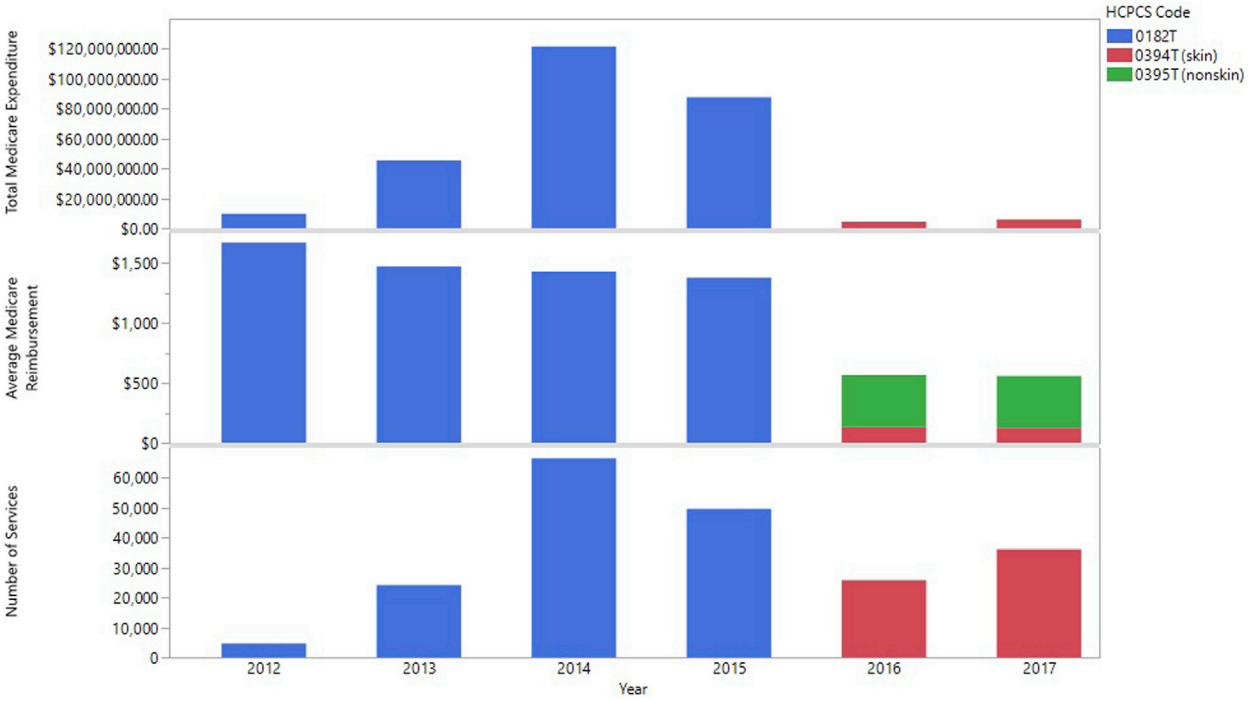

Fig 1. Trends in EBT use, reimbursement, and total Medicare expenditure, 2012-2017. *EBT*, Electronic brachytherapy.

resulted from uncertainty over clinical efficacy as well as markedly lower Medicare reimbursement rates. Limitations of this study include its retrospective design, use of claims data, and lack of correlation with clinical outcomes. Future studies should evaluate EBT in controlled, prospective trials to better assess clinical outcomes and inform cost-effectiveness analyses.

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Serologic characterization of anti-p200 pemphigoid: Epitope spreading as a common phenomenon

To the Editor: Anti-p200 pemphigoid is an autoimmune blistering disease characterized by circulating autoantibodies binding to the dermal side of human salt-split skin (SSS) by indirect immunofluorescence (IIF) microscopy and reactivity against a 200-kDa

protein in the extract of human dermis by immunoblotting (IB).[1] Laminin γ1 has been identified as a major target antigen and can be detected in about 90% of sera.[2] This retrospective single-center study included all 245 anti-p200 pemphigoid sera analyzed between 2008 and 2017 in our routine autoimmune laboratory with a compatible clinical picture and reactivity with the p200 protein. All sera were subjected to 1) IIF on SSS; 2) IB with dermal extract (p200 and type VII collagen), recombinant C-terminus of laminin γ1, and extracellular matrix of cultured human keratinocytes (laminin 332); and 3) a type VII collagen (Col7)-specific enzyme-linked immunosorbent assay (Euroimmun, Lübeck, Germany). Sera that showed reactivity against laminin 332 by IB were also subjected to IIF with HEK293 cells expressing recombinant laminin 332 (Euroimmun) and IB with the recombinant α3 chain of laminin 332. In addition, sera with additional IgG binding to the epidermal side of SSS were tested by BP180- and BP230-specific enzyme-linked immunosorbent assay (both Euroimmun) and IB with conditioned medium of cultured human keratinocytes (LAD-1, the soluble ectodomain of BP180). The study was performed according to the Declaration of Helsinki and was approved by the ethics committee of the University of Lübeck (17-284).

