

Diagnosis, management and prevention of infections in recently arrived refugees

Australasian Society for Infectious Diseases Writing Group

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Introduction

Australia and New Zealand have obligations under the 1951 Geneva Convention relating to the Status of Refugees and the 1967 Protocol Relating to the Status of Refugees to assist in the relocation of individuals who cannot live in their country of origin. Since 1955, more than half a million refugees and displaced individuals have been resettled in Australia, and at present approximately 13 000 individuals (of whom ~40% are children) are granted permanent residency status each year, mainly under the Offshore Resettlement (Refugee and Special Humanitarian) program.¹ New Zealand accepts 750 refugees identified by the United Nations High Commission on Refugees (“quota refugees”) for resettlement each year, in addition to a similar number of asylum seekers who arrive through independent channels.² Recently, the focus of the refugee intake in both Australia and New Zealand has shifted from those displaced by Cambodian and Vietnamese conflicts in the 1970s and the Kosovan crisis in the 1990s, to more recent conflict regions in sub-Saharan Africa, the Middle East and South/South-East Asia.

The Australian Government requires that refugees being considered for migration to Australia receive health checks prior to the issuing of a visa. This assessment includes screening for Human Immunodeficiency Virus (HIV) infection in those 15 years of age or over and for active tuberculosis (TB) infection by chest radiograph in those older than 11 years of age.³ Patients diagnosed with TB are treated prior to being eligible for a visa. Frequently, an additional pre-departure medical assessment (sometimes known as a “fitness to fly” assessment) is performed shortly before departure from the country of origin. Recently, testing for and treatment for malaria and presumptive treatment for helminth infection has been added to the pre-departure medical assessment for many sub-Saharan refugees. However, the pre-departure assessment is neither universal nor comprehensive, and is not intended to guarantee the health and safety of refugees following arrival in Australia.

The New Zealand government also performs offshore screening for HIV and active TB infection prior to the issuing of a visa to refugees (with a maximum of 20 HIV-infected refugees are accepted for resettlement per year), however pre-departure medical screening is not routinely performed. Since 1979, all “quota” refugee arrivals to New Zealand stay at the Mangere Refugee Resettlement Centre (MRRC) in Auckland for 6 weeks following arrival, where post-arrival comprehensive health assessments and other settlement support is provided.⁴

Presentations of recently arrived refugees to hospital emergency departments with acute infectious illnesses are not uncommon in regions or situations where refugees do not have access to timely and appropriate post-arrival health assessment. In addition, refugees carry a disproportionate burden of other chronic infectious diseases that may have been undiagnosed or untreated. Therefore, timely post-arrival screening of refugees for infectious diseases, as part of a more comprehensive health assessment, is clearly warranted.

In recent years, those who provide migrant and refugee health services have noted an increase in the number and variety of infectious diseases in newly arrived refugees, particularly in those resettling from Sub-Saharan Africa.^{4,5} These infections are often unfamiliar to non-specialist health care practitioners, as many of them (e.g. malaria and schistosomiasis) are not endemic to Australia or New Zealand. This has led to a degree of uncertainty and concern among refugees, health care providers and the wider community. Should we be routinely screening for infection in refugees? What tests should be performed? What should we do with the results? What about catch-up immunisations? Who should be funding these activities? In Australia, the States have developed their own responses to these challenges, with approaches varying from no or limited screening, to comprehensive screening for both common and rare infections.⁵⁻⁷ Rural practitioners working with refugees face additional

challenges, including lack of access to on-site interpreters, multidisciplinary refugee services and specialist tertiary services.

In late 2005, the Communicable Disease Network of Australia (CDNA) asked the Australasian Society of Infectious Diseases (ASID) to develop screening and treatment recommendations for infections in recently arrived African refugees to Australia, with the aim of providing practical assistance to general practitioners and others who provide healthcare services to these individuals. The key issues identified by the Writing Group were tuberculosis, malaria, blood-borne viruses (Human Immunodeficiency Virus, Hepatitis B virus and Hepatitis C virus), schistosomiasis, intestinal helminths, sexually transmissible infections (STIs), *Helicobacter pylori* infection and immunisation. Each section of these guidelines has been written by one or more experts in the field and subsequently peer-reviewed by one or more independent experts. Each section also includes discussion of issues specific to refugee children.

Newly arrived refugees have been through significant turmoil and upheaval. The post-arrival health assessment must therefore be sensitive to their feelings of cultural disorientation, vulnerability and sometimes fear and mistrust of authorities. We have recommended a screening approach *based on a single blood draw*, avoiding both routine collection of other specimens and multiple other blood tests wherever possible. Although there will continue to be differences in the way that local services will perform screening, we believe that these guidelines contain a balance between identifying important and treatable infections and over-investigation. Wherever possible, management recommendations are based on published evidence, however there is clearly a need for a broader evidence base to underpin the management of the complex health needs of newly resettled refugees.

These guidelines focus on infectious diseases. However assessment for infectious diseases should only be one part of such a comprehensive overall assessment, including psychological health, nutritional status, sexual and reproductive health, dental health, chronic disease, cancer screening and childhood growth and development, which are beyond the scope of these guidelines. In recognition of the inherent complexity and time required to undertake such an assessment in the general practice setting, in May 2006 the Commonwealth Government introduced Medicare Benefits Schedule item numbers 714 and 716 to provide reimbursement to general practitioners who perform refugee and humanitarian entrant health assessments.⁸ In addition, there are a number of organisations which provide resources for broader issues of refugee health (see table 1). It is important to note that unless the refugees' visa was granted contingent on a specific health undertaking, assessment and screening is offered on a voluntary basis. Refugees should be informed that they may choose which conditions they are screened for and informed consent should be obtained from patients or carers as appropriate.

These guidelines were written primarily for refugees originating from sub-Saharan Africa and arriving in Australia. They may also be useful to less experienced practitioners in the management of non-refugee migrants from these regions. They do not necessarily apply to refugee populations from other regions, however many of the recommendations (e.g. those concerning tuberculosis, blood-borne viruses, STIs, *Helicobacter pylori* and immunisation) will be applicable to refugees arriving from most regions of conflict.

Refugee health assessments should always be undertaken with an appropriate interpreter. In practice, having an interpreter present will usually ease many difficulties that are encountered when discussing past history. In some situations, such as relatively small language groups and regional and rural communities, where the interpreter may be known to the patient personally, a telephone interpreter may

be more appropriate. The Australian Government provides a Telephone Interpreting Service (TIS), which is available *free of charge* to practitioners in private practice who provide a Medicare service to permanent residents who do not speak English. The TIS Doctors' Priority Line (1300 131 450) should be used to access this service. Interpreters may be arranged in advance, ensuring that an interpreter for the specific language is available for the consultation session, although the TIS will often be able to find an appropriate interpreter within a few minutes. Gender issues should also be taken into consideration when working with interpreters, particularly in regard to women's health.

These guidelines are current as of mid-2008, but may require amendment as the health needs of refugees evolve and regions of conflict change. The desktop guide (page may be printed separately and used as a quick guide to tests that should be considered as a part of the initial refugee health assessment. General practitioners and others working in refugee health should make themselves aware of local referral services and what they provide, particularly in regard to infectious diseases, paediatric and psychological services.

We hope you find these guidelines helpful and we welcome any feedback and suggestions for future updates.

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On behalf of the Australasian Society for Infectious Diseases Writing Group

Table 1. Key refugee health resources and services

state	Service	Contact details
NSW	New South Wales Refugee Health Service	phone: 02 8778 0770 http://www.refugeehealth.org.au/
VIC	Asylum Seeker Resource Centre West Melbourne Health Centre	phone: 03 9326 6033 www.asrc.org.au/
	Dandenong Community Health Centre Asylum Seeker Clinic	phone: 03 8792 2200
	Victorian Infectious Diseases Service (Adults) Royal Melbourne Hospital Immigration/Refugee Clinic	phone: 03 9342 7212
	International and Immigrant Health Group University of Melbourne, Department of Medicine Royal Melbourne Hospital	www.internationalhealth.unimelb.edu.au/
	Royal Children's Hospital (Children) Immigrant Health Clinic	phone: 03 9345 5522 www.rch.org.au/immigranthealth/index.cfm?doc_id=10575
	North Richmond Community Health Centre Multicultural Health and Support Service (MHSS)	phone: 03 9342 9700 www.nrhc.com.au/nrhc/programs/mhss.html
	Victorian Transcultural Psychiatry Unit (VTPU) 03 9288 3300	www.vtpu.org.au/
	The Victorian Foundation for Survivors for Torture (Foundation House) Brunswick	phone: 03 9388 0022
	Dandenong	phone: 03 8791 2450 www.foundationhouse.org.au
	Dandenong Hospital Refugee Health Clinic	phone: 03 9554 1000
	Asylum Seeker GP Clinic	phone: 03 8792 2200
	Refugee Health and Wellbeing Action Plan: Current and future initiatives 2005-2008	www.dhs.vic.gov.au/multicultural/html/refugee_action.htm
QLD	Queensland Integrated Refugee Community Health Clinic (QIRCH)	phone: 07 3480 2880 http://www.qpastt.org.au/projects/qirch

	<p>Queensland Program of Assistance to Survivors of Torture and Trauma (QPASTT)</p> <p>Brisbane Actionweb for Refugee Collaboration</p>	<p>phone: 07 3391 6677 http://www.qpastt.org.au/home</p> <p>http://www.barc.org.au/cms/</p>
WA	<p>WA Migrant Health Unit</p> <p>Association for Services to Torture and Trauma Survivors (ASeTTS)</p> <p>Paediatric Refugee Health Clinic, Princess Margaret Hospital for Children</p> <p>Western Australian Refugee Health Network</p>	<p>phone: 08 9219 3222 email: migranthealth@health.wa.gov.au</p> <p>http://www.asetts.org.au/</p> <p>phone: 08 9340 8222</p> <p>http://www.warhn.org/</p>
SA	SA Migrant Health Service	phone: 08 8237 3900
NT	<p>TB/Leprosy Unit Centre for Disease Control Royal Darwin Hospital</p> <p>Melaleuca Refugee Centre</p>	<p>phone: 08 8922 8804</p> <p>phone: 08 8985 3311</p>
TAS	<p>Migrant Resource Centre (Southern Tasmania)</p> <p>Migrant Resource Centre (Northern Tasmania)</p> <p>Royal Hobart Hospital Refugee Health Clinic</p>	<p>phone: 03 6234 9411 http://www.mrchobart.org.au/</p> <p>phone: (03) 6331 2300 http://mrcltn.org.au/</p>
ACT	<p>Companion House Caring for Torture and Trauma Survivors</p> <p>Companion House Medical Service</p>	<p>phone: 02 6247 7227 http://www.companionhouse.org.au/</p> <p>phone: 02 6247 7227</p>
All states	<p>Telephone Interpreter Service (Doctor's Priority Line: available 24h a day, 7 days a week)</p>	<p>phone: 1300 131 450 http://www.immi.gov.au/living-in-australia/help-with-english/help_with_translating/english-speakers/index.htm</p>
	The Forum of Australian Services for Survivors of Torture and Trauma (FASSTT)	<p>phone: 03 9389 8932 http://www.fasstt.org.au/home/index.php</p>

Recommendations for the diagnosis, treatment and prevention of infections in newly arrived refugees

Recommended screening test*	Action
Blood borne viruses	
HIV serology	If positive <ul style="list-style-type: none"> refer to local HIV service advise of transmission risk ensure TB screening has been performed
Hepatitis B serology (sAg/sAb/cAb)	If HBsAg positive <ul style="list-style-type: none"> request HBeAg & liver function tests (LFTs) if HBeAg positive or LFTs abnormal, refer to local hepatitis service advise of transmission risk immunise all non-immune household contacts
Hepatitis C serology	If positive <ul style="list-style-type: none"> request LFTs and HCV RNA advise of transmission risk If LFT abnormal and/or HCV RNA detected, refer to local hepatitis service
Helminths	
Strongyloides serology	If positive <ul style="list-style-type: none"> ivermectin 200 µg/kg PO as a single dose, repeated 14 days following first dose
Faeces microscopy	If <5 yrs, do not give ivermectin; refer to paediatric infectious diseases service If readily obtainable, faeces microscopy followed by directed treatment. If faeces not readily obtainable: <i>no documented pre-departure albendazole therapy:</i> <ul style="list-style-type: none"> empiric single-dose albendazole, FBC in 8 weeks; if eosinophilia still present, Ix
Full blood count (FBC)	<i>documented pre-departure albendazole therapy:</i> <ul style="list-style-type: none"> no eosinophilia: no further treatment or follow-up eosinophilia: repeat FBC in 8 weeks if eosinophilia still present, Ix
Malaria	
Malaria thick / thin film and <i>P. falciparum</i> antigen	If positive <ul style="list-style-type: none"> refer to local infectious diseases service for management. patients with confirmed <i>P. falciparum</i> infection require urgent assessment
Schistosomiasis	
<i>Schistosoma</i> serology	If positive <ul style="list-style-type: none"> obtain stool and urine for ova examination praziquantel 20mg/kg, 2 doses 4 hours apart (30mg/kg if acquired in SE Asia) refer patients with chronic liver disease (including viral hepatitis) or symptoms for further assessment
Syphilis	
Syphilis serology	If positive <ul style="list-style-type: none"> review history including previous treatment treat as per local guidelines discuss all children with positive syphilis serology with paediatric infectious diseases service
Tuberculosis	
Mantoux test or interferon-gamma release assay	If positive <ul style="list-style-type: none"> refer to local tuberculosis service
Other infections	
<i>Helicobacter pylori</i>	Indications for testing Adults with suspected peptic ulcer disease <ul style="list-style-type: none"> Non-invasive tests (eg stool antigen, urea breath test or serology) Children with anorexia, poor weight gain or failure to thrive should be referred to a paediatric migrant health service for assessment
Uncommon infections (eg filariasis, tungiasis)	Discussion, with or referral to, an adult or paediatric infectious disease specialist recommended
Sexually transmitted infections	See guidelines
Catchup immunisations –all ages	
IPV, ADT, DTPa, MMR, Hepatitis B	See guidelines

*Note that only infectious diseases screening tests are detailed here. For additional suggested screening investigations, refer to local protocols or contact the state or territory refugee health service

Tuberculosis

Recommendations

With the exception of those with documented past tuberculosis (TB) disease, all newly arrived refugees, including children, should be assessed for latent TB infection (LTBI) within 2 months of arrival, with the following plan:

- Testing is performed with the intention to treat
- Refer those with a positive Mantoux test result (according to national or local guidelines) or a positive blood-based interferon- γ release assay (IGRA) test to the local TB services, for consideration of exclusion of TB disease and/or treatment of latent TB infection (LTBI). In general, a Mantoux of $\geq 10\text{mm}$ in adults and children ≥ 5 years of age and a Mantoux of $\geq 5\text{mm}$ in those younger than 5 years or those who are HIV-infected warrants specialist referral. Refugees known to be HIV-infected should have a 2-step Mantoux test. In the event that the second test remains $<5\text{mm}$, specialist advice should be sought from TB/HIV services.
- TB (active disease or latent infection) should be managed by clinicians experienced in doing so as part of a centralised, coordinated TB service.

Background

Tuberculosis is a relatively uncommon infection in Australia. This is contrast to many of the countries where refugees originate from or flee to. In countries with political turmoil and war, national health infrastructure is very often markedly compromised; in these circumstances, TB disease frequently goes undetected and under-reported. In addition, the formation of refugee camps results in large groups of people from countries of high TB prevalence living very closely together. This situation, combined with the ongoing African HIV pandemic has amplified the emergence of TB disease in sub-Saharan Africa.

