A review of scrub typhus management in 2000-2001 and implications for soldiers

Jonathan Devine *BAppSc Physiotherapy*

Introduction

Scrub Typhus is an infectious disease caused by a small bacterium of the *Rickettsia* genus. Vast numbers of Australian soldiers were infected during World War II and the Vietnam War. As Scrub Typhus is not a notifiable disease, limited complete statistics are available. Various sources confirm that the disease is still present in areas where Lavarack based soldiers deploy for work or training. The following presentation is directed towards army medics, who are the first point of contact for injured or ill soldiers. The assumed level of knowledge of a medic is a combination of an enrolled nurse and an ambulance officer. In the field, this may extend to prescription of medication, raising IV drips and intubation of collapsed airways. In the first aid posts (RAPs), medics will generally screen basic illness/injury and refer higher-level management to unit doctors.

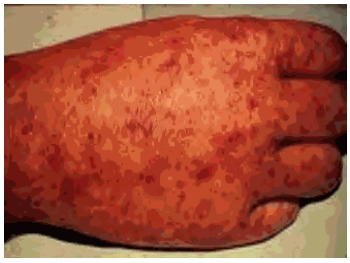
This paper was written to inform you of the presence of an enemy agent who has proven hostile to Australian soldiers. Reports vary on the extent of the enemy's hostility with some reports suggesting an untreated fatality rate of up to 60% after contact. Up to 18,000 allied soldiers experienced hostile contacts during WWII and more were experienced during the Korean and Vietnam Wars. Townsville soldiers were attacked as recently as 1996 and 1997. Thirty-six confirmed attacks occurred in Queensland in 2000, including civilian casualties. The real figure may be far higher.

Scrub Typhus

The first you will know that the enemy has contacted the soldiers under your care is when they present singly or worst case; soldier after soldier after soldier. They may present with sudden fever, chills, headache, backache, profuse sweating, vomiting and enlarged lymph nodes (Gormley 1996, McBride et al 1999). After the onset of fever, a skin ulcer may begin to develop at the site of the enemy's initial contact (Beers and Berkow 1999, Gale Research 1999). The ulcer is approximately 1 cm in diameter and fills with fluid, eventually rupturing and forming a black scab (eschar). Figure 1 shows an eschar. The incubation period for symptoms is between six to twenty one days from exposure. The fever rises during the first week, and may reach 40.5°C. Cough is present during the first week of fever and may worsen to pneumonitis. A red, spotted rash may develop five to eight days after the onset of fever and will rapidly fade, or become intensely coloured and raised. Lymphedema may also develop. Figure 2 shows the rash and lymphedema. If untreated, myocarditis and delirium may occur. High fever may continue for over two weeks. If death occurs, it is usually within two weeks of symptom onset and usually due to bacterial pneumonia, encephalitis or circulatory failure (Peterson and Miller, 1997 sheet).

Figure 1: A typical eschar.

Figure 2: Rash and lymphedema



(Stitt, A. and Nettles, T. Rickettsia. 1999)

As you can see, the enemy, known as Scrub Typhus, can be extremely hostile. Aliases include *Orientia tsutsugamushi* and *Rickettsia tsutsugamushi*. Scrub typhus is a bacterial disease transmitted by the bite of infected mites.

Ecology

Before we talk about management of scrub typhus, it is important to gather some thorough intelligence about the disease. As you all know, it is only through thoroughly understanding your enemy that you will be able to develop a strategic plan for eliminating that enemy or rendering him harmless. Detailed below is information on your enemy's location, lifestyle and habits.

