best tests

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New Zealand Laboratory Schedule: Microbiology

Rural infections series: The Rural Round Up

H. pylori testing

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The New Zealand Laboratory Schedule and Test Guidelines: **Microbiological and Serological Tests**

In October, 2013, the New Zealand Laboratory Test Schedule was published to provide consistent guidance and ensure uniform availability of tests across all District Health Boards (DHBs). The new Schedule divides tests into Tier 1 and Tier 2 to indicate whether all referrers can order the test, i.e. Tier 1, or whether a test must be ordered in conjunction with another health professional with a particular area of expertise, i.e. Tier 2. In this third article of an ongoing series we focus on the new Laboratory Schedule and Guidelines in relation to microbiological and serological tests for infectious diseases.

General Practitioners have access to more than 500 different laboratory tests in New Zealand. From this range the average General Practitioner requests over 4000 tests each year.[1] With this number of tests available, and this volume of testing, selecting the right test, for the right patient, at the right time can be challenging. Emerging evidence, changing guidelines, new testing methods and the ability of infectious organisms to evolve relatively quickly means that best practice inevitably changes with time.

The Laboratory Test Schedule and Laboratory Test Guidelines are available from: **www.dhbsharedservices.health.nz/Site/Laboratory/Laboratory-Schedule-Review-Project.aspx**

How was the infectious diseases section created?

A microbiological and serological Subgroup was formed to review tests for infectious diseases. This was made up of clinical microbiologists (both hospital and community) and public health specialists who examined the currently available tests and made recommendations as to which health professionals required access to each test. The Subgroup will continue to review the infectious diseases section of the Schedule regularly.

For further information see: "The New Zealand Laboratory Schedule and Test Guidelines: What does it mean for general practice?", BT (Nov, 2013).

Important points to note for microbiological and serological tests

The microbiological and serological test section of the Laboratory Schedule includes the following features:

- Alerts have been added to tests for notifiable infections to remind clinicians when notification to the Medical Officer of Health is required
- Tests for organisms causing infectious diarrhoea are now labeled by the suspected organism, rather than by the test that is used to identify them
- The practice of "sentinel testing" has been introduced
- Situations where "screening" tests will not be funded have been specified
- Outdated or unnecessary tests have been removed from the Schedule, where appropriate

Guidance has been provided for some tests in the microbiological and serological Laboratory Schedule to help clinicians request the most appropriate test. These recommendations are based on New Zealand and/or international best practice. Further guidance is likely to be added to the Schedule in future reviews.

Clinicians are invited to provide feedback by suggesting areas where additional information would be helpful. To provide feedback on the Schedule email: **ALLDHBs@dhbsharedservices.health.nz**

Tier 1 and Tier 2 tests for infectious diseases

The Tier 1 category makes the following tests more accessible:

Faecal antigen testing for *Helicobacter pylori* is now considered the most appropriate test for *H. pylori* infection. Previously, faecal antigen testing for *H. pylori* was only funded for hospital laboratories despite most of the requests for this test being made by General Practitioners.

For further information see: "The changing face of *Helicobacter pylori* testing", (Page 20).

The interferon gamma release assay (IGRA, Quantiferon gold test) for tuberculosis exposure or latent tuberculosis infection is now recommended to identify patients who are at high risk of developing active tuberculosis, in preference to older tuberculin tests, e.g. the Mantoux test. The IGRA has greater specificity than tuberculin testing and requires only one patient visit to the clinic. IGRA testing for latent tuberculosis is particularly recommended in the following patients: BCG-vaccinated people, immunocompromised people, e.g. those taking corticosteroids or methotrexate, high risk people who may not attend a second consultation or where a second visit is impractical.[2] IGRA testing in children aged under seven years is not currently recommended.[2] The Mantoux test can still be used to diagnose latent tuberculosis infection and is the preferred test in children aged under seven years.[2] The guideline to the microbiological and serological Laboratory Schedule can provide further information to clinicians when requesting a test for tuberculosis.

Nucleic acid amplification tests (NAAT) to detect *Bordetella pertussis*, *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are Tier 1 tests. Unlike culture tests that were previously used, NAAT tests only need a sample of DNA, and do not require viable bacteria to produce a positive result. Results are also available within hours, compared to cultures which may take three to 12 days.[3] NAAT testing also has the advantages over serology testing of not requiring the patient to have mounted an immune response in order to produce a positive result and of not being complicated by immunisation or past infection.

Influenza virus testing has been included as a Tier 1 test when assisting public health authorities in defining the epidemiology of large scale outbreaks. Previously this was possible but was not recognised in testing guidelines. Under normal circumstances this test may only be requested in primary care after consultation with a public health specialist. The Schedule also has the flexibility to allow other tests to be changed from Tier 2 to 1 as required.

The Tier 2 category will have little effect on general practice

The creation of a Tier 2 category for microbiological and serological testing will not have a significant impact on clinicians in the community as many of the tests in this category were already restricted to specific situations.

The following are examples of Tier 2 tests:

Reflex testing, which occurs automatically when the need for a second test is identified by the laboratory after an initial positive result. For example, when a test for *Toxoplasma gondii* is performed, if the initial test for IgG is positive, and clinical information suggests that this may be an acute infection, the sample is sent for avidity testing to determine if the IgG is a response to a past or recent infection. Screening Gram-negative bacilli that are resistant to cephalosporins for extended β-lactamase production is another example of reflex testing.

Some tests that require invasive sampling by a specialist clinician are classified as Tier 2, e.g. biopsies for *H. pylori* culture and susceptibility testing.

Tests for uncommon pathogens, e.g. arboviruses, are now classified as Tier 2. When considering requesting tests for uncommon pathogens a discussion with an Infectious Diseases Specialist or Clinical Microbiologist may be helpful in assessing the likelihood of a pathogen being present or in interpreting the results of the test. The Tier 2 category promotes consultation in less common situations and improves the quality of requests and the interpretation of test results.

Alerts for notifiable infections

The microbiological and serological Laboratory Schedule now includes an alert column to remind clinicians when notification to a Medical Officer of Health is required, e.g. a positive *Salmonella*, *Shigella*, *Yersinia*, or *Campylobacter* faecal culture. This feature was introduced to increase notifications and to improve understanding of when notification is required.

The Schedule also contains some footnotes relating to case definitions of notifiable diseases, e.g. defining a probable case of pertussis as opposed to a confirmed case.

Tests for faecal pathogens are now specified by pathogen

Test for organisms causing infectious diarrhoea are now labeled in the Schedule by the suspected organism, rather than by the test that is used to identify them. This change was made to encourage clinicians to include clinical information when requesting tests and to allow laboratories to choose the most appropriate test. Listing the patient's risk factors, e.g. recent overseas travel, helps laboratories to optimise testing.

For example, previously, when investigating infectious diarrhoea, if a request for enteric pathogens was made the laboratory performed microscopy and culture, however, different laboratories might culture for different organisms as there was no standardisation in which cultures would be performed. Now clinicians may request the "*Salmonella, Shigella, Yersinia, Campylobacter culture*" test for these common pathogens and additional testing can be added by the laboratory on the basis of clinical information provided.

Sentinel testing may be appropriate in some DHBs

The microbiological and serological Laboratory Schedule allows for DHBs to request health professionals to participate in the reporting of local antimicrobial susceptibility profiles, i.e. sentinel testing, to assist prescribers in the use of empiric antimicrobial treatment. This practice enables laboratory validation of local antibiotic guidelines for the treatment of common conditions. Examples where sentinel testing may

provide useful information in local susceptibility include:

- Females with uncomplicated cystitis, who are generally treated empirically, may have urine samples tested to determine local patterns of antibiotic susceptibility. This was suggested by the Subgroup in response to the introduction of increasingly resistant urinary pathogens, and because the susceptibility of *Escherichia coli* isolates varies geographically.
- *Neisseria gonorrhoeae* is now generally detected by NAAT and therefore susceptibility data is not available in every case
- *Streptococcus pneumoniae* is a common respiratory pathogen with a susceptibility profile that is hard to predict

It is anticipated that sentinel testing will improve the use of tests to diagnose and test for infections and promote the rational use of antimicrobials. Local sentinel testing is not recommended unless initiated by a DHB. Participation in the ESR national surveillance programme of antimicrobial resistance remains important to monitor changes at a national level.

When are "screening" tests not funded?