In 2005, the overall incidence of active TB disease in Australia was 5.3/100 000.¹¹ However the incidence of TB disease amongst those born overseas has been slowly but consistently rising, with a rate of 18/100 000 in 2000 and 20.6/100 000 in 2005; this compares to rates in the Australian-born population of 1.6 and 0.8/100 000 respectively. Sudan, Somalia and Ethiopia have recently been added to the list of countries with the highest TB notifications by country of birth for those notified in Australia as overseas-born.⁹ In 2005, 26% of all overseas-born notifications of TB disease occurred within 2 years of arrival in Australia. In children under 15 years, the rate of TB disease in Indigenous Australians was 0.6 per 100,000 (1 case), the non-Indigenous Australian born rate was 0.7 per 100 000 and the overseas born rate was 18.0 per 100 000.⁹

Other developed countries receiving large numbers of refugees, such as Norway, the United Kingdom and the Netherlands, endeavour to screen migrants for latent tuberculosis infection (LTBI) and offer treatment, with varying levels of success.¹⁰ Canada has also actively advocated screening and LTBI treatment.¹¹ The United States also recognises the importance of LTBI treatment and includes recently arrived refugees in the top priority list for screening and treatment.¹² Rates of active

TB in foreign-born persons in the USA are 21.5/100 000, with the majority of cases occurring in the first 2 years after immigration¹³. For example, in the USA, people from Ethiopia have a rate of active TB of 1515/100 000 in the first year after arrival and 159/100 000 overall,¹³ compared to a rate of 2.7/100 000 in US-born people. Post-arrival screening and LTBI treatment in refugees has been shown to be a cost-effective measure, due to the prevention of TB transmission in the community and numbers of cases and deaths from TB averted.¹⁴ Australia's National Tuberculosis Advisory Committee (NTAC) strongly supports such an approach.⁹

Pre-departure screening

All refugee migrants and special humanitarian visa holders over 11 years of age are screened for active TB disease at the time of visa application, which can occur 6 – 9 months prior to departure. The visa is only issued if active TB is excluded (i.e. chest X-ray and clinical examination exclude active disease). The applicant is not screened for LTBI. If it has been more than 6 months since the chest X-ray until the time of departure the chest X-ray is repeated. If active TB is detected, then the visa is denied until the applicant has completed a suitable course of TB treatment locally. The applicant can then reapply for a humanitarian visa. In the event that the visa is granted, the applicant may be placed on a TB 'health undertaking', which means they must present to local TB services within 4 weeks of arrival in Australia.

In some countries, refugees are offered pre-departure screening for symptoms of active TB disease as part of the process just prior to flight. However the process does not include a chest X-ray, does not screen for LTBI, nor does it screen children.

Post-arrival screening

All newly arrived refugees should have screening for LTBI, ideally within 2 months of arrival. If refugees have acquired their TB infection in the months or year just prior to arriving in Australia (eg in crowded refugee camps) then it is the first 2 years in Australia that they are most at risk of progressing to active TB –and every month that passes without LTBI being identified and treated is an important lost opportunity. This is especially true for children (especially those <3 years), who by definition have been infected relatively recently. The current recommended screening test is the Mantoux test, although some states (e.g. Western Australia) are using blood tests known as interferon gamma release assays in those over 2 years of age instead of Mantoux testing (see below). Those that test positive i.e. induration of $\geq 10\text{mm}$ (and $\geq 5\text{mm}$ in children under 5 years and HIV positive or immunosuppressed refugees) should be referred to local TB services for chest x-ray and evaluation and where appropriate strongly encouraged to have LTBI treatment unless this is contraindicated. Refugees known to be HIV-infected should have a 2-step Mantoux test. In the event that the second test remains $<5\text{mm}$, specialist advice should be sought from TB/HIV services.

The role of interferon-gamma release assays (IGRAs) in the diagnosis of latent tuberculosis infection

In vitro T-cell based interferon- γ release assays (IGRAs) are marketed as a substitute for the Mantoux test for the detection of LTBI. Data suggest that IGRAs using RD1 antigens are more specific and have less cross-reactivity with previous BCG immunisation or exposure to non-tuberculous mycobacteria, potentially offering distinct advantages for the detection of LTBI.^{15,16} However the assessment of IGRAs in differing environments and countries is complicated by the lack of any “gold standard” for diagnosing LTBI (as opposed to active tuberculosis). Currently, there is inadequate data on the use of IGRAs in certain sub-populations such as immunocompromised patients, children and populations from TB-endemic

countries.¹⁶ In addition, IGRAs require blood collection, which can in some instances be more problematic than Mantoux testing in children and the specimen needs to arrive in an appropriate laboratory within 12-16 hours. At present, the Mantoux test remains the preferred method of investigation for LTBI pending further evaluation of IGRAs. However, it is recognised that IGRAs are currently used for LTBI screening in some jurisdictions and may be used more widely in the future. A patient with a positive IGRA test result should be referred to the local TB services for consideration of latent LTBI treatment. NTAC regularly reviews the use of IGRAs and publishes its Position Statements at www.health.gov.au/ntac.

Treatment of latent tuberculosis infection

Treatment of LTBI has been shown to significantly reduce the individual risk of subsequent TB disease. High risk groups for developing active TB are those under 5 years of age, those who are HIV infected and those with signs of previous TB infection on chest X-ray that have never been treated. Those aged 15 – 34 years are also at increased risk. It is vital that these groups in particular have access to screening, as their lifetime risk for developing TB is high. The lifetime risk of TB reactivation for immigrant children less than 5 years of age has been estimated to be 17% and those with HIV infection to be 100%.¹⁷

Most published recommendations advocate 6-9 months of isoniazid for the treatment of LTBI.^{13,18} Latent TB infection treatment is only undertaken when active disease is excluded and should be undertaken by specialised TB units or specialist physicians with considerable experience in the management of TB.

In a study of a school-based programme for LTBI screening and treatment, an independent predictor of LTBI treatment compliance was having ≥ 2 family members

screened and treated at the same time.¹⁹ Therefore, where possible, it is worthwhile screening and treating entire families contemporaneously.

Special considerations in paediatric refugees

Children who are infected with TB have almost always been infected from an adult with pulmonary or laryngeal TB disease. Often this is a household contact or family member, but in crowded refugee camps, transmission outside the household may occur.²⁰ Following exposure, children may develop either LTBI or uncontrolled primary infection. The risk of developing TB disease following exposure is greatest in younger children and in the 12-18 months following exposure.²¹ Young children also have the greatest risk of developing extra-pulmonary TB, including TB meningitis.²² Therefore, TB (both LTBI and TB disease) is an important diagnosis in refugee children.

All refugee children should be screened for TB. There are currently only limited data on IGRA tests in young children, in whom they appear to be less sensitive.^{20,23} Clinical signs of TB disease are often subtle in children and include chronic cough, malaise and weight loss or failure to thrive.²⁴

The investigation and treatment of TB in children should be undertaken by those with the experience and resources to do so. Management of all infected family or household members by the same service is recommended.

Malaria

Recommendations

- All refugees should be tested for malaria after arrival in Australia, other than those who have never resided in or travelled through a malarious region.
- This includes those individuals who have had documented testing and / or treatment for malaria at the time of pre-departure assessment.

Epidemiology

Malaria is one of the world's most important public health challenges. It causes hundreds of millions of infections and an estimated one million deaths per year worldwide, many of which occur in children.²⁵ Four species of human malarial parasites are recognised, of which *Plasmodium falciparum* is both the most common and the most dangerous.

Sub-Saharan Africa bears a significant proportion of the worldwide burden of malaria. It is the leading cause of morbidity and mortality in many countries from which African refugees either originate, or are resident in, prior to migration to Australia. For example, 20-30% of all outpatient attendances and 30% of hospital admissions in Sudan are for malaria, whereas in Uganda, a frequent country of refuge for displaced Sudanese migrants, malaria is responsible for 40% of all hospital admissions, 25% of hospital admissions and 14% of all deaths.²⁶ In addition, asymptomatic malaria infection is common in many African countries, particularly in adults.

The intensity and seasonality of malaria transmission varies significantly both within and between countries in the region and thus risk of malaria will vary between geographical locations, the age and ethnicity of the migrant and the time of the year. Refugees arriving in Australia from malaria-endemic countries may have had screening for and/or treatment of malaria at some stage prior to departure. However documentation of treatment may be unreliable or non-existent, the agents used may not be optimal, and re-infection may occur if treatment is not administered shortly prior to departure.²⁷

Rationale for screening

In a recent study of almost 2 000 adult African refugee migrants presenting for health screening after arrival in Western Australia, 3.5% were diagnosed with malaria. The majority of these infections were caused by *Plasmodium falciparum* and were either asymptomatic or minimally symptomatic.²⁸ Importantly however, immunity to malaria can wane, and thus subsequent symptomatic disease or persistent parasitaemia may present many years after arrival in Australia.²⁹ In children, in whom anti-disease immunity is often incomplete and malaria may be life-threatening, screening and treatment of malaria is extremely important.

Australia was declared free from endemic malaria in 1981, however much of Australia above latitude 19°S remains receptive to malaria due to the presence of patent mosquito vectors (*Anopheles* spp).³⁰ Malaria transmission in Australia due to re-introduction of infection into a receptive area has occurred on more than one occasion since 1981 and is a constant threat to this “malaria-free” status.^{31,32} Therefore, the detection and treatment of malaria in individuals arriving into Australia from malaria-endemic areas is of significant public health importance. We recommend that all refugees migrating from malaria-endemic regions should be screened for malaria as soon as possible after arrival and treated if found to be infected.

Diagnosis

The “gold standard” test for the diagnosis of malaria remains the thick and thin blood film examination for malaria parasites by light microscopy. This test is widely available throughout Australia, although the quality of diagnosis can vary greatly between laboratories. Hence, rapid diagnostic tests (RDT) that detect antigens of *Plasmodium* spp. are also frequently used in Australian laboratories to supplement

blood film examination. There are several RDTs available, but the most commonly used in clinical practice detect only *P. falciparum* infection. A combination of blood films and RDT has relatively high sensitivity for the detection of *P. falciparum* infection and is therefore recommended for initial screening. If malarial parasites are detected on thick and / or thin films, they should be characterised and quantitated whenever possible. Mixed infections with more than one *Plasmodium* spp. are not infrequent.²⁸ If the species of *Plasmodium* cannot be confidently identified by microscopy, detection of *Plasmodium* DNA in blood by polymerase chain reaction (PCR) can be performed,³¹ but this test is not widely available at present. If a patient has symptoms consistent with malaria but negative initial blood films and / or RDT result, a minimum of 2 repeat blood films, should be performed in an attempt to demonstrate malarial parasites and (if available) a *Plasmodium* spp. PCR test may also be useful in this setting.³³

Management

***Plasmodium falciparum* malaria**

Uncomplicated infection

All patients with falciparum malaria should be referred to physician with experience in the management of malaria. Children with malaria may deteriorate quickly, even if asymptomatic and should be referred urgently, ideally to a paediatric infectious diseases physician.

Patients with asymptomatic or uncomplicated falciparum malaria who are able to tolerate oral medication should be treated with oral antimalarial therapy. Factors that will influence the choice of therapy in this population include the species of infection,

efficacy and toxicity profile of the drug and age and pregnancy status of the patient. Current Australian and WHO guidelines for the treatment of uncomplicated falciparum malaria recommend the use of artemisinin-based combination therapy (ACT) in uncomplicated *P. falciparum* infection.^{25,34} This recommendation is primarily intended to counter the growing threat of antimalarial resistance and to optimize treatment outcomes, particularly in malaria-endemic regions. The only ACT product available in Australia at present is artemether-lumefantrine (Riamet®). Artemether-lumefantrine is a fixed dosed combination regimen that is effective against all species of Plasmodia including that acquired in areas with high prevalence of multidrug resistance. In general, more than 95% of people have cleared their parasites and are afebrile within 48 hours following treatment. Furthermore in malaria-receptive regions, the artemisinin derivative (artemether) has activity against gametocytes, therefore reducing the duration of infectivity for local vectors and the likelihood of local transmission. However the dosing schedule of artemether-lumefantrine is complex (see table) and needs to be carefully explained to the patient to maximize compliance. Ideally, therapy should be directly supervised by healthcare staff. Importantly the bioavailability of lumefantrine varies considerably during acute disease. To ensure adequate drug levels tablets should be taken with a small fatty meal, such as a biscuit or glass of milk.

Alternative treatment options include atovaquone-proguanil (Malarone®), mefloquine (Lariam®), or quinine sulphate plus doxycycline (doxycycline should only be used in those >8 years of age). Atovaquone-proguanil and mefloquine are effective treatments for falciparum malaria acquired in Africa, however there have been occasional reports of therapy failures and resistance. These agents have the advantage of relatively simple dosing regimens. Mefloquine is contraindicated in individuals with a history of neuropsychiatric illness or epilepsy. Treatment with quinine sulphate and doxycycline has the disadvantage of a longer dosing period (7 days) and frequent side effects (cinchonism with quinine, photosensitivity and

mucocutaneous candidiasis with doxycycline, which should also be avoided in young children).

Current Australia recommendations suggest that all patients with falciparum malaria should be admitted to hospital, at least for the initial part of their treatment.³⁴ However, individuals with non-severe malaria infection in malaria-endemic regions are usually treated entirely as outpatients.²⁵ A recent study reported on a cohort of 57 adult African refugees diagnosed with asymptomatic or non-severe malaria after arriving in Western Australia. The majority of patients were treated as outpatients, following supervised administration of the first dose of antimalarials in hospital. No treatment failures were noted, and although the findings are limited by the relatively small size and non-controlled, retrospective design, this study suggests that this approach may be safe and effective in this low-risk population.²⁸ A similar study in 90 African refugee children with falciparum malaria showed that with careful patient selection, some children could be managed in ambulatory paediatric care.³⁵

Careful instructions regarding dosing schedules, side effects and what action to take if therapy is not tolerated or the patient deteriorates, should be given to the patient or their guardian, in a language they understand. It is particularly important that the family are able to access emergency hospital care if necessary. Mosquito avoidance measures (e.g. bed nets, insect screens on windows and doors, long sleeves, DEET-based insect repellent and avoidance of outdoor activity at dawn and dusk) should be instituted in individuals with malaria infection who reside in malaria-receptive areas. In such areas, patients are admitted to hospital if gametocytes are present on the blood film.

Complicated infection

All patients with malaria who have symptoms and/or signs of severe malaria (see table) or are unable to tolerate oral medication should be urgently referred to an Infectious Diseases Physician at a tertiary hospital for treatment. Options for treatment include intravenous artesunate or intravenous quinine (plus oral doxycycline). A recent large randomized controlled trial demonstrated that artesunate was superior to quinine sulphate and doxycycline for the treatment of complicated falciparum malaria in South East Asia;³⁶ this effect is likely to be the same for patients with severe malaria acquired in Africa, although studies addressing this are ongoing. Due to manufacturing and regulation issues, the availability of artesunate in Australia is limited at present; access is via the Specialised Access Scheme through tertiary hospital pharmacies.