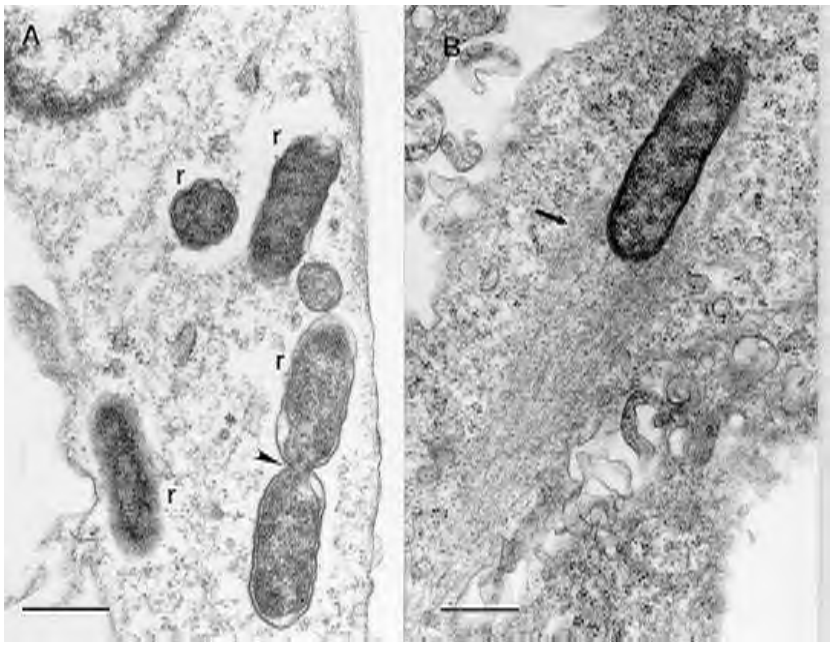
Figure 3: Location of scrub typhus in Australia (http://www.ianr.unl.edu/ianr/entomol/scrub_typhus_map_au.htm - Original image redrawn from Harwood, R. and James, M. Entomology in human and animal health. Macmillan, New York, 1979)

Scrub typhus has been found throughout Southeast Asia, the Western Pacific and the Northeast coast of Australia. Pockets of infestation have been found in the Northern Territory and Western Australia. Of particular local concern is the Cowley Beach Training area where two major outbreaks have occurred amongst soldiers (McBride et al 1999). Figure 3 details the geographical distribution of scrub typhus in Australia.

The disease is caused by a tiny organism known as *Orientia* (*Rickettsia*) *tsutsugamushi*. Figure 4 shows the *Rickettsia* within a cell. The last part of the name comes from two Japanese words; tsutsuga, meaning small and dangerous, and mushi, meaning creature (Gale Research 1999).

This is a simple but appropriate name for a parasite that has been reported to be fatal in up to sixty percent of cases. Scrub Typhus is propagated in a moderately complex relationship involving the *Rickettsia* bacterium, small forest marsupials and rodents, and *Leptotrombidium* mites. Humans are not normally part of this cycle, and are accidental hosts.

Figure 4: *Rickettsia* within a cell



(Stitt, A. and Nettles, T. Rickettsia. 1999)

The bacterium is an intracellular organism living and breeding within the cells of its host. Although it is difficult to isolate *R. tsutsugamushi* from the host cell, achieving this will allow a microscopic view of a long rod shaped organism (Gale Research 1999). The bacterium is of particular concern because it can bypass the body's defence system, white blood cells known as phagocytes. When attacked by a phagocyte, the bacterium will actually breed within the phagocyte. The host's body recognises *R. tsutsugamushi* as foreign particle and sends the phagocytes to destroy it. The phagocyte engulfs the *R. tsutsugamushi* and attempts to digest it, however the bacterium escapes and divides within the cell (Walker 1999). New *R. tsutsugamushi* cells escape from the cell back into the circulation to continue

the cycle. *R. tsutsugamushi* can also enter and reproduce in cells other than phagocytes. In humans, the majority of clinical symptoms arise from infection of vascular endothelial cells.