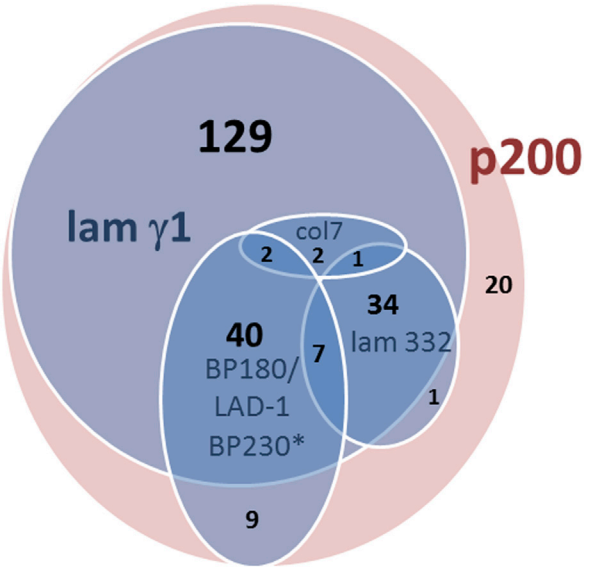

Fig 1. Epitope spreading in anti-p200 pemphigoid. The numbers of sera with IgG reactivity to the different antigens are shown. *Including sera with additional binding to the epidermal side of salt-split human skin by indirect immunofluorescence microscopy but unidentified epidermal target antigen. *col7*, Collagen type VII; *LAD-1*, linear IgA dermatosis antigen 1; *lam γ1*, laminin γ 1; *lam 332*, laminin 332; *p200*, p200 protein.

Table I. Fine autoantibody specificities of 245 anti-p200 pemphigoid sera

Target antigen	IgG reactivity
p200 protein, n/total (%)	245/245 (100)
Laminin γ1, n/total (%)	215/245 (88)
Laminin 332, n/total (%)*,†	43/239 (18)
α chain, n	42
β chain, n	6
γ chain, n	3
BP180, n/total (%)‡	50/245 (20)
NC16A	22/245 (9)
LAD-1	15/245 (6)
Full length	14/245 (6)
BP230, n/total (%)§	15/245 (6)
Col7, n/total (%)§	5/245 (2)
Unidentified,‖ n/total (%)	4/245 (2)

Col7, Type VII collagen; *LAD-1*, linear IgA-dermatosis antigen 1; *NC16A*, extracellular noncollagenous domain.
*Six sera could not be analyzed for autoantibodies against laminin 332 because of a limited serum amount.
†Three patients with anti-laminin 332 reactivity had predominant mucosal involvement.
‡Ten of 50 (20%) patients had predominant BP180 reactivity.
§No patient had predominant anti-BP230 or anti-Col7 reactivity.
‖Binding to the epidermal side of salt-split human skin by indirect immunofluoresence microscopy in addition to the dermal side but unidentified epidermal target antigen.

There were 91 women and 154 men with a mean age ± standard deviation of 74 ± 11 years (range, 28-95 y) included in the study. Compatible with the inclusion criteria, all sera contained antibodies against the p200 protein by IB of dermal extract. By IIF on SSS, IgG antibodies against the dermal side were identified in 223 (91%) sera, and IgA labeling of the dermal side was seen in 1 (0.4%) serum. IgG4 reactivity to laminin γ1 was found in 215 (88%) sera. IgG4 reactivity to laminin 332 by IB was observed in 43 (18%) patients, with 42 (98%) sera recognizing the α3 chain. Anti-laminin 332 reactivity was confirmed in 30 of 43 (70%) sera by IIF with HEK293 cells expressing recombinant laminin 332 and/or IB with the recombinant full-length laminin α3. IgG autoantibodies to Col7 were detected in 5 (2%) patients. In addition to IgG reactivity against the dermal side, IgG and IgA labeling of the epidermal side of SSS was observed in 58 (24%) and 2 (0.8%) sera (directed against C-terminal epitopes of BP180), respectively. In 54 of 58 (93%) sera with additional IgG labeling to the epidermal side, reactivity against BP180 and/or BP230, detailed in the Table I, were detected. All 4 additional target antigens in our patients with anti-p200 pemphigoid are autoantigens of other pemphigoid diseases, that is, mucous membrane

pemphigoid (BP180, laminin 332), bullous pemphigoid (BP180, BP230), and epidermolysis bullosa acquisita (Col7). In line with our study, autoantibodies against these 4 antigens have previously been described in patients with anti-p200 pemphigoid in case reports and a case series.[3-5]

In 82 (33%) anti-p200 pemphigoid sera, reactivity against a single antigen in addition to p200/laminin γ1 was detected, and in 15 (6%) sera, reactivity against 2 additional antigens was detected (Fig 1). In some patients with dual autoantibody responses, the final diagnosis remained elusive because of no predominant autoantibody reactivity.

The study was limited by its retrospective, monocentric design and lack of clinical information that did not allow any correlation analyses between autoantibody specificities with a particular clinical phenotype, disease duration, or treatment responsiveness.

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Response of dermatomyositis to the antimalarial quinacrine: A retrospective cohort study

To the Editor: Quinacrine (QC) is an antimalarial taken with hydroxychloroquine or chloroquine to treat dermatomyositis (DM).[1,2] QC is prescribed at a constant dosage (100 mg/d), is well tolerated, and does not require blood or vision monitoring, but it may be associated with reversible skin yellowing.[2-4] In 2019, the US Food and Drug Administration placed the manufacturer of QC on import alert.[5] This is concerning because the lack of QC may increase reliance on steroids or immunosuppressants. To characterize the importance of the effects of QC on DM disease activity and quality of life, we present a retrospective study from a prospectively collected database of patients with DM.

Inclusion criteria included adult patients with an initial visit before starting QC, a follow-up visit at least 2 months after initiating QC, and no changes in immunosuppressive therapy between the 2 visits. Patients were followed up for up to 36 months. Data collected included Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) activity scores and the Skindex-29 parameters of symptoms, emotions, and photosensitivity. Patients were QC responders if the follow-up CDASI activity score decreased by at least 5 points or 20% from the initial visit. QC nonresponders did not meet either criteria. Wilcoxon signed rank tests and rank sum tests were performed to compare paired and unpaired variables, respectively, with a significance level of .05.

Of the 321 database patients, 20 started QC while in the database and had a follow-up visit