***P. vivax*, *P. ovale* and *P. malariae* infection**

Chloroquine is the treatment of choice for infection caused by *P. vivax*, *P. ovale* and *P. malariae* (see table). Chloroquine resistance (CQR) in these *Plasmodium* species has not been described in Africa, although significant CQR in *P. vivax* is prevalent in Indonesia, Papua and East Timor. Antimalarial agents used in the treatment of falciparum malaria (e.g. doxycycline, artemether-lumefantrine, atovaquone-proguanil, mefloquine) are also efficacious against these *Plasmodium* species, therefore chloroquine does not need to be added to therapy for patients with mixed falciparum infection to clear the asexual stages. Hypnozoite eradication therapy (or “radical cure”) should be attempted in patients with *P. vivax* or *P. ovale* infection, to reduce the likelihood of subsequent relapses. Primaquine is the agent of choice for hypnozoite eradication with alternative agents limited; tafenoquine and bulaquine are under development but not currently available in Australia. Eradication therapy with primaquine is not always effective; furthermore, in individuals with glucose-6 phosphate (G6PD) deficiency, administration of primaquine causes red blood cell

haemolysis of varying severity. Therefore, individuals should be screened for G6PD deficiency prior to receiving primaquine; those with severe deficiency should not receive the drug, whereas those with mild deficiency can be treated with reduced doses with careful monitoring.

Pregnancy

Pregnant women with malaria are at increased risk for severe malaria, severe anaemia and delivery of a low birth weight infant. Antimalarials considered safe in all stages of pregnancy include quinine sulphate, chloroquine, proguanil (but not atovaquone), clindamycin, pyrimethamine and sulphadoxine. No adverse foetal outcomes have been observed in over 1000 patients treated with artemisinin derivatives in the second and third trimester of pregnancy. The WHO have recommended that ACT are considered suitable alternatives to quinine sulphate in the later stages of pregnancy, however there is little safety data available for lumefantrine.²⁵ Thus we recommend the combination of quinine and clindamycin for pregnant patients. This should, at least initially, be given as supervised inpatient therapy.

Post-treatment follow-up

Patients should be assessed one month post-treatment and have follow up blood films performed to ensure the infection has been successfully treated, as recrudescence / relapses can occur despite initial eradication of infection and full compliance. Rapid diagnostic tests and PCR should not be used for this purpose, as they may remain positive for several weeks after successful treatment. Patients with *P. vivax* or *P. ovale* infection should be advised that recurrence of infection may occur and to represent for treatment if symptoms develop.

Table 2. Diagnosis and treatment of malaria in African refugees

<p>Tests</p> <ul style="list-style-type: none">• Thick and thin film• Malaria rapid diagnostic test (RDT) or antigen detection test ^a
<p>Treatment</p> <p><i>P. falciparum</i></p> <p>Adult with asymptomatic or minimal symptoms, not pregnant, no indicators of severe malaria^b AND likely to be adherent with oral therapy</p> <p>artemether-lumefantrine 20mg + 120mg : 4 tablets with fatty food at 0, 8, 24, 36, 48 and 60h (i.e. 24 tablets in 6 doses)</p> <p>or</p> <p>atovaquone / proguanil 250 + 100mg: 4 tablets with fatty food, daily for three days</p> <p>or</p> <p>mefloquine 750mg, followed by 500mg 8-12 hours later</p> <p>or</p> <p>quinine sulphate 600mg three times daily PLUS either doxycycline 100mg twice daily or clindamycin 300mg three times daily for 7 days</p> <p>Pregnancy:</p> <p>quinine sulphate 600mg three times daily for 7 days PLUS clindamycin 300mg three times daily for 7 days</p> <p>Children:</p> <p>assess need for admission on individual basis or on local protocols.</p> <p>atovaquone-proguanil (dosage by body weight) with fatty food daily for three days.</p> <p>or</p> <p>artemether-lumefantrine (dosage by body weight) is an alternative, taken with fatty food, although dosing schedule is more complex and treatment may need to be supervised.</p> <p>Severe falciparum malaria^b:</p> <p>Refer urgently to Infectious Diseases Physician for further inpatient management</p> <p><i>P. ovale, P. vivax or P. malariae</i></p> <p>chloroquine 620mg base (4 tablets) initially, then 310mg (2 tablets) at 6h, 24h,</p>

48h (total of 10 tablets)

Hypnozoite eradication therapy (*P. vivax*, *P. ovale*)

primaquine

<50kg: 0.3-0.5mg/kg/day (in one or two doses) for 14 days^c

>50kg: 15mg daily PO (*P.ovale*) or 30mg daily PO (*P.vivax*) for 14 days

- a. A variety of RDTs are available, which may detect *P. falciparum* antigen, or both *P. falciparum* and *P. vivax* antigens. Refer to local laboratory for details. RDTs can remain positive for several weeks after successful therapy.
- b. WHO criteria for severe malaria: altered consciousness, jaundice, oliguria, severe anaemia or hypoglycemia, parasite count >100 000/ μ L or >2%, or patient vomiting or clinically acidotic
- c. exclude G6PD deficiency prior to administering primaquine

Blood-borne viral infections (Human immunodeficiency virus[HIV], hepatitis B[HBV] and hepatitis C[HCV])

Recommendations

- Screening for HIV, hepatitis B and hepatitis C infection should be offered to all refugees.
- All screening tests should be performed with the knowledge and informed consent of the individual or their legal guardian.
- Discussion of these screening tests and communication of results must be carried out with utmost respect for the privacy of the individual.
- Practitioners should explicitly state their obligations to protect patient confidentiality, but also their obligation to notify the relevant authorities of the diagnosis.
- Practitioners should explain that the results of screening tests do not have adverse implications for the refugees' status as Australian residents.
- Testing the mother for HIV infection should not be used *in lieu* of direct testing of the child.

Epidemiology

Many refugees who settle in Australia originate from, or have transited through countries with a high prevalence of blood-borne viral infections. Such regions include sub-Saharan Africa, South East Asia, Papua New Guinea and parts of Central Asia, Eastern Europe, the Caribbean and Latin America. The conditions of conflict and temporary refuge may increase the exposure of refugees to blood borne and other infections.^{37, 38}

Human Immunodeficiency Virus (HIV)

The current estimated prevalence of HIV infection in Australian adults is <0.1%. Over 70% of people living with HIV in Australia are men who acquired the infection through homosexual sex, but in recent years, an increasing number of people diagnosed with HIV infection have been heterosexual men and women born in regions of high HIV prevalence, such as sub-Saharan Africa. Among these are people who have arrived as refugees.^{37, 39}

Current Australian immigration policy requires applicants for a permanent residency visa to pass a health requirement before being granted a visa. Part of the medical assessment is a test for HIV infection. In Australia, a combined HIV antibody/antigen test is used, but if testing is performed abroad, an antibody-only test may be used. The test is required for applicants aged 15 years and over, children for adoption and (less commonly) people with a specific risk factor for HIV infection such as a history of blood transfusion.^{4,40} Applicants with a positive HIV test result generally fail the health requirement, however a history of HIV testing as part of pre-migration medical assessment does not exclude the possibility of HIV infection in a newly arrived refugee. Some refugees applying for a visa are granted a waiver of the health requirement, but there are no formal arrangements in place between DIAC and the

health departments of the states and territories to ensure that such individuals are systematically referred for follow-up treatment, or examination for medical conditions other than tuberculosis.⁴⁰ In addition, individuals may acquire HIV infection during the interval between the visa application test and the time of migration, which may be several weeks or months;⁴¹ additionally, HIV screening tests performed in resource-poor settings may fail to detect recently acquired infection.^{42,43} Allegations of falsified test results are periodically made,⁴¹ but considering the large number of visa applications (over 4 000 000 per year) and health assessments (over 400 000 per year), apparent false negative HIV tests may sometimes occur through processing or clerical error.⁴⁰

A retrospective cohort study of over 2 000 newly arrived refugees to Western Australia between 1 January 2003 and 31 December 2004, in whom HIV testing was done for people aged 18 years and over (or by parental request), found 2 to be HIV-infected, giving a prevalence of 0.01% (or 0.16% among those were aged 15 years and above). Both of the people diagnosed with HIV infection after arrival tested negative for HIV infection at the time of the “visa medical”.⁵ This draws attention to the need to consider the possibility of recent HIV infection when assessing the health of newly arrived refugees.

Hepatitis B virus (HBV)

Hepatitis B virus is transmitted via sexual contact, sharing injecting equipment, unsafe medical procedures (e.g. injections, surgery, blood transfusions), household contact, pregnancy and childbirth. The risk of persistent HBV infection is higher for those infected at a younger age (90% for those infected at birth, falling to around 5% for those infected as adults). Persistent infection progresses to cirrhosis in 14% and hepatocellular carcinoma in 5%. The risk of disease progression increases if chronic hepatitis C is also present, to 31% and 9%, respectively.^{44,45}

The incidence of HBV infection in non-Indigenous Australians is low, due partly to the policy of universal infant immunisation adopted in 1997. However many refugees come to Australia from countries in which HBV is highly prevalent. Regions of high endemicity include sub-Saharan Africa, East Asia and South East Asia. In these regions, HBV is the major cause of hepatocellular carcinoma. In Australia, birth in the Asia/Pacific or African/Mediterranean region or being a remote-dwelling Indigenous person substantially increases the likelihood of past or present HBV infection.^{44, 46 - 48}

In a study of over 2 000 newly arrived refugees in Western Australia, the prevalence of current HBV infection among people born in Europe and the Middle East was 0.0%; those born in South-East Asia had a prevalence of 6.5%; those born in South Asia, 3.5%; those born in North Africa 6.8% and those born in sub-Saharan Africa, 6.4%.⁵ Another study of 185 recently arrived African refugees in Victoria demonstrated that 8% had chronic HBV infection, but only 26% of 1 - 14 year olds and 60% of those aged 15 years and above were immune to HBV through immunisation or past infection.⁴⁹ Therefore, there are significant numbers of individuals in this population who are susceptible to HBV and are also likely to have regular and close contact with HBV-infected individuals.

Hepatitis C virus (HCV)

Hepatitis C is transmitted via through sharing or reusing needles, exposure to blood products and via medical procedures using contaminated equipment. Sexual transmission is rare. Mother to child transmission can occur during pregnancy and childbirth, at rates of 4 – 7%. The risk of transmission is substantially higher for mothers infected with HIV. Acute hepatitis C infection is commonly asymptomatic, however 75 - 85% of those infected will develop chronic infection, and of these, 10 - 20% progress to cirrhosis and approximately 5% will develop hepatocellular

carcinoma. The risk of disease progression is increased by alcohol use, older age at infection, male gender and co-infection with HIV or HBV.^{50 - 54}

The epidemiology of HCV infection is very variable and poorly understood in much of the developing world, particularly Africa. In a Ugandan study, the prevalence of HCV infection among blood donors was 4.1%⁵⁵ whereas in Burkina Faso, the prevalence among blood donors was 2.2% and among pregnant women 1%.⁵⁶ A study of refugees from the Mekong region of Indochina found a prevalence of 3% among Laotian refugees and 8% among refugees from Cambodia,⁵⁷ whereas a study of Kurdish refugees in Turkey found a prevalence of 0.1%.⁵⁸ However prevalence rates between and within countries vary widely according to risk factors, such as a history of medical procedures or unsafe injections. For example, a study in an incarcerated population in Ghana found that the prevalence of HCV infection was 19.2%, whilst the prison officers had a prevalence of 23.2%.⁵⁹ In Egypt (a country of transit for many African refugees), a high prevalence of HCV infection has been found among recipients of mass treatment for schistosomiasis prior to 2000; in some rural villages, the prevalence of HCV is 40% among older adults, compared to 2.7% in young adults.⁶⁰

Rationale for screening

As discussed above, a negative HIV test result at the time of pre-migration health assessment does not exclude the possibility that a few people who arrive as refugees may have undiagnosed HIV infection. The pre-migration health assessment HIV test should be considered an administrative tool; it is not a screening test contributing to the provision of health care for individual migrants and refugees. The current Australian National HIV Testing Policy includes, as indications for offering HIV

testing, “being from a country of high HIV prevalence” and “having recently travelled overseas.” Most refugees will have at least one of these indications for HIV testing.⁶¹

Screening for HBV is not routinely performed as part of pre-migration medical assessment for all refugees (HBV surface antigen is currently tested for in pregnant women and unaccompanied minors). Susceptible individuals arriving as refugees (particularly children) are at high risk of being exposed to HBV infection through contact with chronic carriers. The aim of HBV screening is to identify susceptible individuals requiring vaccination and chronic carriers requiring follow up and treatment.⁶²

Hepatitis C testing does not form part of the pre-migration medical assessment and is often currently not routinely performed after arrival, even at clinical services focusing on refugee health. In a recent study, only 68/258 (26%) of recently arrived African refugees were screened for hepatitis C; anti-hepatitis C antibodies were detected in only one case.⁴⁹

Acute or chronic infection with HIV, HBV or HCV is frequently asymptomatic and may have a long “latent” period prior to the development of symptoms, but can be readily detected at most stages of infection by a blood test. HIV, hepatitis B and hepatitis C, although potentially life-threatening, are all preventable and treatable. Given the prevalence of these infections in many regions from which refugees originate, screening of all newly arrived refugees is warranted; This approach has also been adopted in the United States.^{63,64}

Diagnosis

HIV

HIV infection is diagnosed by the detection of antibodies to HIV by enzyme immunoassay (EIA) or Western Blot, detection of HIV antigens (e.g. p24 antigen) or detection of HIV nucleic acid by PCR. The test most frequently used in Australia for HIV screening is a “combo” test, which detects both anti-HIV antibodies and p24 antigen.

For many people arriving in Australia as refugees, a diagnosis of HIV is associated with fear, stigma and discrimination. Disclosure of an individual’s HIV serostatus to other community members can lead to ostracism and social isolation. For this reason, discussion regarding HIV testing should be undertaken with due regard to privacy and confidentiality. The professional confidentiality of interpreters is critical in this situation.^{41,65}

HBV

Hepatitis B infection is diagnosed by the presence of anti-HBV core antibodies (HBcAb, anti-HBc), detection of viral proteins such as HBV surface antigen (HBsAg) and hepatitis B e antigen (HBeAg), or by detection of HBV DNA by nucleic acid testing. A positive HBcAb results indicates past or current infection; the presence of HBsAg and/or HBeAg indicates a high risk of transmission to contacts and detection of HBV DNA by PCR indicates ongoing viral replication and risk of progression to chronic liver disease or hepatocellular carcinoma. Detection of HBsAb (anti-HBs) indicates immunity following past infection or immunisation. Using a combination of three tests (HBsAb, HBsAg and HBcAb), most individuals can be categorised as either HBV susceptible, immune (past infection), immune (immunised), or chronically infected. One pattern of serological results that is difficult to interpret is detection of HBcAb in the absence of detectable HBsAg or HBsAb. Such individuals may have past HBV infection with low levels of HBsAb (immune), chronic HBV infection without

detectable HBsAg (“occult” chronic hepatitis B infection), or acute hepatitis B infection (in which case HBcAb IgM should be detectable). In low-prevalence countries the HBcAb may be a false positive result. The likelihood of chronic infection is higher in among individuals from high-prevalence countries and those with HIV or hepatitis C co-infection. At present the Medicare Schedule does not provide a rebate for HBV PCR testing in the primary care setting. Specialist advice or evaluation is recommended when trying to interpret this pattern of results.⁶⁴

HCV

Past or current infection with HCV is detected by the demonstration of anti-HCV antibodies. Although anti-HCV antibodies are usually detectable 1 - 3 months after infection, anti-HCV antibody testing is unreliable for acute infection, as up to 30% of acutely infected individuals will have undetectable antibodies at the onset of their symptoms. HCV RNA testing can be used to diagnose both acute and chronic infection. Detection of HCV RNA indicates ongoing viral replication and a higher risk of transmission. Undetectable HCV RNA in peripheral blood usually indicates clearance of the infection (either spontaneously or following treatment). The Medicare Benefits Schedule provides a rebate for HCV RNA PCR testing in the primary care setting for people in whom anti-HCV antibodies have been detected.⁵²

Management

HIV

All patients diagnosed with HIV infection should be referred for specialist assessment and management. It is not necessary for primary health care providers to request CD4 counts or HIV viral loads prior to referral. It is not possible to cure HIV infection using currently available treatments, However treatment with antiretroviral therapy can prevent progression to AIDS, prolong survival and improve quality of life for most people infected with HIV. Antiretroviral therapy can also significantly reduce the likelihood of further sexual or mother to child transmission.⁴³

Transmission of HIV can be prevented by avoiding exposure to blood and body fluids. Post-exposure prophylaxis of uninfected individuals after a high-risk sexual or other exposure may reduce the risk of transmission and is offered at some specialist services.

