted.

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