NUTRITION INFORMATION CENTRE
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TUBERCULOSIS (TB) AND NUTRITION

The information explosion in the science of nutrition very often creates the impression that available information is contradictory. Consequently, it is no longer easy to distinguish between fact, misinformation and fiction. The Nutrition Information Centre of the University of Stellenbosch (NICUS) was established to act as a reliable and independent source of nutrition information.

The disease is spreading like a wildfire

The disease is called by some, "The Mother of Diseases" and is as much a social disease as an infectious disease. TB is associated with poverty, overcrowding, alcoholism, stress, drug addiction and malnutrition and is by far the most common disease in South Africa. The disease spreads easily in overcrowded, badly ventilated places and among people who are undernourished. This has lead to TB being known as a disease of poverty. The Coloured population in the Western Cape seems to be at greatest risk with incidence rates in excess of 700 per 100 000 being reported in 1994. The WHO has declared TB to be a global emergency and has called for urgent and extraordinary action. TB has infected approximately a third of the world's population and there were an estimated 8.8 million new TB cases in 2005, with the concentration of cases being in poor countries. A total of 1.6 million people died of TB, including 195 000 patients infected with HIV. South Africa was classified as a high-TB burden country and was ranked 7th by the WHO, [according to rank based on estimated number of incident cases (all forms)] in 2005.

The combined burden and effect of TB and HIV/AIDS co-infection is immense. The global burden of TB is increasing, largely due to the spread of HIV/AIDS. HIV-infected persons are far more susceptible to TB, are more difficult to diagnose, and in addition, are also more difficult to treat. HIV-infected people have a much higher mortality in the period following TB treatment, with 30% dying within a year of diagnosis and treatment. With the HIV epidemic continuing to spread at startling rates in South Africa and globally, it is highly probable that this will contribute to the increasing numbers of TB cases.

Effective treatment of TB is available, but even though clear guidelines and standardised drug formulations exist in South Africa, cure rates remain unacceptably low. In the year 2000, not a single South African province has reached the 85% cure target set by the WHO.

Inconsistent treatment protocols, behavioural patterns, increased incidence of side effects and malabsorption of drugs due to associated diarrhoea may contribute to the development of multidrug-resistant (MDR) TB. The rate of MDR TB is estimated to be at 1.7% in South Africa (6.6% of treatment cases), with over 6000 cases per annum. Due to South Africa's large TB caseload, this translates into the highest absolute number of MDR TB cases in the world. With the HIV epidemic continuing to spread at startling rates both nationally and globally, it is highly probable that this will contribute to the increasing numbers of TB cases and the combined burden and effect of HIV/AIDS and TB co-infection is immense.

The WHO estimates that infected adults lose an average of 3-4 months of work while recuperating from TB disease and an average of 15 years of economic activity is lost from each adult TB death.

What are the symptoms of TB?

Adults with pulmonary TB have chest pain and severe cough, sometimes with blood in the sputum. Exhaustion, night sweats, fever, loss of appetite and weight loss are symptoms of pulmonary and extra-pulmonary TB. These effects are produced, partly, by the fever and other consequences of

excessive production of tumour necrosis factor-α and other pro-inflammatory cytokines produced by a well-intentioned immune system as a result of persistent TB infection. The disease can go undetected amongst children as it has non-specific symptoms that could be the result of a number of childhood illnesses. They may cough, have a fever or diarrhoea for more than a month, have unexplained weight loss, enlarged glands, fits and neck stiffness.

NUTRITIONAL FACTORS THAT INCREASE YOUR RISK FOR TUBERCULOSIS

The risk of complications including death from infections is influenced by the nutritional status of an individual, but the nutritional status of an individual and utilization of nutrients are also adversely affected following an infection.

- ### Protein-energy malnutrition

Under nutrition can be considered as one of the risk factors in the development of TB, since under nutrition is known to adversely affect the immune system. Still there remains a question as to whether malnutrition predisposes to tuberculosis, or whether it is a consequence of the disease. Irrespective, a vicious cycle is known to exist between tuberculosis, HIV and malnutrition such that one is promoting the other(s).

Some of the key signs and symptoms of TB, for example wasting, anaemia, loss of lean and fat mass, are also signs of malnutrition. Tuberculosis results in anorexia, cachexia and generalized weakness. Nutritional deficiencies are generally associated with increased risk for and severity of tuberculosis by adversely affecting precisely those immunological mechanisms that are crucial for the successful control of mycobacterium, namely the functions of T-lymphocytes and a variety of phagocytic cells.

