

Codfish allergy in adults

Identification and diagnosis

Hansen TK, Bindslev-Jensen C. Codfish allergy in adults. Identification and diagnosis.

Allergy 1992; 47: 610–617. © Munksgaard 1992

Ten adult patients with a medical history of immediate allergic reactions following ingestion of minute amounts of codfish were examined together with 27 control subjects (8 nonatopics, 7 pollen allergics, and 12 suffering from atopic dermatitis) all regularly ingesting codfish without experiencing reactions. All 37 subjects were evaluated by skin prick test, RAST, and histamine release test in order to determine the value of these commonly used diagnostic tests. The results were compared to titrated, oral, double-blind, placebo-controlled food challenges (DBPCFCs) with fresh codfish undertaken in the 10 patients, whereas all control subjects were classified as challenge-negative according to their questionnaires. Totally, 7 of 10 medical histories were confirmed by DBPCFC, and in these most of the reported symptoms proved reproducible. Oropharyngeal itching and swelling occurred as the first symptom, always preceding the onset of any accompanying symptom. For identification of DBPCFC-positive subjects, skin prick test and RAST proved to be the most sensitive tests (7/7), and all tests showed specificities of 90–97%. The skin prick test still seems reliable but does not, however, exclude the need for DBPCFC.

Clinical aspects

A diagnostic procedure for oral testing with codfish is described. Doses eliciting symptoms varied between 6 mg and 6.7 g of freshly prepared codfish, and by DBPCFC, reproducibility was found in 70% of the codfish-hypersensitive patients. The potential of commercial codfish allergen extract was tested in commonly used diagnostic tests. Results show that a negative skin prick test is an excellent indicator of no clinical codfish hypersensitivity, while a positive result requires further evaluation. Specificities of 90–97% in skin prick test, RAST, and histamine release test reveal that DBPCFC are still needed to identify clinically allergic individuals.

T. K. Hansen, C. Bindslev-Jensen

Food Allergy Unit, National University Hospital,
Copenhagen, Denmark

Key words: adult; double-blind method; fish; food hypersensitivity; histamine liberation; IgE; radioallergosorbent test; skin tests.

Tine K. Hansen
Food Allergy Unit TTA 7523
National University Hospital
20 Tagensvej
DK-2200 Copenhagen N
Denmark

Accepted for publication 6 March 1992

Ingestion of codfish has been reported to be one of the most common causes of allergic reactions to food, but no clinical studies of codfish-induced hypersensitivity reactions have been conducted with the particular purpose of investigating this problem in adults. Allergy to different food items in children has been carefully investigated in studies using diagnostic tests such as skin prick test (SPT), RAST, histamine release (HR), and double-blind food challenges (1, 2, 9, 10, 11, 14, 15, 23, 26, 27). Double-blind, placebo-controlled food challenge (DBPCFC) is now considered to be the "gold standard" for determining the presence of immediate food hypersensitivity (8, 11, 12, 14, 21, 24, 25), and recently this procedure has been applied with the aim of diagnosing adverse reactions to different foods in adults.

These studies reveal that about 30 to 53% of adults suspected of adverse reactions to food can be confirmed in DBPCFC (7, 8, 13, 18, 22).

The purpose of this study was to identify a group of adults with immediate adverse reactions to codfish by DBPCFC with fresh food; to characterize the symptoms appearing; and to investigate the diagnostic reliability and accuracy of tests (SPT, RAST, HR) commonly used.

Material and methods

Patients and control subjects

Based on their medical histories, 10 adult patients, (average age 26 years, range 21 to 31 years), with suspected food allergy to codfish were included in

the study. Inclusion criteria included histories of codfish allergy, manifested by local irritation, itching and swelling in mouth, oropharynx, and eventual itching of ears (OPIS); rhinoconjunctivitis; asthma; gastrointestinal (GI) symptoms such as vomiting and diarrhoea; urticaria; angioedema; erythema; and/or anaphylactic shock. All patients reported objectively measurable symptoms within 30 min after ingestion of small amounts of codfish, and none of them had ingested codfish within 4 weeks to several years prior to this investigation. Each patient was evaluated on the basis of clinical history, SPT, RAST, HR, and DBPCFC with codfish allergen (Fig. 1).