The microbiological and serological Laboratory Schedule now outlines situations when tests are not funded. This will make it clear for laboratories and DHBs under which situations tests will not be funded, when they are negotiating contracts. Tests are not funded in the following situations:

- Occupational testing, e.g. pre-employment drug testing
- To provide evidence of immunity for travel purposes
- Providing information for insurance or for visa applications
- Tests required by sports groups, e.g. testing for prohibited substances in athletes or proof of HIV status to obtain a professional boxing license
- Testing pre- or post-vaccination, e.g. hepatitis A testing to determine a patient's immunity before or after vaccination

Tests that are no longer necessary have been removed

Microbiological and serological tests which were not considered necessary have been removed from the schedule include:

- Chlamydia IgG tests have not been found to be useful for the routine diagnosis of Chlamydia infections. NAAT is considered a better test for patients suspected of having a Chlamydia infection.
- *H. pylori* serum antibody tests were routinely used to test for *H. pylori*. This test has been superseded by the use of *H. pylori* faecal antigen tests using monoclonal antibodies. A guideline will be released to assist clinicians in the use of this test.
- Hepatitis C antibody immunoblot and hepatitis C confirmatory immunoblot have been replaced by hepatitis C NAAT tests for viral detection and confirmation of patients with active infection
- TORCH screening for perinatal infections in newborn infants is no longer recommended and is not funded. Individual tests should be ordered when a congenital infection is suspected.
- Typhoid serology is not funded because culture for *Salmonella typhi* is considered to be a better test

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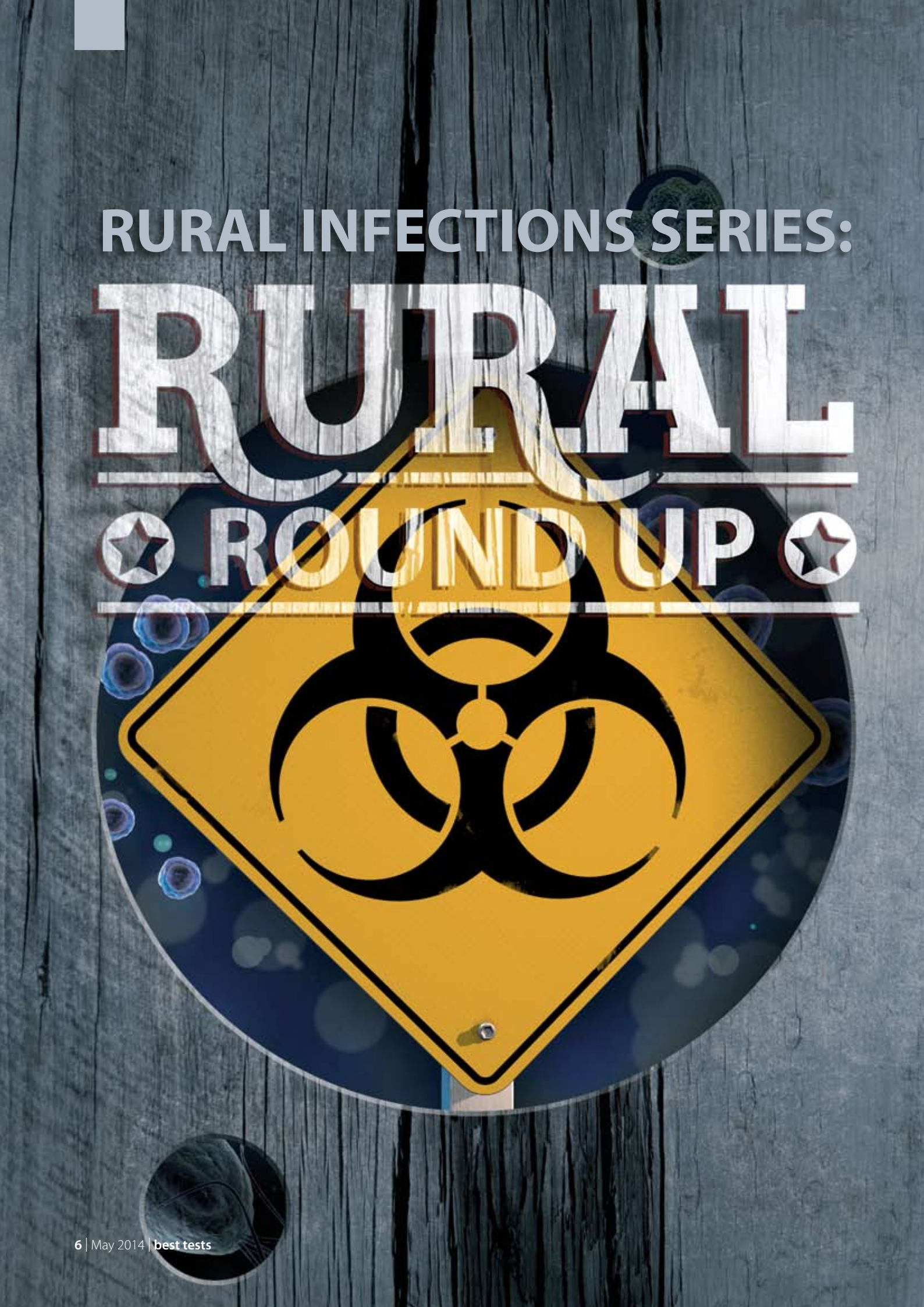
RURAL INFECTIONS SERIES:



In the final instalment of the rural series we present a round-up of infections that may be seen in patients living in, working in or visiting a rural environment. Most of these infections will be rarely encountered, but it is useful to be aware of their features and recommended management.

People who live, work or undertake recreational activities in a rural, agricultural or horticultural setting, are potentially exposed to a large number of infectious pathogens that can cause disease. Individually, most of these infections are rare, but the possibility of a rurally-acquired infection should be considered in symptomatic patients who have been exposed to this setting.

Many infections that were once prevalent in rural New Zealand have now been eliminated, e.g. hydatid parasites and brucellosis. However, some infections, e.g. leptospirosis, orf and *Listeria*, are still occasionally seen in rural communities.

Leptospirosis, campylobacter enterocolitis, salmonella enterocolitis, cryptosporidiosis and giardiasis are the most common rurally-acquired infections in New Zealand; these have been covered in previous articles in the rural infections series.

To round up the list of other rural infections, we have categorised them by their primary risk factors, which are:

- Consumption of unprocessed foods and untreated water
- Exposure to animals
- Exposure to plants or soil

N.B. Many of these infections have more than one contributing cause, and some are not unique to the rural environment.

Infections acquired via consumption of unprocessed foods or untreated water

Many people living in a rural community do not have access to a reticulated water supply, and collect and store their own water for household use. A rural lifestyle also often involves raising, growing and gathering food, e.g. raw milk, home-butchered or recreationally-caught meat and seafood. These practices are all associated with an increased risk of infectious diseases.

Drinking unpasteurised (raw) milk

Drinking milk "straight from the cow" is a way of life for many people living or working on a farm. The consumption of raw milk products is also gaining popularity in the wider community. However, although regarded as "wholesome" or "healthy", drinking raw milk actually increases a person's risk of illness.

Milk from cows, goats and sheep can be contaminated with bacteria, such as *Campylobacter jejuni*, *Escherichia coli*, *Listeria monocytogenes*, *Mycobacterium bovis*, *Salmonella enteritidis*, *Shigella spp*. and *Yersinia enterocolitica*. Pathogens can pass into milk directly via an infection in the animal, e.g. mastitis in the udder, or indirectly from the farm environment during the milking process, e.g. faecal contamination.[1] Commercially produced milk is pasteurised to destroy these bacteria. Pasteurisation is a heat treatment process which usually involves milk being rapidly heated to 72°C for 15 seconds.

There have been several small outbreaks of infectious diarrhoea associated with raw milk consumption in New Zealand in recent years.[1] The Ministry for Primary Industries monitors dairy products in New Zealand; an ongoing survey has found *Listeria monocytogenes*, Shiga-toxin producing *E. coli* and *Campylobacter jejuni* in raw milk.[1] In the United States, the Centers for Disease Control and Prevention (CDC) states that "the consumption of non-pasteurised dairy products cannot be considered safe under any circumstances".[2]

Facts about pasteurised milk:[1, 3]

- Pasteurisation is a highly reliable method for eliminating pathogens in milk
- Pasteurisation has a minimal effect on the fat and protein composition of milk
- Pasteurisation does not affect mineral content, stability or gastric absorption of milk
- Riboflavin, vitamin B6 and B12 are reasonably heat stable so remain in pasteurised milk at high levels
- Pasteurisation reduces the vitamin C content in milk by approximately 10%, however, milk is not a significant dietary source of vitamin C
- Some enzymes in milk are inactivated during the pasteurisation process but these are not thought to be important for human health

It is recommended that:[1]

- Raw milk products should not be consumed by young children, elderly people, pregnant women or people who are immunocompromised
- If raw milk is consumed, ensure it is from a source where good hygiene practices are adhered to during milking and storage (this reduces, but does not eliminate, the risk of contamination)
- Refrigerate raw milk at ≤ 4 ° C (this will not eliminate *Listeria* – see below)
- Discard raw milk if it has been at room temperature for more than two hours
- If diarrhoea develops after ingestion of raw milk, consider the possibility of an infectious pathogen as the cause

For further information on *Salmonella*, *Campylobacter* and *E. coli*, which can all be contaminants in unpasteurised milk, see: "Rural infections series: Investigating and managing people with diarrhoea", Best Tests (Feb, 2014). For information on *Listeria*, also a milk contaminant, see below.

A focus on *Listeria*

Listeria monocytogenes is a foodborne pathogen found in unpasteurised milk or unpasteurised milk products (e.g. cheeses), and also in items such as processed meat products (e.g. salami, paté), cold pre-cooked meats, uncooked seafood and raw vegetables, e.g. stored salads. *L. monocytogenes* can survive and multiply in food items at standard refrigeration temperatures.[4] People may also be exposed to *L. monocytogenes* via contact with potentially infective farm material, such as aborted animal foetuses.[4]

Listeriosis, the illness caused by *L. monocytogenes*, is characterised by diarrhoea, nausea, vomiting, fever, myalgia and fatigue, which typically resolve within one to three days.[5] More severe complications, such as the development of septicaemia or meningoencephalitis, are more likely to occur in vulnerable groups, such as pregnant women, young infants, elderly adults and immunocompromised people. Listeriosis also causes risks to a pregnancy, including miscarriage, premature labour and stillbirth. *Listeria* infection can be transferred to an infant during childbirth, which can result in serious illness and death for the infant.[6] There are approximately 25 notified cases of listeriosis per year in New Zealand (see: "Listeriosis in New Zealand", next page).[4]

Listeriosis is often an unexpected diagnosis and rarely considered before being identified by laboratory testing. The time between exposure and onset of symptoms is variable, with cases being reported between 1 – 70 days after exposure to a contaminated food.[4, 5] It is estimated that the median incubation period of *Listeria* is three weeks.[4] In practice it will be difficult to differentiate listeriosis from other diarrhoeal illnesses caused by pathogens, such as *Giardia*, *Salmonella*, *Campylobacter* and *E. coli*. Laboratory investigation is recommended in patients presenting with persistent diarrhoea and risk factors, e.g. exposure to a rural environment. It can be important to ask people their occupation when they present with persistent diarrhoea as they may live in an urban area, but work in a rural/agricultural environment.

