

Policy Statement

Neutropenic Dietary Advice for Haematology Patients

Summary

This BDA Policy Statement provides guidance for the provision of consistent advice on neutropenic dietary restrictions for haematology patients. It provides evidence/ best practice guidance for haematology patients undergoing chemotherapy as well as those with more profound neutropenia undergoing stem cell/ bone marrow transplantation. This is a guideline for those units who chose to continue to advise dietary restrictions during neutropenia. It is not intended for people with neutropenia of a non-haematological cause.

Introduction

After chemotherapy and stem cell transplantation, patients are at a greater risk of infection from bacteria or fungus in food. This is for the following reasons:

- The white blood cells (neutrophils) that would usually fight food poisoning bacteria are at a low level. This is called neutropenia
- The gut lining which acts as a barrier between bacteria and the bloodstream is damaged by chemotherapy and radiotherapy. This makes it easier for bacteria to cross into the bloodstream

The 'Neutropenic Diet' has remained a controversial area across Haematology Units in the UK. The evidence for dietary restriction during immunosuppressive therapy and/ or neutropenia is still limited and some institutions have removed restrictions without any corresponding increase in infection rates (1). However an UK audit of neutropenic dietary advice revealed a variety of practices continue (2). Many well established units still follow tradition and restrict intake of multiple foods highlighting the need for consensus regarding the advice given.

Due to concerns regarding inconsistent and inappropriate dietary advice during neutropenia, the Haematology Group of the British Dietetic Association established recommendations that were published by Leukaemia and Lymphoma Research in 2007 (3). 5 years later our group recognised that the evidence for this guidance needs to be re-visited. Further literature search and consultation has now led to updated recommendations. These are shown, according to the level of neutropenia in tables 1 and 2. The following article highlights some of the more contentious areas and summarises changes to the previous advice which have been summarised in table 3.

Aims

To standardize neutropenic dietary advice provided to haematology patients undergoing treatment throughout the United Kingdom using evidence/ best practice guidelines.

Objective

To enable dietitians working with haematology patients to confidently be able to advise about neutropenic dietary restrictions.

Recommendations

Reheating food and rice

Previous advice to avoid reheating cooked food was reviewed in the context of known risk and potential benefit to the patient. There was no evidence that correctly reheated food, increases food poisoning risk in immunocompromised individuals. Therefore guidance on cooling, storing and reheating cooked food safely has been added to the recommendations. The exception to this advice is reheating cooked rice. The spores of *Bacillus cereus* and *Bacillus subtilis* found in rice, survive the cooking process. These develop into bacteria that multiply very quickly at ambient temperatures and may not be adequately killed during reheating. Therefore rice should be served hot and eaten immediately after it is first cooked.

Water

There was no evidence to support any change to the existing recommendations regarding water. *Campylobacter* has been found and can flourish in bottled and mineral water (4-6) and *Legionella*, *Pseudomonas aeruginosa* and *Pseudomonas fluorescens* have been isolated from commercially available bottled still water (5;7;8). Non-carbonated bottled water may also contain large amounts of gram negative bacteria such as *Stenotrophomonas maltophilia* (9). Therefore recommendations continue to support avoiding non-carbonated bottled water, mineral water and water from fresh wells during neutropenia < 0.5.

Clarification regarding water from water coolers and dispensers has been added to the current consensus. Contamination and poor maintenance of dispensers can again be a risk factor in the immunocompromised for cryptosporidiosis (9;10), *Pseudomonas aeruginosa* (11;12) and *Pseudomonas fluorescens* (9;13).

Ice

Ice is now stipulated as safe if made from the appropriate water sources. With regards to commercially available ice based drinks such as “slush puppy” the group reached consensus to avoid these due to unknown source of ice production, storage conditions and potential risk of contamination from the machine dispenser.

Ice cream

Ice cream is used as a quick high calorie snack for many of our patients. There is inadequate research available to give evidence based guidance; therefore the recommendations are based on group consensus. When considering the manufacturing process it was felt that ice cream is unlikely to present a significant risk, provided it has been stored at the correct temperature, had not previously thawed, was individually wrapped and from a reputable source. This excludes ice cream sold from mobile vans including ice cream from soft serve machines that may harbour unacceptable levels of bacteria.

Probiotics

There is no evidence that ingested Lactobacilli and bifidobacteria are any greater infection risk than commensal strains, e.g. those found in the mouth, ileum and colon (14). Reported infections from specific probiotics are mainly limited to *Saccharomyces boulardii*/ *cerevisiae*, the soil organism *Bacillus Subtilis* and *Lactobacillus rhamnosus* LGG (15;16). In some cases of bacteraemia, the methods for matching the particular strain of bacteria to that consumed has been criticised. *Lactobacillus* and

Bifidobacteria identification verified by DNA based approaches at species level is required but this is rarely carried out routinely (17).