The control group comprised three subgroups: 8 non-allergic subjects; 7 pollen-allergics; and 12 suffering from atopic dermatitis, 6 having serum-IgE concentrations >2000 kIU/l and 6 <2000 kIU/l. Altogether there were 17 female and 10 male subjects, aged 17 to 48 years; average 32 years. The control subjects underwent the same diagnostic programme as

the patients; however, the challenges were omitted due to regular unsymptomatic ingestion of codfish.

Preparation of codfish for provocations

Fresh codfish was used in oral challenges. The fresh, raw, white meat of codfish was stored at -20°C for a maximum of 7 days before use. Immediately before the challenges, the codfish was homogenized in distilled water for 2×3 min using a thermostatically controlled Waring blender (Waring Products Division, New Hartford, Connecticut). The codfish suspension was mixed with concentrated blackcurrant juice (without dyes or preservatives), and dilutions were made with blackcurrant/distilled water (1:4). Doses ranging from 5 μg to 100 mg of codfish were easily masked in a volume of 50 ml dilution, whereas 0.5, 1, and 5 g required 100 ml. The placebo preparations were prepared the same way, omitting the codfish, and were administered in equal numbers and volumes. The preparations were tested by volunteers using a nose-clip in order to minimize any possible taste of the content. No one could identify the active content from the placebos up to 1 g, but a minority reported a slight difference in texture but not in taste at a dose of 5 g. Two patients both noted a change of texture once, which was not reproducible. All challenge preparations were prepared by the same person, and the randomization was made by the dietician of the clinic. The challenge preparations were kept cool until use and administered in opaque plastic cups with lid and straw.

Medication

On the day of challenge the patients were told to arrive early in the morning and to be fasting and free of any symptoms which could either be caused by eating codfish or would mask the registration. They were instructed to discontinue antihistamines for 5 days (astemizole 6 weeks) and systemic steroid for 1 month, and that local β_2 -agonists should be withheld for at least 4 h before the challenges.

Skin prick test

Skin prick test was performed in quadruplicate on the forearms of all 37 subjects according to the European Academy of Allergology and Clinical Immunology Guidelines (28). Extracts used throughout the study were from the same batch of commercial, glycerinated allergen of codfish, 1:20 w/v, (Soluprick, ALK Laboratories, Hørsholm, Denmark). Histamine dihydrochloride 10 mg/ml was used as positive control, and a diluent of glycerol/sodiumchloride as negative control. Prior to testing, oral antihistamines were discontinued for 5 days (astemizole 6 weeks), systemic steroids for 1 month and topical steroids on

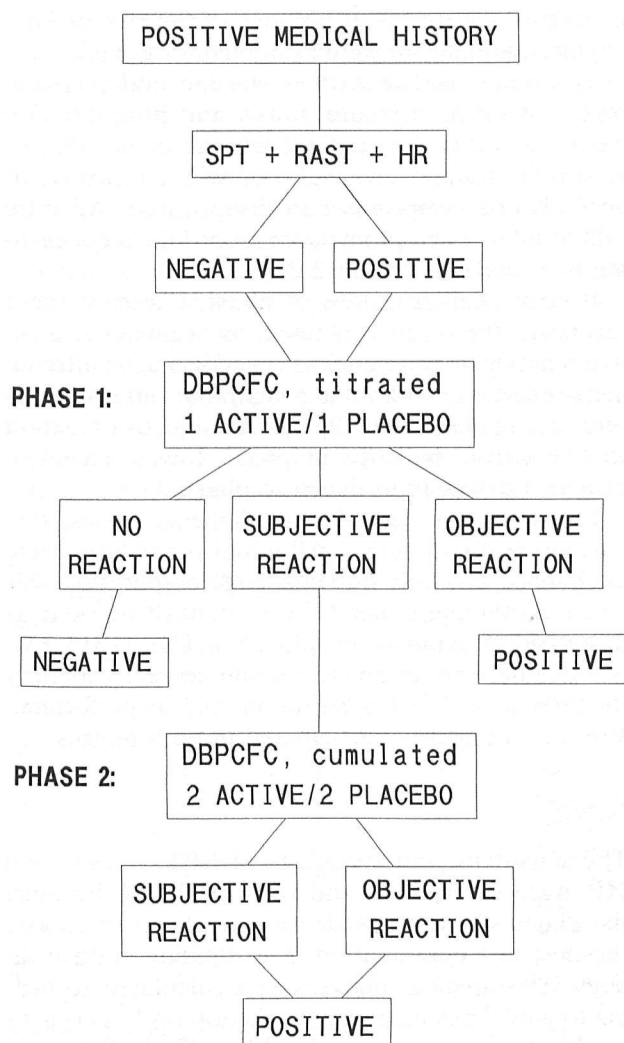


Fig. 1. Chart of the diagnostic procedure.