If listeriosis is suspected (e.g. risk factors present and other likely pathogens have been ruled out), this can be discussed with an Infectious Diseases Specialist or Clinical Microbiologist. The best test for *L. monocytogenes* is blood culture; stool culture for *Listeria* is not routinely performed. Listeriosis is a notifiable disease and cases (suspected or confirmed) must be notified to the local Medical Officer of Health.[4]

Management of listeriosis is usually in conjunction with an Infectious Diseases Specialist. Depending on the clinical situation, patients with listeriosis may be managed at home if their signs and symptoms are mild. Patients with severe signs and symptoms, and those most at risk of serious illness are managed in a hospital setting.[4] Antibiotics may be considered for symptomatic and asymptomatic people who are at high risk of complications (e.g. infants, pregnant women, elderly adults, immunocompromised people), if they are known to have ingested a food implicated in an outbreak.[5] Listeriosis is treated with amoxicillin 1 g, three times daily, for 10 – 14 days.[7] Co-trimoxazole is an alternative.[5] Other antibiotic choices for treatment may be considered in a hospital setting.[6]

Patients with listeriosis can remain infectious to others for several months after resolution of symptoms,[4] however, other than transplacental transmission (mother to foetus), there are few, if any, reported cases resulting from person to person transmission.

Eating home-kill and recreational catch meat

In the rural community, many families will consume meat which has been butchered on the farm (home-kill) or hunted (recreational catch). As these methods are not subject to any hygiene or safety regulations, there is a potential for transmission of infectious diseases and toxicity via handling or ingestion of raw or under-cooked meat.

The main risks are:[9]

- Bacterial contamination from the animal via external wounds or contents of the gut or other infected organs
- Bacterial contamination from the environment, e.g. soil, grass, hunting knife
- Chemical contamination via the animal eating pest control poisons or carcasses of poisoned animals, or if transporting the carcass in a vehicle used to carry chemicals, e.g. weed killer or fuel

Bacterial contaminants in home-kill and recreational catch meats include *Salmonella* (particularly birds), *Campylobacter*, *Cryptosporidium* (particularly calves and lambs), *Giardia* and, rarely *Trichinella* (particularly pigs – see over page).

The Ministry for Primary Industries has guidelines on safe practices for home-kill meat. A consumer information brochure can be found here: **www.foodsafety.govt.nz/elibrary/consumer/Homekill-brochure-2012-web.pdf**

And further information found here: **www.foodsmart.govt.nz/food-safety/hunting-collecting-fishing/**

Listeriosis in New Zealand

In New Zealand, epidemiological data on listeriosis is collected by the Institute of Environmental Science and Research Ltd (ESR). In 2012 (latest reported data) there were 25 notified cases of listeriosis (0.6 per 100 000 population). Two of these cases were perinatal, which resulted in death of the foetus. Of the remaining cases most were in people aged 50 years and over (21 cases). The majority (16 cases) also had an underlying co-morbidity, and four cases resulted in death. The 25 notified cases were from nine DHBs, including five from Counties Manukau, five from Bay of Plenty and four from Hawke's Bay. There was one outbreak of listeriosis reported in 2012, linked to an infected ready-to-eat meat product. The notification rate of listeriosis has been relatively stable over the past 15 years, following a peak of cases in 1997 (0.9 per 100 000 population).[8] It is likely that the actual rate of *Listeria* infection in the population is higher than the notified rate, taking into account cases of sub-clinical or mild infection which are not reported.

A focus on Trichinella

Trichinella spiralis is a parasitic round worm that can be found in carnivorous animals, such as feral cats and rats. There have been historical cases of infection among the domestic pig population in New Zealand, from pigs eating carcasses and faeces of infected animals.[10] However, the risk of *T. spirialis* in commercial piggeries in New Zealand is now regarded as very low. Although extremely rare (only three notifications since 1988),[8] infection in humans can occur after ingestion of raw or under-cooked meat, i.e. pork, that contains encysted *Trichinella* larvae. *Trichinella* cannot be transmitted from human to human.[10]

Trichinella can be destroyed by cooking meat until it reaches an internal temperature of ≥ 60°C for at least one minute, or by freezing meat at ≤ −15°C (standard home freezer temperature) for at least 20 days. Curing, salting, smoking or microwave cooking will not destroy *Trichinella*.[10]

Trichinellosis, the illness caused by *T. spiralis*, typically begins one to two days after ingestion of infected meat, with general discomfort, abdominal pain and diarrhoea, lasting up to one week. Headache, fever and excessive sweating may develop three to four days after ingestion. Further systemic features may occur within 8 – 15 days after ingestion (range 5 – 45 days), such as facial oedema (usually periorbital), myalgia (most commonly affecting the trunk and limbs) and severe weakness.[10, 11] Patients with trichinellosis almost always have eosinophilia, which can persist for several weeks to months.[11] Other characteristic laboratory parameters include increased muscle enzymes and increased total IgE. Differential diagnoses of trichinellosis include influenza, infectious diarrhoea and auto-immune disease.[11]

Patients with suspected trichinellosis should be referred to an Infectious Diseases Specialist. Trichinellosis is confirmed by a positive serological test or detection of larvae in muscle tissue biopsy. Treatment usually involves an anthelmintic (e.g. mebendazole), analgesics, corticosteroids and supportive care.[10, 11] Trichinellosis is a notifiable disease so all cases, suspected or confirmed, should be notified to the local Medical Officer of Health.

For further information about trichinellosis, see: FAO/WHO/OIE Guidelines for the surveillance, management, prevention and control of trichinellosis. Available from: **www.trichinellosis.org/uploads/FAO-WHO-OIE_Guidelines.pdf**

Drinking tank water

Using collecting tanks or a natural ground water source for household water supply is common in rural communities in New Zealand. Depending on the source of the collected water, e.g. stream, bore, rainwater, and the household storage and filtering system used, contamination with infectious pathogens, heavy metals, trace elements and agricultural chemicals is possible.

Blastocystis: unknown role in infection

Blastocystis is a protozoan parasite which can be found in the gastrointestinal tract of many animals. Humans may acquire infection from animals (particularly from cattle, pigs or birds) or from person-to-person oral-faecal contact. Whether blastocystis is a cause of human disease is very uncertain. Some people found to have stool carriage of blastocystis are asymptomatic, whereas some have diarrhoea and other gastrointestinal symptoms. It is thought that people who are immunocompromised may be more susceptible to infection.[16] Most mild symptomatic cases are self-limiting; no specific treatment is required. However, in rare cases, gastrointestinal symptoms may be persistent. In these cases, other pathogens, e.g. *Giardia*, should first be ruled out as a cause for the symptoms. If the symptoms appear to be attributable to blastocystis, a course of metronidazole may be trialled. There has been mixed evidence of the success of metronidazole in eradicating infection. If treatment with metronidazole has failed, or is contraindicated, co-trimoxazole is a second-line option.[16]

Human or animal waste is the most likely source of pathogenic micro-organisms in water supplies. Bacteria are also found naturally in ground water and surface water.[12]

Drinking water may be contaminated from seepage from a septic tank, run-off from pastures, heavy rains causing overflowing storm water, animal faeces (e.g. on a roof used for collecting rainwater), or improperly sealed storage tanks or wells.[12]

E. coli is one of the most common infectious pathogens in collected water and is used as a marker of faecal contamination. *Cryptosporidium*, *Giardia*, *Campylobacter*, *Salmonella* and *Shigella* are also common contaminants. Other micro-organisms found in water include helminths (thread worms, tape worms, nematodes) and viruses, such as norovirus, rotaviruses and hepatitis A.[12] These organisms can be found in faecal waste of humans and animals (e.g. pigs, deer, sheep, cows, birds, possums) and also in raw milk.[12] Most of these pathogens cause gastrointestinal illness, and the most susceptible groups are young infants, elderly adults and people who are immunocompromised. In some cases, people who have a prolonged exposure to a pathogen can develop immunity to it. Therefore members of a household with a contaminated water supply may not display and signs and symptoms, but visitors drinking the contaminated supply may become ill.[12]

If a patient presents with persistent diarrhoea and has a history of drinking from a tank water supply, testing for infectious pathogens would be indicated. A faecal sample should be sent for culture (which tests for *Campylobacter*, *Salmonella*, *Yersinia*, *E. coli* (VTEC) and *Shigella*) and antigen testing for *Giardia* and *Cryptosporidium*. Note risk factors and relevant clinical details on the laboratory request form.