R. tsutsugamushi is usually carried by native marsupials and rodents and transmitted to and from parasitic larval mites (chiggers) of the *Leptotrombidium deliense* family when they feed on the animals. The newly infected host then becomes a new reservoir for *R. tsutsugamushi*. Spread of disease is dependent on mammalian hosts and will therefore present the greatest risk where concentrations of host animals are greatest (Traub and Wisseman 1974). Some of these regions can be highly localised and are called scrub typhus islands. Areas several hundred metres away may be relatively safe. Host animals will often tend to reside in regions with transitional or scrubby vegetation, hence the name scrub typhus. This vegetation is preferred as the scrub offers a safe harbour with ease of movement for the animals. The small marsupials and rodents will often shelter in unused buildings, and will approach camping areas to scavenge for food. These activities on the part of the host animals bring the mites into closer contact with humans.

The mites have a four-stage lifecycle: egg, larva, nymph and adult. The chigger (adult) phase (Figure 5) is the only stage that is parasitic on animals or humans, and hence infected mites are only dangerous at this point.

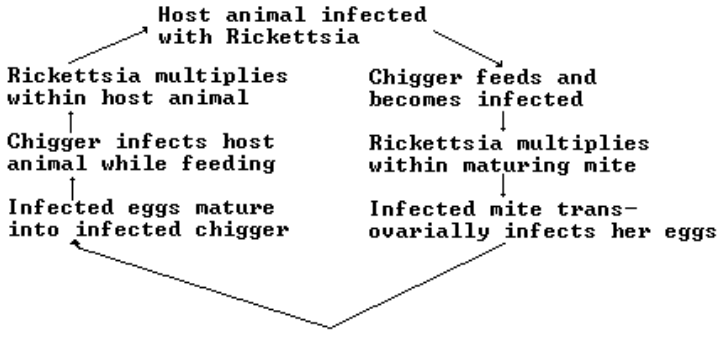
Figure 5: A microscopic view of a chigger (Photograph by D.E. Walter & C. Meacham)

Infected adult female mites transmit *R. tsutsugamushi* to their offspring in a process known as transovarial transmission. The female usually lays all of her eggs in one location only. This is a second reason that scrub typhus tends to localise in scrub typhus islands.

When the offspring reach the larval stage of development, they congregate on scrubby bushes and tall grass in order to attach themselves to passing animals. Chiggers are most commonly found in damper areas, out of direct sunlight. Previously cleared areas with scrubby regrowth, riverbanks and grassy regions provide optimal conditions for the chiggers to thrive (Gale Research 1999). These are often the areas where soldiers will perform their activities or camp for the night.

Once the chiggers have grasped a passing host, they prefer to feed near vulnerable areas of skin. This is usually where the skin is thin, tender or wrinkled. Chiggers also like areas where clothing is tight. Chiggers do not usually pierce the skin when feeding, preferring to insert their mouthparts down hair follicles or pores. Once attached, they inject a liquid that dissolves the tissue around the feeding site. This liquefied tissue is then sucked up as sustenance for the chigger (Koehler 1999). As large numbers of the *R. tsutsugamushi* organisms are found in the salivary glands of the chigger, they are injected into its host when it feeds. (Peterson and Miller 1997). After feeding, the engorged chigger will drop off its host, burrow into the ground and transform into the more mature nymphal version of the mite. Figure 6 explains the relationship between the disease, mite, and animal host.

Figure 6: *R. tsutsugamushi* ecology diagram



R.tsutsugamushi is injected into humans when bitten by the infected chiggers. It spreads widely via the blood stream of the infected soldier and attacks endothelial cells in the microcirculation. Damage to the small vessels in the skin gives a rash, in the lung gives pneumonitis and in the brain gives encephalitis.

Mechanism of exposure

Soldiers will be exposed to scrub typhus when they deploy to areas of endemic typhus infection; the scrub typhus islands mentioned previously. Cowley Beach training area is one such location. McBride et al (1999) have described two outbreaks amongst soldiers who have deployed in this area. The first involved 17 soldiers in 1996. This represented twenty-five percent of a group that had spent five days undertaking Infantry Minor Tactical (IMT) training. The second involved 11 soldiers, ten percent of a group that deployed in 1997. For the benefit of the hospital based medics, and those who have not gone 'bush' for a long time, I will describe the clothing and activities of soldiers whilst deployed for IMTs at Cowley Beach.