HBV

All patients diagnosed with possible chronic HBV infection (detectable HBcAb +/- HBsAg) require further assessment to determine a) whether the infection is active and b) whether there is evidence of liver disease (i.e. hepatitis, fibrosis, cirrhosis or hepatocellular carcinoma). Recommendations regarding investigation and management of such patients can be obtained from local hepatitis treatment services. Specialist centres can provide treatments that slow the progression of disease in people with chronic hepatitis B. It is not necessary for primary health care providers to request abdominal ultrasound prior to referral to specialist services. Individuals who are susceptible to HBV infection (HBsAb titre <10mIU/mL, without

detectable HBcAb) should be offered hepatitis B immunisation, although this is not presently subsidised for adults in Australia.^{45,46}

Transmission of HBV can be prevented by avoiding exposure to blood and body fluids and by immunisation of susceptible individuals. Immunoglobulin may be offered to exposed individuals in some circumstances.

HCV

As for HBV infection, all patients diagnosed with detectable anti-HCV antibodies require further assessment to determine a) whether the infection is active and b) whether there is evidence of liver disease (i.e. hepatitis, fibrosis, cirrhosis or hepatocellular carcinoma). Recommendations regarding investigation and management of such patients can be obtained from local hepatitis treatment services. Effective treatments are available for HCV infection that can prevent progressive liver damage and clear the infection. Treatment is most effective early in acute HCV infection. To avoid delays in assessing the need for treatment, it is helpful for primary health care providers to request an HCV RNA PCR test when referring an individual with detectable anti-HCV antibodies to specialist services for evaluation and possible treatment. It is not necessary to arrange abdominal ultrasound or other investigations prior to referral.^{53,68}

Hepatitis C infection is preventable by avoiding exposure to potentially infected blood or blood products. There is no effective vaccine, and immunoglobulin administration following exposure is not effective at preventing transmission.

Box 1. Initial screening tests for blood-borne viral infections

Discuss reasons for testing

Risk of infection despite pre-migration screening

Asymptomatic infection

Benefits of early diagnosis and treatment

Risk of transmission to others e.g. partners, family, unborn child

Discuss obligation to maintain confidentiality

Discuss need for notification of diagnosed infections to health authorities

Reassure regarding security of immigration status regardless of results

Initial investigations for hepatitis B

HBcAb, HBsAg, HBsAb

Initial investigations for hepatitis C

HCV antibody

Initial investigations for HIV

HIV antigen / antibody

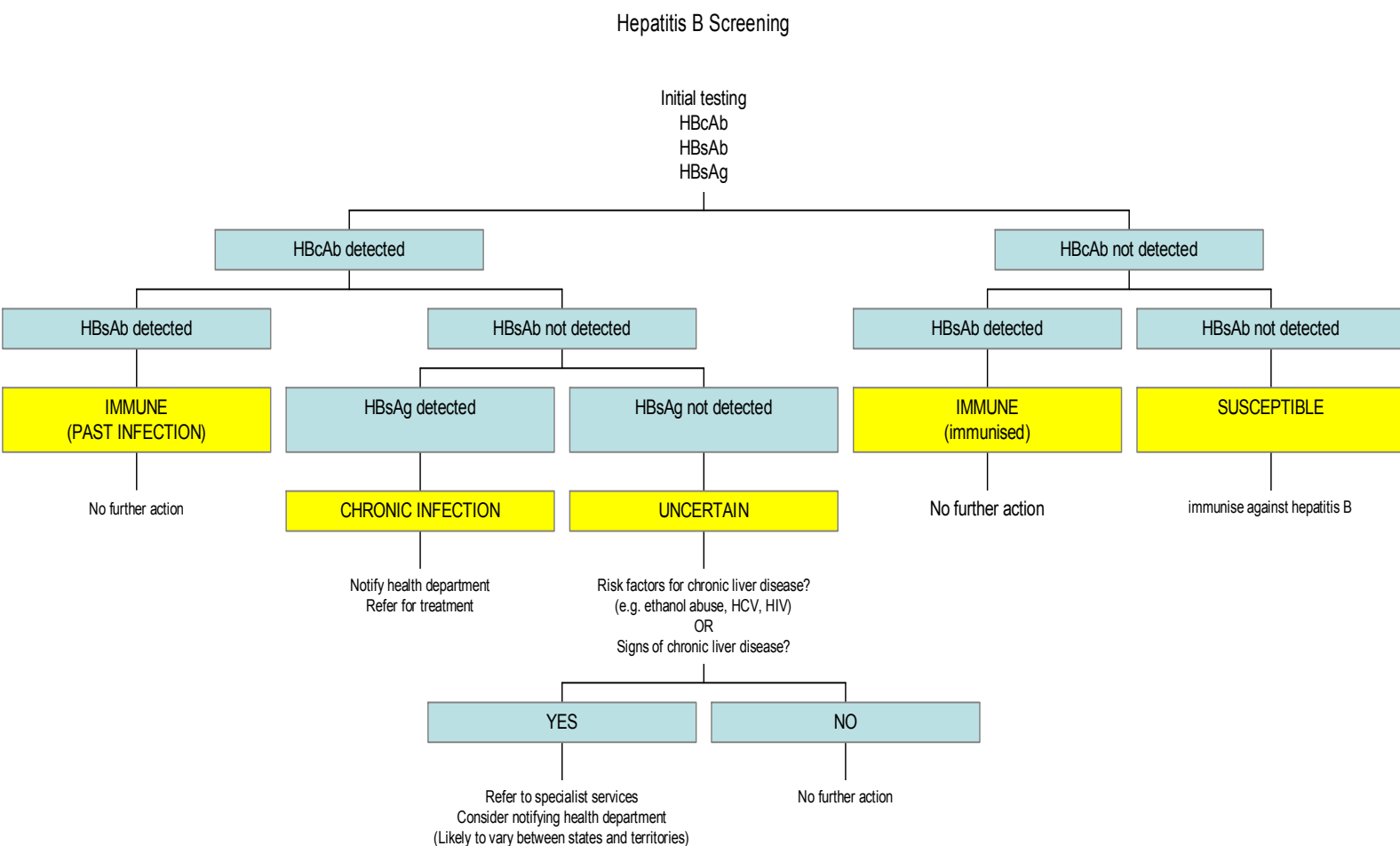
Subsequent visit:

Discuss results of initial testing

Further testing (e.g. HCV RNA PCR), referral and notification to health department as necessary.

Figure 1. Testing algorithms for blood-borne viral infections

Hepatitis B .



HBCAb: Hepatitis B core antibody.

HBsAb: Hepatitis B surface antibody.

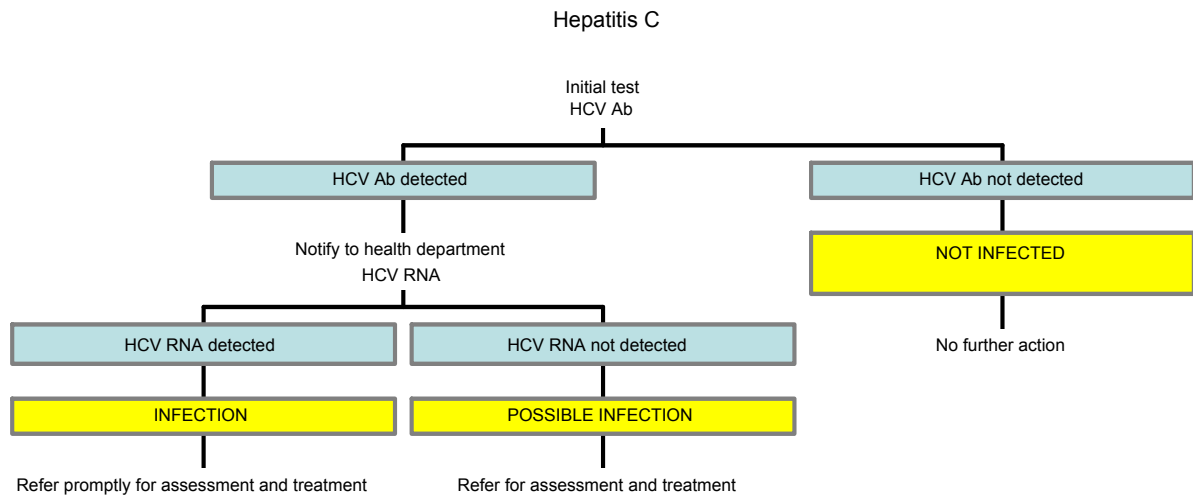
HBsAg: Hepatitis B surface antigen.

There is no consensus about the management of patients in whom only HBCAb is detected. This may be the sole serological marker of HBV infection in up to 10% of cases. Some of these cases are persistently infected.⁶⁶

Our suggested approach is to perform a hepatitis B DNA test on peripheral blood and to refer for specialist follow up those individuals with either detectable hepatitis B DNA or with another risk factor for chronic liver disease (e.g. hepatitis C infection, HIV, or excessive ethanol consumption). The requirement to notify health authorities about possible (but unconfirmed) cases of chronic hepatitis B may vary between states and territories.

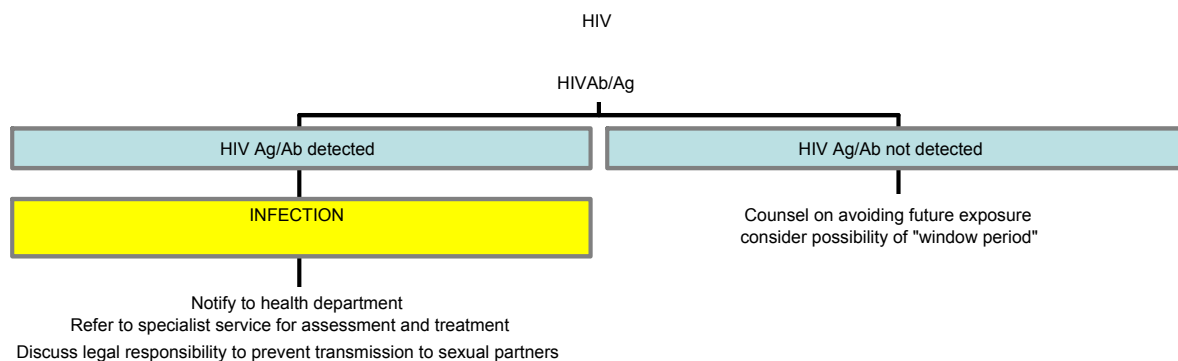
Hepatitis C

NB. If exposure has occurred within the last three months and HCV antibody is negative, repeat screening in three months. If HCV Ab is detected, a test for hepatitis C RNA PCR should be requested and the individual referred to specialist services to further investigation and management of hepatitis C.



1. HCV Ab: Hepatitis C antibody. Marker of past or current infection.
2. HCV RNA: Hepatitis C RNA (tested by PCR). Indicates current infection (acute or chronic) or used to assess response to therapy for HCV infection.

Human immunodeficiency virus (HIV)



1. HIV Ag/Ab: HIV antigen/antibody "combo" assay.

If recent exposure (within past three months):

1. asymptomatic: Repeat HIV Ab/Ag testing at 1, 3 and 6 months post-exposure.⁶¹
2. symptomatic (fever, rash, lymphadenopathy or other symptoms suggestive of acute HIV infection): Discuss with HIV specialist and health department. Test for HIV Ab/Ag or HIV viral load. Refer to HIV specialist for follow up.

Schistosomiasis

Recommendations

- Schistosomiasis serology should be offered to all recently arrived African and South East Asian refugees
- Those with negative serology require no treatment or further follow-up
- Those with positive serology should be treated with praziquantel (40mg/kg in two doses of 20/mg/kg, 4 hours apart for refugees from Africa; 60mg/kg in two doses of 30mg/kg, 4 hours apart for refugees from South East Asia). They should also have faeces and urine examination for schistosoma ova to determine if further follow-up is required (see flow-chart).

Epidemiology

Schistosomiasis affects 200 million people worldwide, 85% of whom live in Africa. It has recently been estimated that there are 130 000 deaths in Africa each year due to portal hypertension from intestinal schistosomiasis, and there are 70 million people with haematuria and 10 million with hydronephrosis due to urinary schistosomiasis.⁶⁹ Schistosomiasis is highly prevalent in nearly all regions of Africa. Urinary (*Schistosoma haematobium*) and intestinal (*S. mansoni*, *S. intercalatum*) forms are both present in the areas from which most African refugees currently originate. Schistosomiasis also occurs in South-East Asia, where *S. japonicum* and *S. mekongi* are the common infecting species.

Many centres in Australia routinely screen African refugees for schistosomiasis using serology, and in some cases with faeces and urine examination for *Schistosoma* ova. Positive schistosomiasis serology has been found in 37% of African refugees arriving in Newcastle, NSW,⁷⁰ 38% arriving in Hobart⁶ and 41% arriving in Sydney (Mitchell Smith, personal communication 2006). This gives a pooled seroprevalence of 38% for 653 African refugee adults and children arriving in Australia, predominantly from Liberia, Burundi, Tanzania and Sudan. These patients were part of screening programs for all new arrivals and are thus likely to be representative of the population of new African refugee arrivals as a whole. A multivariate analysis of the Newcastle data showed that schistosomiasis serology was much more likely to be positive in those from East Africa (OR 14.5) and West Africa (OR 5.5) than from the Sudan region (OR 1.0).⁷⁰ In those who had faeces and urine examination in these cohorts, urinary schistosomiasis is uncommon, with >95% of those with positive microscopy having *S. mansoni* in faeces.

Rationale for screening

Schistosomiasis is predominantly a chronic disease which is generally asymptomatic until the late stages, when there is significant end-organ damage. Treatment is safe, simple and usually highly effective. The consequences of not diagnosing and treating chronic schistosomiasis range from none (in a light infection) to early mortality from portal hypertension, renal failure or bladder malignancy. There can also be substantial morbidity and long-term cost to health services as a result of intestinal polyposis, oesophageal varices, hydronephrosis and urogenital fibrosis. Adult worms can live in venous plexuses for 20-30 years after the patient has left an endemic area. Thus, schistosomiasis meets criteria for a condition which should be screened for, ie a) a high prevalence; b) a long asymptomatic phase; c) effective diagnostic tests and treatment are available, and d) cure with early detection and treatment.

Diagnosis

Examination of faeces and/or urine for ova is the 'gold standard' diagnostic method for schistosomiasis. It is 100% specific, but has poor sensitivity unless multiple specimens (at least 3) are submitted to an experienced laboratory that uses a validated concentration technique. It has been estimated that 3000-6000 eggs need to be excreted per day to be detectable by microscopy in a concentrated faeces specimen.⁷¹ Therefore, a light-to-moderate worm burden may not be detected by faeces examination alone, particularly in a laboratory that does not perform faecal concentration for parasites.

It is often logistically difficult to collect multiple faeces samples from recently arrived refugees, particularly at a single initial screening visit. It is also considered invasive by some refugees and is expensive and labour intensive for the laboratory to concentrate, fix and thoroughly examine multiple faeces specimens. Similar considerations apply to the examination of urine in suspected urinary schistosomiasis.