the test site for 24 h. The reaction to the positive control was assessed after 10 min and the codfish reactions after 15 min by outlining the wheal contour using a fine-tip rolling pen, and the reaction outlines were transferred to a record sheet using transparent tape. All SPTs were applied and measured by the same investigator. The size of the skin reaction was recorded as the average of the longest and the mid-point orthogonal diameters $((D + d)/2)$, measuring the inner contour of the wheal outline. The reaction to the skin test was considered to be positive when the wheal induced by the codfish extract had a net diameter 3 mm larger than that of the negative control in all 4 punctures.

Total and specific IgE

Total serum-IgE was measured in all patients and control subjects by the commercially available PRIST kit (Pharmacia, Uppsala, Sweden). Codfish-specific IgE analyses were measured in duplicate by Phadebas RAST (Pharmacia Diagnostics AS, Hillerød, Denmark) and the results expressed in RAST classes 0–4 according to the Phadebas RAST scoring system. A result of RAST class 1 or more was considered to be positive. The results were given in PRU/ml.

Histamine release test

Histamine release from basophil leukocytes was measured in all 37 subjects according to the method developed by Skov (17, 30), and performed at the Referencelaboratorium, Denmark. As provocative allergen, Soluprick extract of codfish 1:20 w/v from ALK was coated onto microtiter wells and 25 µl of whole blood were applied. The codfish allergen was tested in six concentrations. The microtiter plates were incubated at 37°C for 1 h, protein residues were enzymatically removed, and histamine bound to the microfibrils was measured spectrophotofluorometrically.

Responses were considered to be positive if yielding a histamine release ≥ 20 ng/ml. A histamine release of < 20 ng/ml following anti-IgE challenge, i.e. non-responding basophils, was classified as inconclusive.

Procedure of double-blind, placebo-controlled food challenges

All patients underwent oral, titrated challenges with fresh codfish, except one who was challenged outside this study. The control subjects reported no adverse reactions when ingesting codfish, and accordingly they were not challenged but were classified as challenge-negative based on the questionnaire. The challenge procedure was divided into two

phases, and both were performed at the clinic. Phase 1 consisted of titrated double-blind, placebo-controlled challenges performed on 2 separate days; one day with active challenge preparations, containing doses from 0.5 µg up to 5 g, masked as described above, and one day with placebo. Each day the first challenge comprised placebo in order to permit a baseline registration of reactions. Then either increasing doses of active preparation (9 challenges, a total dose of 6.7 g) or an equal number of placebos was given every 30 min if no symptoms appeared. Before each ingestion, relevant parameters such as lung function, oral examination and symptoms elicited by ingestion were recorded; challenging was continued until either objective reactions were observed or the maximum dosage had been reached. While drinking, a nose-clip was always used in order to minimize any possible taste of the content. All reactions were described with regard to type, severity, time of onset, and duration, and the physician serving the challenge preparations and evaluating the reactions was unaware of the content. Certain precautions were taken because of the risk of anaphylaxis: initially all were examined for the presence of symptoms, and an intravenous line, and measurements of blood pressure, pulse, and lung function were standards. No patient left the clinic until at least half an hour after ingestion of the last dose or until elicited symptoms had disappeared. All were told to fill in a symptom score record form concerning late reactions within 2 days.

If both challenge days of phase 1 were without reactions, the result was taken as negative. A positive reaction was defined as objective signs after an active challenge without any symptoms after the corresponding placebo challenge. A subjective reaction to the active challenge in phase 1 was accepted, provided it was reproduced in phase 2.

Phase 2 consisted of four challenge series, two placebo and two active. All initial procedures were unchanged but only one challenge preparation was given containing either 6.7 g of codfish masked as described previously or placebo. The DBPCFC-positive patients in phase 2 could correctly identify the three active challenges among the six performed. Five of 10 patients participated in both phases.

Statistics

The sensitivity and specificity of SPT, RAST, and HR were determined and the correlation between the diagnostic tests used was calculated to choose the best test combination in estimating codfish allergy. All statistical analyses were calculated according to guidelines from the Workshop on Experimental Methodology, edited by Metcalfe & Sampson (16).