There are several ways in which nutritional deficiencies could influence the prevention and management of TB. A central way in which malnutrition may change the pathogenesis of TB is to increase the risk of progression from TB infection to primary disease in the short term, or to increase the risk of reactivation of TB disease in the longer term. Furthermore, nutritional status may also influence the progression from TB infection to disease by altering the availability of essential nutrients to meet the metabolic needs of the pathogen and the individual.

Additionally, concomitant malnutrition could diminish the pharmacodynamic effectiveness of anti-mycobacterial drug regimens, which must be taken for several months to cure the patient. Malnutrition-induced loss of some immune functions is reversed fairly rapidly upon correction of the nutritional deficiencies. Thus, nutritional intervention in combination with appropriate pharmaceutical therapy, as is the case in HIV infected patients, could improve the outcome in malnourished TB patients. Malnutrition could also impair the protective efficacy of Bacillus Calmette-Guérin (BCG) vaccine, thereby increasing the disease burden in vaccinated populations that are nutritionally vulnerable or deficient.

- ### Micronutrients and immune function

Since most of the reliable data on the role of micronutrients in immunity to tuberculosis have been generated on experimental animal models, the relevance for humans of the conclusions drawn from such studies must be interpreted cautiously. It is known that deficiencies of zinc, vitamin D, vitamin A, vitamin C, and iron can cause profound impairment of immunity (and precisely the cell types that are critical to "fight" tuberculosis). It is therefore not unreasonable to propose that dietary deficiencies of these micronutrients may be important determinants of tuberculosis resistance.

NUTRITIONAL RESPONSE TO INFECTION

Acute infectious illnesses, such as tuberculosis, are accompanied by a complex variety of nutritional and metabolic responses within the body. The response to infection is associated with an increase in the energy expenditure of the patient and various degrees of tissue breakdown. Additionally, in the body's attempt to fight the infection energy expenditure is increased, thereby increasing energy needs in the TB patient. Patients characteristically present with loss of appetite

and body weight. Complex changes occur in the metabolism of all the macronutrients, i.e. protein, carbohydrate and fat. An increase in protein breakdown for example, leads to muscle wasting in these patients. TB patients are also known to have high losses of protein (nitrogen), which may result in malabsorption due to diarrhoea, loss of fluids, electrolytes and other nutritional reserves. The breakdown of protein and other reserves due to fever may also worsen under nutrition and further impair resistance against the infection. There is also good evidence that underweight, in itself, is a risk factor for the development of tuberculosis in infected persons.

The response to infection also includes a profound impact on the micronutrient status of the patient. Vitamins and minerals are compounds that are essential for normal growth and maintenance of body functions, playing key roles in many different metabolic processes in both health and disease. The increased energy expenditure and tissues breakdown associated with infection are thought to increase the requirements of micronutrients such as vitamin A, E, B_6, C, D and folate. It is also known that a decrease in blood levels of trace elements such as iron, zinc and selenium occur during the infection.

Infectious diseases, such as tuberculosis, are therefore associated with increased requirements of both the macro- and micronutrients. A causal relationship between nutrition and tuberculosis has not yet been established, because of the difficulties involved in separating the influence of nutrition from economic, environmental and genetic factors, which characterize high-risk populations. There remains the question still as to whether malnutrition predisposes to tuberculosis, or whether it is a consequence of the disease.

NUTRITIONAL TREATMENT OF TUBERCULOSIS

Clinically, it has long been noted that the risk and morbidity of infections are influenced by the nutritional status of the individual. Likewise, the nutritional status and the intake and utilization of foodstuffs are profoundly altered during the body's response to infection. The association between malnutrition and disease is well recognized, but the explanation for the association is complex. In the context of TB and HIV/AIDS, attention should be focused on specific symptoms, such as weight loss, diarrhoea, loss of appetite, nausea, and specific disorders such as micronutrient deficiencies, known to occur commonly among TB and HIV-infected individuals and to impact adversely in the short- or the longer-term outcomes. Factors that affect food intake, such as food availability, appetite, eating patterns, medication side effects, traditional food taboos, lifestyles (smoking, alcohol, physical activity, caffeine intake, use of social drugs), psychological factors (stress and depression), stigma, and economic factors are also very important to consider.

The South African National Department of Health produced the “National guidelines on nutrition for people living with TB, HIV and AIDS and other chronic debilitating conditions” in 2001. These guidelines are currently being revised.