Serology for the detection of anti-*Schistosoma* antibodies is widely used for the diagnosis of schistosomiasis. The most commonly performed tests are enzyme immunoassay and indirect haemagglutination assays. The reported sensitivity and specificity of serology varies with the method used.⁷² In Australia, many laboratories use a non-commercial or “in-house” EIA test, developed at the Institute for Clinical Pathology and Medical Research in NSW, which uses extracted egg antigens from *S. mansoni*. This technique has had excellent reported results in other centres, with reported sensitivity and specificity for chronic infection with *S. mansoni* of 93.3% and 98.2% respectively.⁷³ However, serology remains positive after effective treatment or after the infection has run its course, and therefore cannot differentiate between current and past infection.⁷⁴ Most people living in endemic areas are repeatedly infected due to bathing or washing in contaminated water sources either until they leave the area, or effective local control measures are put in place. This, combined with the fact that worms can survive for decades, means it is likely that the majority of refugees with positive serology have current infection. Similar considerations apply to serology for *S. haematobium*.

Evaluation for the end-organ effects of schistosomiasis is important. This includes history taking for past episodes of haematemesis or haematuria and physical examination for signs of portal hypertension (e.g. ascites, caput medusae and splenomegaly).

Laboratories not infrequently report schistosomiasis serology as “equivocal”. In this situation, the specimen should be tested a second time using a different serological method. If this is not possible, or the result remains equivocal despite repeat testing, the patient should be treated as if their serology were positive. This is because the pre-test probability is high; the consequences of missing an infection in the long term are potentially severe; and the treatment is safe and effective.

Management

Praziquantel (40mg/kg in two divided doses of 20mg/kg, taken four hours apart) has been shown to have excellent cure rates in schistosomiasis acquired in Africa and is generally safe and well tolerated.⁷⁴ Higher doses (60mg/kg) are recommended for *S. japonicum* and *S. mekongi* infection, which occur in South East Asia. Mild adverse effects occur in 5-30% of patients and include nausea, dizziness, headache, diarrhoea and pruritis. These may be immune reactions to the dying worms rather than direct adverse effects of the drug itself. There is a theoretical concern of precipitating seizures in patients who have cerebral *Taenia solium* infection (neurocysticercosis). However this complication is exceedingly rare and it has not thus far been reported in Australian refugee clinics. Screening by cerebral imaging to exclude concurrent neurocysticercosis should therefore not be routinely performed prior to praziquantel treatment.

Treatment failure rates after praziquantel have been reported to range from 1.3% to 40%.⁷⁵ However, even if the infection is not cured, a single treatment will significantly decrease the worm burden. Treatment failure is more likely with a recently-acquired infection (the migrating larvae (schistosomulae) are relatively insensitive to praziquantel) or with a heavy worm burden. True praziquantel resistance in *S. haematobium* has yet to be reported and is very rare in *S. mansoni*.

We recommend performing faeces and urine examination in adults and children for schistosome ova only for those patients with positive schistosomiasis serology (see attached flow chart for treatment and follow-up recommendations). This is not as a screening test, but as a risk-stratification tool, to detect patients with high worm burdens. Only those with positive serology and macro- or microscopic haematuria (using dipstick urinalysis) should have their urine tested for ova.

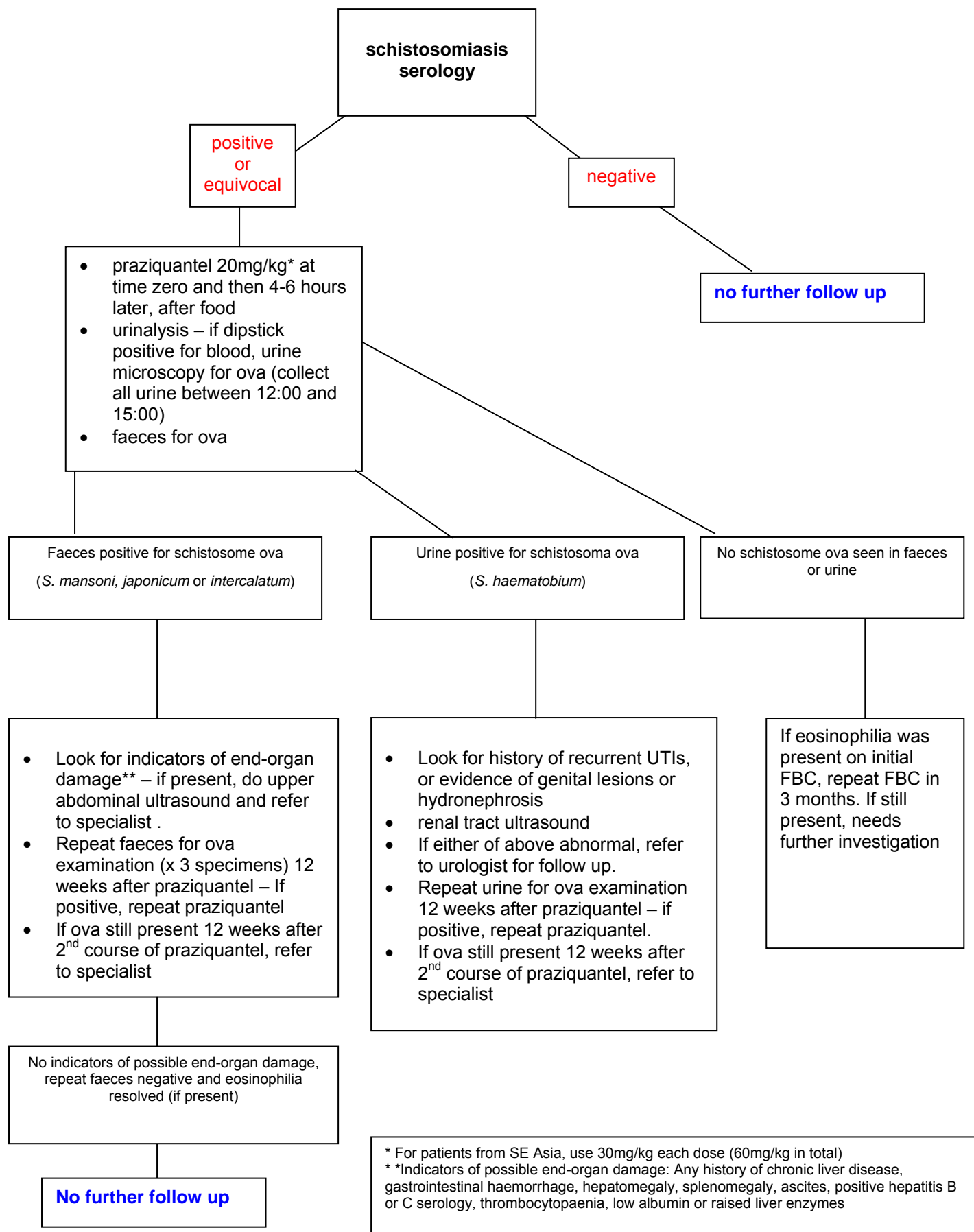
Those patients with positive faeces or urine microscopy for schistosome ova require further assessment following treatment. This includes repeat faeces or urine microscopy to document cure, and evaluation for end-organ damage. For *S. mansoni*, *S. japonicum* or *S. mekongi* infection, those with indicators suggestive of hepatic impairment should have imaging with upper abdominal ultrasound to exclude “pipe-stem” fibrosis and portal hypertension, which are well-recognised complications of chronic intestinal schistosomiasis. These indicators include: i) History – any history of chronic liver disease, gastrointestinal haemorrhage, hepatitis B or C infection or ascites, ii) Examination – hepatomegaly, splenomegaly, ascites or peripheral oedema. iii) Blood tests – positive hepatitis B or C serology, thrombocytopenia, low albumin or raised liver enzymes. If an abnormality is found, referral for specialist assessment may be indicated. For *S. haematobium* infection, all patients with ova in urine should have a renal tract ultrasound as well as physical examination looking for hydronephrosis and genital disease. Those with macroscopic haematuria, recurrent urinary tract infection, abnormalities on imaging or genital disease should be referred to a urologist for consideration of cystoscopy and further follow up. After successful treatment, ova can continue to be excreted for 6 weeks or more. Therefore, if undertaken to document cure, it is recommended that repeat faeces or urine examination for *Schistosoma* ova should be delayed for 12 weeks following treatment that, Those with faeces or urine positive for ova despite treatment with praziquantel should have the treatment repeated. If faeces or urine remains positive for ova more than 12 weeks after a second course of praziquantel, the patient should be referred to an Infectious Diseases physician.

Pregnancy

Praziquantel is classified as category B1 drug for use in pregnancy. It is therefore controversial whether asymptomatic schistosomiasis should be treated in pregnant

women. Waiting until after delivery runs the significant risk of loss to follow-up. There is limited evidence of the safety of praziquantel in pregnancy and no convincing evidence of teratogenicity. The WHO now recommends that pregnant women in endemic areas are not excluded from mass treatment programs. We recommend that praziquantel treatment be withheld during the first trimester, but should be offered during the second or third trimester of pregnancy, after discussing the risks and benefits of treatment with the patient.

Figure 2. Management of schistosomiasis in recently arrived refugees



Soil-Transmitted Helminths (Worms)

Recommendations

- *Strongyloides* serology
 - If equivocal or positive, treat with two dose of ivermectin 200 micrograms/kg , two doses two weeks apart
 - If less than 5 years of age, do not give ivermectin – refer to paediatrician
 - If from West or Central Africa, consider risk of loiasis before giving ivermectin – see below

- Screening / treatment for other helminth infections:

Option One (faeces specimen readily obtainable):

- Faeces microscopy for ova, cysts and parasites. Treat appropriately if helminths identified (see background document).

Option Two (faeces specimen not readily obtainable):

- Full blood count (FBC) with differential white cell count for eosinophilia.
- If eosinophilia present, investigate and treat appropriately (eg for allergy, drugs, helminths, filariasis, schistosomiasis, strongyloides, tapeworm infection). NOTE: If predeparture albendazole was given, eosinophilia may still be present for 1-2 months despite predeparture eradication of the helminth. In this case, recheck FBC at least 8 weeks after arrival to ensure that the eosinophilia has resolved.
- If no cause found of eosinophilia found, treat presumptively with single-dose albendazole (see below for doses).

Introduction

Intestinal parasite infections are a major disease burden in most developing countries and they are among the most prevalent and easily treated communicable diseases occurring in immigrants and refugees.^{76,77} A survey of recently arrived African refugees in Melbourne in 2005 found one or more pathogenic organisms in the faeces of 30 of 193 (16%) refugees tested.⁴⁹

Strongyloides stercoralis

Epidemiology

Estimates of the worldwide prevalence of *Strongyloides stercoralis* infection (strongyloidiasis) vary widely between 3 million and 100 million individuals.⁷⁸ Strongyloidiasis is endemic in tropical and subtropical regions (including Africa) and occurs sporadically in temperate areas. It is relatively common in some regions of Australia (eg. Aboriginal people living in East Arnhem land) but is considered rare in more heavily populated regions.

A survey of newly arrived African refugees in Melbourne in 2005 found a positive strongyloides serology in 6 of 66 African refugees (9%).⁴⁹ Surveys in Melbourne and Perth have found a prevalence of strongyloides larvae in stool of 0-2%.^{5,49} Surveys in longer-term immigrants from Cambodia and Laos found positive or equivocal serology in 42% and 24% of participants respectively.^{76,77}

Most individuals with strongyloidiasis are asymptomatic, however they can maintain infection with a small number of worms by autoinfection.⁷⁹ *S. stercoralis* infection may persist for decades, causing recurrent skin rashes, abdominal pain and occasionally life-threatening disseminated infection in those who later become

immunocompromised. A cutaneous linear eruption (larva currens) and urticarial skin rashes in the buttocks and waist areas also occur. Intestinal symptoms may include intermittent watery diarrhoea, nausea, vomiting, abdominal pain and weight loss. Additionally, pulmonary symptoms (Loeffler-like syndrome) and eosinophilia may occur as migrating larvae penetrate alveolar spaces.

Diagnosis

Peripheral eosinophilia is present in the majority of individuals with chronic strongyloidiasis. For example, eosinophilia was present in 57% of immunocompetent patients with *S. stercoralis* in stool presenting to Royal Darwin Hospital in 1993 and 78% of Laotian refugees with positive serology and/or *S. stercoralis* in stool.^{76,80}

Microscopy of a single faeces specimen is insensitive for the diagnosis of strongyloidiasis. Multiple specimens and concentrates need to be examined to achieve acceptable sensitivity.⁸¹ Multiple stool samples are, however difficult to collect and therefore should only be undertaken in special circumstances. Harada culture and the agar plate technique (collectively referred to as coproculture) increase the sensitivity of faecal microscopy, but are labour intensive and expensive. Agar-plate culture has a sensitivity of approximately 90%, however it is resource intensive, takes 2-3 days and is not practical for screening large numbers of specimens and can miss a significant proportion of infected subjects.⁸²

The anti-*Strongyloides* antibody enzyme-linked immunosorbent assay (EIA) detects IgG antibodies and has been used for both screening and diagnosis, as well as for post-treatment monitoring.⁸³ Difficulties in assessing the performance of serology for the diagnosis of strongyloidiasis include: i) the lack of a sensitive “gold standard” for comparison,^{81,83} ii) cross reactivity with other helminths may occur and iii) uncertainties exist with respect to persistent seropositivity representing past treated or

current infection,⁸³⁻⁸⁶ although more evidence is emerging to support the role of serology in post-treatment assessment .^{83,84} At present, given the lack of practical alternate methods for diagnosis, the likelihood of long term infection in an untreated patient and the availability of a safe drug for treatment of infection, a serology-guided approach to diagnosis and management is recommended in these guidelines.

Management of adults and children greater than 5 years of age

Effective treatment of an individual will prevent the transmission of strongyloidiasis to others. It will also eliminate the potential for disseminated disease if the patient becomes immunosuppressed in the future. In addition, it will eliminate the likelihood of auto-inoculation and resulting long-term infection and chronic symptoms. Exogenous re-infection is unlikely to occur if the person remains in Australia.

Those individuals with positive *S. stercoralis* serology should be given two doses of oral ivermectin 200microg/kg, two weeks apart. Two doses are given to ensure that developing larvae migrating through tissues at the time of the first dose are exposed to the drug with the second dose.¹² In 2 randomised trials, 3 days of albendazole therapy had an efficacy of 38% and 45% respectively, compared with 83% in both trials for a single dose of ivermectin for the treatment of strongyloidiasis.^{87,88}, therefore this albendazole is now considered “second line” therapy for this infection.

Loiasis is infection with the filarial roundworm *Loa loa*. It is endemic in West and Central Africa (for example in Nigeria, Cameroon, the Central African Republic, Equatorial Guinea, Gabon and the Democratic Republic of the Congo). In people with loiasis and a high burden of microfilaraemia, there is a potential risk of severe encephalopathy and even death if ivermectin is given. This is thought to be due to an immunological response to rapidly dying microfilariae in the central nervous system. Factors which would make one consider the possibility of co-infection with *L. loa* include country of origin, history of migratory subcutaneous swellings (“calabar swellings”) or an “eye-worm“. If these risk factors are present, a blood film taken at approximately midday should specifically be examined for microfilariae (this can be performed at the same time as the malaria thick/thin film). Although this approach (as opposed to serology or multiple blood films) will miss light infections with *Loa loa*,

these patients are at very low risk of encephalopathy if treated with ivermectin. If a patient is known or suspected to have loiasis, ivermectin should **not** be given and the patient should be referred to an infectious diseases specialist for further management. In these cases, strongyloidiasis can be treated with albendazole 400mg daily for 3 days.