Results

The reported symptoms associated with codfish ingestion in the sensitive group and the results of SPT, RAST, HR, and DBPCFC are detailed in Table 1. The majority of patients reported subjective local reactions such as irritation, itching, and swelling of oropharynx (OPIS), gastrointestinal symptoms (GI), and cutaneous reactions. OPIS was reported as the initial symptom occurring within 10 min after ingestion of minute amounts and often followed by systemic symptoms. No late reactions were reported. The age at onset of symptoms is shown in Table 1.

Eight of the 10 patients with histories of codfish sensitivity had positive SPT; 8/10 had positive RAST; and 5/9 positive HR, one (being DBPCFC-positive) was classified as inconclusive regarding HR because of nonresponding basophils, and was excluded from calculations. Ninety percent of the medical histories were accompanied by at least one positive test result, and 5/9 (one inconclusive in HR) had a positive reaction to the suspected food item in SPT, RAST, and HR.

In 7 of 10 patients with histories of immediate allergic adverse reactions to small amounts of codfish, the diagnosis was clinically confirmed by DBPCFC (70%). In phase 1, one showed clear objective signs at 1.656 g. In both phases 1 and 2, additionally, five patients correctly identified active challenges with subjective symptoms in 6 of 6 randomized challenges. Further, four of these five patients showed objective signs at least once in the two active challenges in phase 2. The one who had been challenged according to another protocol and experienced a severe anaphylactic reaction was included in this study as challenge-positive (patient No. 6) – a rechallenge was considered to be unethical. The remaining three patients received the maximum dose

of 6.7 g of codfish without any reactions, and they were classified as DBPCFC-negative. A total number of 194 single challenges (mean: 19.4; range 2–24) were performed, of which 93 (47.9%) contained active and 101 (52.1%) placebo. Mild subjective symptoms were reported to a single placebo challenge only in one case (1/101, 1%) – these symptoms could not be reproduced during rechallenge and therefore were not recorded as a definite reaction. Patient No. 6 has not been considered in the following description of symptoms.

Table 2 summarizes the results of DBPCFC with codfish in this study. All patients developed OPIS (6/6); erythema and/or angioedema (facial, especially around the mouth) developed in 4/6, blisters on lips in 4/6, nausea in 2/6, and vomiting in 1/6. No nasal or pulmonary symptoms were seen. OPIS always preceded the onset of any accompanying symptom. When OPIS had disappeared and the challenge dose was increased, it would reappear together with objective signs. Dyspnoea was not seen in any of the OPIS reactions. Doses eliciting symptoms varied between 6 mg and 6.7 g. Five of 9 patients showed objective signs following 6.7 g or less, and the lowest dose was 56 mg eliciting perioral erythema. In one case we did not feel convinced of the validity of a reaction (erythema, patient No. 2), so the titrated challenges were continued.

Table 3 shows results of SPT, RAST, and HR in the control subjects. All had negative SPT; 2/27 had a positive RAST; and 1/27 a positive HR. These reactions appeared in individuals with a total IgE > 2000 kIU/l. Since these three subjects had ingested codfish recently – and never had experienced any adverse reactions to codfish ingestion at all – they were not challenged (blind or open) according to the protocol.

Table 4 shows the sensitivity and specificity of

Table 1. Characteristics of the codfish-allergic patients

Subject No.	Age (yr) when studied	Sex	Age (yr) at onset	Symptoms reported	DBPCFC	SPT	RAST	HR	IgE
1	23	M	2–3	OPIS OPIS, AE, RC, N, V, AP, D	–	–	–	–	83
2	28	F	1	A, P, E, B	+(2)	+	+	–	880
3	28	M	2–5	OPIS, V, P, E	–	+	–	–	102
4	21	M	10	OPIS, AP, P, E, U, AE	+(6)	+	+	+	579
5	31	M	child	OPIS, (A), AE OPIS, RC, AE, A, ANAF	+(6)	+	+	+	14600
6	28	F	4–5	AP, V, E	+(2)*	+	+	+	858
7	26	F	19	OPIS	+(6)	+	+	+	435
8	25	F	15	AE, RC, P, E	–	–	+	–	15900
9	28	F	child	OPIS, N, V, AP, ANAF, AE	+(6)	+	+	IC	215
10	22	F	2	OPIS, N, V, AE, E	+(6)	+	+	+	29

A: asthma; AE: angioedema (not incl. oropharynx); ANAF: anaphylactic shock; AP: abdominal pain; B: blisters; D: diarrhoea; E: erythema; N: nausea; OPIS: oropharyngeal itching/swelling; P: pruritus; RC: rhinoconjunctivitis; U: urticaria; V: vomiting.