Nutritional needs in tuberculosis

- **Energy**

Energy needs of TB patients are increased because of the disease itself. The current recommendations for TB patients are based on the nutrient and energy requirements for hyper catabolic and undernourished patients. (Approximately 35 - 40 kCal per kilogram of ideal body weight). The WHO technical consultation on HIV and nutrition stated that energy requirements are likely to increase by 10% to maintain body weight and physical activity in asymptomatic HIV-infected adults and this should then be added to the DRI requirements for healthy adults. During symptomatic HIV, and AIDS, energy requirements increase by 20-30% to maintain body weight. In the case of co-infection, the highest recommendation should be implemented, based on the individual’s needs and other requirements.

- **Protein**

The protein intake of the diet is important to prevent the wasting of body stores (for example muscle tissues). An intake of 1.2 - 1.5 g per kilogram body weight or 15% of energy of total daily intake or approximately 75 - 100 g per day will be sufficient.

- **Micronutrients**

Despite extensive studies, little is known about the exact vitamin and trace element requirements in infection and the effects of micronutrient supplementation on TB treatment outcomes, clinical complications, and mortality are uncertain. A good multivitamin and mineral supplement, therefore providing 50% -150% of the recommended daily allowance, is advisable since it will be most unlikely that a person with TB will be able to meet the increased requirements for vitamins and minerals with diet alone (due to a poor appetite).

Recently one study found that supplementation with vitamin E (140 mg alpha-tocopherol) and selenium (200ug) reduces oxidative stress and enhances total antioxidant status in patients with pulmonary TB treated with standard chemotherapy.

A link between tuberculosis and vitamin D deficiency has been postulated and fish liver oils and sunlight were sometimes used to treat tuberculosis before the advent of antimicrobial drug treatment. Low serum vitamin D levels are associated with higher risk of active tuberculosis and vitamin D deficiency has been postulated. In addition to its role in mineral and skeletal homeostasis, vitamin D (1, 25 $(OH)_2D$) regulates the growth and function of a broad spectrum of cells, including cells of the immune system. It is now known that the principle source of vitamin D is sunlight and that plasma concentrations of vitamin D have striking seasonal variation with peak levels after summer and the lowest levels in the spring. The occurrence of tuberculosis has been reported to be related to the seasonal variation in vitamin D status in some, but not all countries.

It was also found that there is a massive local production of active vitamin D (metabolites of vitamin D) in the TB lesions in the lungs and other affected tissues of people with tuberculosis. There is some uncertainty though as to whether this is part of the body's protective system against the disease. Recent evidence, however, indicates that a vitamin D supplement (single oral dose of 2.5 mg vitamin D) corrects hypovitaminosis D at 1 week but not at 8 weeks post-dose in TB patients. The potential role of vitamin D supplementation in people with tuberculosis should be evaluated, especially since there is still some uncertainty whether Vitamin D enhances antimycobacterial immunity and improves disease outcomes. Emerging evidence however does indicate that a vitamin D supplement (single oral dose of 2.5 mg vitamin D) enhances antimycobacterial immunity in humans. Such supplements therefore could be considered in the appropriate settings. The public health implications of these observations remain to be clarified and vitamin D supplementation is not routinely prescribed to tuberculosis patients as of yet.

- **Drug -nutrient interactions**

Isoniazid is one of the most frequently anti-tuberculosis drugs used in the treatment of the disease. The drug is an antagonist of vitamin B6 (pyridoxine) and may case peripheral neuropathy (relatively rare) due to a nutritional deficiency of vitamin B6. It is standard procedure to supplement adults with 25 mg of vitamin B6 per day (in the form of supplements). Children are not routinely given vitamin B6, but if their blood levels are low or if they get large (more than 10 mg of isoniazid per day) dosages of isoniazid, they will also need 25 mg of vitamin B6 in the form of supplementation.

TB Antibacterial Drugs: Potential side effects and drug –nutrient interactions

TB Antibacterial Drugs			
Drug	**Guidelines**	**Potential side-effects**	**Potential drug-nutrient interactions**
Isoniazid	Take on empty stomach, 30 minutes before or 2 hours after meal	Increased requirements for pyridoxine, folate, niacin (vitamin B_3) and magnesium Hepatitis Constipation Anaemia Fatigue	May decrease absorption of pyridoxine, calcium, vitamin D May react with bananas, beer, pickled fish, yeast and yoghurt.
Rifampin	Take on empty stomach, 30 minutes before or 2 hours after meal Supplement with 10mg vitamin B_6 daily Not to be taken with alcohol	GI irritation Anaemia Jaundice Pancreatitis Altered taste Anorexia	May interfere with folate and vitamin B_{12}

Source. FANTA, 2001

NUTRITIONAL NEEDS OF CHILDREN WITH TUBERCULOSIS

The rapid growth periods of infancy and childhood can only be maintained if a child's nutrient intake is optimal. Insufficient intake can cause impaired growth and result in diseases such as malnutrition. Because of the previously described link between malnutrition and TB, all children presenting with malnutrition or with failure to gain adequately in weight must be evaluated for possible TB. Studies of children presenting with different forms of malnutrition indicate that TB can be found in 12- 30% of cases. When weight gain patterns of children with TB are studied, it is evident that 66% of cases fail to gain weight or show loss of weight prior to diagnosis.