Children <5 years of age with positive strongyloides serology should be referred to a paediatrician for assessment and management.

Hookworm (*Ancylostoma duodenale*, *Necator americanus*)

Epidemiology

Hookworm infection is found mostly in poor and rural communities worldwide, especially where there is faecal contamination of soil and high humidity. Of 1245 refugees from Sub-Saharan Africa screened in Perth in 2003-04, 5% had hookworm ova in faeces.⁵

Hookworm larvae penetrate through intact skin, especially in areas where footwear is not commonly worn (*A. duodenale* can also be transmitted via the oral route). Larvae migrate through the lungs, and subsequently develop into adult worms that live in the lumen of the small intestine. Here they feed from the small intestinal mucosa causing chronic blood loss. Adult worms have a life span of up to 5 years.

Diagnosis

Hookworm is diagnosed by the microscopic finding of ova in faeces. Concentration methods are necessary to detect light infections. Peripheral eosinophilia may be present. Iron deficiency and anaemia are clues to moderate-heavy infections.

***Ascaris lumbricoides* (Round Worm)**

Epidemiology

There is a worldwide distribution of this nematode with an estimated 1.4 billion people infected, predominantly in Asia, Africa and Latin America. Ascariasis is most common in children in tropical and subtropical regions and areas with inadequate sanitation. Infection is usually asymptomatic (eg an incidental finding in the faeces, or a history of passing a worm) or there are mild gastrointestinal symptoms such as abdominal pain, distension, nausea and occasional diarrhoea. Occasionally a worm is coughed up. Nutritional disorders may occur in children with moderate to heavy worm burdens. Pulmonary ascariasis (eosinophilic pneumonitis or Loeffler's syndrome) may occur 4-16 days after infection and presents as a self-limiting pneumonia-like syndrome of cough, dyspnoea and haemoptysis.

Diagnosis

Ascariasis is diagnosed by the finding of ova on faeces microscopy. Peripheral eosinophilia may be present. The history of the passage of a roundworm from the anus, mouth or nose is highly suggestive of ascariasis. In pulmonary ascariasis, the chest X-ray usually shows diffuse pulmonary infiltrates and the peripheral eosinophil count often exceeds 20% of the total white blood cell count.

***Trichuris trichuria* (Whip worm)**

Epidemiology

This infection is most prevalent in children aged 5-15 years. Estimates suggest that 800 million individuals are infected worldwide, especially in warm, moist areas with poor sanitation. Transmission of this nematode is by the ingestion of eggs from soil-contaminated hands or food. The eggs then hatch in the small intestine and release larvae that mature and establish themselves as adults and attach in the appendix, caecum and ascending colon. The unembryonated eggs appear in faeces about two months after infection. The life span of adult worms is about 1 year. *T. trichuria* is often found together with *A. lumbricoides*.

Patients are usually asymptomatic or have mild abdominal discomfort. In heavily infected individuals there may be epigastric pain, vomiting, anorexia and weight loss. Some patients develop bloody diarrhoea and rectal prolapse. In severe chronic cases, anaemia and growth retardation have been reported.

Diagnosis

T. trichuria infection is diagnosed by the microscopic identification of ova in faecal specimens. A history of bloody diarrhoea without other explanation, or of rectal prolapse is suggestive of trichuris infection.

Management of hookworm, *A. lumbricoides* and *T. Trichuria* infection

Some refugees will have received empirical pre-departure treatment for helminth infestation with albendazole prior to arrival in Australia. This is given by the International Organisation for Migration (IOM) on behalf of the Australian government at major points of embarkation in Africa and elsewhere. In those who have received such treatment, diagnosis and management of intestinal helminthiasis is difficult

(peripheral eosinophilia can persist for several weeks after successful treatment). If the person had a hookworm infection, it is likely to have been cured by this predeparture treatment. If the person had *Trichuris* or *Ascaris* infestation, a proportion of people will have been cured, but some will have persisting infection and stool microscopy will not be helpful initially in these patients because the albendazole may have reduced ova production to undetectable levels without curing the infestation. If pretreated patients have an eosinophilia on a screening full blood count (FBC), they should have a repeat FBC performed at least 8 weeks after their treatment. If the eosinophilia has resolved on re-testing and the patient is asymptomatic, they do not need further treatment. If the eosinophilia is still present, they should have further investigation to determine the cause, which is most likely persistent helminth infection (eg strongyloidiasis, schistosomiasis, filariasis, hookworm, or tapeworm infection).

Ideally, at least one stool sample for parasite microscopy should be collected from every recently arrived refugee, whether or not they have received predeparture antihelminthic therapy. The likelihood of identifying pathogenic parasites in stools will depend on the country of origin, transit experience, predeparture treatment and length of time in Australia; *Ascaris* and *Trichuris trichuria* are relatively short lived, whereas hookworm, *Strongyloides stercoralis*, *Taenia solium* and *Opisthorcis* spp. can persist in an individual for many years.⁸⁹ However, in some settings, collection of a stool sample is logistically difficult, expensive and may be considered by some refugees to be invasive, especially during an initial clinic visit. All patients with symptoms or signs suggestive of intestinal helminthiasis (eg diarrhoea, abdominal pain, anaemia or eosinophilia) or those from known high risk groups should have a stool sample collected for microscopy for ova, cysts and trophozoites as a priority. In those with no symptoms, no pretreatment and peripheral eosinophilia, a presumptive dose of albendazole (doses as below) should be given after common causes of eosinophilia have been ruled out, with repeat FBC in 8 weeks to document resolution of eosinophilia. If eosinophilia persists, referral to or discussion with an Infectious

Diseases physician is recommended. If iron deficiency or iron deficiency anaemia are present on screening, possible causes other than helminth infection (e.g. dietary deficiency, menstrual blood loss, pregnancy, gastrointestinal malignancy) should be considered. After treatment of the primary cause, the patient will need iron replacement therapy and follow-up to ensure a satisfactory response.

Where hookworm, *Ascaris* or *Trichuris* infection are identified, use:^{89, 90}

albendazole*: person >10 kg: 400 mg orally daily (1 dose for hookworm or *Ascaris*, 3 daily doses for *T. Trichuria*).

person ≤ 10 kg: 200 mg 1 dose orally daily (1 dose for hookworm or *Ascaris*; 3 daily doses for *T. Trichuria*)

* *NOT to be used in pregnancy or in children < 6 months of age. For these groups specialist advice should be sought. Also caution in patients who have symptoms and/or a travel history that could be compatible with neurocysticercosis (such as epilepsy, CNS symptoms, subcutaneous nodules, Taenia solium positive in faeces or serology) as treatment with albendazole alone can exacerbate CNS disease.*

Helicobacter pylori

Recommendations

- Routine screening for *H. pylori* infection is not recommended
- Non-invasive tests for *H. pylori* infection are recommended in the initial investigation of those with symptoms and/or signs of peptic ulcer disease. If *H. pylori* infection is detected in this setting, then eradication therapy should be offered
- patients with *H. pylori* infection who also have anorexia, weight loss, dysphagia, vomiting, gastrointestinal bleeding or an abdominal mass should be referred for further assessment, including endoscopy

Epidemiology

The spiral bacterium *Helicobacter pylori* is estimated to infect half the world's population. Infection with *H. pylori* causes gastritis, peptic ulcer disease and gastrointestinal malignancy; it is considered to be the most common cause of infection-related malignancy worldwide.⁹¹ Transmission of *H. pylori* is person-to-person, presumably via oral-oral and/or faecal-oral routes, but other modes of transmission (eg via flies) have also been proposed.⁹² Infection generally occurs in childhood, with studies reporting seroprevalence rates of 50-55% in the first decade of life.⁹³⁻⁹⁶ Childhood infection appears particularly common in high-density populations with low socioeconomic status.⁹⁷ Based on seroprevalence surveys, infection rates in adults are as high as 60-100% in sub-Saharan Africa countries and indigenous populations, including Australian Aboriginals,^{92,94,98-100} compared to 30-40% in Caucasian Australian populations.^{101,102}

The significance of *H. pylori* infection in children and its relationship to gastrointestinal symptoms, extra-gastrointestinal manifestations and subsequent risk of malignancy in adulthood remain controversial.^{103,104} *H. pylori* infection has been suggested as a contributing factor in growth retardation in Gambian children.⁹⁵

Some researchers have described an apparent disassociation between high *H. pylori* infection rates and the incidence of *H. pylori* associated disease in African populations, a phenomenon referred to as the "African enigma".¹⁰⁵ However studies of pooled data from prospective studies including over 20,000 African patients undergoing upper gastrointestinal endoscopy suggest that rates of *H. pylori*-associated peptic ulceration and gastric cancer are as expected in populations with high rates of *H. pylori* infection, and are consistent with rates described in other high-prevalence regions.^{93,106,107}

Rationale for screening

Upper gastrointestinal symptoms are commonly reported by recently arrived refugees. In a study of 66 East African migrants settling in the United States, 68% reported “dyspepsia” symptoms (pain, reflux, nausea, vomiting, or indigestion) when assessed shortly after arrival; 93% of these patients had detectable anti-*H. pylori* antibodies in serum.¹⁰⁸ As many individuals with *H. pylori* infection are asymptomatic, and “dyspepsia” symptoms may be due to other infections that are also very common in these populations (eg intestinal helminths, schistosomiasis and malaria), detection of anti-*H. pylori* antibodies in this population does not mean that the patient has *H. pylori*-related disease. For these reasons, routine screening of all recently arrived refugees for *H. pylori* infection is not currently recommended in adults or children.

Diagnosis

Non-invasive tests to detect *H. pylori* infection include detection of anti-*H. pylori* antibodies by serology, detection of *H. pylori*-specific antigen in stool, or detection of urease (an enzyme produced by *H. pylori*) by urea breath test. Serology is the most convenient test to perform, however the sensitivity and specificity of serology can vary considerably depending on the test used and is less reliable in young children.¹⁰⁹ In addition, serology cannot accurately distinguish between current and past *H. pylori* infection. The urea breath test is a very sensitive and specific test for *H. pylori* infection; however, the test takes up to an hour to perform, requires specialised equipment to detect radiolabelled CO₂, and is difficult to perform in children. Detection of *H. pylori* antigen in stool by monoclonal enzyme immunoassay is also a highly sensitive and specific test for *H. pylori* infection and the specimen can be collected at the individuals convenience.¹¹⁰ Polyclonal stool antigen testing or rapid immunochromatographic tests do not perform as well as monoclonal assays.¹¹¹

Other tests (eg detection of *H. pylori* DNA in stool by polymerase chain reaction) have been evaluated and show significant promise, but are not currently in routine clinical use.¹¹²

Upper gastrointestinal endoscopy remains the “gold standard” investigation for the detection of *H. pylori* infection and disease, as it allows direct visualization of the stomach and duodenal mucosa, and it provides an opportunity to obtain biopsies for histopathological examination and culture / susceptibility testing of the organism. Biopsy specimens can be examined for the presence of *H. pylori* by the detection of urease activity using laboratory rapid tests (eg the *Campylobacter* Like Organism [CLO] test) and/or bacterial microscopy and culture. Additionally, histopathological examination of biopsies can demonstrate the presence of the organism and any associated disease.

Given the very high *H. pylori* seropositivity rate and the frequency of dyspepsia symptoms in refugee migrants, some have recommended that symptomatic patients should be treated with *H. pylori* eradication therapy without testing for *H. pylori* infection.¹⁰⁸ However a prospective study of 97 dyspeptic patients in rural African settings noted that *H. pylori* seropositivity rates were similar in patients with endoscopically documented peptic ulcer disease when compared to rates in asymptomatic individuals. In addition, the authors of this study noted that, if *H. pylori* eradication therapy had been given to all patients on the basis of symptoms alone, 3 patients with gastric cancer would potentially have had a significant delay in diagnosis.¹¹³

In adult refugees aged less than 50 years of age with dyspepsia and no “alarm features” (eg anorexia, weight loss, dysphagia, vomiting, gastrointestinal bleeding or abdominal mass), a reasonable approach would be to perform a non-invasive test for *H. pylori* infection (eg serology, urease breath test or stool antigen detection) and if

positive, offer treatment for *H. pylori* infection. The choice of test will depend on factors such as availability, expense and the local performance characteristics of the particular test. This “test and treat” approach is recommended in several consensus guidelines.¹¹⁴⁻¹¹⁶

Treatment

Current Australian guidelines for the treatment of *H. pylori* related disease in adults recommend a 7 day course of acid suppression therapy with either a proton pump inhibitor (PPI) (eg omeprazole, esomeprazole, lansoprazole, rabeprazole or pantoprazole) or ranitidine-bismuth-citrate, combined with antimicrobial therapy (see table 1).¹¹⁴ Longer courses of treatment (10-14 days) are often recommended in children. For patients with beta-lactam hypersensitivity, metronidazole is suggested as an alternative to amoxicillin. However susceptibility testing of *H. pylori* isolates obtained from African subjects have reported high rates of metronidazole resistance (100% in a recent study),¹¹⁷ therefore this regimen would be expected be less efficacious in this group. The importance of adherence to the complex dosing schedule and completing the full course of treatment should be explained carefully to the patient in a language they understand.

Table 3. Treatment of *Helicobacter pylori* – associated peptic ulcer disease

	drug therapy	duration of treatment
Option 1^a	proton pump inhibitor (PPI)^b PLUS clarithromycin 500mg twice daily^c PLUS amoxicillin* 1g twice daily^d	adults: 7 days children: 14 days
Option 2	ranitidine-bismuth^f-citrate PLUS clarithromycin 500mg twice daily^c PLUS amoxicillin*1g twice daily^d	adults: 7 days children: 14 days
	<p>a. Single-prescription “combination pack” options available in Australia include omeprazole/amoxicillin/clarithromycin (Klacid HP7[®]) and esomeprazole/amoxicillin/clarithromycin (Nexium HP7[®]).</p> <p>b. options include: omeprazole, esomeprazole, rabeprazole (all 20mg twice daily) lansoprazole (30mg twice daily), or pantoprazole (40mg twice daily). Dosages in children: omeprazole: less than 10 kg: 5 mg; 10 to 20 kg: 10 mg; child greater than 20 kg: 20 mg; lansoprazole: less than 10 kg: 7.5 mg; child 10 to 20 kg: 15 mg; child greater than 20 kg: 30 mg</p> <p>c. clarithromycin dosage in children: 7.5 mg/kg, up to 500mg.</p> <p>d. amoxicillin dosage in children: 25 mg/kg, up to 1g.</p> <p>e. bismuth is only available via the Special Access Scheme (SAS).</p> <p>* patients with hypersensitivity to beta-lactams: metronidazole resistance in <i>H. pylori</i> is common: seek specialist advice</p>	

Follow-up

Treatment of *H. pylori* infection results in organism eradication rates of >90% and healing of peptic ulcer disease in the majority of patients in clinical trials.¹¹⁸ Due to a range of factors, response rates in non-trial settings may be considerably lower than this. Therefore, treatment outcomes should be assessed in all patients undergoing *H. pylori* eradication therapy.

