

diabetes, morbid obesity, chronic kidney disease, multiple strokes and multiple myocardial infarctions. His obesity had persisted despite having a gastric band *in situ*.

Physical examination revealed an indurated erythematous plaque on the left side of the abdomen. There was marked lymphoedema and abdominal asymmetry (Fig. 1a). There were several erosions within the plaque. The rest of the body was clear.

We were uncertain whether the lymphoedema was secondary to lymphatic damage from a primary inflammatory dermatosis, or due to lymphatic compression from the large abdomen, with resulting secondary inflammation. Hence, the differential diagnosis included immunobullous disorders, and skin changes due to chronic oedema.

Histological examination (Fig. 1b) revealed dermal oedema, dermal scarring and a small capillary proliferation without a lymphocytic infiltrate. Direct and indirect immunofluorescence was negative.

A diagnosis of LPA was made, based on the clinical and histopathological features.

The patient was treated with topical clobetasol and potassium permanganate soaks, with some improvement, but his symptoms recurred following cessation of treatment. He presented to a tertiary lymphoedema centre, where he was prescribed a Velcro® compression garment. The patient did not engage with the compression therapy and his condition has progressed. His abdomen continues to expand, leading to worsening lipodermatosclerosis, chronic pain and recurrent infections. He now has permanent lymphoedema, causing breathing difficulty and distortion of his lumbar spine. He was referred again to the bariatric surgeons, but they could not offer further intervention.

We hope that awareness of LPA will allow early recognition and referral to specialist lymphoedema and bariatric services. Antigravity measures such as bed rest, together with early treatment of lymphoedema and obesity may prevent irreversible lymphoedema and secondary complications.

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Four-year data from use of the nut and soya allergy testing protocol before treatment with isotretinoin and alitretinoin

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We previously reported crossreactive soya allergy in patients with peanut and other nut allergy.¹ In the UK, around 1 in 20 patients who are allergic to peanut are also allergic to soya, and an unknown number of patients with other nut allergies are also soya-allergic. Both isotretinoin and alitretinoin contain soya oil. We report on a patient developing an allergic reaction after testing isotretinoin, and describe an allergy-testing protocol (Fig. 1) for patients under consideration for treatment with isotretinoin/alitretinoin. Nut and soya allergy causes tingling or swelling at sites of contact (lips, tongue, mouth or throat), nausea, urticaria following allergen absorption and/or anaphylaxis.

Our index case had a known cashew nut allergy and developed swelling of her eyelids and lips requiring emergency treatment after taking isotretinoin. She was subsequently tested for soya allergy using the blood test for specific IgE antibodies against Gly m4, m5 and m6 blood test, and she had a positive Gly m4 result.

Consequently, we proposed a protocol that safely identifies those patients with a known nut allergy who are suitable to be treated with isotretinoin or alitretinoin, and those for whom they should be avoided.

In the past 4 years since designing the protocol, 16 consecutive patients with a nut allergy have been tested (Table 1). Of these, four (25%) were identified to have a crossreactive allergy to soya. Including the index patient, three of the five cases of crossreactive allergy were caused by cashew nuts. We clearly demonstrate a higher risk in patients with cashew nut allergy than with peanut.

The product literature for isotretinoin and alitretinoin states that they are contraindicated in those with peanut allergy, but no mention is made of other nuts. We urge the manufacturers of isotretinoin and alitretinoin to change the product literature to contraindicate the use of these drugs in all patients with a known nut allergy who have not been tested with this protocol.