+ = positive; – = negative. (X) = number of challenges. * not in this study. IC: inconclusive. Total IgE given in kIU/l, normal range 0–150 kIU/l.

Table 2. Doses eliciting symptoms

Sympt:	OPIS	Erythema	Nausea	Vomiting	Angioedema	Anaphylactic shock	Blisters
Cumulated dose (g):							
0.006	2						
0.056		2					
0.156							
0.656			2				
1.656	9			2			
6.656	4,5	4,9	10		4,9	6*	4,7
	7,10	10			10		9,10

Numbers indicate patient numbers. * outside this study, 25–50 g; OPIS: oropharyngeal itching and swelling.

Table 3. Test results obtained in the control groups

	Age(yr)/Sex when studied	Med. hist.	SPT	RAST	HR	IgE kl U/l
8 normal subjects	26–43 7 F; 1 M	all neg.	all neg.	all neg.	all neg.	< 150
7 pollen allergics	25–48 2 F; 5 M	all neg.	all neg.	all neg.	all neg.	< 150 (one with 401)
12 with atopic dermatitis						
IgE < 2000	17–32 5 F; 1 M	all neg.	all neg.	all neg.	all neg.	< 5 to 1883
IgE > 2000	20–38 3 F; 3 M	all neg.	all neg.	–	+	5210
				–	–	11780
				+	–	15834
				–	–	2153
				+	–	10342
				–	–	3894

All 27 control subjects were classified as challenge negative.

+ = positive; – = negative.

Table 4. Correlation between the test results and the challenges

		DBPCFC/negative medical history		
		+	–	
SPT	+	7	1	Sens. 7/7
	–	0	29	Spec. 29/30 = 96.7%
				Conc. 36/37 = 97.3%
RAST	+	7	3	Sens. 7/7
	–	0	27	Spec. 27/30 = 90%
				Conc. 34/37 = 91.9%
HR	+	5	1	Sens. 5/7 (1 IC)
	–	1	29	Spec. 29/30 = 96.7%
				Conc. 34/36 = 94.4%
Med. history	+	7	3	
	–	0	27	Conc. 34/37 = 91.9%

n = 37.

IC: Inconclusive.

Conc.: Concordance (efficiency).

SPT, RAST, HR, and medical history were all in significant concordance with DBPCFC ($P < 0.05$).

Discussion

This study aimed at characterizing adults suspected of codfish allergy and determining what aspects of their history or immunological tests could predict objective food hypersensitivity reactions. To estimate the reliability and efficacy of tests commonly used in diagnosing food allergy, 10 patients with medical histories of immediate adverse reactions to codfish underwent DBPCFC. In these highly selected patients together with 27 control subjects, SPT, RAST, and HR were performed.

The outcome of DBPCFC

Other studies by several investigators have found DBPCFC to be useful in the diagnosis of food reactivity in children, and apparently this procedure is excellent for studying adults, too. Previous studies on children (10, 11, 14, 15, 27) have revealed that about 30–60% of patients suspected of adverse reactions to food reacted during challenge. Similar studies in adults have indicated that about half the patients regarded as allergic to a specific food item reacted when challenged under controlled conditions (7, 18, 22). Of the 10 patients we examined, 7 (70%) were identified as clinically allergic during DBPCFC. Generally, it is possible to obtain strong positive or negative evidence of codfish allergy through the medical history alone. But a convincing medical history cannot exclude DBPCFC in the diagnosis of clinical food allergy, because 3/10 medical histories could not be verified in DBPCFC.

In patients undergoing positive challenges in this

SPT, RAST, and HR. The result of DBPCFC was used as the true diagnosis in the codfish-sensitive patients, whereas in the control groups, the negative medical history was considered to be true. Hence, SPT and RAST gave the highest sensitivity (7/7), followed by HR (5/7). However, SPT and HR showed a specificity of 0.97 as compared with RAST (0.90). Accepting a RAST score of 2 or more as positive did not in any way change the sensitivity in the same groups, but slightly improved specificity (data not shown). Raising the cut-off to 3 (as suggested by Sampson, 27), reduced sensitivity (5/7) but gave the best specificity (1.00); a high sensitivity would be important if potential DBPCFC-positive patients should not be missed. The highest concordance was found between DBPCFC and SPT: 97.3% (36/37). It was considered to be an important factor that the medical history corresponded with the result of blinded challenges in 91.9% of the cases.