In patients with mild-moderate symptoms who clinically respond to therapy, retesting for *H. pylori* eradication is not recommended unless symptoms recur. In patients with endoscopically documented peptic ulcer disease or a documented history of complicated ulcer disease, non-invasive testing should be performed to determine the efficacy of *H. pylori* eradication therapy, as it allows documentation of treatment response and determination of the risk of recurrence.¹¹⁴⁻¹¹⁶ Current Australian guidelines state that the urea breath test is the investigation of choice for determining the efficacy of *H. pylori* eradication therapy. Both urea breath testing and *H. pylori* stool antigen tests can give false positive results for 4 weeks or longer after successful eradication therapy and acid suppression therapy should be withheld for at least 2 weeks prior to testing. Serology is not useful for the evaluation of treatment success, as anti-*H. pylori* antibody titres fall very slowly after successful therapy.¹⁰⁹

The persistence of dyspeptic symptoms after *H. pylori* eradication therapy does not always correlate with treatment failure. If symptoms persist despite documented eradication of *H. pylori* infection, endoscopy should be considered and other diagnoses, including gastric carcinoma, should be sought.

***Helicobacter pylori* in children: special considerations**

Refugee children share many of the adult risk factors for *H. pylori* acquisition and although there are few published data, the prevalence of active *H. pylori* infection in refugee children is high - probably 70-80% in African children.¹¹⁹ The association between *H. pylori* infection and gastrointestinal symptoms in childhood is unclear and therefore, at present, routine screening of all refugee children is not justified or recommended.¹⁰³ Refugee children with chronic abdominal pain, early satiety or anorexia should have other common causes of their symptoms considered in addition to *H. pylori* infection. These include somatic manifestations of post-traumatic stress disorder, unfamiliarity with food and other infections, including tuberculosis, helminths and malaria. *H. pylori* infection is more reliably associated with iron deficiency in children.¹²⁰ In a child with persistent iron deficiency, *H. pylori* infection should be sought and treated if present.¹¹⁵

The diagnosis of active *H. pylori* infection in children is challenging and the issues are often compounded in recently arrived refugees. Endoscopy may be difficult in children and hospital admission is disruptive and often upsetting for families. Similarly, urea breath testing is often impractical or unavailable and serological testing is not of diagnostic value for current *H. pylori* infection.¹⁰³ Monoclonal faecal antigen testing using ELISA has excellent sensitivity and specificity in children^{121,122} and is probably the current diagnostic method of choice, although this test is not widely available at present.

Treatment of children with *H. pylori* infection is similar to that of adults, with amoxicillin, clarithromycin and a proton-pump inhibitor given for 14 days.¹⁰³ Treatment courses shorter than two weeks may be unsuccessful.¹⁰³ Metronidazole resistance is likely to be common in refugee groups¹²³ and this drug is not well-tolerated by children. As for adult refugees, if symptoms resolve, repeat screening to document eradication of *H. pylori* infection is probably unnecessary, but clinical follow-up following treatment is warranted.

Sexually transmitted Infections

(for HIV, Hepatitis B and Hepatitis C infection, see “blood borne viruses” section)

Recommendations

- All refugees should have serologic testing for treponemal infection (syphilis), with an intention to treat all those with positive results where there is no documented history of prior treatment.
- All adult refugees should be tested for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* genital infection using a nucleic acid detection test on first- void urine. This should also be done in any youth who is sexually active, or is suspected of having been sexually assaulted.
- All adult female refugees should be offered a 'well women's check' including screening for cervical cancer. A cervical swab should be collected at the same time for a nucleic acid detection test to detect *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infection.
- Investigation for other sexually transmitted infections should be performed according to history, symptoms and signs elicited at the initial assessment. It should be noted that sexual assault of men and children occurs in some settings.

Epidemiology

The World Health Organisation has estimated that 340 million cases of curable sexually transmitted infections (STIs) occur per year worldwide.¹²⁴ In developing countries, STIs and their complications are among the top five diseases for which adults seek health care.^{124,125} Many refugees arriving in Australia have resided in countries where sexually transmitted infections (STIs) are considerably more prevalent. Poverty, powerlessness, social instability, mobility and lack of protection against sexual violence will facilitate transmission of STIs in the refugee population.¹²⁶ The limited data available suggest that many children have also been subject to sexual violence.¹²⁷ Refugees will usually have had limited access to health care prior to arrival, however reproductive health and STIs other than HIV are not likely to have been a priority for either themselves or the health professionals caring for them.

Of the world's estimated 35 million refugees, approximately 70-80% are women and children.¹²⁸ Women, especially those on 'Woman at Risk' (subclass 204) visas, are at particularly high risk for STIs during conflicts and the refugee experience. It is estimated that up to 50% of women will have been exposed to rape, forced prostitution, sexual slavery or sexual violence during their flight and refugee camp experiences,¹²⁹ though the majority of them will not disclose this fact. In one study of asylum seeking children in the UK, over one-third of those <17 years old had been raped.¹²⁵ Similarly, boys and young men (particularly unaccompanied minors) may have been exposed to sexual violence and also be at a higher risk of STIs. Usual family, cultural and social norms may be disrupted and adolescents may begin sexual relations at an earlier age or may be coerced into having sex to obtain their survival needs.³ In addition, some STIs (e.g. hepatitis B and HIV), can be transmitted

through non-sexual routes (eg via contaminated medical equipment, blood transfusions or by vertical transmission).¹³⁰

Data on the prevalence of STIs in conflict-affected areas is very limited. Studies in refugee populations in Africa, including the Kakuma refugee camp in Kenya (the source of many Sudanese refugees who come to Australia), showed a prevalence of syphilis of 3.4-12.2%.¹²⁶ In 1994, when large numbers of refugees moved from Rwanda to Tanzania, over 50% of those attending an antenatal clinic were infected with agents causing vaginitis (*Trichomonas vaginalis*, bacterial vaginosis or *Candida albicans*) and 3% had gonorrhoea.¹²⁵ In the Azerbaijan Reproductive Health Study reported by the US Centers for Disease Control, 88% of women tested had bacterial vaginosis and 27.5% had trichomoniasis.¹²⁸

Rationale for screening

All applicants for permanent entry into Australia over the age of 15 years are initially assessed against a health requirement (the “visa medical assessment”), which includes HIV serology (and occasionally also syphilis serology). In addition, most humanitarian entrants also undergo a pre-departure medical screening and treatment for certain prevalent conditions. STIs other than HIV are not routinely tested for at either of these assessments. Failure to diagnose and treat STIs at an early stage may result in serious complications and sequelae for the individual, including infertility, miscarriage, ectopic pregnancy, anogenital cancer and premature death, as well as neonatal and infant infections.¹³¹ The presence of an STI can increase both the likelihood of acquisition and transmission of HIV.¹²⁴

Diagnosis

Refugees may not be aware of how STIs are transmitted and will probably not have had access to condoms whilst fleeing or in exile.¹²⁸ Women and children may also have had no or very limited ability to negotiate safe sex.¹²⁹ Feelings of shame, guilt and fear will decrease the likelihood of patients and families asking for testing for STIs after they arrive in Australia. It is important that questions about sexual health be asked with sensitivity, to reassure the patient that the health professional understands that in their culture they may not be asked such questions and to apologise for any embarrassment or intrusion into their personal life. The health professional will need to emphasise that in order to improve the patient's health and wellbeing, it is important to ask these questions and that they will be asked of all patients who attend the clinic.¹³² Having a standard form that is filled in helps to reassure the patient that these are standard questions asked of everyone. Questions that might be asked are detailed in box 1.

Box 2. Questions that may be asked during history taking for sexually transmitted infection

- Do you have a current sexual partner/s?
- Have you had any other partners in the last 12 months?
- Have you ever had any sexual health infections?
- Have you ever had an abnormal discharge from your genital area?
- If yes, did you have any treatment?
- Do you have lower abdominal pain, post coital bleeding or pain during sexual intercourse?
- Some people have had painful or frightening sexual experiences, especially at times of conflict and whilst fleeing or in exile. Has this ever happened to you?
- Have you ever been made to have sex you did not want to have?
- Are you aware if your partner has other partners?
- Do you have concerns about a past or current experience of physical or emotional violence?
- Is there anywhere you don't feel safe?

Adapted from the Well Women's History Form, Migrant Health Service, Adelaide ¹³²

The WHO has developed and implemented syndromic guidelines for urethral discharge syndrome (UDS) in men, genital ulcer syndrome (GUS) in men and women, and flow charts for the management of vaginal discharge and/or lower abdominal pain, which may have been used by health care workers if an STI was suspected in the country of origin.¹³³ Algorithms for screening for urethral and vaginal discharge, penile or vulval lesions, and syphilis are available for Australian practitioners that more adequately address the difficulties in diagnosis, particularly of vaginal discharge.¹³³ Diagnosis will include appropriate cervical, urethral and vaginal swabs for microscopy and culture, viral swabs, blood tests and urine for polymerase chain reaction (PCR).

As most patients will be asymptomatic or have few symptoms, the majority of STIs are detected through screening, contact tracing or further screening for those already diagnosed with an STI. The care of a patient with an STI must involve more than just diagnosis and medication with the aim of cure and reduced infertility. It should also include history taking, clinical examination, correct diagnosis, early and effective treatment, advice on sexual behaviour, promotion and/or provision of condoms, partner notification and treatment, case reporting and clinical follow-up.¹³¹

Diagnosis and treatment of some of the more common STIs is summarised below. Guidelines will differ in different areas and up-to-date and more expanded information can be accessed from websites such as the WHO,¹³¹ the Sexually Transmitted Diseases Treatment Guidelines from the CDC in Atlanta, USA¹³⁴, the Clinical Guidelines for the Management of Sexually Transmissible Infections Among Priority Populations from the Chapter of Sexual Health Medicine of the Royal Australasian College of Physicians,¹³⁵ or the Diagnosis and Management Guidelines of the Sexually Transmitted Diseases Services at the Royal Adelaide Hospital.¹³³

Syphilis

Infection with subspecies of *Treponema pallidum* causes syphilis, yaws, bejel/endemic syphilis and pinta. Presently, *T. pallidum* is the only treponeme endemic to Australia, however the other *Treponema* species and sub-species have been reported from most African countries and throughout the tropics.¹³⁶ Screening algorithms for the diagnosis of syphilis will vary from laboratory to laboratory, but none will differentiate between the various types of treponemal infection. Therefore, a positive serologic test for treponemal infection might be caused by non-sexually acquired infection with non-venereal *T. pallidum* subspecies, by congenital transmission from an infected mother (syphilis only) or by consensual or non-consensual sexual exposure (syphilis only).¹³⁶ Because it is rarely possible to determine with certainty which type of treponemal infection has resulted in a positive treponemal serology result in an asymptomatic patient, patients should always be treated if there is no documented prior treatment of treponemal infection. If the patient is a child and the biological mother's treponemal test is negative, congenital syphilis can be excluded.

A serological diagnosis of treponemal infection requires:

1. A reactive specific treponemal test [e.g. IgG enzyme immunoassay, *T. pallidum* haemagglutination assay (TPHA), *T. pallidum* particle agglutination (TPPA) assay, *T. pallidum* immobilisation assay (TPIA)], which is confirmed either by a reactive non-specific treponemal test (e.g. VDRL or RPR), OR reactivity on a different specific treponemal test such as fluorescent treponemal antibody absorption (FTA) if the non-specific treponemal test is non-reactive;

AND

2. The absence of a history of documented previous adequate treatment of syphilis or endemic treponemal disease (e.g. yaws).¹³⁷

Gonorrhoea

Genital infection with *Neisseria gonorrhoeae* is readily curable, but if untreated can cause infertility and occasionally result in disseminated infection. Men may be asymptomatic or have dysuria, usually with a penile discharge. In women there are often no symptoms or signs, but some women may have a yellow vaginal discharge, low abdominal pain, irregular menstrual bleeding or pelvic inflammatory disease. In both sexes, infection of the rectum may occur during anal sex and infection of the throat may follow oral sex. Diagnosis is made with a Gram's stain and culture of a urethral swab (if there is a urethral discharge) and/or detection of *Neisseria gonorrhoeae* DNA by nucleic acid testing (NAT) on a urethral swab or first-void urine in men. In women, if cervicitis is present on examination, then an endocervical swab (ECS) for Gram's stain and culture should be taken together with a specimen for detection of *N. gonorrhoeae* DNA by NAT. If the female patient is asymptomatic and does not wish to be examined, a Self Obtained Low Vaginal Swab (SOLVS) for NAT for a number of organisms, including *N. gonorrhoeae*, can be collected. Wherever possible, patients with positive NAT for *N. gonorrhoeae* should have the diagnosis confirmed with microscopy and culture before treatment is instituted. Nucleic acid testing for throat and rectal specimens has not been validated for the diagnosis of *N. gonorrhoeae* infection, therefore swabs for culture should be taken if the history or examination suggest infection at these sites.

Chlamydia

Genital infection with *Chlamydia trachomatis* is common worldwide, particularly among young, sexually active people. Most individuals with chlamydia are asymptomatic, however women may have a vaginal discharge, low abdominal pain or irregular menstrual bleeding and men may have dysuria or penile discharge. Untreated chlamydia is the most common cause of pelvic inflammatory disease and infertility in women.¹³³ Diagnosis is made by detection of *C. trachomatis* DNA by NAT in males on a first-void urine or urethral swab (if a urethral discharge is present) and in females on a first-void urine, an endocervical or a self-collected vaginal swab. In females without a cervix or in whom swabs cannot be taken, a first-void urine or a Self Obtained Low Vaginal Swab can be tested for *C. trachomatis* by NAT. Rectal chlamydial infection can be detected with rectal swabs for chlamydia DNA by NAT in those who may have contracted the infection during unprotected anal intercourse.

Trichomoniasis

Infection with the protozoan parasite *Trichomonas vaginalis* is also ubiquitous in sexually active individuals worldwide. Infection can cause an unpleasant discharge and vaginitis in women. Men are usually asymptomatic, but may need to be treated to prevent re-infection of their partners.¹³³ Diagnosis is by detection of trichomonads in vaginal discharge by wet-preparation microscopy and culture, or by NAT where available (although this test is currently not validated to National Pathology Accreditation and Advisory Council standards). In males, microscopic examination of centrifuged urine may reveal trichomonads, but this test lacks sensitivity, and a NAT from first-void urine may be a more sensitive test if it is available.

Bacterial Vaginosis

This is caused by an alteration in vaginal flora and is not an STI *per se*. It produces an offensive smelling discharge, but the vagina is usually not inflamed. Diagnosis requires all of the following criteria: - homogeneous white vaginal discharge, "clue" cells on vaginal swab microscopy and vaginal fluid with a pH > 4.5. If *Candida* spp or *Trichomonas* spp are present, these should be treated and the patient reassessed.

Management

The aim of treatment is for microbiological cure, alleviation of signs and symptoms, prevention of sequelae and prevention of transmission.¹³⁴

Syphilis

Treatment is usually best done in the context of a specialised sexual health or infectious diseases unit and will usually require parenteral penicillin.

Gonorrhoea

Treatment of non-complicated infection is ceftriaxone 250mg IM in 2ml of 1% lignocaine or ciprofloxacin 500mg orally stat if the organism is known to be susceptible to this agent.¹³⁵

Chlamydia

Treatment is with azithromycin 1g orally as a single dose, doxycycline 100mg orally twice daily for 7-10 days, or roxithromycin 300mg daily for 7-10 days¹³⁵

Trichomoniasis

Treatment is with metronidazole 400mg orally 12 hourly for 5 days, metronidazole 2g orally as a single dose, or tinidazole 2g orally as a single dose.¹³⁵

Bacterial Vaginosis

Treatment is only offered to patients with clinical symptoms or signs, if intrauterine instrumentation (e.g. termination of pregnancy) is anticipated and to some pregnant

women. Standard therapy is with metronidazole 400mg orally 12 hourly for 5 days or tinidazole 2g orally as one dose.¹³⁵

Considerations in paediatric refugees

Although child and young adult refugees are at high risk of sexual violence, this information is rarely volunteered by families. If there is a disclosure of such information, or if an STI is suspected for other reasons (e.g. vaginal discharge, genital ulcers, chronic lower abdominal pain), then referral to a service experienced in managing child sexual abuse is recommended.