Clothing consists of DPCU 'cam' trousers and a long sleeved shirt. This clothing is dipped in a permethrin solution prior to departing for Cowley Beach. Sleeves are often buttoned closed, and the trouser legs are sealed against the boots with elastic straps. Long, thick socks are worn and the top of the socks is often folded over the top of the boots. Boots are leather and sealed. The newer boots have breathing holes in the base to allow water to enter whenever the soldier stands in a puddle! Boots come to just below mid-tibial height. A floppy bush hat is worn on the head. Whenever patrolling, the soldier will usually wear his webbing, a belt with shoulder straps holding his water and other basic equipment (Figures 7 and 8).

Figure 7: Typical 'bush' military dress (Photo by WO2 L. Green 2000. Used by permission of Lt T. Mayne SO3 PR, 3rd Brigade Public Affairs Office)

The Cowley Beach training area consists of coastal scrub, and a variety of drier grassy scrub and dense jungle. On initial deployment soldiers will transfer their equipment to their accommodation. This consists of old timber-framed weatherboard huts set in a grassy clearing. Most of the grass is closely mown, and thick coastal scrub surrounds the area. For several nights the soldiers will sleep under 'hoochies', small canvas shelters above a relatively flat patch of ground. Sleeping bags, if used, will be laid directly on the dirt.

During the day, soldiers will undertake various activities. Depending on environmental considerations, they may 'dig in'. This involves excavating shallow trenches to shelter from enemy fire. Soldiers will take turns on watch, sheltering in the pits and scanning the area for enemy activity.

Figure 8: Soldiers going to ground (Unknown photographer. Photo in public domain, 2000)

Patrols may be undertaken to search for signs of enemy activity or to march to a specified location. 'Contact drills' may be practiced in ambush situations, where soldiers will dive to the ground and roll to available shelter, else they may lay in wait while setting up their own ambushes (Figure 8). Practice at loading and unloading men and equipment may also be undertaken with army landing craft. Both work and leisure activity will generally involve close contact with the ground and associated shrubbery.

Clinical diagnosis

Initial presentation of scrub typhus may mimic a variety of febrile illnesses. Dengue fever and malaria are the most common differential diagnoses that spring to mind. Knowing that the affected soldier has recently been in geographical locations where scrub typhus occurs is one of the most significant clues. The maculopapular rash and eschar, if present, greatly assist in differential diagnosis. Definitive diagnosis is made by laboratory testing of blood samples.

Laboratory Diagnosis

Initial laboratory diagnosis may be difficult since antibody levels may be low during early infection, and there is a great diversity of antigenic strains (Panbio 1997). One of the most widely used tests is the Weil-Felix agglutination test. This test is based on the principle that antibodies developed during specific infections will react with certain strains of Proteus bacteria, causing them to clump together (Gale Research 1999). This clumping is known as agglutination and can be observed under a microscope. This test is inexpensive, easy to perform and is used widely. However, the Weil-Felix test lacks sensitivity and specificity (Panbio 1997), reacting to leptospirosis (often endemic in regions where scrub typhus is found) and assorted febrile illnesses. It is also not effective until the second week of fever.

The Dot ELISA offers a rapid diagnostic technique, however this also lacks sensitivity and specificity (Panbio 1997). The most accurate laboratory diagnosis is offered by indirect immunofluorescent antibody testing. This uses fluorescent markers that attach to antibodies formed during infection, allowing easy identification (Gale Research 1999). The main drawback of this technique is that specific antigenic 'tags' need to be available and a lack of them will hamper effective diagnosis. This was demonstrated several years ago by delayed recognition of an outbreak that occurred amongst soldiers who had been to the Cowley Beach training area (McBride et al 1999).

