表1 対　象

	男	女	計	年齢
健常者	1例	4例	5例	49.6±14.2歳
炎症性筋疾患患者	2例	4例	6例	49.3±7.7歳
多発筋炎患者	1例	3例	4例	
皮膚筋炎患者	1例*	1例	2例	

* 再燃例

表2 健常者及び多発筋炎患者における増多クローンのサイズの検討

27歳女性 健常者	BV1 5.7 %	BV11 1.8 %		
35歳女性 多発筋炎患者	BV6S2+6S4 12.0 %	BV9 7.8 %	BV22 1.3 %	BV24 0.3 %
52歳女性 健常者	BV1 5.3 %	BV7 4.5 %	BV15 5.4 %	
52歳女性 皮膚筋炎患者	BV2 5.4 %	BV11 0.5 %	BV15 5.9 %	BV24 0.5%

図1 TCR CDR3 length spectratyping

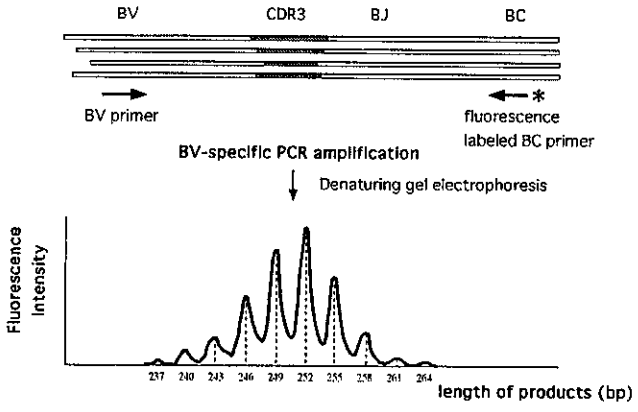
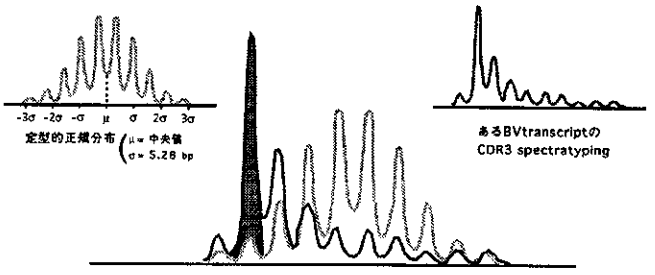


図2 クローン性増多の判定基準



(各ピーク値とそれに対応する定型的正規分布でのピーク値の差)≧50%の時クローン性増多ありと判定する (Monteiro, Molecular Medicine, 1995)