It is recommended that home water supplies are frequently tested for *E. coli* (also called faecal coliforms) to monitor faecal contamination. At home kits are available or a sample can be sent to a commercial laboratory. An effective water filtering system, e.g. a UV filter, will help to minimise risk.

For further information on managing diarrhoea in a rural population, see: "Rural infections series: Investigating and managing people with diarrhoea", Best Tests (Feb, 2014).

For further information about drinking water guidelines, see: **www.health.govt.nz/our-work/environmental-health/drinking-water**

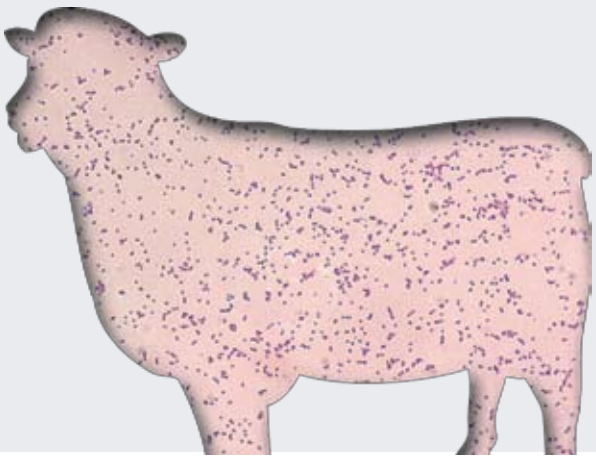
Brucellosis: once endemic in New Zealand but now rare

Brucellosis is a granulomatous infectious disease caused by the ingestion of *Brucella* bacteria in raw milk or meat from infected animals, or through contact with animal faeces or carcasses. Most cases of brucellosis in humans are caused by *B. melitensis*, but *B. abortus*, *B. suis* and *B. canis* can also cause human illness.[13]

Brucellosis is a notifiable disease and between 1997 and 2012, 13 cases were reported in New Zealand.[8] However, these patients are presumed to have acquired the infection in other countries because the only *Brucella* species that remains in New Zealand is *B. ovis*, which infects sheep, but is not pathogenic to humans. *B. abortus* was once endemic in cattle in New Zealand but was eradicated by 1996; since then, there has been no evidence of locally-acquired brucellosis in humans.[14]

People with brucellosis usually present with acute febrile illness, general malaise and respiratory tract symptoms.[15] "Drenching", malodorous perspiration is a characteristic feature.[13] Physical examination is generally nonspecific, however, lymphadenopathy, hepatomegaly or splenomegaly may be present.[13] If untreated, complications can include granulomatous hepatitis, arthritis, spondylitis, anaemia, thrombocytopenia, meningitis, uveitis, optic neuritis, endocarditis and neurological disorders collectively known as neurobrucellosis.[13]

Patients with suspected brucellosis should be referred to an Infectious Diseases Specialist. Laboratory confirmation of brucellosis involves serological testing and culture.



Infections acquired via contact with animals

People with agricultural occupations, such as farmers, dairy workers and meat processors, and people who live on farms, are exposed to a large number of infectious pathogens via contact with animals. For example, leptospirosis, which passes from mammals, such as pigs and cattle, to humans, is the most common occupationally acquired infectious disease in New Zealand.[17]

Animal-to-human contact is associated with respiratory infections, such as tuberculosis, and skin infections, such as pox viruses, dermatophyte and erysipeloid infections and granulomas.

For further information about leptospirosis, see: "Rural infections series: Leptospirosis", Best Tests (Nov, 2013).

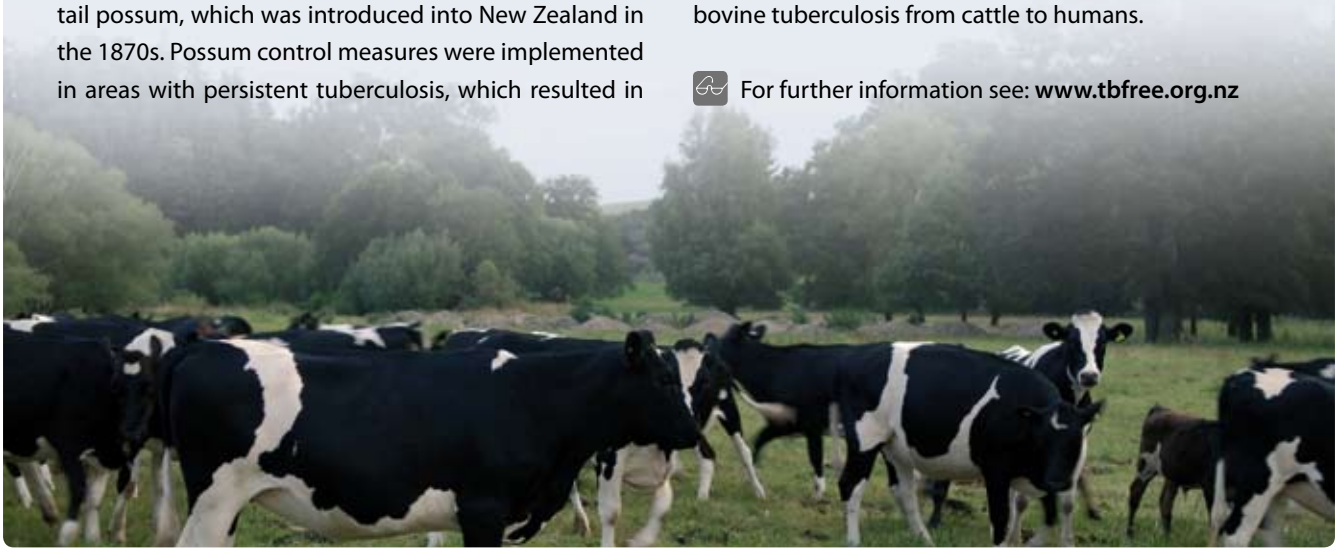
Tuberculosis

In 2013 there were 278 cases of tuberculosis in New Zealand.[18] Tuberculosis is now mostly seen in immigrants and seasonal workers. *Mycobacterium tuberculosis* is the typical bacteria associated with tuberculosis, and is transmitted from human-to-human. Atypical infections with other *Mycobacterium* species also occur. There are multiple causative species, but the most common are *M. kansasii* and *M. avium-intraceullulare*, which can be found in water, milk, bird excrement, soil and house dust. Atypical mycobacterial infections are more commonly seen in children, often presenting as an inflammation of the lymph nodes. Rarely, *M. bovis* (bovine tuberculosis) can be transmitted from infected animals (cattle, deer, possums and ferrets) to humans via handling or ingestion of contaminated animal products, including raw milk, or by airborne droplet spread to people who work closely with animals.[19]

Bovine tuberculosis in New Zealand livestock

It is thought that bovine tuberculosis was first established in New Zealand in the 1800s when cattle and deer were introduced. Control measures were implemented in the mid 1900s and by the 1970s all cattle herds were undergoing regular testing for tuberculosis and post-mortem inspection for disease. Bovine tuberculosis was eradicated in several regions, but there was unexplained disease in some areas, such as the West Coast of the South Island. It was found that livestock were being infected via the Australian brush-tail possum, which was introduced into New Zealand in the 1870s. Possum control measures were implemented in areas with persistent tuberculosis, which resulted in significant declines in livestock infections. When possum control measures were later relaxed in the 1980s, bovine tuberculosis returned, peaking in the mid-1990s at rates much higher than in other developed countries. In the past decade, renewed efforts to control bovine tuberculosis and cooperation between herd owners have resulted in levels which are at an all-time low. It is hoped that in the near future, New Zealand cattle herds will become "TB-free". There have been no reported cases in New Zealand in recent years of transmission of bovine tuberculosis from cattle to humans.

For further information see: **www.tbfree.org.nz**



Symptoms of tuberculosis are dependent on the organ system involved, e.g. pulmonary, intestinal, bone, lymphatic system. Pulmonary symptoms are most common, including dry cough which becomes productive, haemoptysis, pleuritic chest pain and breathlessness, along with anorexia, fatigue, fever and night sweats.[19]

Patients with suspected tuberculosis should be discussed with an Infectious Diseases Specialist. Chest x-ray and sputum culture are usually the initial tests. Further testing, e.g. QuantiFERON Gold assay, may also be required. Tuberculosis is a notifiable disease so all suspected or confirmed cases must be notified to the local Medical Officer of Health.

Combination antibiotic treatment is required for up to one year, or longer in some cases.[19] Tuberculosis can remain latent for many years, and in some cases reactivation may occur years after the original exposure.[19] People with active pulmonary tuberculosis are infective to others for several months to years.[19]

For further information see: "The guidelines for tuberculosis control in New Zealand", available from: **www.health.govt.nz**

Orf

Orf, also referred to as contagious ecthyma, contagious pustular dermatitis or scabby mouth, is a virus that commonly affects sheep (usually lambs) and goats, that can be transferred to humans.[20] It is caused by the parapoxvirus orf virus.[20] Other livestock, such as deer and cattle, are affected by similar poxviruses (see: "Milker's nodules"). Although orf can be a life-threatening disease in sheep and goats, it is a relatively mild and self-limiting condition in humans.