Although testing for HIV infection is not considered mandatory in those <16 years, this test should be routinely discussed with the child's parents or guardian, as early diagnosis allows monitoring, treatment and age-appropriate education. Using the mother as a quasi-surrogate for HIV testing her children is not recommended, as she may not be child's biological mother, or the child may have acquired the infection non-vertically (e.g. via sexual violence or blood transfusion). Families declining HIV testing may be referred for more detailed discussion with a specialist. HIV-infected children should be referred to the local paediatric HIV service.

All child and young adult refugees should be screened for syphilis infection by serology.¹³⁶ Patients who return a positive treponemal serology result should be discussed with (and possibly referred to) a paediatric infectious diseases physician.

Other infections and infestations

A number of other infections are not uncommonly encountered in recently arrived African refugees. Whilst these infections are rarely life-threatening, they may cause considerable morbidity. Some of the more frequently seen infections are detailed below. Discussion with or referral to an adult or paediatric infectious disease physician is recommended.

Filarial infections

These include infections caused by helminths that reside in various tissues and produce microfilaria. Filarial infections are found throughout the tropical regions of Sub-Saharan Africa and can cause considerable morbidity and mortality if not diagnosed and treated. An otherwise unexplained eosinophilia can be a clue to a filarial infection and warrants referral to an infectious diseases specialist.

Onchocerciasis (river blindness)

This is caused by infection with *Onchocerca volvulus*, transmitted by species of blackflies (*Simulium* spp). It affects approximately 18 million people worldwide and is endemic in 28 countries across sub-Saharan Africa.¹³⁸ The adult worms live and breed in subcutaneous nodules which are not infrequently visible or palpable under the skin (usually in the pelvic region). Migration of microfilaria through the skin and the eye causes a range of symptoms and complications, which if left untreated can result in blindness and chronic skin disease.

The diagnosis of onchocerciasis is made by demonstrating microfilaria in a skin-snip or in the anterior chamber of the eye. As there are well-established onchocerciasis control programs throughout Africa, patients will often have already been diagnosed

with onchocerciasis prior to arrival in Australia and may have been commenced on treatment. Referral to a dermatologist or an infectious diseases specialist is recommended if the diagnosis is suspected.

Standard treatment is with periodic ivermectin (usually yearly), which is microfilaricidal but does not have an effect on adult worms. Therefore, treatment needs to continue until the female adult worm dies or becomes sterile (which can take 9-11 years).¹³⁹ It has recently been shown that doxycycline has a profound inhibitory effect on embryogenesis in female adult *O. volvulus* due to activity against endosymbiotic *Wolbachia* spp, resulting in more long – lasting microfilaricidal activity than ivermectin.¹⁴⁰ On the basis of this evidence, some authorities currently recommend administering doxycycline initially, combined with periodic (half-yearly to yearly) ivermectin.

Loasis

This filarial infection, found across Western and Central Africa, is transmitted by tabanid flies of the genus *Chrysops*. Loasis is usually asymptomatic, however if the adult worm (*Loa*) traverses the conjunctivae or a lymphatic channel, it may produce transient symptoms. Diagnosis can be suggested by intermittent asymmetric limb swelling (Calabar swelling) and can be confirmed either by identification of the passage of an adult worm across the conjunctivae, or demonstration of microfilaria in blood films. Treatment is with diethylcarbamazine (DEC), which is not readily available in Australia.

A potentially fatal encephalopathy can occur in patients who are infected with both *O. volvulus* and *L. loa* if they are given ivermectin to treat onchocerciasis or other parasitic infection. This reaction is thought to be due to death of *L. loa* microfilaria in

the brain. Therefore, infection with *L. loa* should be excluded in patients with onchocerciasis (see “intestinal helminths” section for further details).¹⁴¹

***Mansonella perstans* infection**

Infection with *Mansonella perstans* is found across sub-Saharan Africa and is not infrequently encountered in sub-Saharan African refugees.¹⁴² The majority of infections with this infection are asymptomatic and are diagnosed on routine blood film examination. However some patients describe abdominal pain, pruritus and other symptoms, which are probably the result of immune response to the adult worms. Diagnosis is by demonstration of microfilaria in thick or thin blood films. It is controversial whether *Mansonella* infections need to be treated; However in the presence of attributable symptoms, treatment is recommended. The treatment of choice is not known, however albendazole has been used with some reported success.

Other filarial infections

Lymphatic filariasis caused by *Wuchereria bancrofti* also occurs across Africa and Asia in geographically restricted areas, but at present is not commonly seen in sub-Saharan or South East Asian refugees.

Infestations

Tungaisis is a skin infestation caused by the sandflea *Tunga penetrans*, also known as “chigoe flea or jigger flea”. It is found across Eastern and Central Africa, as well as South Asia, Latin America and the Caribbean. Tungaisis has recently been reported in refugee children arriving in Australia from refugee camps in Tanzania.¹⁴³

The gravid female flea buries into the skin (most commonly on the feet) and lays innumerable eggs onto the skin, which are then released into the immediate environment. The flea causes an intense local inflammatory response often accompanied by secondary bacterial infection. Tetanus and sepsis due to bacterial infection are recognised complications.

Treatment consists of management of secondary bacterial infection, tetanus prophylaxis and occasionally removal of the flea.

Other infections

A number of other infections are endemic in regions from which African refugees originate. These infections and may not be detected at pre-migration screening or may not become symptomatic until after arrival in Australia. These include bacterial infections (e.g. meningococcal disease, African Tick Typhus), viral infections (e.g. Rift Valley Fever) or other parasitic infections and infestations (e.g. scabies, myiasis).

Immunisation

Recommendations

- Catch-up immunisation is recommended for all refugees, unless reliable written documentation of previous immunisation is provided.
- Routine serology for vaccine-induced immunity to determine which vaccines have been received is not indicated.
- Catch-up immunisation should be performed so refugees are vaccinated in accordance with the Australian Standard Vaccination Schedule (as per the current version of the Australian Immunisation Handbook).
- Clinical examination for BCG scar is recommended.

Epidemiology

Many vaccine preventable diseases (VPD) are endemic and/or epidemic in the countries of origin and transit of refugees. Refugees may present with a VPD, or may remain susceptible to VPD due to inadequate immunisation, often as a result of disruption of preventive health care services. Immunisation coverage in countries experiencing internal conflict such as Somalia and Sudan has deteriorated over recent years.¹⁴⁴ Refugees have documented higher rates of VPD such as rubella, congenital rubella and tuberculosis after settling in new destination countries, both from previous exposure and from exposure after arrival.¹⁴⁵⁻¹⁴⁷

Most refugees do not have written documentation of immunisation. Completed Expanded Program of Immunisation (EPI) records are neither a visa medical nor pre-departure requirement. The EPI recommends immunisation against tuberculosis, tetanus, diphtheria, pertussis, measles, poliomyelitis, hepatitis B and rubella. Most African countries of origin of refugees do not include rubella or hepatitis B immunisation in their current EPI schedules and rates of immunisation for schedule vaccines may be less than optimal. For example, in Somalia rates of immunisation against tuberculosis are 50% and as few as 35% of children are immunised against measles.¹⁴⁴ Routine screening of refugee children in Melbourne between 2002-2005 has shown protective antibody levels against VPD vary significantly, with 46-69% protected against diphtheria, 52-88% against tetanus and 74-82% against rubella.¹⁴⁸

Specific recommended immunisation schedules by country are listed at: <http://www.who.int/topics/vaccines/globalsummary/immunization/countryprofileselect.cfm> .

Rationale for catch-up immunisation schedule

Written documentation of previous vaccination is generally considered reliable evidence. Debate continues regarding the validity of parental or self-recall of immunisations received in the absence of written records.^{149,150} In the absence of documentary evidence of prior vaccination, the benefits of complete revaccination are considered to substantially outweigh the disadvantages. However the presence of a BCG scar in the deltoid, forearm or scapular region is evidence of BCG vaccination against tuberculosis (TB), which does not need repeating.

Catch-up immunisation regimen

The recommended catch-up immunisation schedule for individuals is summarised in Table 4, adapted from the Australian Immunisation Handbook.¹⁵¹ The period/s in brackets after each vaccination is/are the minimum interval before subsequent doses. Consult the Australian Immunisation Handbook for contraindications to immunisation and for dosing instructions. For hepatitis B, varicella, polio and mumps/measles/rubella vaccines, no adverse reactions are associated with additional doses in immune individuals. Additional doses of diphtheria and tetanus containing vaccines may be associated with an increase in local and systemic reactions; if such a reaction occurs, review prior to giving further doses.¹⁵¹

Consideration should also be given to medical conditions that require extra vaccine protection, such as children with anatomic or functional asplenia, HIV infection, chronic illnesses and haemoglobinopathies. Consult the Australian Immunisation Handbook or the local public health unit for specialist guidance on the vaccines required in such conditions.

Table 4. Catch-up immunisation schedule for newly arrived refugees

Vaccine type	Age and number of doses	Minimum dosing interval (months)	Notes
MenCCV	> 12 months*, 1 dose	-	Funded at 12 months of age if born after 1/1/2002. Disease has bimodal peaks in incidence of < 5 years and 15-24 years, *catch-up previously funded to 19 years
Diphtheria Tetanus Pertussis vaccines	< 8 years, 4 doses DTPa	1,1,6*	3 doses for primary series then *4 th dose at 4 years of age or 6 months after primary course Combination vaccines available in various jurisdictions. If combined with hepatitis B, dosing interval changes (2 months between doses 2 and 3)
	≥ 8 years, 3 doses (dTpa, ADT, ADT)	1,1	No safety data on 3 doses of dTpa, therefore recommend dTpa, ADT, ADT. (dTpa, single dose, is funded age 15-17 years)
MMR	< 8 years, 2 doses	1	2 nd dose currently recommended at 4 years if < 4 years at first dose
	≥ 8 years (born ≥ 1966), 2 doses	1	
IPV	Any, 3 doses*	1,1	*4 th dose at 4 years if < 4 years for primary course. Available as monovalent IPV or in combination vaccines
Hepatitis B	< 11 years, 3 doses	1,2	Combination vaccines are available
	11 – 15 years, 2 doses adult formulation*	4	*Adult formulation is 1 ml dose, alternate regimen is 3 doses paediatric formulation as above
	≥ 16 years, 3 doses**	1,2	**Age 16 – 19 years 3 paediatric doses, ≥ 20 years 3 adult doses
Hib	2 – 11 months, 2 or 3 doses then booster*	1 or 2*	Not required over 5 years of age. Usually combined with Hepatitis B vaccine. *Refer to handbook for catch-up schedule in younger children – different vaccines require different catch-up schedules with different dosing intervals
	12 – 14 months, 1 dose then booster	varies*	
	15 – 59 months, 1 dose	-	
7vPCV	2 – 6 months, 3 doses	1,1	Not required in low risk children over 2 years of age. People with medical risk factors require extra doses of 7vPCV and 23vPPV
	7 – 17 months, 2 doses	1	
	18 – 23 months, 1 dose	-	
VZV	18 months – 13 years, 1 dose ≥ 14 years (non immune*), 2 doses	- 1	Funded if born after 1/5/2004 (at 18 months) or between 10 – 13 years if no history clinical varicella. VZV is recommended in non immune adolescents ≥ 14 years and adults (*no clinical history and negative serology; check serology if no history of varicella)

HPV	13 – 26 years (females), 3 doses	2, 4	Catch-up funded until June 30, 2009
BCG	Varies*, 1 dose	-	<p>Criteria:</p> <ul style="list-style-type: none"> • *Exposure to active pulmonary TB < 16 years • *Travel to high prevalence area > 3 months aged < 5 years • *Consider in all children in families of a refugee background if no previous BCG • BCG is only given if no record/scar and no evidence TB infection (latent or active) and no other contraindications (which include Mantoux test > 5mm). Perform a Mantoux test prior to BCG if age > 6 months

Specific Issues

Immunisation of adults and children with DT containing vaccines

Childhood diphtheria-tetanus vaccine (CDT) is no longer available, so catch-up vaccination of children less than eight years of age has been simplified to using pertussis-containing vaccines (DTPa, DTPa-IPV, DTPa-IPV-Hib-HepB, DTPa-HepB, DTPa-HepB-IPV). The catch-up vaccine recommended for children over eight years of age and adults; dT (ADT), contains reduced dose diphtheria, to reduce the risk of significant local reactions. In recent years, pertussis-containing vaccines with lower doses of diphtheria and acellular pertussis components have been used as booster vaccines for adolescents and adults previously vaccinated against pertussis (dTpa, or dTpa-IPV). There are no studies to date on the safety or immunogenicity of multiple doses of these newer vaccines as catch-up vaccines, However the potential advantage in providing pertussis immunity and reducing the number of injections by including IPV is considerable.

We recommend that despite the absence of data, where funded, dTpa be used as at least one of the dT containing catch-up vaccines in children ≥ 8 years.

Inactivated polio vaccination

Wild poliovirus continues to circulate in the African subcontinent, with cases reported in 2006 in Kenya, Nigeria, Ethiopia, Democratic Republic of Congo, Angola and Namibia.¹⁵² Cases have been reported in both adults and children. Oral polio vaccination is part of routine immunisation, but despite additional National Polio drives to eradicate polio, polio vaccine coverage rates remain sub-optimal. In the absence of written immunisation records, it is recommended that all arrivals receive IPV as part of the global polio eradication strategy.

Hepatitis B immunisation for adults who are not household contacts of a HBV case

In Australia, hepatitis B vaccination is part of the routine childhood vaccination schedule and is currently offered to all children and adolescents and to adults who are household or intimate contacts of acute and chronic hepatitis B carriers. Hepatitis B vaccination is not routinely offered as part of standard immunisation programmes in sub-Saharan Africa. Recent data from the UK emphasizes the burden of hepatitis B infected individuals in the UK is in the overseas-born from high prevalence areas and that household contact is a means of transmission in children.¹⁵³ The role that travel to endemic countries plays in transmission of hepatitis B remains unclear. Nevertheless, it seems reasonable to recommend hepatitis B vaccination to people who may in the future travel to endemic countries and are potentially at risk of acquiring the infection through sexual and household contact.

BCG Immunisation

Although BCG vaccine is not a routinely administered vaccine under the National Immunisation Program, it is recommended for children within communities at high-risk of TB transmission. BCG is generally accepted as a safe and efficacious vaccine against childhood TB and recent data is supportive for efficacy against adult TB, despite long-standing controversy regarding the role of BCG in adults.^{154,155} While prior BCG vaccination needs to be considered in the interpretation of Mantoux tuberculin skin testing (TST), the increasing use of *in vitro* assays (unaffected by prior BCG), can help resolve this issue in adolescents and adults.

Following appropriate screening to rule out latent or active TB infection, BCG vaccination should be considered for children under 5 years old without prior evidence of BCG immunisation, who will be travelling to live in high countries of high TB prevalence for longer than three months (WHO defines 'high-risk' countries as those with an annual incidence of TB in excess of 100 per 100 000 population.) unless contraindicated. State and Territory guidelines should be consulted for advice on children > 5 years who will be travelling or living for extended periods in countries with high prevalence of tuberculosis. BCG is also indicated for those aged < 16 years (without contraindications, including therapy with isoniazid) exposed to an individual with active pulmonary tuberculosis and for neonates born to patients with leprosy or tuberculosis. Contraindications to BCG include TB infection/disease, immunodeficiency and pregnancy. BCG should be delayed if HIV is suspected, until HIV has been excluded.

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