Without the use of the protocol, the tested 16 patients would have been unsuitable for treatment with isotretinoin due to the unknown crossreactive allergy incidence, but with its application 12 (75%) of the 16 patients were successfully treated and the remaining 4 were safely

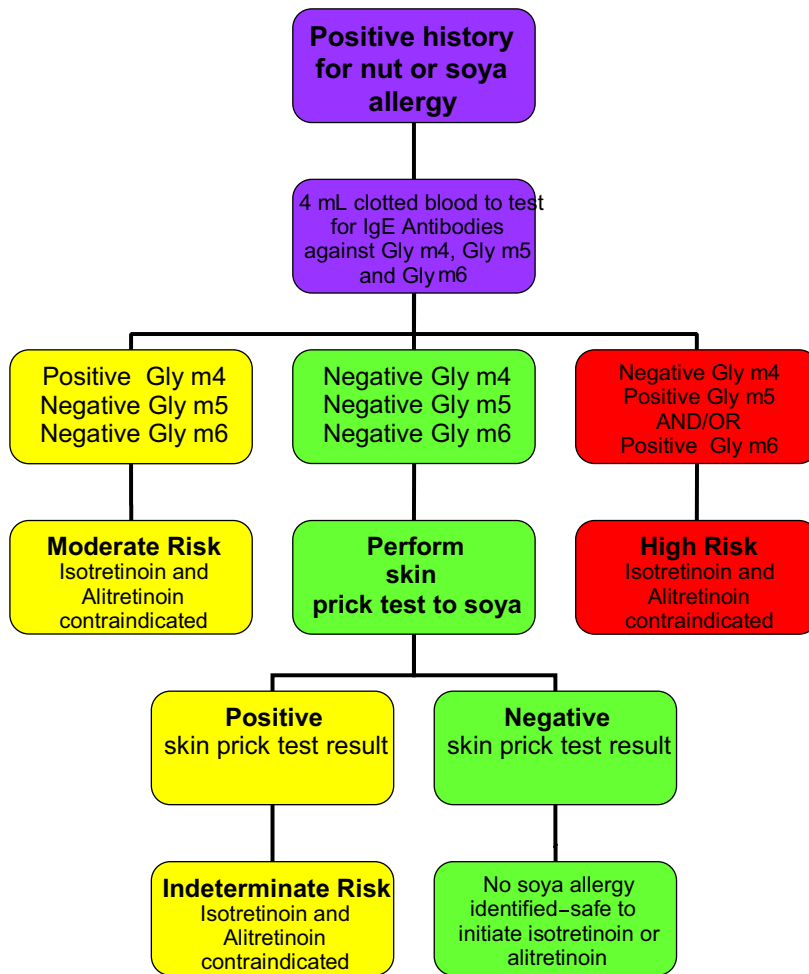


Figure 1 Protocol for investigation of possible soya allergy in patients being considered for treatment with isotretinoin or alitretinoin.

Table 1 Case series of 16 patients tested using the soya allergy protocol.

Patient	Which nut(s) allergic to	Result	Outcome
1	Cashew	Gly m4 positive	Not treated
2	Peanut	Gly and prick test negative	Treated successfully
3	Peanut	Gly m5 positive	Not treated
4	Peanut	Gly and prick test negative	Treated successfully
5	Peanut	Gly and prick test negative	Treated successfully
6	Sesame	Gly and prick test negative	Treated successfully
7	Peanut	Gly negative, prick test negative	Treated successfully
8	Multiple, including peanut	Gly negative, prick test negative	Treated successfully
9	Peanut, almond	All positive	Not treated
10	Peanut, hazelnut	Gly and prick test negative	Treated successfully
11	Peanut, cashew	Gly and prick test negative	Treated successfully
12	Cashew	Gly and prick test negative	Treated successfully
13	Multiple, including peanut	Gly and prick test negative	Treated successfully
14	Peanut	Gly and prick test negative	Treated successfully
15	Cashew	Gly m4 positive	Not treated
16	Peanut	Gly and prick test negative	Treated successfully

identified as unsuitable for treatment. Seven cases of anaphylaxis have been reported via the Yellow Card reporting scheme since 1983, none of which were fatal. Use of this protocol would minimize the risk of anaphylaxis and fatality while allowing patients with a nut allergy but no soya allergy to be safely identified.

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patients being considered for treatment with isotretinoin or alitretinoin. *Clin Exp Dermatol* 2016; **41**: 326–7.