Orf is most frequently seen in farmers, shearers, meat processors, veterinarians and people bottle-feeding lambs.[21] Orf is characterised by the development of a 2 – 3 cm tender, flat-topped, red-to-blue papule or pustule on the dorsum of the index finger or hand (less commonly on the forearm or face), approximately one week after contact with an infected animal (Figures 1 and 2).[20, 21] The lesion will eventually crust over and resolve within two months. Usually only one lesion develops, but in some cases there may be multiple lesions.[21] Lymphadenopathy may be present, along with red streaks marking the lymph channels.[21] In some cases, patients may develop erythema multiforme, which is a secondary rash on distal limbs, characterised by target lesions with central blistering. The rash may persist for two to three weeks. Orf lesions may be more progressive and destructive in patients who are immunocompromised.

Orf can be diagnosed based on the appearance of the lesion and a history of contact with animals; laboratory investigation is not usually required. Standard microbiology culture will be negative. Skin biopsy typically shows ballooning of keratinocytes, necrosis and inclusion bodies.

No specific treatment is indicated, unless secondary bacterial infection is present; staphylococcal infection is most likely, which would be treated with flucloxacillin or cephalexin (see New Zealand Formulary or bpac^{nz} antibiotic guide for further details). Lesions can be covered to prevent cross-contamination. Patients with large lesions may require shave

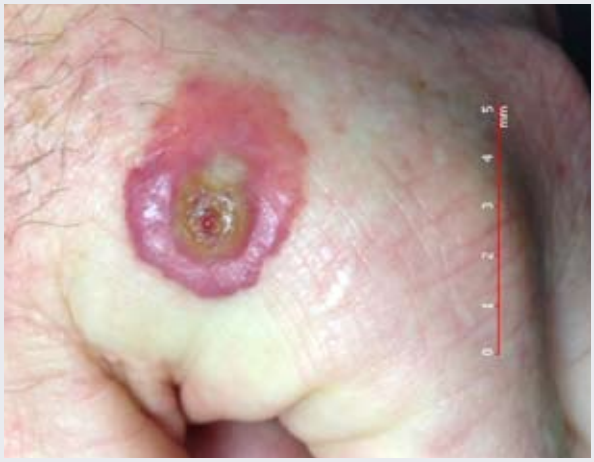


Figure 1: Typical orf lesion. Image provided by DermNet NZ (Courtesy of Dr Bert Rauber)

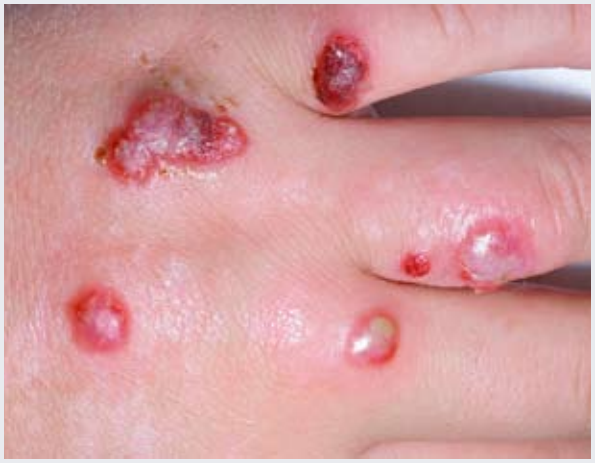


Figure 2: Multiple orf lesions. Image provided by DermNet NZ

excision, and should be referred to a Dermatologist.[21] There is some evidence that imiquimod cream is effective in treating orf,[22] however, this is an off-label use of this medicine and would not meet Special Authority criteria for subsidy.

For further information on orf and other parapox viruses, see Dermnet: **www.dermnetnz.org**

Milker's nodules

Milker's nodules are caused by a parapox virus that affects cattle. Infection is carried on the teats or in the mouth of cows ("ring sores") and can be passed to humans while milking or examining the animal.[23] It is sometimes referred to as "cowpock" and is often confused with cowpox, which is a viral skin infection caused by the vaccina-type cowpox virus (part of the family of viruses that also includes smallpox).[24] Cowpox is extremely rare and unlikely to be seen in New Zealand.

Milker's nodules develop 5 – 14 days after exposure to the virus. They begin as small, red, raised, flat-topped lesions, and over the course of approximately one week, they become red-blue, firm, tender vesicles or nodules, that may develop a greyish skin and small crust. The nodules usually appear on the hands, and less commonly on the face. There may be one or two nodules, or several.[23] As with orf, secondary bacterial infection and erythema multiforme may occur in some cases.

Laboratory investigation is usually not required as milker's nodules can be diagnosed based on the appearance of the lesions and a history of contact with cattle. However, if there is any doubt about the diagnosis, a skin biopsy can be performed.[23]

Management is the same as for orf. Nodules should be covered to prevent contamination, and patients advised to wear gloves if milking. Antibiotic treatment may be required if secondary bacterial infection is present.[23]

See: **www.dermnetnz.org/viral/milkers-nodules.html** for images of milker's nodules

Dermatophyte infections: ringworm

A dermatophyte infection is a skin, nail or hair infection caused by fungi which use keratin for growth. Infections may be acquired from a human (anthropophilic), animal (zoophilic) or soil (geophilic) source. Tinea corporis, known as ringworm, is an example of a dermatophyte infection. The anthropophilic dermatophyte *Trichophyton rubrum* is the most common cause of tinea corporis in New Zealand, and originates from infection in the feet (tinea pedis) or nails (tinea unquium). Tinea corporis caused by *T. rubrum* most often affects people with lowered immunity, e.g. people with diabetes or people treated with oral or topical corticosteroids. It is characterised by annular plaques which expand slowly.

Microsporum canis (from cats and dogs) and *T. verrocosum* (from cattle) are the most commonly implicated zoophilic dermatophyte infections responsible for tinea corporis.[25] Patients with zoophilic (or geophilic) ringworm usually present with single or multiple itchy, inflamed, skin lesions that form irregular expanding rings with a raised, distinct border (Figure 3). There are often scattered follicular pustules and loss of hair within affected areas. The lesions are usually located in exposed areas. Dermatophyte infections rarely occur on or near mucous membranes, helping to differentiate

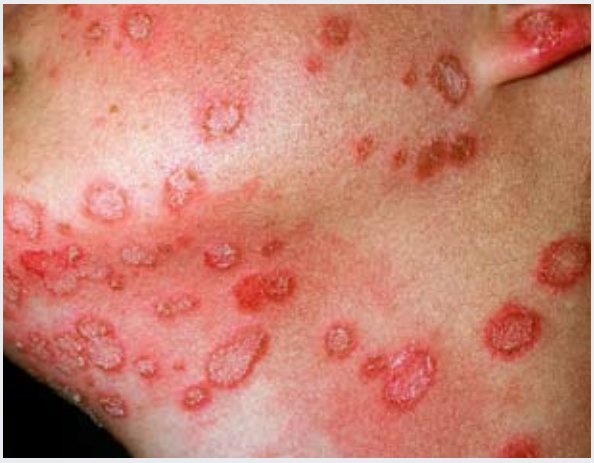


Figure 3: Zoophilic tinea corporis (*M. canis*)
Image provided by DermNet NZ

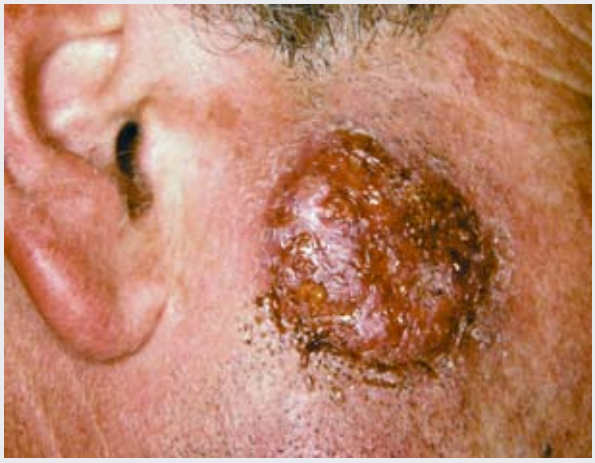


Figure 4: Kerion (*T. verrocosum* – cattle ringworm)
Image provided by DermNet NZ

them from candidal infections.[26] Adults and children in rural areas may present with kerion (fungal abscess – Figure 4).

Diagnosis of tinea corporis can be made by clinical appearance, but should be confirmed by laboratory analysis of skin scrapings and extracted hair shafts. Patients should not use topical anti-fungal medicines for three days prior to a sample being taken as this can prevent identification of the dermatophyte.

Patients with tinea corporis affecting a small area of skin can be treated with topical antifungals (e.g. miconazole or clotrimazole cream). If topical treatment fails, the rash is extensive, there is follicular involvement or the patient has kerion, oral antifungals are appropriate, e.g. terbinafine 250 mg, once daily, for four weeks – sometimes longer.

For further information on collecting skin scrapings, see: "Collecting specimens for the investigation of fungal infections", Best Tests (Mar, 2011)

Erysipeloid infection

Erysipeloid is an infection caused by *Erysipelothrix rhusiopathiae*. It is transferred to humans via contact with raw meat, poultry, fish and shellfish, when bacteria enter the skin through an open wound. Farmers, meat processors and veterinarians are most at risk of infection.[27]

Patients with erysipeloid can be affected in three ways: most often they will present with localised skin lesions, in very rare cases a diffuse cutaneous reaction occurs with multiple lesions across the body, and also rarely, a systemic infection affecting multiple organs can occur. Localised lesions are red-purple, with a smooth, shiny surface. The lesions slowly expand over several days, and develop a sharp or curved border, with very small blisters.[27] The lesions may feel warm, and pain, tenderness and a burning sensation may be reported.[27] Most lesions occur on the hands or fingers, but can form on any skin area exposed to the infected meat or animal.[27]

Laboratory investigation is not required; diagnosis is based on clinical examination. Lesions will resolve spontaneously within two to four weeks.[27] Antibiotic treatment can be considered to shorten the healing time. Oral flucloxacillin is an appropriate treatment; erythromycin or doxycycline are alternatives.[27]

Search: **www.google.com/images** for images of Erysipeloid

Foreign body granulomas: wool handlers

A foreign body granuloma is a non-immunological reaction to an exogenous material (e.g. wood or metal fragment, fibres) that has penetrated the skin. The foreign body is encapsulated within granulation tissue (which contains a proliferation of inflammatory and giant cells) and can mimic a soft tissue tumour. In some cases, a sinus is formed, which can result in infection.