There is a growing body of evidence that probiotics are safe in other immunocompromised groups e.g. HIV and neonates (14;16) (18) (19) and there may be benefits to the haematology patient in terms of graft versus host disease (20) gastrointestinal health or immune function (21). However disruption of the intestinal epithelial barrier during cancer treatment could theoretically lead to translocation of Lactobacilli or bifidobacteria. Other risk factors for the pathogenicity of probiotics have also been suggested i.e. immune compromise, presence of a central venous catheter or jejunal administration of the probiotic (15;16). One or more of these risk factors may be present in a neutropenic patient.

Therefore, the recommendations to avoid probiotic cultures if patients are immunosuppressed have not changed. This approach is endorsed by the product manufacturers themselves. The advice is based on uncertainty rather than robust evidence of harm and these recommendations will require on-going review as further evidence becomes available.

Live Yogurt

All yogurts are made using the live bacterial starter cultures *Lactobacillus delbrueckii* subsp. *bulgaricus* and/ or *Streptococcus thermophilus*. Historically patients with a low neutrophil count have been advised to avoid yogurt containing live cultures and choose pasteurised products. However, the majority of yogurts are not pasteurised post production. Often where the term pasteurised is found on a yogurt label it relates to the milk used. Hence immunocompromised individuals already (unwittingly) consume live yogurt cultures.

Unlike probiotic bacteria, starter cultures cannot survive in the human stomach and are not normal human commensals. These cultures have been used safely since the early 1900s to produce yogurt and are considered by the food industry as non-pathogenic. A literature review in 2004 found no reports linking lactic acid bacteria from fermented milk to infection in humans (22). Therefore previous advice, which considered live yogurt with probiotic cultures, has been revised. Live yogurt is not potentially harmful and no restriction is necessary. This represents a significant change to neutropenic dietary advice and will greatly improve choice for this patient group.

Of note is the lack of legislation surrounding product labelling of live cultures or probiotics. Hence there is a risk some yogurts may contain unlabelled probiotic bacteria (17). However it is unlikely that significant numbers of probiotic bacteria would be added to a product unless that product was to be marketed for its probiotic content/ benefits. Therefore unless a product specifically makes reference to its probiotic content then no restriction is necessary. Due to the lack of clear definition of the term "bio" it was felt prudent to avoid these products also.

Honey

The microbes of concern in honey are primarily yeasts and spore-forming bacteria. Bacterial spores, particularly those in the *Bacillus* genus are regularly found in honey. Although the antibacterial property of honey discourages growth or persistence of many microorganisms it is recommended that the following types of honey are avoided when following a neutropenic diet: raw honey, unpasteurised honey, strained honey, fresh honey comb. Honey that is labelled as pasteurised has undergone heat treatment to destroy the yeast cells. Filtered honey is heated and strained to remove fine particles such as pollen, dust, and nectar which can contaminate the honey. The neutropenic diet therefore allows pasteurised and filtered honey to be consumed. It is recommended that where possible single serving or small jars of pasteurised or filtered honey should be used as there is a potential for large jars to become contaminated with microorganisms from the normal environment and from food handlers and/or equipment being used (23).

Nuts and dried fruit

Salmonella and *Escherichia coli* have been linked to the consumption of nuts. Peanuts, almonds, pistachios, pecans, pine nuts, macadamias, hazelnuts, Brazil nuts, and walnuts have all been

involved in product recalls due to salmonella. Recent evidence of unacceptable levels of *Salmonella spp* in ready to eat nuts supports the avoidance of "raw" nuts (24).

The most common method for reducing pathogens in nuts is the application of heat (25). Therefore if the nut has undergone a process of heating such as roasting then these can be consumed when neutropenic. It is recommended that raw and unshelled nuts/nut products should not be consumed. Similarly cooked and processed dried fruit is not considered high risk, allowing consumption of products such as flap jacks, cereal bars, fruit cakes or scones.

Vegetable and Fruit Smoothies

The guidelines have now clarified that the packaging on any commercially bought juice or smoothie should state that it has undergone pasteurisation or heat treatment. Homemade smoothies can be made from washed and peeled fruit allowed from the original list or from tinned or frozen fruit and vegetables.

Smoked fish

Previous advice to avoid ready to eat smoked fish during neutropenia was based on potential risk for contamination with *listeria monocytogenes*. However a recent Food Standards Agency survey found only 3 samples that breached the legal limit in 3000 samples of ready to eat smoked fish at point of sale in 1000 outlets (26). As a result the group felt that ready to eat smoked fish from a vacuum packet was safe to eat where neutrophil counts > 0.5 provided it was consumed within 24 hours of opening. This is in line with the FSA advice to other vulnerable groups i.e. pregnant women, where ready to eat smoked fish is not restricted (27). Due to uncertainty surrounding risk from low levels of bacteria the group have continued to recommend avoidance of ready to eat smoked fish where neutrophils < 0.5 .

Conclusion

Evidence and the lack of it remains a problem when providing advice to neutropenic individuals. However, it is felt by many that immunocompromised patients should avoid all unnecessary risk for potentially life threatening infections. Therefore consensus of advice remains valuable to avoid unnecessary and impractical restrictions being recommended in this patient group. Ensuring a consistent and sensible approach to the dietary advice given during neutropenia should help minimise both the risk of food borne infection and worsening malnutrition at a time when nutritional intake can be severely compromised.