図3 健常者(27歳女性)のTCR CDR3 spectratyping

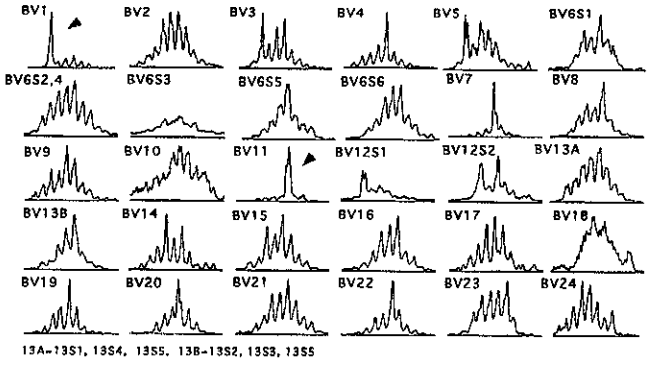


図4 多発筋炎患者(35歳女性)のTCR CDR3 spectratyping

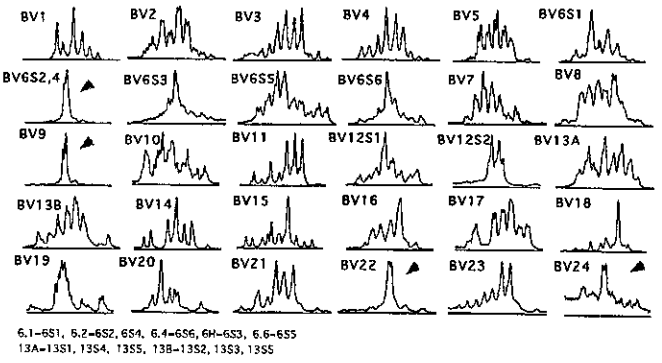


図5 健常者と多発筋炎/皮膚筋炎患者のCD8T細胞クローン性増多数の比較

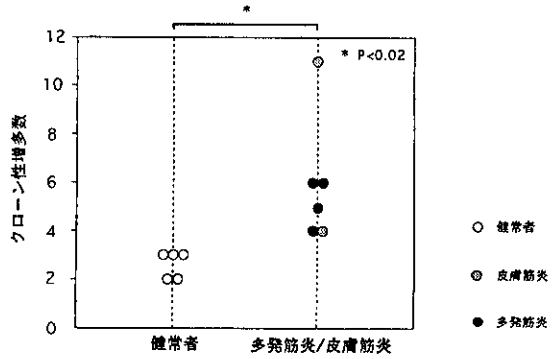
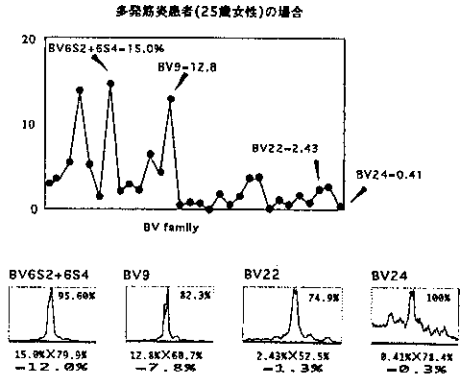


図6 各クローンの末梢CD8T細胞における頻度の推定



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シェーグレン症候群改訂診断基準

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［研究要旨］シェーグレン症候群の診断基準については、厚生省研究班で定められた基準（１９７８）[1]が長く用いられてきており、本格的な改訂は行われていなかった。日本シェーグレン症候群研究会においてはシェーグレン症候群の診断基準の改訂に関する検討を行ってきており、厚生省特定疾患自己免疫調査研究班平成７年度研究報告書[2]において中間報告としてその改訂試案を提案し、またその後も検討作業を継続していたが、平成１０年度の第８回日本シェーグレン症候群研究会[3]において、シェーグレン症候群改訂診断基準が定められたのでその内容について報告する。

［研究目的］シェーグレン症候群（ＳＳ）の診断基準としては我が国では厚生省特定疾患シェーグレン病調査研究班で定めた基準[1]がいわゆる厚生省基準として広く用いられてきた。一方、米国では Fox ら[4]の診断の感度は低いが特異性の高い分類があり、ヨーロッパでは１９９３年ＥＣ各国が共同して診断基準を統一して発表した[5]。このような背景のもと我が国でも従来の基準をもととして、長年の使用経験をふまえて、診断の客観性、診断技術の進歩、国際的普遍性などを考慮した再検討と、その結果による診断基準の改訂が必要ではないかと考えられ、日本シェーグレン症候群研究会において具体的な作業を行ってきた。

［研究方法］１９９４年の第４回日本シェーグレン症候群研究会において上述の趣旨による診断基準改定のために小委員会を発足させることが決議され、筆者らの７名が委員となった。小委員会では改訂案作成の具体的方法について議論し、７名の委員が自験例より１次性シェーグレン症候群（ＳＳ）と考える症例１５例、２次性ＳＳと考える症例１５例、および１次性ＳＳの対照となる正常または他疾患を１５例、

２次性ＳＳの対照となるＳＳを合併しない膠原病疾患例を１５例の合計６０例を原則的に持ち寄ることとし、その結果４１９例が小委員会症例として集積した。このうち前２者をＳＳ確実例、後２者を対照例として以下の検索を行った。すなわち口腔乾燥自覚症状、眼乾燥自覚症状、唾液分泌量、唾液腺シンチグラフィー、唾液腺造影撮影、口唇腺生検組織像、Schirmer 試験、Rose-Bengal 試験、蛍光色素試験、BUT、涙腺生検組織像、合併自己免疫疾患、Rheumatoid 因子、抗核抗体、抗 SS-A 抗体、抗 SS-B 抗体、高ガンマグロブリン血症などの諸検査や項目のＳＳ診断に対する感度(Sensitivity)、特異度(Specificity)、および精度(Accuracy)を次式より求めた。

Sensitivity(%)=[True Positive/(True Positive+False Negative)]x100
Specificity(%)=[True Negative/(True Negative+False Positive)]x100
Accuracy(%)=[(TP+TN)/(TP+FN+FP+TN)]x100

ついで、これらの各検査法を組み合わせ厚生省基準の改定を念頭にして、いくつかの診断基準の素案を作成し、それらの感度、特異度、精度を算定しつつ改良を重ねてＳＳ診断基準改定試案第１、第２、第３案を作成した。１９９５年の第５回日本シェーグレン症候群研究会においてその試案を示し、１９９６年３月発行の厚生省特定疾患自己免疫疾患調査研究班平成７年度研究報告書にも記載した[2)]。

