

lium sensitivity.<sup>8</sup> Instead, the beryllium lymphocyte proliferation test should be used. It is a useful and safe test in individuals who are exposed to beryllium from dental prostheses and devices.

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#### In reply

We acknowledge the points raised by Pigatto et al regarding our research team's recent publication on allergy to mercury and OLP.<sup>1</sup> Pigatto et al report that the presence of organic mercury in dental plaque and calculus is caused by bacterial biotransformation of inorganic mercury associated with dental amalgam fillings. Our team found that cross-reactivity between the inorganic mercurials (ammoniated mercury, metallic mercury, and amalgam) and the organic mercurials (thimerosal and phenylmercuric salts) may also be important in the pathogenesis of OLP. In 2 patients with OLP, patch-test reactions were positive to ammoniated mercury, metallic mercury, and thimerosal.<sup>1</sup> This underlies the clinical importance of patch testing with both organic and inorganic mercury compounds in patients with OLP.<sup>2,3</sup>

Increased dental plaque or calculus has been reported to be associated with a significantly higher incidence of gingival OLP lesions.<sup>4</sup> Generally, improvement of poor oral hygiene in patients with OLP is very important.<sup>5</sup> Regarding the comment on the clinical characteristics of the patients, potential association between OLP and hepatitis C viral infection has since been reported.<sup>6</sup>

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### Defective Prelamin A Processing Resulting From LMNA or ZMPSTE24 Mutations as the Cause of Restrictive Dermopathy

Armbrust and colleagues<sup>1</sup> report a case of a child with restrictive dermopathy (RD) who had unusual symptoms: a transposition of the great arteries and a microcolon. The authors state that RD is an autosomal recessive disorder of unknown cause and suggest that the *FATP4* gene is pathogenetically involved.

We were surprised by their article. The authors must have missed our recent articles<sup>2,3</sup> in which we demonstrated that RD is caused either by mutations in the *LMNA* gene, encoding A-type lamins, or in the *ZMPSTE24* gene, encoding a metalloprotease essential for the posttranslational processing of prelamins A to mature lamin A.<sup>2,3</sup> As such, RD can be either autosomal dominant, as in the case of de novo splicing mutations in *LMNA*, or autosomal recessive, as in the case of loss of function mutations in *ZMPSTE24*.<sup>2,3</sup> In the latter case, patients with these mutations have been found to be either homozygous or compound heterozygous.<sup>3</sup> We have examined a total of 12 patients with RD and have identified mutations in all of them. Furthermore, major nuclear disorganization was observed, with accumulation of either truncated or normal-length prelamins A.<sup>2,3</sup> Accumulation of lamin A precursors has a dramatically toxic effect on RD cells, as confirmed in recent studies<sup>4</sup> performed on knockout mouse models for *LMNA* and *ZMPSTE24*. Our findings rule out mutations in the *FATP4* gene as a potential cause for most cases of RD, despite the features resembling RD described in targeted disruption of *FATP4* in mice.<sup>1</sup> To date, the closest model for RD corresponds to the *ZMPSTE24* knockout mouse.<sup>5</sup> Thus, RD can be added to the group of laminopathies that consists of more than 10 different disorders. It most resembles the premature aging disorder progeria, which was previously associated with lamin A truncation.<sup>6</sup>

Studies of *LMNA* and *ZMPSTE24* may still be possible in the patient reported by Armbrust and colleagues.<sup>1</sup> Because their patient died after 24 days of life, which is somewhat unusual for patients with RD, the possibility exists that residual activity of the *ZMPSTE24* gene is maintained together with mature lamin A or that a heterozygous mutation lies in the specific *LMNA* region encoding the lamin A isoform.

Their patient had symptoms that were unusual for RD. It may be possible that the heart defect in this child was related to the heart defect in her sibling and is in fact unrelated to the RD. Evaluation of the child's sibling, perhaps using fluorescence in situ hybridization to search for a microdeletion of chromosome 22q11-13, seems warranted. Like the authors, we think these additional symptoms are unrelated to the RD. Finally, Armbrust et al<sup>1</sup> mention that a uniparental disomy was identified in a sibling with Silver-Russell syndrome. We are not informed which chromosome was involved, but it may be useful to search for a similar molecular mechanism in the proband as well. The presence in a single family of various and different disorders pleads for extensive additional studies to explain this and to provide adequate genetic counseling for the parents.

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### In reply

We appreciate the helpful comments of Levy and colleagues. The very recent results from studies of Navarro et al,<sup>1,2</sup> subsequent to submission of our manuscript, on mutations in the LMNA and ZMPSTE24 genes are indeed important findings for elucidating the etiology of restrictive dermopathy (RD).

Previously, RD had not been associated with Silver-Russell syndrome (SRS). According to the proposed diagnostic criteria defined by Price et al,<sup>3</sup> growth retardation is the only sign of SRS that our patient had, whereas Herman et al<sup>4</sup> concluded that no single finding is pathognomonic. The distinctive facial appearance of SRS was not seen in our patient, whereas the most striking symptoms in patients with RD, including ours, are microstomia and micrognathia, together with a taut, translucent skin that is often described as having the appearance of an "Asian porcelain doll."

Gastrointestinal complications are frequently seen in patients with SRS, but these are more functional than mor-

phological, and specific gastrointestinal diseases have not been recognized as major features.<sup>5</sup> After our patient died, her parents were no longer available for further diagnostic investigations, particularly for uniparental disomy.

Most infants with RD die within the first days or weeks of life, mainly because of respiratory insufficiency resulting from thoracic stiffness.<sup>6</sup> Because we were unaware of the lethal condition the child had, our patient was ventilated and thus survived for some time. Cases of typical RD with longer survival times of up to 4 months are rare but have been described.<sup>7</sup>

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### VIGNETTES

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#### Drug-Induced Bullous Pemphigoid Caused by a Generic Canadian Medication Obtained Over the Internet

A 40-year-old man with a medical history of ulcerative colitis presented with a 2-week history of a pruritic, bullous eruption (**Figure 1**). He reported that he had been taking 5-aminosalicylic acid for years and had not recently taken any new medications. Despite his young age, bullous pemphigoid was suspected clinically. A biopsy was performed and prednisone therapy was initiated.

Routine hematoxylin-eosin staining revealed an eosinophil-rich, perivascular infiltrate and a subepidermal blister. Direct immunofluorescence studies revealed 2+ coalescing granular and linear IgG deposits along the basement membrane zone, 2+ coalescing granular and lin-