study, reactions generally occurred within 30 s to 10 min of ingestion, and no one developed delayed reactions. However, it cannot be excluded that administration of higher doses of codfish (open challenges) might have caused reactions in one or more of the three DBPCFC-negative patients. The dose of 6.7 g was chosen as a maximum because of lack of experience in challenging adults with codfish, based on literature dealing with food challenges (1, 13, 15, 19, 26), and because of the limitation of the masking procedure. So the amount of codfish eliciting immediate allergic reactions seems larger than expected. The reported pattern of symptoms was reproduced during the challenges. The reduced number of reactions could be due to a variation in sensitivity to codfish with time, or to the quantity of antigen used.

In this study no definitive reactions to a placebo challenge were registered. Bernstein et al. (8) found that 20% of adults tested with placebo reacted positively, while Pastorello (22) reported 30%; and in Nørgaard's study (18) positive reactions were seen in 2/162 single placebo challenges, while Daul (13) had none. The low incidence of reactions to placebo observed in our study may be explained by the fact that our patients were highly selected according to a clear history of immediate hypersensitivity excluding doubtful cases.

OPIS

All patients reported oropharyngeal swelling and itching as their first symptom, always at lower doses of codfish than those provoking their positive objective signs. The appearance of blisters on lips was related to the location of the straw – which explains that more cases were seen during challenges than those reported. In other investigations this symptom has been described as the oral allergy syndrome (OAS) often seen in fruit- and pollen-sensitive patients (5, 20) but also in DBPCFC-positive adults (7).

An important concern in this study was provoking relevant reactions to ingestion, so instead of capsules containing freeze-dried extracts, fresh codfish was used. Possible alterations of the antigen resulting from preparation were thus prevented. Furthermore, it was administered orally in order to present the antigen in the normal fashion and to avoid bypassing the oropharynx. Oropharyngeal symptoms would not have been experienced if the first contact with the food item took place in the GI tract.

Diagnostic tests

Reviewing the literature, the assessed value of SPT and RAST in diagnosing clinical food allergy shows

marked differences. Some consider RAST to be superior to SPT, whereas others find it inferior and non-specific. Recently, a study on milk and egg allergy in adults (18) has shown that SPT, RAST, and HR using commercial extracts cannot exclude the need for DBPCFC. In children the correlation of SPT results with the result of DBPCFC has strongly suggested an association between a positive challenge and a positive SPT to the same specific food (11, 27). Sampson (27) recommended SPT as a major diagnostic test (sensitivity varied between 0.73 and 1.00, and superior to the combination SPT/RAST). Few studies (with different food items) have evaluated the use of SPT in comparison to DBPCFC in adults, and the results vary with sensitivities between 0.30 and 0.90 (6, 8, 13, 18, 22). Our study, however, demonstrates a high concordance between SPT with commercial extracts and DBPCFC with fresh codfish. All challenge-positive patients showed positive SPT whereas control subjects did not react. Even if the cut-off was raised to 7 mm, the concordance between SPT and DBPCFC was not changed. Sampson and Vierrucci (26, 27, 29) have demonstrated false positive SPT in patients having atopic dermatitis with high serum IgE. In this study where 7/10 codfish patients had elevated serum IgE, no positive SPT were found in the control groups – not even in those having serum IgE > 2000 kIU/l. Thus, judging from the sensitivity and specificity (97%) found, the SPT seems to be useful (Table 4).

Concerning the RAST analysis, sensitivity is also high, having a slightly reduced specificity (90%) due to positive reactions in two control subjects with high serum IgE. One SPT-negative and DBPCFC-negative patient demonstrated specific IgE to codfish. On the other hand, a study by Daul (13) has indicated that shrimp RAST provides useful information when diagnosing shrimp-sensitive subjects – contrary to SPT, which failed to identify clinically allergic subjects. Bernstein (8) reported a correlation of only 7.6% between RAST and DBPCFC in adults, whereas RAST was the most sensitive test (sensitivity = 1.00) in a study of egg/milk allergic adults (18). Our study is in concordance with findings in children, where Aas, using a purified codfish allergen, demonstrated high diagnostic reliability of SPT and RAST compared to the medical histories (2, 4).

