showed IgE reactivity in the patient's serum to one band with an apparent molecular mass of 35 kDa, in both crude and heated quinoa extracts (Fig. 1B). No specific IgE binding was observed for the control sera (Fig. 1C).

Exceptional food allergies to spinach or beets and cross allergy to latex have been reported (2–4). No case is recorded in the CICBAA data bank including 1400 food allergic patients.

The major quinoa seed storage proteins included: 11S-type globulins named chenopodin and a high-cysteine 2S fraction. Two heterogeneous sets of polypeptides in the size ranges 30–40 kDa (acidic subunits) and 20–25 kDa (basic subunits) joined by disulphide bonds in the native protein characterize the 11S-type of seed proteins (5). The band near 35 kDa evidenced by immunoblot therefore may belong to the class of chenopodin A acidic subunits.

Highly soluble proteins of quinoa seeds can be used for developing functional foods and as potential ingredients that could be substituted for soy or lupin flour, with additional advantage of avoiding mandatory labelling (6). For this reason, this first case of anaphylaxis documenting a thermostable allergen is of particular interest.

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Pholcodine caused anaphylaxis in Sweden 30 years ago

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Key words: anaphylaxis; immunoglobulin E antibody; neuromuscular blocking agents; pholcodine; Tussokon.

The prevalence of anaphylaxis to neuromuscular blocking agents (NMBA) during the induction of anaesthesia varies greatly between countries (1), e.g. Norway had approximately 10 times as many cases as Sweden (2). It was recently proposed, the pholcodine (PHO) hypothesis, that the reason was that in Norway, but not in Sweden a cough syrup containing PHO was available and without prescription (2). Pholcodine shares the disease-related allergenic epitope, the quaternary ammonium ion (QAI), with NMBA and also with morphine (MOR). In blood samples collected in 2002 in Norway, 6% of blood donors had immunoglobulin E (IgE) antibodies to PHO and 5% to MOR, while no case was found in Sweden. Results from a similar multinational screening support the PHO hypothesis (S. G. O. Johanson et al., unpublished data).

Availability in Sweden during 1970s/1980s of a pholcodine antitussive paralleled IgE-sensitization and anaphylaxis to neuromuscular blocking agents.

Pholcodine is a very potent IgE-sensitizer, but, in addition, even a very low dose of a cough syrup containing PHO for 1 week stimulates a 100-fold increase of polyclonal IgE in sensitized persons (3, 4). Based on these findings, the only PHO-containing drug in Norway was withdrawn from the market in March 2007.

It was recently noticed that there had been such a drug, Tussokon, on the market in Sweden in the 1970s and 1980s. It was available by prescription both as tablets, with 10 mg PHO, and as syrup with 2 mg/ml PHO. The tablets were withdrawn from the market from 1 August 1985 and the syrup from 1 July, 1989 because of 'changes in recommendations for treatment of cough and because other, more effective pharmacological preparations had become available'. There is no mentioning of any possible relation to anaphylaxis during anaesthesia.

Table 1. Reported cases of anaphylaxis during anaesthesia accumulated during the 10-year period, in parenthesis per million of inhabitants, average pholcodine (PHO) consumption, as Tussokon, in kg per year and, in parenthesis, per million and prevalence of IgE antibodies (>0.35 kU_A/l) to PHO, morphine (MOR) and suxamethonium (SUX)

	Reported anaphylaxis (per mill.)	PHO consumption (kg/mill.)	No. samples tested	PHO % pos	MOR % pos	SUX % pos
1970–1979	37 (4.5)	19.6 (2.4)	49	6.1	10.2	2.0
1980–1989	15 (1.8)	7.6 (0.9)	161	5.6	6.2	6.2
1990–1999	0	0	170	2.4	4.1	2.9
2002	0	0	300	0	0	0

Data from 2002 from Florvaag et al., 2005 (2).

The average PHO consumption in Sweden was the highest during 1970s (Table 1), but dropped in the 1980s. The consumption was in the same order as the currently mid-consuming countries like The Netherlands and Finland, but 10-fold less than high consuming ones like UK and France (S. G. O. Johanson et al., unpublished data).

The accumulated number of reported cases of anaphylaxis was high in the 1970s, but no case was reported after 1990 (Table 1) when the drug was no longer on the market.

We were lucky to have serum samples in our freezers, collected between 1970 and 1999 from patients selected for an IgE-mediated allergy. Atopic sera, defined as having a positive Phadiatop®, were analysed for IgE antibodies to MOR and PHO and one NMBA, suxamethonium (SUX), using the ImmunoCAP® Specific IgE assay (Phadia AB, Uppsala, Sweden). High percentages of sera from the 1980s and also the 1970s, although the sample is very small, had IgE antibodies to PHO and MOR and, interestingly, also to SUX (Table 1). Maybe the figures are a bit high due to the special selection of sera. During the 1990s, the prevalences continued to drop and two studies of sera from 2002 (2) and 2006 (S. G. O. Johanson et al., unpublished data) did not find any sample positive to PHO or SUX.

The availability of information about consumption of Tussokon, number of reported cases of anaphylaxis after NMBA exposure and sera for analyses of IgE-sensitization during and after the years when Tussokon was on the market has provided important information. The PHO hypothesis is strengthened, and thus a general, global withdrawal of all drugs containing PHO should be seriously considered, as morbidity will be reduced and lives saved from the reduction or disappearance of anaphylaxis to NMBA (5). Interestingly, although it was not possible to analyse serum samples from each year after the withdrawal of Tussokon, when exposure is stopped, IgE-sensitization to both PHO and SUX as well as anaphylactic reactions to NMBA seems to decrease quite rapidly, i.e. within a few years. Thus, it seems that we do not have to wait for a new generation that has never been exposed to PHO.

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