Foreign body granulomas have been reported in people who handle sheep, e.g. wool handlers, shearers, pressers and rousies, although there is little published literature on this. When the wool is handled, wool fibres (especially when wet) may penetrate areas of exposed skin, e.g. the limbs and neck. This is also reported to occur in the breast and nipple area, when fibres penetrate through clothing. The resulting painful, swollen lesion is colloquially referred to as a "grease ball". This condition is similar to trichogranulomas that affect hairdressers or dog groomers, when hair penetrates the skin, usually between the fingers, and there is a foreign body reaction to the presence of keratin in the dermis.

A foreign body granuloma can be diagnosed with histopathology (fine needle aspiration or excision biopsy), which will show characteristic cell formation. Foreign bodies can sometimes be detected on ultrasound, but this is unlikely to reveal a wool fibre. Patients with infected lesions may require local incision and drainage, and antibiotics. Historically, topical application of methylated spirits has been used as a treatment for "grease balls". Protective clothing and gloves, and the use of a barrier (moisturising) cream on exposed skin can help to prevent foreign body granulomas from occurring.

Infections acquired via contact with plants or soil

There are many infectious pathogens which pose a risk to people working in outdoor occupations. For example, bacterial or fungal skin infections can occur in crop and field workers, and there is a risk of tetanus being transferred to a wound from soil. Some less common skin and soft-tissue infections are contracted via water-borne microbes through minor abrasions, e.g. *Aeromonas hydrophila*, a rare cause of cellulitis and abscess, and *Mycobacterium marinum*, a cause of chronic granulomatous plaques.

For further information on Aeromonas skin infection see: **www.dermnetnz.org/bacterial/aeromonas.html**

Paronychia

Horticultural workers are at risk of skin infections due to repeated minor trauma, e.g. from thorns and vines. Paronychia is inflammation of the nail folds, caused by bacterial, viral or yeast infection of the fingers or, less commonly, the toes.[28] It occurs when there is penetration between the proximal nail fold and the nail plate, allowing microbial entry. Disruption of the nail seal can also occur due to a contact irritant or excessive moisture.[28]

Paronychia can be acute or chronic. Acute paronychia is caused by bacterial infection, most commonly *Staphylococcus aureus*, and sometimes *Streptococci* and *Pseudomonas* organisms,[28] or by herpes simplex virus. Chronic paronychia is when symptoms have been present for more than six weeks, and is usually due to a fungal infection, e.g. *Candida albicans*. It is more likely in people who have repeated exposure to water containing chemical irritants or exposure to moist environments.[28] Chronic paronychia may also arise as a complication of hand dermatitis.

Patients with acute paronychia (Figure 5) present with localised pain, tenderness and swelling of the perionychium (epidermis bordering the nails). Discharge may be present if an abscess has formed and infection may extend into the nail bed. The nail may be discoloured or distorted.[28] Laboratory investigation is not required unless the infection is severe. If there are signs of significant bacterial infection, oral antibiotic treatment is recommended; flucloxacillin is an appropriate choice. Incision and drainage is recommended if there is an abscess.[28]

In chronic paronychia (Figure 6), several nails and perionychium appear swollen and tender, with "boggy" nail folds. There is thickening, transverse ridging and discolouration of the nail plate, and separation of the nail from the cuticle and nail folds.[28] Microbiological analysis of nail scrapings can be considered to identify the causative agent. Treatment with a combination of topical corticosteroids and a topical antifungal (when yeast infection is present) is usually successful. If symptoms do not resolve, an oral azole antifungal or antibiotic, depending on the microbes present, can be considered. If medical treatment is unsuccessful and the case is severe, surgical intervention may be considered; this may involve removal of the nail.[28]

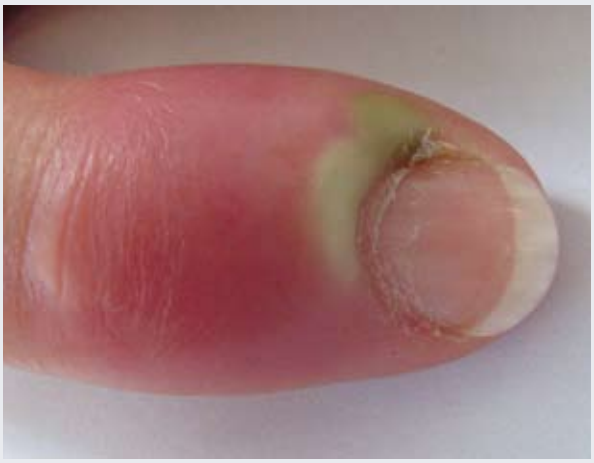


Figure 5: Acute paronychia. Image provided by DermNet NZ

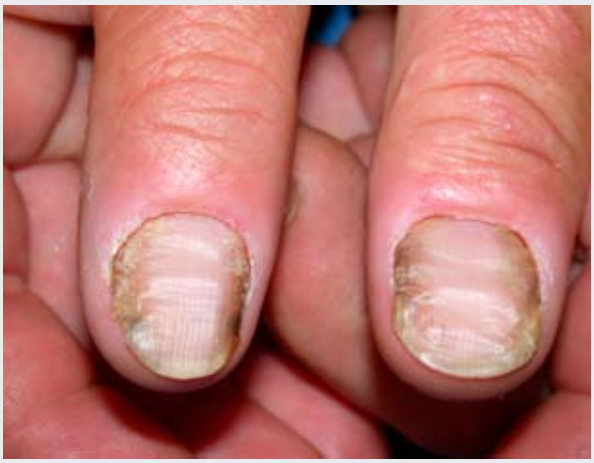


Figure 6: Chronic paronychia. Image provided by DermNet NZ

Tetanus

Clostridium tetani, the causative organism of tetanus, is present in soil, dust and animal faeces. People are at risk of tetanus if infected soil or other matter enters a wound. Once in an anaerobic environment in the wound, *C. tetani* multiplies and releases a toxin which causes the characteristic symptoms of tetanus: muscular rigidity and contraction spasms. Symptoms develop 3 – 21 days after exposure (ten days on average).[29] Initial symptoms include weakness, stiffness or cramps and patients may report difficulty chewing or swallowing food. Muscle spasms usually begin one to four days later. The mortality rate for people with tetanus is approximately 10%, but is higher in older people.[29]

Tetanus is rare in New Zealand due to an effective immunisation programme which was introduced for infants in 1960.[29] Prior to this, only people in the armed forces were likely to have received a primary series of tetanus vaccinations. Most cases of tetanus occur in older people (particularly older women) as they are less likely to have been immunised or to have received booster vaccinations. Between 2000 and 2010, there were 34 people in New Zealand hospitalised with tetanus; 23 of these people were aged over 60 years.[29]

If a patient presents with a tetanus-prone wound, it should be cleaned and dressed, and they should receive a tetanus booster immunisation if they have not had one within the last five to ten years (Table 1). Td (ADT Booster) or Tdap (Boostrix) can be used. Patients with no history of previous tetanus immunisation and a tetanus-prone ("dirty") wound should receive a primary course of tetanus vaccination (three doses) and should also receive tetanus immunoglobulin (TIG). The recommended dose is 250 IU, IM (one ampoule), but this should be increased to 500 IU if the wound occurred more than 24 hours previously or if there is a risk of heavy contamination.[29]

Patients with features suggestive of tetanus should be referred to hospital for further assessment and management.

Table 1: Guide to tetanus prophylaxis in wound management (adapted from Immunisation Handbook, 2011)[29]

Vaccine history	Time since last dose	Type of wound	Tetanus vaccination required?	Tetanus immunoglobulin (TIG) required?
≥ 3 doses	< 5 years	Tetanus-prone	No	No
≥ 3 doses	5 – 10 years	Clean/minor	No	No
≥ 3 doses	5 – 10 years	Tetanus-prone	Booster dose	No
≥ 3 doses	> 10 years	Tetanus prone	Booster dose	No
< 3 doses		Clean/minor	Complete course of three doses	No
< 3 doses		Tetanus-prone	Complete course of three doses	Yes

Assess tetanus status at age 45 and 65 years

The tetanus immunisation status of adults should be reviewed at age 45 and 65 years. If it has been more than ten years since receiving a tetanus vaccination, patients should be offered a booster vaccination: Td (ADT Booster) or Tdap (Boostrix). If they do not have a reliable history of tetanus vaccination a primary course should be given, which is three doses of Td or Tdap, at least four weeks apart. A booster dose is then recommended in ten years.