Table 1. Food safety advice where neutrophil counts < 2.0 x 10⁹/litre

Avoid	Alternatives
All unpasteurised dairy products eg milk sold on local farms	Any pasteurised milk, soya milk, Jersey milk or UHT milk
Soft cheeses made with unpasteurised milk eg feta, parmesan Homemade/deli paneer and labnah Mould-ripened cheeses eg Camembert, Brie, goat's cheese Blue veined cheeses eg Danish blue and Stilton	Cheeses made with pasteurised milk, processed cheese eg Dairylea, Kraft, Philadelphia, mesh and halloumi Pasteurised parmesan, pasteurised mozzarella. Paneer made with pasteurised milk Vacuum-packed pasteurised and hard cheeses eg cheddar and Edam
Raw or lightly cooked shellfish	Well-cooked shellfish eg prawn Curry
Raw/undercooked meat, poultry or fish eg meat which is still pink, sushi, caviar and oysters Smoked meats eg salami Avoid smoked salmon unless eaten directly from a freshly opened packet	Well cooked meat, poultry and fish; tinned meat and fish Vacuum-packed cold meats such as turkey and ham stored below 3°C and eaten following the manufacturer's instructions Vacuum packed fish eaten straight from a new packet. This includes smoked salmon.
Raw eggs or undercooked eggs eg homemade mayonnaise, homemade ice cream, mousse, egg-nog, meringue, Hollandaise sauce and béarnaise. Any dressing containing raw eggs eg home/restaurant-made Caesar salad dressing	Hard boiled eggs; shop-bought mayonnaise and other products made with pasteurised egg
Probiotic or "bio" foods, drinks or supplements eg Yakult, Actimel, ProViva Yogurt which is described on the label as bio or probiotic	Any yogurt that does not describe itself as bio or probiotic including live, plain, Greek and fruit yogurts
Meat paté, vegetable paté	Pasteurised paté and paste in tins or jars that do not need to be refrigerated

Table 2. Further food safety advice where neutrophil counts < 0.5 x 10⁹/litre

Avoid	Alternatives
<p>Raw unpeeled fruit or vegetables including salad items, stuffed vine leaves, fatoosh and taboulleh</p> <p>Raw dried fruit, products containing these eg muesli, Bombay mix, confectionary</p> <p>Damaged or over-ripe fruit or vegetables</p> <p>Unpasteurised or freshly squeezed fruit or vegetable juice or smoothies</p>	<p>Good quality fruit and vegetables that are well cooked or peeled</p> <p>UHT or long-life fruit juices – in cartons or jars</p> <p>Pasteurised smoothies Tinned fruit</p> <p>Cooked dried fruit eg in fruitcake, flapjacks or cereal bars</p>
<p>Fresh nuts, nuts in shells</p>	<p>Cooked nuts, nuts in cans</p> <p>Peanut butter, roasted nuts</p>
<p>Uncooked herbs, spices and pepper</p>	<p>Cooked herbs, spices and pepper</p>
<p>Cold smoked salmon</p>	<p>Cooked dishes containing smoked salmon</p>
<p>Non-drinking water, bottled mineral or spring water, water from wells, water from coolers, domestic water filters and water fountains</p>	<p>Freshly run tap, carbonated water Please check with your hospital for guidance</p>
<p>Ice when away from home eg in a restaurant and slush puppies</p>	<p>Ice made from appropriate water sources (see above)</p>
<p>Ice cream from ice cream vans</p>	<p>Ice cream from reputable sources, individual portions, wrapped, small pots</p>
<p>Unpasteurised or 'farm fresh' honey and honeycomb</p>	<p>Pasteurised or heat-treated honey Ideally try to use individual sachets or portions</p>
<p>Unnecessarily large packets of food items from pick and mix, universal jars</p> <p>Deli counter foods eg olives, houmus, shawirma and baklava</p>	<p>Ideally, packets should be individual portions eg butter, sweets, pickles</p>

Table 3. Summary of main changes in consensus from 2007 to 2016

	2007	2016
Neutrophil counts < 2.0 x 10⁹/litre		
REHEATING MEALS	Avoid	Follow risk reduction guidelines and consume within 24 hours of cooking or defrosting
REHEATING RICE	No restriction.	Avoid. Serve rice hot and eat immediately.
SMOKED FISH	Avoid	Allow if eaten directly from a freshly opened packet
PROBIOTICS AND YOGURT	Avoid all probiotic, live and bio products	Avoid products marketed as probiotic or bio. No restriction on any other yogurts including those containing live cultures.
Neutrophil counts < 0.5 x 10⁹/litre		
ICE CREAM	Ice cream supplied according to local Trust policy	Avoid only ice cream from vans and soft serve ice cream/ dispensers
ICE	Not specified	Allow where made from suitable water source
NUTS	No restriction	Avoid fresh nuts
SMOOTHIES	Avoid	Allow where pasteurised or appropriately homemade

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