The provision of adequate energy and nutrients for a child with TB is very important, since the child has increased requirements as a result of both growth and TB. In meeting their requirements, it should be born in mind that children have limited stomach capacity and appetites and as such meeting nutrient requirements presents a difficult challenge. It is therefore necessary to modify and plan the diet carefully to ensure adequate intake of food. (See recommendations.) The best way to monitor weight gain and detect malnutrition in children is to use the aid of a "Road to Health" card (curve that illustrate the growth pattern of a child).

RECOMMENDATIONS

- There is no documented evidence that any specific food on its own can alter the course of the disease or can for that matter be effective in the treatment of malnutrition. TB and HIV/AIDS patients are encouraged to eat a healthy varied diet.
- Pulmonary disease often adversely affects nutritional intake, due to poor appetites, making patients at risk for malnutrition. Six smaller meals per day are indicated instead of three meals.
- The meals should be appetizing in appearance and taste and provide enough energy and protein.
- Commercially available high energy and protein drinks (balanced in terms of micro-and macronutrients) may be used effectively to meet the increased requirements.
- Household ingredients, such as sugar, vegetable oil, peanut butter, eggs and non-fat dry milk powder can be used in porridge, soups, gravies, casseroles or milk based drinks to increase the protein and energy content without adding to the bulk of the meal.

- At least 500 - 750 ml of milk or yogurt should be consumed daily to ensure adequate intakes of vitamin D and calcium.
- At least 5-6 portions of fruit and vegetables should be eaten per day. Pure fruit juice can be used to decrease the bulk of the diet. Approximately 1/2 a glass of fruit juice is equal to one portion of fruit.
- The best dietary sources of vitamin B6 (pyridoxine) are yeast, wheat germ, pork, liver, whole grain cereals, legumes, potatoes, bananas, and oatmeal.
- Alcohol should be avoided.
- Adequate fluid intake is important due to increased losses (at least 10-12 glasses per day).
- A good multivitamin and mineral supplement, providing 50%-150% of the recommended daily intake, is advisable since it will be most unlikely that a person with TB will be able to meet the increased requirements for vitamins and minerals with diet alone (due to a poor appetite). Supplements however should preferably be given after consulting an expert health professional.
- Safe food handling and personal hygiene is very important. The following precautions for preventing or minimizing food or waterborne diseases are recommended in The South African National Guidelines on nutrition for people living with TB, HIV/AIDS and other chronic debilitating conditions:

Food Safety Principles
Raw and undercooked chicken, meat, fish and eggs, unpasteurised milk and water that do not come from a tap are the main dangers. **Cooking and Eating Defensively** Children are often taught about hygiene from a very early age. It becomes second nature in adults and may easily be taken for granted in healthy people. People with HIV/AIDS are at a higher risk of infections by germs that are carried in food and water. Extra care and awareness of the steps to take to lower this risk is needed.
Personal hygiene around food • Always wash hands thoroughly with soap and water (preferably warm water) before touching food. Do this every time between touching raw and cooked food. • It is very important to wash your hands after touching pets and other animals, after visits to the toilet and after sneezing or blowing your nose. • Cover all wounds to prevent contamination of food during preparation and handling.
Clean and safe water • In South Africa it is generally safe to drink water from a tap. If you get your water from a river or well, drink the water only after boiling it. • Use the bleach method to make the water safe when it is not possible to boil the water. Add 1 teaspoon (5 ml or one capful if the bottle has a screw cap) of bleach to 25 litres of water. Mix it well and let it stand for 2 hours (or preferably overnight) before using it. • Store clean and safe water in a clean container with a lid or covered with a cloth. • Cool drinks and ice cubes should also be made with water that is clean and safe.
Safe food shopping • It is safer to buy food in amounts that can be eaten before they spoil. It is sometimes cheaper to buy food in bulk, but without a fridge for safe storage this is not useful. For example, any meat not used within two days should be frozen. • Do not use canned food if the can bulges or if it is dented or leaking. Do not be tempted by discounts on damaged cans. • When buying cold meats and cheese, pre-packed and sealed products are safer. Cold meats that have been in the display case for some time are not safe. • Do not buy cracked eggs. It is wise to inspect the eggs in the shop before they are bought. • Many foods now have “Sell by”, “Best before” and “Use by” dates. Read the labels. It is not safe to buy foods after their “Sell by” date. Do not be tempted to do so even if the price is marked down. Check the food in your kitchen and throw away any food that has reached the “Best before” or “Use by” date, even if it still looks good. Do not taste food that you think might be spoiled. You might not have done these things in the past and never got sick. Remember that things are different with HIV/AIDS.