Extragenital lichen sclerosis successfully treated by topical maxacalcitol/betamethasone butyrate propionate

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Lichen sclerosis (LS) is a benign chronic inflammatory skin disorder affecting the anogenital and extragenital areas. It is an autoimmune disease characterized by autoreactive T cells. Clinically and histopathologically, LS and scleroderma are similar.¹ Patients are usually asymptomatic or may present with slightly itchy, white papules with progressive development of parchment-like skin.

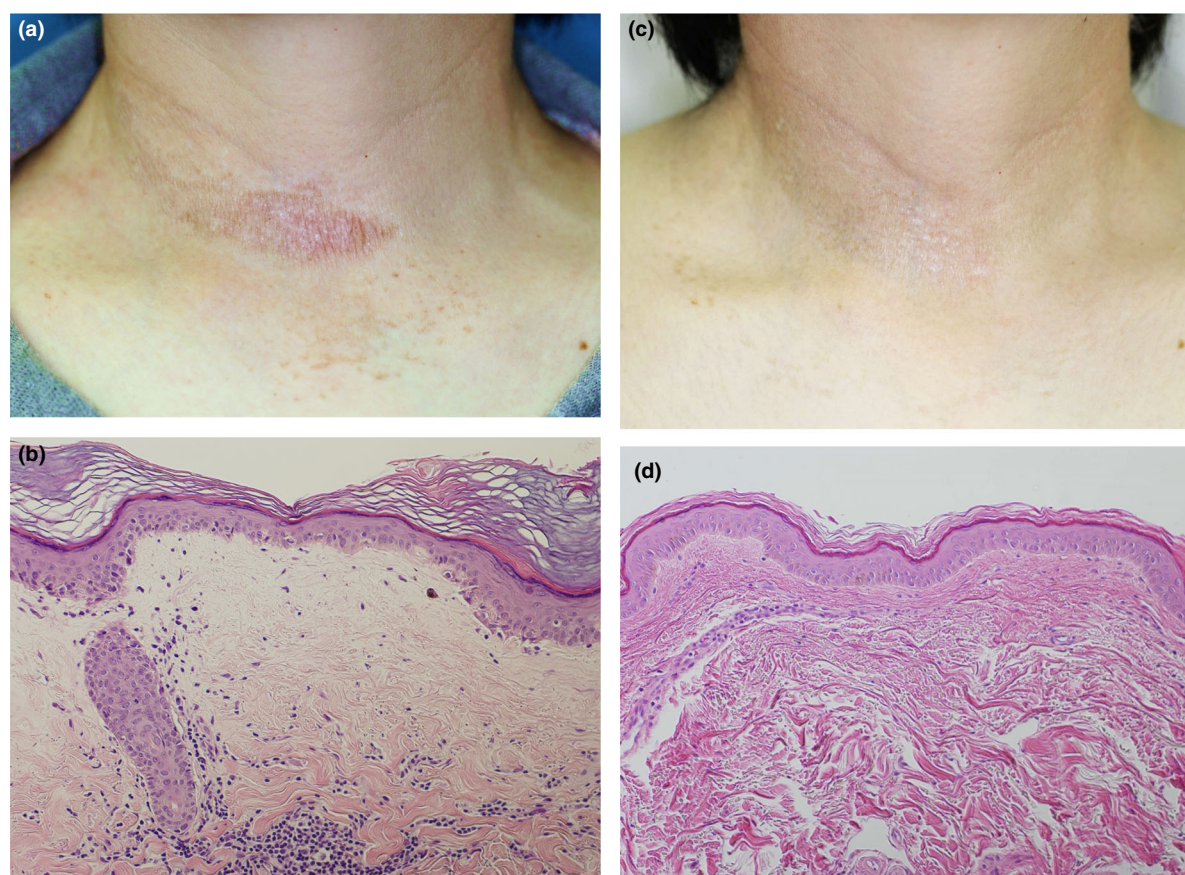


Figure 1 (a) Sclerotic and atrophic plaques with brownish comedo-like hyperkeratotic lesions on the patient's neck. Partial hyperkeratosis, epidermal thinning, loss of rete ridges, liquefaction degeneration of the epidermal–dermal junction, hyalinized collagen, oedema and mild dermal infiltration of inflammatory cells (haematoxylin and eosin, original magnification $\times 200$). (c) After 4 months of application of topical maxacalcitol/betamethasone butyrate propionate, the skin lesions showed significant improvement. (d) Marked increase in the number of collagen fibres and disappearance of the dermal oedema, as well as the previously observed inflammatory cell infiltration (haematoxylin and eosin stain, original magnification $\times 200$).