Control of scrub typhus

Control of scrub typhus can be considered in three phases: prevention, prophylactic treatment, and curative treatment once the disease is present. I will introduce control as recommended by various sources, and then I will describe current Army management as a comparison.

Prevention

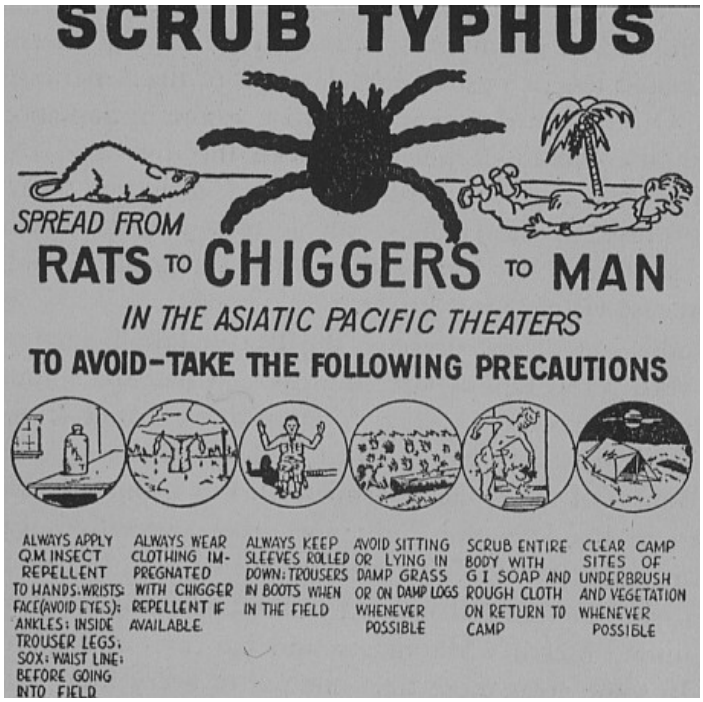
Prevention generally works best when a threat is perceived as real. The presence of potentially infected chiggers can easily be determined by placing a small piece of black cardboard edgewise on the ground (Koehler 1999). The chiggers will climb to the top of the card and congregate there. Tiny yellow or pink dots moving across the card will confirm the presence of the chiggers. The Northern Territory Health Service (NTHS) has published some preventative guidelines for people entering Litchfield Park, a scrub typhus endemic region. They suggest that people entering an exposed area wear closed in footwear such as boots with socks, and long trousers. Exposed areas of skin and clothing itself should be treated with mite repellents. Repellents containing DEET, dusting sulphur, dimethyl phthalate or benzyl benzoate have been suggested as suitable agents (Koehler 1999, Beers and Berkow 1999, NTHS scrub typhus pamphlet). Those people working in infested areas should consider impregnating clothing with permethrin. When sitting around or camping, groundcovers and tents with closed floors should be used (NTHS scrub typhus pamphlet).

If people are in one location for an extended period of time, area control of chiggers can be achieved by removing protective cover by clearing scrub and mowing grass short (Koehler 1999). The application of residual insecticides will help to reduce or eliminate local mite populations (Beers and Berkow 1999). Koehler (1999) suggested a number of commercial formulations containing pyrethrins and piperonyl butoxide as suitable to apply in camping areas. The NTHS suggests area application of any insecticide containing DEET. Koehler (1999) also suggests that lathering with soap in a hot bath or shower will remove both attached and unattached chiggers. Presumably, decreasing the chigger's feeding time can reduce the bacterial load transmitted, hence decreasing the potential for Scrub Typhus. Control of the rodent and marsupial reservoirs may also assist to prevent chiggers coming into areas where humans are living and working. Simple options such as sealing food containers and burying waste will help with this. The US Armed Forces produced interesting posters during World War II to assist troops deployed in scrub typhus endemic areas to avoid the disease (Figure 9).