Safe foods

- If you are not sure where food comes from or how it has been prepared, it is safer not to eat it. If you have any doubt, do not eat it.
- Make sure the food is kept away from pets and other animals.
- Always keep food well covered to prevent flies and other insects from reaching it.

Fruits and vegetables

- Wash all fresh fruits and vegetables. If it is not possible to wash them properly, peel your fruits and vegetables. A mixture of 1 teaspoon of bleach added to one litre of clean water can be used to wash fruits and vegetables.
- Throw away any fruits or vegetables that are mouldy or rotten.
- Milk and dairy products
- Use only pasteurised milk. Pasteurisation is a process whereby milk is heated to a very high temperature, which destroys harmful germs. Look for the word "PASTEURISED" on the label. It might not be safe to drink home-produced milk. Home-produced milk should be boiled before use.
- Throw away mouldy cheese. Cutting off the mouldy part of the cheese is not good enough. Avoid blue-veined cheese and soft cheese which contain live moulds. This is not considered safe for people with HIV/AIDS.

Meat

- Do not eat raw meat, poultry and fish, not even in small amounts.
- Cook meat thoroughly until it is cooked right through. If it is still pink inside, it is not safe for you. When eating in a restaurant, order your meat well done.

Eggs

- Do not eat raw eggs. Always cook eggs until the white is cooked and the yolk (the yellow section) is firm.
- It is not safe to add raw eggs to milk shakes.
- Do not use cracked eggs. The cracks allow germs to enter.
- Wash the eggs before breaking them.

Keep cold foods cold and hot foods hot

- Keep frozen foods frozen.
- Hurry home with frozen food. Food warms up and defrosts in warm vehicles. This allows germs to grow before you get home to re-freeze the food.
- Plan your shopping and pick up frozen foods last. If you know you are going to be long, pack the frozen food in a cooler bag.
- Foods frozen at home can be kept safely for 30 days only in the freezer compartment of a fridge. Germs can grow even in the freezer.
- Once frozen food has been defrosted, it should be used as soon as possible. It is not safe to freeze the defrosted food again.
- It is not safe to defrost frozen meat at room temperature. Room temperature gives germs the chance to grow and they may make you sick. Defrost frozen meat or other frozen foods in a fridge if you have one. Microwave ovens are also good for defrosting frozen food quickly.
- If you do not have a fridge, keep the food in a cool place away from the sun while it is defrosting.
- Once food has been cooked it should be eaten as soon as possible. It is not safe to store foods that have cooled down at room temperature.
- Any leftovers should be stored in a fridge if possible. Warm foods should be allowed to cool down before putting it in a fridge. Food should not be left out for any longer than 2 hours. Use airtight containers or cling wrap to protect foods in storage. If you do not have a fridge, keep the food covered and in a cool place.
- Do not keep food at room temperature for more than two hours. Be careful about eating cold cooked food that has been kept at room temperature for longer than this. This often happens at parties and large functions such as weddings. Many healthy people have suffered stomach upsets after such events. When you are infected with HIV you need to be extra careful.
- When you eat leftovers of cooked food, you should reheat them to a high temperature to make sure that you kill all germs first. It is not safe to simply warm the food up.

Take extra care when travelling

Food safety standards are not the same everywhere. When people travel they come into contact with new germs that their bodies are not used to. Our immune systems are not

prepared for this and it can be a problem even for healthy people. Diarrhoea is a common consequence. When the immune system is weakened by HIV/AIDS, it is easier to get sick from food and water that does not cause problems in uninfected people. Extra precautions should be taken when travelling. It is advisable to drink water only after boiling. Alternatively only bottled and canned drinks or water should be drunk. Do not use ice in drinks, the water used for this.
Keep a safe kitchen Guidelines on proper food handling and cleaning of kitchen utensils (See source for full details).

Source: DOH, 2007

For further, personalized and more detailed information, please contact NICUS or a dietician registered with the Health Professions Council of South Africa

References from the scientific literature used to compile this document are available on request.

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