

Appendix S3.

Indications for chronic spontaneous urticaria (CSU) diets and reintroduction of items

Diets

Pseudoallergen-free diet (based on the protocol described by Zuberbier et al. (22))

	Permitted: pure, natural foods without artificial additives or flavours	Prohibited: all foods containing artificial additives, e.g. convenience food, sweets
Beverages	Pure water, mineral water, coffee, black tea, milk, buttermilk	Herbal, rose hip or fruit teas, water and tea with aroma (e.g. citrus, bergamot, vanilla), flavoured instant coffee
Basic foods	Potatoes, noodles (without egg), rice, pure bread and rolls, flour (not self-raising), rice cakes and unprocessed cereals (e.g. pure corn flakes)	All others: e.g. bread or rolls with herbs, raisins, nuts or oil seeds (e.g. sunflower, pumpkin, flax seeds), potato chips, crisps, cakes, biscuits
Fats	Butter, refined plant oils	All others (e.g. margarine, cold-pressed plant oils)
Milk products	Milk, pure cream, pure buttermilk, pure curd, cream cheese without additives, young gouda (mild)	All others (e.g. fruit yoghurt, cacao, herbal cheese, spread cheese and all other flavoured milk products)
Meat, fish, eggs	Fresh meat without any additives or seasonings (only prepared with salt and oil)	All others: fish, eggs and meat with seasonings or additives
Vegetables	All except those listed as forbidden (e.g. lettuce, carrots, zucchini, cabbage, broccoli)	Tomatoes and tomato products, sweet peppers, olives, spinach, rhubarb, mushrooms, peas, artichokes, onions
Fruits	None	All kind of fruits including fruit juices, puree, stewed and dried fruits (e.g. raisins)
Herbs, spices	Salt, sugar, pure vinegar to dilute with water (without herbs, balsamic, wine aromas)	All other including chives, pepper, chilli, herbs, garlic or other seasonings, sweeteners
Sweets, spreads	Honey, sugar beet molasses, (mild gouda)	All other

Low-histamine diet

List of allowed food:

Dairy products: milk, cream and sour cream, butter milk, cream cheese, soured milk, curd cheese	Meat and eggs: eggs, cooked ham, not cured beef, veal, pork, lamb, chicken
Fish (fresh or fresh frozen): plaice, coalfish, codfish, haddock, trout, hake, perch	Spread: butter, margarine, honey, homemade jam (permitted fruit only)
Sweets and snacks: fruit drops, fruit gums, chewing gum, popcorn	Desserts: cold sweet soup, rice pudding, stewed fruit*, sorbet and ice cream, fruit yoghurt or curd cheese with fruit*, vanilla custard *(permitted fruit only)
Fruits: everything, except for strawberries, raspberries, citrus fruit, bananas, kiwis, plums, papaya	Vegetable: any fresh or frozen vegetable, except for tomatoes, spinach, avocados, egg plant
Cereals/potatoes/noodles: bread and pastries, pasta, all kind of potatoes, cereals, grains (rice, corn, millet seed, buckwheat)	Beverages: soda water, homemade fruit and vegetable juices* *(permitted fruit only)

Reintroduction tests

Double-blind, placebo-controlled oral histamine provocation (DBPCOH)

Verum [75 mg histamine (equivalent to 125 mg histamine dihydrochloride) plus 125 mg of sucrose] and placebo (125 mg sucrose) were placed in identical gelatine capsules, which were swallowed by the patient. Verum and placebo were administered in a randomized fashion at the same time on alternate days, 6 h after the last meal and 6 h before the next meal. Patients avoided alcohol, non-steroidal anti-inflammatory drugs and strenuous exercise on challenge days. Both physicians and patients recorded the appearance of symptoms, e.g. weals, itching, redness, angioedema and diarrhoea, which occurred within 24 h of each challenge.

Incremental build-up food

IBUF contained 6 1-week steps with different cumulative food ingredients

Step I: It contained foods that are not highly suspected to act as pseudoallergens [e.g. organic (bio) eggs, cold-pressed olive oil, fresh sea fish, pears], to increase the compliance for further intervention. These foods also reappear later in a processed manner.

Step II: It contained foods with high amounts of biogenic amines (e.g. tuna, well-matured cheese, bananas and walnuts). We chose biogenic amines at this time point, because there are foods containing biogenic amines but no other additives or seasonings: pure cheese without herbs, pure tuna in plant oil and salt without other additives. Beta-carotene, nitrite and nitrate are permitted at this step because these ingredients can be found in many pure natural foods, which have already been consumed within the PAD (e.g. vegetables).

Step III: Natural flavours, aromatic compounds, such as p-hydroxy benzoic or salicylic acid were the main ingredients of this step (e.g. fruits, herbs, tomatoes and isolated spices). Up to step III are only pure foods with no considerable artificial food additives or flavours. For this reason, nutritional consultation with patients is highly important, not using convenience foods such as flavoured teas or broth (containing glutamate).

Step IV: It contained all foods supplemented with different additives (glutamate, sulphite, preservatives, anti-oxidants, flavours), with the exception of food dyes. Many convenience foods do not contain any artificial dyes, but contain other additives or seasonings. For this reason, step IV (food additives exceptionally dyes) must be given before step V (food dyes) and after step III (herbs, natural aromatic compounds).

Step V: All coloured food and beverages were permitted and patients were advised to choose preferential sweets and beverages containing different food dyes (E100–E199) [44, 45]. Furthermore, conventional [non-organic (non-bio)] eggs were now allowed, because hen feed can be supplemented with dyes (canthaxanthin), which can be found in the egg yolk.

Step VI: Alcohol was permitted only in the last step, because alcohol has been known to elicit urticaria directly and may lead to increased resorption of possible pseudoallergens.

Steps	Cumulative ingredients	Food selection
I	None	Whole flour bread, onions, garlic, organic (bio) eggs, cold-pressed olive oil, fresh sea fish, pears, watermelon, honey melon
II	Biogenic amines, nitrite, nitrate	Well-matured cheese without herbs and other food additives such as nitrate, nitrite and beta-carotene: e.g. Emmentaler, Cheddar, Gouda, Camembert, Appenzeller, Edamer; Scombroidae: tuna, mackerel, herring, sardine; pickled cabbage, kohlrabi, spinach, beetroot, avocado, banana, walnut
III	Natural phenolic substances such as p-hydroxy benzoic acid, cumaric acid, salicylic acid, natural flavours, ethereal oils	All fruits, fruit juice, all vegetables (e.g. tomatoes), other nuts, isolated herbs and spices (no instant broth), natural herbal and fruit teas (without any flavouring)
IV	Food additives (without dyes), industrial aromas	Foods are permitted, if no dyes (E100–E199) are added (exception: beta-carotene and riboflavin as natural dyes used for colouring cheese and butter), e.g. instant soup or broth, convenience food, sauces, chips, pizza, nut nougat creme, sweets, soft drinks, chocolate, cacao, all flavoured foods, e.g. teas
V	Food dyes (E100–E199)	Eggs, coloured foods with natural and artificial food dyes, e.g. coated chocolate lenses, bubble gum, drops, bonbons, soft drinks, ice cream, wine gums, custard, gelatin-containing dessert
VI	Alcohol	Beer, wine, liquor, spirits