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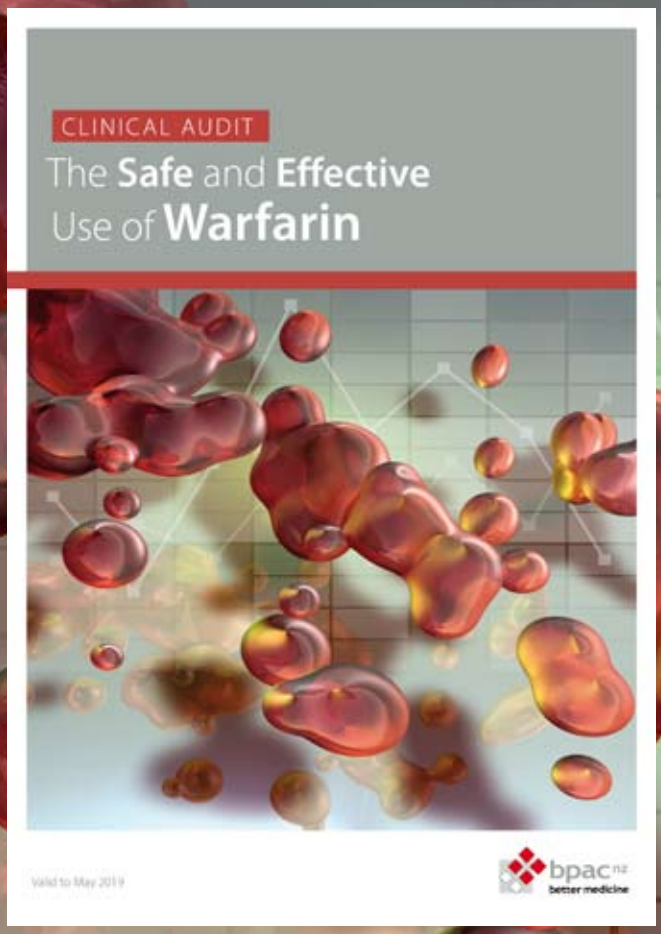

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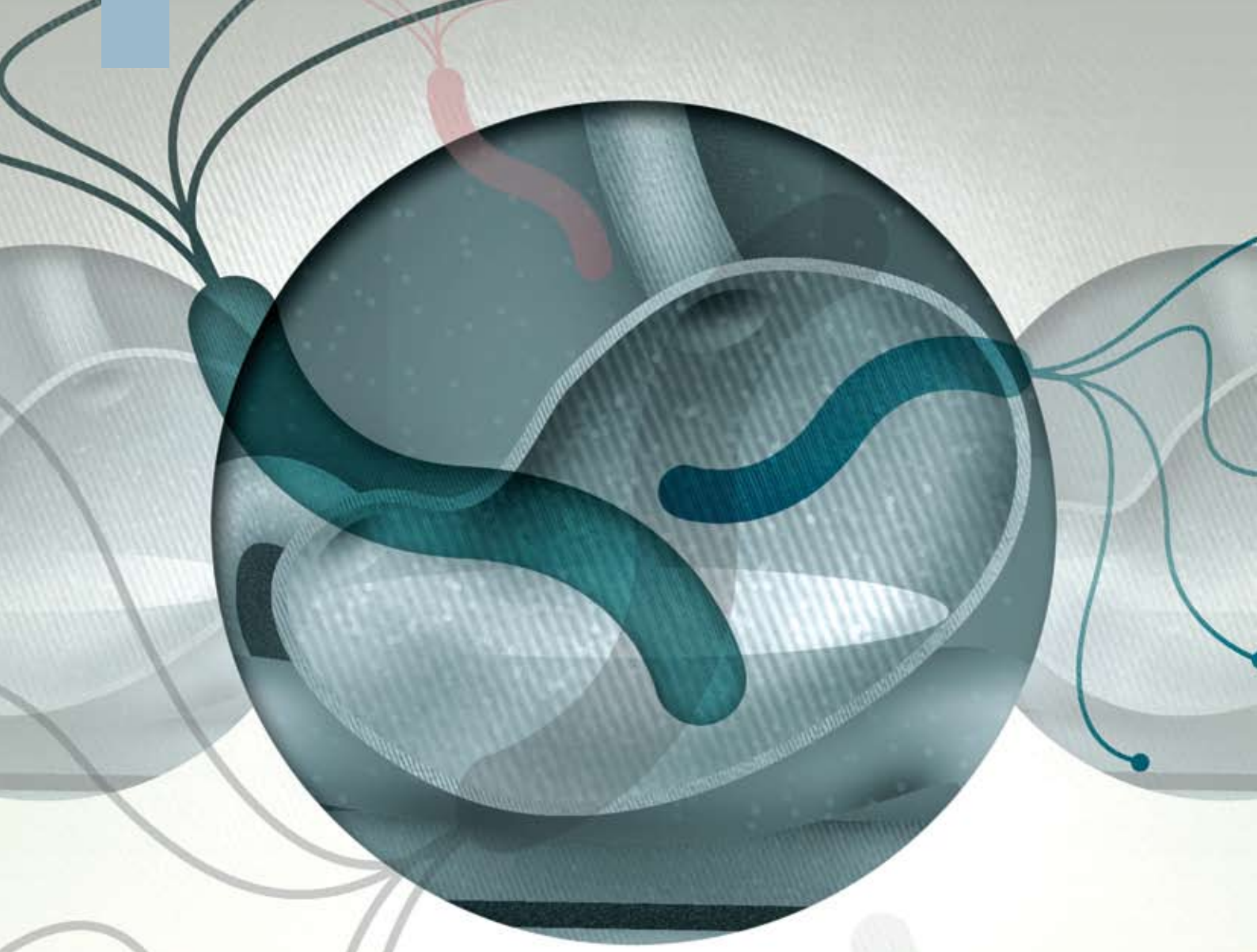

The changing face of ***Helicobacter pylori*** testing

There is ongoing debate in the literature about which is the best test to request for the detection of infection with *Helicobacter pylori*. The most appropriate test is influenced by several factors, such as the pre-test probability of *H. pylori* infection (reflected by prevalence), the patient's specific clinical circumstances and the cost and availability of the test.[1] In New Zealand, like many other countries, the advice has changed over recent years, however, the current thinking is that the *H. pylori* faecal antigen test is now the preferred option in patients who require investigation for *H. pylori* (see: "The New Zealand Schedule and Test Guidelines update, Page 2). Infection with *H. pylori* is known to increase the risk of peptic ulcer disease and gastric cancer due to chronic inflammation and atrophy of the stomach mucosa.[2]

The prevalence of *H. pylori* in New Zealand is low by world standards

In New Zealand the overall prevalence of *H. pylori* is lower than many other developed countries, although there is limited data and prevalence differs throughout the country.[3] A recent small study in South Auckland, traditionally an area with rates of *H. pylori* > 30%, recruited patients undergoing endoscopy, and reported an overall prevalence of *H. pylori* for adults of all ethnicities of 18.6%. However, rates varied between people from different ethnic groups: for New Zealand Europeans, prevalence was reported as 7.7%, which ranks among the lowest rates for *H. pylori* in the world,[4,5] but a significantly higher prevalence was noted in Māori (34.9%), Pacific (29.6%), Asian (23.8%) and Indian (19.2%) peoples.[4]

The overall global prevalence of *H. pylori* is > 50%. Prevalence has declined in many countries due to improvements in treatment and in standards of living, however, there continues to be a marked variation between, and within, countries.[5,6] This is because infection with *H. pylori* is influenced by a number of factors, including ethnicity, socioecomonic status, gender and age.[5] Rates remain higher in developing countries due to associations with increased transmission in areas with overcrowded living conditions, poor sanitation and unsafe drinking water.[1,5,6]

H. pylori is typically acquired during childhood and does not usually resolve spontaneously. Infection tends to be acquired at a very young age in children in developing countries compared to developed countries.[5] For example, in Bangladesh, 50 – 82% of children aged < 9 years are infected with *H. pylori* and this rises to > 90% in adults.[5] In comparison, a rate of 7.1% is reported for young people aged 5 – 18 years in Canada, rising to 20 – 30% in adulthood.[5]

Prevalence of *H. pylori* in adults is high in most Asian countries, e.g. Japan and China (50 –70%), South American, Eastern European and Middle Eastern countries, e.g. Chile (73%), Bulgaria (61.7%), Egypt (90%) and Saudi Arabia (80%).[5,6] Lower rates are reported for countries such as the United Kingdom (13.4%), Switzerland (11 – 26%), and Australia (15 – 20%).[5,6]

Do we still need to test patients for H. pylori?

The decreasing prevalence of *H. pylori*-related peptic ulcer disease and gastric cancer has begun to alter management recommendations when a patient presents with dyspepsia, or *H. pylori* is suspected.[7,8] It is suggested that testing for *H. pylori* may not be needed, or helpful, in people who live in areas with low prevalence,[8,9] which applies to people in many areas of New Zealand.