Prophylactic treatment

Prophylactic treatment usually consists of dosing with broad-spectrum antibiotics. Several regimes have been recommended. Oral Chloramphenicol or Tetracycline given once every 5 days for thirty-five days (Gale Research 1999) or weekly doses of Doxycycline during and for 6 weeks after exposure (Walker 1999) have both been shown to be effective regimes. Resistance to antibiotics has been noted in several areas, therefore prophylaxis with antibiotics cannot be guaranteed. No effective vaccine has been developed for Scrub typhus.

Figure 9: Scrub Typhus poster developed by the American Armed Forces during WWII (public domain http://www.maldivesculture.com/maldives_scrub_typhus.html)



Treatment

Treatment for Scrub Typhus involves antibiotic therapy. Ponponratn et al (1996) showed that Tetracycline, a broad-spectrum antibiotic induced deleterious changes in *Rickettsia* organisms cultured from infected livers. These changes included depletion of essential organelles within the *Rickettsia*, and central vacuolation, mostly in dividing cells. Panpanich and Garner (2000) in a Cochrane review of antibiotics found that Tetracycline and Doxycycline were both effective treatments. One hundred mg of Doxycycline twice a day for a fortnight has been used successfully in soldiers infected at Cowley Beach (McBride et al 1999) and a soldier infected in Japan (Gormley 1996). Vig (2000) found that this dose was effective in most cases in a Northern Thailand trial, however 900 mg/day of Rifampicin for a week showed quicker recovery with no relapses. Four hundred mg of Chloramphenicol daily until the patient has been afebrile for 24 h may be as effective as tetracycline (Beers and Berkow 1999). Early treatment appears to universally show better outcomes and faster resolution than delayed treatment.

Implications for Lavarack Soldiers

In Northern Australia, soldiers routinely deploy for exercises in scrub typhus endemic areas and are therefore vulnerable to infection by the disease. We have seen current research and recommendations for preventing and treating the disease and will now look to apply it to soldiers.

To help soldiers realise the potential for the disease, a demonstration that chiggers are present will be useful. It may be helpful to carry a piece of black card as described previously. Check first that some are around before you do a public demonstration and damage your 'cred' (bush credibility)! If deploying to Cowley Beach, the grounds around the huts you initially stay in generally have the scrub cleared for a good distance with the lawns mown. It may pay to contact range control prior to deploying to see if this, and spraying, has been done recently. If deployed elsewhere, your Environmental Health Officer may be able to arrange necessary area control of chiggers. These actions will considerably lower the risk of encountering chiggers while located in one area. Do not forget basic hygiene. Burying waste and covering food will keep scavenging animals, potentially carrying infected chiggers, away from your living areas. I know that all the soldiers appreciate hot showers when they are available. Remind them to scrub well with soap and a cloth to help remove any chiggers that may have attached.

Lavarack soldiers deploying to known endemic areas are currently given 200mg of Doxycycline on the first and last day of deployment, and 200 mg every week they are in location. This period seems shorter than the literature suggests, however anecdotal evidence by unit doctors suggests this has been effective since being instituted after the last outbreak at Cowley Beach. 'Dipping sessions' are organised prior to soldiers deploying. All uniforms are dipped in a permethrin solution, and this practice should be continued. Treated uniforms constitute a large chemical and physical barrier against infected chigger bites. One important personal protective measure that should be implemented is to use repellents on exposed skin. The current army mosquito repellent contains DEET and should be spread over the soldiers' hands, faces, necks and feet. This is important, as soldiers will routinely be 'going to

ground' with their hands and faces brushing past foliage that may contain chiggers. Remember 3 D's: Dipping, Doxy, and DEET. These are essential, as when your soldiers are in the 'real' scrub area, area control may be impossible due to military and environmental considerations, and the only available protection will be personal measures.