In our study no false negatives were seen except 1/6 in HR, which makes the HR test seem less sensitive than the other tests, but very specific and acceptable for confirming codfish allergy (Table 4). Bernstein (8), who found a sensitivity of HR of only 0.15 compared with DBPCFC in adults, regarded the test as without any real diagnostic value (as did Pastorello, 21), whereas investigations of egg and

milk (18) have shown a sensitivity of 0.63. However, it has to be taken into account that the results of all these studies on sensitivities vary according to the particular food item, the amount investigated, the selection of subjects, and the quality of the allergen extract. In our study the need for DBPCFC seems less pronounced, as compared with other investigations on these specific food items. This observation might be due to a better quality of commercial extracts of codfish used for SPT, RAST, and HR than of those available for testing egg and milk allergy; furthermore the stability of the cod M allergen is well known (3). This means that commercial food allergen extracts vary in reliability and quality, so their individual potential has to be tested.

In the challenge-negative patients some of the screening tests were positive (Table 3), so for a correct diagnosis in clinically allergic adults, DBPCFC has to be applied. Assessing the correlation between tests, a combination of SPT and DBPCFC (97%) shows an obvious clinical importance in diagnosing codfish allergy. In summary, in our limited material, no advantage of RAST or HR alone or in combination with SPT was demonstrated in the evaluation of codfish hypersensitivity, as compared with SPT alone. The negative predictive accuracy, i.e. the number of negative skin tests truly representing absence of clinical codfish hypersensitivity, is high (29/29). Regarding the quality of the screening tests used (Table 4), the correct predictive value of positive challenges is 7/8 using SPT, HR 5/6, and RAST 7/10. Generally, SPT should be considered to be a reliable test for excluding immediate codfish allergy. But still DBPCFC is of clinical importance in diagnosing allergy to food items including codfish. However, variations of sensitivity and specificity in different investigations (8, 13, 20, 21, 22, 27, 29) and the correlation between tests depend on the criteria for diagnosing and on the quality and potential of the commercial food allergen used for testing.

In conclusion, we confirmed 70% of the medical histories of immediate allergic reaction to codfish in a selected group of adults. All symptoms provoked during double-blind, placebo-controlled challenges were characteristically associated with an IgE-mediated allergic response, and the SPT and RAST data provide supporting evidence of this reaction in the challenge-positive patients. Further, a negative SPT is an excellent indicator of clinically absent codfish hypersensitivity. In contrast, positive SPT suggests a specific codfish allergy requiring further evaluation with other tests. We therefore conclude that the need for DBPCFC in diagnosing allergy to codfish seems less pronounced than in allergy to other food items, such as egg and milk (18). On the other hand, a definite clinical allergy can only be verified by DBPCFC.

Acknowledgments

The technical assistance of Mrs Helle Vestergaard, dietician, and the secretarial assistance of Ms Anne Larsen are highly appreciated.