When a person first presents with dyspepsia, therefore, the clinician should consider how likely it is that *H. pylori* will be present, whether red flags are present (see: "Red flags"), if there are other factors that may be influencing their symptoms, such as NSAID use, and how the test result will influence the management of the patient.[9] Routinely testing all patients with dyspeptic symptoms for *H. pylori* or prescribing empiric eradication treatment for *H. pylori* without testing is not recommended.[10]

The decision to treat dyspeptic symptoms empirically with a proton pump inhibitor (PPI) in people who are less likely to have *H. pylori* , or to "test and treat" for *H. pylori* can be, in part, based on:

- Where they live – prevalence is generally higher in the north of New Zealand than in the south[3]
- Their ethnicity – if the person is of New Zealand European ethnicity, the prevalence is likely to be approximately ≤7%, but in Māori, Pacific, Asian and Indian peoples prevalence will be much higher[4]
- Where they were born – even allowing for expected diffrences due to ethnicity, if the person was born in New Zealand, the chance that they will have *H. pylori* is likely to be lower than many people born overseas (depending on their country of origin). If the person was born in a developing country, there is at least a 50% chance that they will have *H. pylori*, and research shows that adults who immigrate retain a prevalence of *H. pylori* similar to their country of origin.[11]
- The presence of any red flags (see: "Red flags")

Red flags for people presenting with dyspepsia

A patient with any of the following factors has an increased risk of significant organic disease and may require referral for endoscopy:[3]

- Age ≥ 50 years at first presentation (the incidence of gastric cancer increases with age)
- Age ≥ 40 years at first presentation for people of Māori, Pacific or Asian descent (gastric cancer tends to occur a decade earlier in these groups)
- Family history of gastric cancer with age of onset < 50 years
- Dyspeptic symptoms that are severe or persistent
- Previous history of peptic ulcer disease, particularly if complicated
- The use of aspirin or NSAIDs (also check over-the-counter use)*
- Signs and symptoms of chronic gastrointestinal bleeding, such as malaena, anaemia
- Iron deficiency anaemia
- Difficulty in swallowing
- Persistent regurgitation or protracted vomiting
- Palpable abdominal mass
- Unexplained weight loss

* If a person taking NSAIDs has no other red flags and symptoms are mild, initial management is to stop the NSAID and then re-assess symptoms

For further information, see: "Managing dyspepsia and heartburn in general practice – an update", BPJ 34 (Feb, 2011).

There is also evidence that the majority of people with dyspeptic symptoms and an absence of red flags will have normal findings at endoscopy and that empiric treatment with a PPI for symptom control is considered an effective, safe strategy.[12]

Taking these factors into account for an individual patient can help determine the most appropriate management strategy.

For patients with dyspepsia who are at:

Lower risk of *H. pylori* infection – the most pragmatic approach is to prescribe a PPI and review the patient in a month to assess whether their symptoms have improved. If the patient's symptoms have not improved, reassess for the presence of red flags and consider testing for *H. pylori* . Ideally the PPI should be stopped for two weeks prior to testing for *H. pylori* to reduce the rate of false negative results.

Higher risk of *H. pylori* infection – consider testing for *H. pylori* with a faecal antigen test. If the patient has a positive result for *H. pylori* , they should be prescribed eradication treatment. If the result is negative, empiric treatment with a PPI can be initiated after reassessing for red flag features.

Faecal antigen testing is now recommended to detect *H. pylori* infection

There are three non-invasive tests for *H. pylori*. These are the:

- Faecal antigen test
- Carbon-13 urea breath test
- Serum antibody test

Table 1 summarises the advantages and disadvantages of these three tests.

Faecal antigen testing is now included as a Tier 1 test on the New Zealand Laboratory Schedule, and is widely available throughout community laboratories in New Zealand. When faecal antigen tests for *H. pylori* were first introduced they relied on polyclonal antibodies and the results were often unreliable.[13] The use of monoclonal antibody-based techniques to assess faecal samples has improved the accuracy of the test.[13, 14] The test detects the presence of antigens to *H. pylori* in a faecal sample and can be used to diagnose active infection and, if required, to confirm that eradication treatment has been successful.[14] Sensitivity and specificity of faecal antigen testing is similar to that reported

Table 1. Advantages and disadvantages for non-invasive tests for *H. pylori*:[5, 7, 9, 13, 14]

Test	Sensitivity	Specificity	Positive predictive value	Advantages	Disadvantages
Faecal antigen test	94 – 95%	94 – 97%	84%	Determines active infection Can be used as a test of cure No cost to patient as the test is funded in New Zealand	The accuracy of the test may be reduced if the patient has upper gastrointestinal bleeding or if the stool sample is unformed or watery Patient should not have antibiotics for four weeks, or PPIs or bismuth for two weeks, prior to testing. Advice varies regarding whether H_2-receptor antagonists and antacids are able to be continued.
Urea breath test	95%	96%	88%	Determines active infection Can be used as a test of cure	Cost to patient as test is not funded in New Zealand Limited availability Patient needs to be fasted The patient should not have antibiotics for four weeks, or PPIs for two weeks, or H_2-receptor antagonists for 24 hours, prior to testing
Serology	85 – 92%	79 – 83%	64%	Convenient for the patient The test is not affected by medicines such as antibiotics, PPIs or H_2-receptor antagonists	No longer funded in New Zealand (however, the test is relatively inexpensive) Variable specificity; most accurate if there is high prevalence of *H. pylori* Cannot distinguish between past and present infection – a positive result means the patient has been exposed but may not mean the patient has active infection Cannot be used as a test of cure

Sensitivity – reflects the ability of the test to correctly identify patients with the condition being tested for, therefore a test with high sensitivity reduces the likelihood of a false negative result

Specificity – reflects the ability of the test to correctly identify patients without the condition, therefore a test with high specificity reduces the likelihood of a false positive result

Positive predictive value – reflects the probability that if a result is positive, the patient does have the condition being tested for

For further information see "Deciding when a test is useful: how to interpret the jargon", Best Tests (Feb, 2013).

for carbon-13 urea breath testing.[1, 13, 14] False negative results can occur if the patient has been taking medicines that may decrease the load of *H. pylori* in the stomach, or the contents of the stomach are less acidic, e.g. if a patient has been taking a PPI (Table 1).[1, 7] However, there is some limited evidence that monoclonal antibody-based faecal antigen tests may be less influenced by PPI use than urea breath tests.[15]

Carbon-13 urea breath testing is still regarded in the literature as the gold standard for testing for *H. pylori,* however, the test is time consuming and expensive to perform.[7] In New Zealand the test has limited availability and is not funded. The test provides an indirect measure of the presence of *H. pylori*-associated urease which is detected by a change in CO_2 in the patient's breath after ingestion of labelled urea.[16] Both sensitivity and specificity of the test are comparatively high, although, as with faecal antigen testing, false negative results can occur with medicines that decrease the bacterial load or suppress gastric acid.[13]

Serum antibody testing (serology) for *H. pylori* has previously been recommended as the most appropriate test in New Zealand. However, with the improved availability and accuracy of faecal antigen tests, serology is no longer the preferred test, and it is no longer funded in New Zealand. Serological testing detects the presence of IgG antibodies to the *H. pylori* bacteria. Although the sensitivity of the test is comparable with the other non-invasive tests, the specificity is variable and when prevalence of *H. pylori* is low the positive predictive value of the test declines.[1, 9] Serology also cannot distinguish between infection that is past or current, and because antibody levels decrease slowly over 6 – 12 months or longer after eradication treatment, it cannot be used as a test of cure.[1, 7]

Invasive testing for *H. pylori* requires endoscopy which can provide biopsy material for histology, rapid urease testing and culture.

Eradication treatment for *H. pylori*

If a positive result for *H. pylori* is obtained, the patient should be prescribed eradication treatment, i.e. "do not test if not intending to treat". [5]

A recommended triple treatment regimen for the eradication of *H. pylori* is a seven day course of:[17]

- Omeprazole 20 mg, twice daily
- Clarithromycin 500 mg, twice daily
- Amoxicillin 1 g, twice daily (or metronidazole 400 mg twice daily, if allergic to penicillin)

Other regimens using different dosing intervals, or other PPIs e.g. lansoprazole, can also be used.[17] For further information refer to the New Zealand Formulary.

Confirmation of eradication of *H. pylori* after a triple treatment regimen is not required for the majority of patients.[3] A test of cure may be considered in patients with a recurrence of symptoms, a peptic ulcer complication or with important co-morbidities.[3] Faecal antigen testing can give accurate confirmation of eradication if required.[14]

Recently there have been concerns in New Zealand and worldwide about increasing resistance of *H. pylori* to the antibiotics used in the various eradication regimens.[4, 7] Resistance to clarithromycin and metronidazole was reported in a recent New Zealand study and, in particular, resistance to clarithromycin has doubled since the 1990s.[4] Although the study was based on a small number of participants, rates of clarithromycin resistance varied with ethnicity – no resistance was reported in New Zealand Europeans while a rate of 25% was reported for Māori.[4]

If an initial seven day eradication regimen has failed (i.e. symptoms have recurred) an alternative two week quadruple regimen can be used or referral for endoscopy considered. Bismuth-based quadruple treatment is comprised of:[4,10]

- Omeprazole 20 mg, twice daily
- Tripotassium dicitratobismuthate 120 mg, four times daily (to be taken as: one dose 30 minutes before breakfast, midday meal and main evening meal, and one dose two hours after main evening meal)
- Tetracycline hydrochloride 500 mg, four times daily
- Metronidazole 400 mg, three times daily

In New Zealand, tripotassium dicitratobismuthate (or colloidal bismuth subcitrate) and tetracycline hydrochloride are unapproved medicines, supplied fully subsidised under Section 29. Tetracycline hydrochloride requires a Special Authority, which only applies to its use in this *H. pylori* eradication regimen.[17] Doxycycline is not recommended as an alternative tetracycline as it results in a significantly lower eradication rate for *H. pylori*.[4] Adhering to optimal timing of the medicines in the quadruple regimen can be challenging for patients.

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