その後研究会参加の各施設においても検討され、１９９６年の第６回、１９９７年の第７回の各研究会において、第１案を主体に検討すること、小委員会症例のみでなく、症例をより多施設より集積して、病理組織診断の単独性や眼科的診断基準とくに van Bijsterveld スコアの陽性基準について再検討することにした。そこで日本シェーグレン症候群研究会において登録症例を公募し、各施設から自己施設診断で１次性ＳＳ、２次性ＳＳ、正常または他疾患、非ＳＳ膠原病と診断した原則的に各５例計２０例を提出することとした。その結果１９施設から４０４症例の登録があった。小委員会症例４１９例に公募症例４０４例を加えると合計検索対象症例は８２３例となった。

［結果と考察］１）改訂試案第１案の診断精度の対象例による変化は

	対象例数	感度（%）	特異度（%）	精度（%）
小委員会症例	４１９	９１．９	９１．８	９１．８
公募症例	４０４	８８．５	９１．６	８９．８
合計症例	８２３	９０．２	９１．７	９０．９

２）改訂試案第１案では病理組織所見で陽性であればその第１条件のみで確定診断陽性となっているのを、病理、口腔、眼、血清の４項目を同等に扱い、この４項目のうちいずれか２項目以上陽性で確定診断

陽性とした場合は

検索対象	感度（%）	特異度（%）	精度（%）	除外症例数
８２３例	８３．２	９４．６	８８．１	１５例

3）van Bijsterveld スコアの記載のある１１６例での検索で、陽性条件をスコアで１以上（原案)、３以上、４以上と変更した場合の診断精度の変化は

陽性条件	感度（%）	特異度（%）	精度（%）	除外数
スコア１以上	７２．６	９２．７	７９．８	2
スコア３以上	７０．３	９２．７	７８．３	1
スコア４以上	６８．９	９２．７	７７．４	1

4）Rose-Bengal 試験結果の記載のある５６０例で RB＋の解釈を van Bijsterveld スコアで次のようにした場合の診断精度の変化は

RB＋の解釈	感度（%）	特異度（%）	精度（%）	除外数
スコア１以上	９０．２	９１．７	９０．９	１２
スコア３以上	８９．６	９２．０	９０．７	１０
スコア４以上	８９．４	９２．０	９０．５	１０

5）高齢者で False Positive が増加しないかについて、年齢を６０歳以上と未満、７０歳以上と未満に分け検定を行ったが、高齢者群での False Positive の増加は見られず、精度の低下はわずかであった。

6）これらの結果を総合して改訂診断基準について１９９８年の第８回日本シェーグレン症候群研究会において討論した結果、診断基準改訂試案第１案のうち、上述した（１）病理組織所見陽性を単独陽性で確定診断陽性とせず、口腔、眼、血清とともに４項目中の１項目とし、４項目中いずれか２項目以上で確定診断陽性とすること、（２）眼の Rose-Bengal 検査は van Bijsterveld スコアで３以上で陽性とすることの２点を改訂して診断基準とすることが合意された。したがって改訂診断基準は次の結論ごとくである。

［結論］

シェーグレン症候群の改訂診断基準（１９９９年）

１．生検病理組織検査で次のいずれかの陽性所見を認めること

A）口唇腺組織で４mm^2あたり１focus（導管周囲に５０個以上のリンパ球浸潤）以上

B）涙腺組織で４mm^2あたり１focus（導管周囲に５０個以上のリンパ球浸潤）以上

２．口腔検査で次のいずれかの陽性所見を認めること

A）唾液腺造影で Stage Ⅰ（直径１mm 未満の小点状陰影）以上の異常所見

B）唾液分泌量低下（ガム試験にて１０分間で１０ml以下またはサクソンテストにて２分間で２ｇ以下）があり、かつ唾液腺シンチグラフィーにて機能低下の所見

3．眼科検査で次のいずれかの陽性所見を認めること

A）シャーマー試験で５分間に５mm以下で、かつローズベンガル試験（van Bijsterveldスコア）で３以上

B）シャーマー試験で５分間に５mm以下で、かつ蛍光色素試験で陽性

4．血清検査で次のいずれかの陽性所見を認めること

A）抗ＳＳ－Ａ抗体陽性

B）抗ＳＳ－Ｂ抗体陽性

＜確定診断基準＞

上の４項目のうち、いずれかの２項目以上に該当すればシェーグレン症候群と確定診断する。

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〔Ⅴ〕研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

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