References

1. AAS K. Studies of hypersensitivity to fish. A clinical study. *Int Arch Allergy* 1966; 29: 346–63.
2. AAS K. The diagnosis of hypersensitivity to ingested foods. *Clin Allergy* 1978; 8: 39–50.
3. AAS K. Fish allergy and the codfish allergen model. In: BROSTOFF J, CHALLACOMBE SJ, eds. *Food allergy and intolerance*. London: Baillière Tindall, 1987: 356–66.
4. AAS K, LUNDKVIST U. The radioallergosorbent test with a purified allergen from codfish. *Clin Allergy* 1973; 3: 255–61.
5. AMLOT PL, KEMENY DM, ZACHARY C, PARKES P, LESOFS MH. Oral allergy syndrome (OAS): symptoms of IgE-mediated hypersensitivity to foods. *Clin Allergy* 1987; 17: 33–42.
6. ATKINS FM, STEINBERG SS, METCALFE DD. Evaluation of immediate adverse reactions to foods in adult patients. I. Correlation of demographic, laboratory, and prick skin test data with response to controlled oral food challenge. *J Allergy Clin Immunol* 1985; 75: 348–55.
7. ATKINS FM, STEINBERG SS, METCALFE DD. Evaluation of immediate adverse reactions to foods in adult patients. II. A detailed analysis of reaction pattern during oral food challenge. *J Allergy Clin Immunol* 1985; 75: 356–63.
8. BERNSTEIN M, DAY JH, WELSH A. Double-blind food challenge in the diagnosis of food sensitivity of the adult. *J Allergy Clin Immunol* 1982; 70: 205–10.
9. BOCK SA. A critical evaluation of clinical trials in adverse reactions to foods in children. *J Allergy Clin Immunol* 1986; 78: 165–73.
10. BOCK SA, BUCKLEY J, HOLST A, MAY CD. Proper use of skin tests with food extracts in diagnosis of hypersensitivity to food in children. *Clin Allergy* 1977; 7: 375–83.
11. BOCK SA, LEE WY, REMIGIO LK, MAY CD. Studies of hypersensitivity reactions to foods in infants and children. *J Allergy Clin Immunol* 1978; 62: 327–34.
12. BOCK SA, SAMPSON HA, ATKINS FM, et al. Double-blind, placebo-controlled food challenge (DBPCFC) as an office procedure: a manual. *J Allergy Clin Immunol* 1988; 82: 986–97.
13. DAUL CB, MORGAN JE, HUGHES J, LEHRER SB. Provocation-challenge studies in shrimp-sensitive individuals. *J Allergy Clin Immunol* 1988; 81: 1180–6.
14. MAY CD. Objective clinical and laboratory studies of immediate hypersensitivity reactions to food in asthmatic children. *J Allergy Clin Immunol* 1976; 58: 500–15.
15. METCALFE DD. Food hypersensitivity. *J Allergy Clin Immunol* 1984; 73: 749–62.
16. METCALFE DD, SAMPSON HA. Workshop on experimental methodology for clinical studies of adverse reactions to foods and food additives. Washington, DC, Nov 1988. *J Allergy Clin Immunol* 1990; 86: 421–42.
17. NOLTE H, STORM K, SCHJØTZ PO. Diagnostic value of a glass fibre-based histamine analysis for allergy testing in children. *Allergy* 1990; 45: 1–11.
18. NØRGAARD A, BINDSLEV-JENSEN C. Egg and milk allergy in adults. Diagnosis and characterization. *Allergy* 1992 (in press).
19. ONORATO J, MERLAND N, TERRAL C, MICHEL FB, BOUSQUET J. Placebo-controlled double-blind food challenge in asthma. *J Allergy Clin Immunol* 1986; 78: 1139–46.
20. ORTOLANI C, ISPANIO M, PASTORELLO EA, ANSALONI R,

- MAGRI GC. Comparison of results of skin prick tests (with fresh foods and commercial food extracts) and RAST in 100 patients with oral allergy syndrome. *J Allergy Clin Immunol* 1989; 83: 683-90.
21. PASTORELLO A, STOCCHI L, BIGI A, et al. Value and limits of diagnostic tests in food hypersensitivity. *Allergy* 1989; 44 (Suppl. 9): 151-8.
 22. PASTORELLO EA, STOCCHI L, PRAVETTONI V, et al. Role of the elimination diet in adults with food allergy. *J Allergy Clin Immunol* 1989; 84: 475-83.
 23. SAMPSON HA. Role of immediate food hypersensitivity in the pathogenesis of atopic dermatitis. *J Allergy Clin Immunol* 1983; 71: 473-80.
 24. SAMPSON HA. IgE-mediated food intolerance. *J Allergy Clin Immunol* 1988; 81: 495-504.
 25. SAMPSON HA. Immunologically mediated food allergy: the importance of food challenge procedures. *Ann Allergy* 1988; 60: 262-9.
 26. SAMPSON HA. Comparative study of commercial food antigen extracts for the diagnosis of food hypersensitivity. *J Allergy Clin Immunol* 1988; 82: 718-26.
 27. SAMPSON HA, ALBERGO R. Comparison of results of skin tests, RAST, and double-blind, placebo-controlled food challenges in children with atopic dermatitis. *J Allergy Clin Immunol* 1984; 74: 26-33.
 28. Skin tests used in type I allergy testing. Position paper. Subcommittee on Skin Tests of the European Academy of Allergology and Clinical Immunology. *Allergy* 1989; 44 (Suppl. 10): 22-33.
 29. VIERRUCCI A, NOVEMBRE E, DE MARTINO M, LUCCI A, DINI A. Reliability of tests for specific IgE to food in atopic dermatitis. *Allergy* 1989; 44 (Suppl. 9): 90-6.
 30. ØSTERGAARD PA, EBBESEN F, NOLTE H, STAHL SKOV P. Basophil histamine release in the diagnosis of house dust mite and dander allergy of asthmatic children. *Allergy* 1990; 45: 1-5.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.