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Comment on 'Four-year data from use of the nut and soya allergy testing protocol before treatment with isotretinoin and alitretinoin'

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Linked articles: Alden K *et al.* *Clin Exp Dermatol* 2020; **45**: 627–9. Alden K *et al.* *Clin Exp Dermatol* 2016; **3**: 326–7.

We read with interest the recent article by Alden *et al.* in *Clinical and Experimental Dermatology*,¹ in which they asserted that isotretinoin and alitretinoin are contraindicated in nut-allergic patients unless tested using their previously proposed protocol.¹ We feel that this is an unsupported step, limiting treatment options for adolescents with two very common conditions: nut allergy and acne.

The index case's eye and lip swelling occurring very late (12 h) after isotretinoin,¹ do not automatically represent drug allergy and are inconsistent with IgE-mediated mechanisms as seen in peanut allergy.^{1,2} Continued exposure to an allergen, as described in the report, would cause rapid escalation of IgE-mediated symptoms. A subjective report of 'throat tightness'^{1,2} while admittedly difficult to ignore, cannot be accepted as proving allergy. Without IgE-mediated symptoms, screening for IgE-mediated crossreactivity does not seem logical. Other unidentified triggers might be responsible. Crucially, a drug provocation test was not performed, therefore an adverse reaction to isotretinoin, whether IgE-mediated or not, remained unconfirmed.

An allergy diagnosis, needs reproducible, typical symptoms upon repeated exposure, supported (not replaced) by appropriate *in vivo* or *in vitro* testing. The original case report commented that the index case was 'unaware of any soya allergy', implying that she did not have clinical symptoms, i.e. she was not soya-allergic. Her extremely low-level positive specific (s)IgE levels were therefore, by definition, false-positive results.

Soya, a legume, is an uncommon cause of allergy, rarely seen in infants without coincident cow's milk allergy. P34, a major protein in soya, shares 50–70% sequence homology with casein in milk, and 70%

homology to Ara h 1, a major peanut protein.³ Despite this, clinical crossreactivity with peanut is very uncommon, with only 3% of peanut-allergic individuals showing reactivity to soya.^{3,4} Testing peanut-allergic individuals for sensitization to soya is not recommended, owing to a high rate of false positives. Allergists do not advise such patients to avoid soya, as crossreactivity with soya is not considered a clinical risk. Crossreactivity between soya and tree nuts has not been described outside the context of pollen–food allergy syndrome related to Gly m 4 sensitization, which is associated with a much lower risk of systemic reactions compared with primary food allergy. The index case in the report by Alden *et al.*¹ had a very low level of splgE to Gly m 4 and was asymptomatic.

Isotretinoin and alitretinoin contain refined soya oil, with very low levels of soya protein and minimal IgE binding. At these levels, it would be expected that soya-allergic individuals would need to consume very large volumes (over 1 L) to experience a reaction.⁵ The European Food Safety Authority and the US Food and Drug Administration do not require fully refined soya oil to be declared as an ingredient in foods. Therefore, the report's published precautions about soya oils used in medicines¹ appear to be based on theoretical principles rather than clinical evidence.

More evidence-based and clinically useful protocols would include either formally investigating the safety of isotretinoin and alitretinoin in a large number of well-phenotyped, nut-allergic patients with skin prick testing to the active drug and its constituents, or to do that in any individual patient allergic to peanut, tree nut or soya allergic who was being considered for isotretinoin therapy. These are studies that many allergists would be keen to support to finally prove or disprove the questions raised in the two reports by this group.

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