If all else fails, and a soldier presents to you some time after exposure with fevers, rash etc., suspect scrub typhus in your differential diagnoses. Let the doctor know of your suspicion so that appropriate treatment can be implemented. Remember that outcomes are better with early treatment, and it may not be necessary to wait for a confirmed diagnosis before implementing antibiotic therapy. The current treatment approach of 100mg of Doxycycline twice daily for a fortnight seems to be effective and should be continued. Even though Rifampicin may be more potent, most of the Doctors here won't prescribe it due to unpleasant side effects. Bear in mind that the Rifampicin trial applied in areas where Doxycycline resistant scrub typhus is found. That is not yet the case here in Australia, but should be considered with overseas deployments. Although scrub typhus is not a notifiable disease, and comprehensive data is unavailable, the efficacy of Army management to date can be seen quite clearly. Despite large numbers of soldiers having worked in endemic areas, Area Health Service - North Queensland staff indicate that only two cases have been discovered to date this year.

The following is a summary of the 'take home' measures you should consider when dealing with scrub typhus.

- Establish the enemy's presence with black card. Show soldiers the chiggers.
- 3 D's. Doxy, dipping and DEET. These are personal preventative measures.
- Do not remove your uniform in the field. It constitutes a barrier.
- Clear scrub and keep grass short if possible. Spraying with insecticides helps as well
- Keep the rodents and marsupials away to limit chiggers spread. Basic food hygiene will help.
- If you have access to showers, wash well to remove chiggers.
- Recognise the symptoms of scrub typhus in order to institute early, appropriate treatment.

When it comes to scrub typhus, Army medics are the first line of defence for soldiers and failure to act will result in sickness and death. Recognise your enemy, understand his habits and weaknesses, be prepared, and you will defeat him. Good luck.

Acknowledgments

Russell Symons of the Queensland Rickettsial Reference Laboratory at Coopers Plains for providing details of the number of annual positive tests for Scrub Typhus.

Area Health Service – North Queensland for informing me of reported cases in Townsville.

Unit Medical Officers at Lavarack Barracks for background on incidence of scrub typhus, cases reported, and management practices for the disease.

Bibliography

Beers M and Berkow H (1999) Merck Manual of Diagnosis and Therapy. Whitehouse Station, NJ, USA.

Gale research (2000) Scrub typhus information page for Mylifepath. California Blue Shield. http://www.mylifepath.com/article/gale/100267397.

Gormley T (1996) A diagnosis of scrub typhus. Navy Medicine, 87: 20-22.

Koehler P (1999) ENY-212 Chiggers. Florida Cooperative Extension Service, Institute of Food and Agricultural Science, University of Florida.

McBride W, Taylor C, Pryor J and Simpson J (1999) Scrub typhus in North Queensland. Medical Journal of Australia, 170: 318-320.

NT Disease Control Centre (1999) Scrub typhus. Health information pamphlet for Litchfield Park, NT. Disease Control Centre, Northern Territory Health Service, Darwin.

Panpanich R and Garner P (2000) Antibiotics for treating scrub typhus. The Cochrane Library, Issue 2. Oxford: Update Software.

Peterson R and Miller G (1997) Insects, Disease, and History, University of Nebraska. http://www.ianr.unl.edu/ianr/entomol/history_bug.htm.

Pongponratn E, Rigantil M, Wilairatana P, Punpoowong B, Maneerat Y and Viriyavejakul P (1996) Pathology of *Rickettsia tsutsugamushi* infected liver after treatment with tetracycline: a case report. Fourteenth Annual Conference of the Electron Microscopy Society of Thailand, December 11-13. Oral presentation.

Panbio (1997) Scrub typhus. Scrub typhus fever technical information. Panbio website, http://www.panbio.com.au/scrubfever.htm.

Traub R and Wisseman C (1974) The ecology of chigger borne rickettsiosis. Journal of Medical Entomology, 11: 237-303.

Vig P (2000) Thai study: Rifampicin is more active than doxycycline against scrub typhus. Lancet, 356: 1057-1061.

Walker D (1999) Medical Microbiology, 4th edition. University of Texas Medical Branch, Galveston, Texas.

