Guidance for testing and preventing infections and updating immunisations in asymptomatic refugee children and adolescents in Switzerland

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Introduction

Worldwide there are an estimated 60 million displaced individuals, of which 50 % are children and adolescents. Globally, the number of refugees is steadily increasing and in Switzerland more than 28000 individuals were provisionally granted asylum in 2014, of which 66 % were children ≤ 7 years of age, and this number will be significantly higher in 2015. Refugee children and adolescents in Switzerland are heterogeneous in terms of native country. In 2014, the most common places of origin were Eritrea, Somalia, Sri Lanka, Syria and Afghanistan. Refugee children and adolescents may be in a reduced state of health when arriving as a result of lack of healthcare infrastructure in their country of origin, malnutrition and violence and challenging living conditions during their escape. They are at increased risk for infectious diseases and other physical and mental health problems[1), 2)]. Upon arrival in Switzerland, challenges to migrant health may be compounded by limited language proficiency, insufficient knowledge about the local health care system and lack of documentation including immunisation records. Furthermore, asylum seekers often live in crowded dwellings and have to change residence frequently.

After arrival in Switzerland refugees seek asylum and are admitted to one of the the reception and registration centres (EVZ/CEP) and are classified as asylum seekers (permit N). Their request for asylum is evaluated within weeks up to several months after which they are provisionally admitted (permit F), recognised refugees (permit B) or rejected. Every person including children and adolescents requesting asylum in Switzerland has a health check and is given health related information during admission at EVZ/CEP[3)]. This health check is performed by a nurse based on an online questionnaire featuring pictograms, spoken and written text mainly covering signs and symptoms of tuberculosis (TB) disease (http://www.tb-screen.ch). An integrated scoring system also including the country of origin of the refugee helps to decide who needs further investigations for TB disease. In case of suspected TB disease or another acute disease needing further management the asylum seeker is referred to the physician responsible for the respective EVZ/CEP. The questionnaire also includes an item «assessment of the general health condition» of the refugee judged by the nurse as «good» or «bad», which may lead to a referral for other health conditions. The Federal Office of Public Health (FOPH) currently recommends immunisations for refugees during admission in EVZ/CEP only for children <5 years of age (for more details see section on immunisation below).

Switzerland has ratified – as did the majority of countries worldwide – the Convention on the Rights of the Child in 1997[4)]. By ratification of this convention Switzerland commits to recognise the right of the child for the highest attainable standard of health and the right to access facilities for treatment. In addition, any child who is seeking refugee status or who is considered a refugee should receive appropriate protection and humanitarian assistance.

The following recommendations are intended for a health check-up of healthy-looking/asymptomatic children and adolescents ≤ 18 years of age who have recently requested asylum in Switzerland. Implementation of these recommendations should ideally be started at the first visit of a health care provider, preferably within weeks to few months after arrival in Switzerland. Children and adolescents with signs and symptoms of disease are not the focus of this guidance and should be diagnosed and treated according to clinical diagnosis. Recommendations about general health aspects of immigrant children and adolescents are not part of this document and covered in a separate article in this issue. Our aim is to provide guidance for healthcare providers for routine investigations of infectious diseases in asylum seekers and updating their immunisations. We also suggest roles of and the collaboration between primary healthcare providers and paediatric infectious disease specialists.

Guideline development process

A working group was convened among members of the Paediatric Infectious Disease Group in Switzerland (www.pigs.ch) in June 2014. A list of priority infectious diseases was determined by the writing group. Nine individuals were assigned section writing responsibilities. The first drafts of the sections were internally reviewed in May 2015. The second draft was then sent to representatives of the Swiss Society of Paediatrics, the Swiss Tropical and Public Health Institute and the Federal Office of Public Health (FOPH) for review and endorsement in June 2015. The third and final draft was reviewed by all co-authors in November 2015 and approved by the FOPH.

Collaboration of primary healthcare providers with infectious diseases specialists

A number of diagnostic steps can and should be provided as part of primary paediatric care in an office setting. In addition, close involvement of a specialist service is always desirable whenever primary care providers feel they will benefit from such advice. However, in immigrant children and adolescents there is also the possibility of severe or complex infections not commonly seen in Switzerland, or chronic disease, which requires input from

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a specialist service. Our proposed approach for the collaborative management of infectious diseases in immigrant children and adolescents is shown in *table 1*. Further details on specific criteria for referral to a paediatric infectious disease specialist will be provided below.

History taking

History taking for refugee children and adolescent is challenging. An independent interpreter (i.e. not a family member or friend) is advisable whenever possible however this may not always be feasible. All interpreters and families should be advised that the information discussed is strictly confidential. Questions should be short and simple. The following information relevant to infectious diseases and immunisations should be obtained.

- Country of origin, route and duration of escape, date of the arrival in Switzerland, current permission status for Switzerland.
- Previous admissions to a hospital or medical treatments: in the country of origin, during escape, after arrival in Switzerland.
- Endured physical abuse.
- Current symptoms: e.g. diarrhoea, vomiting, cough, or (recurrent) fever.
- Immunisations received in the country of origin, during escape, after arrival in Switzerland. Documentation of immunisation from the country of origin or from Switzerland.
- History of any family member suffering from or died of tuberculosis, HIV or other illness.

Primary health care provider provides	Paediatric infectious diseases specialist provides
• immediate diagnostic workup and treatment of ill-appearing children; referral as needed for severe, unfamiliar or chronic infectious diseases • testing of treatable and/or contagious infectious diseases in healthy-looking/ asymptomatic children • treatment of common infectious diseases (e.g. parasitic diseases) • immunisation catch-up program	• completion of diagnostic workup in newly diagnosed infectious diseases • treatment of severe, complex or chronic infectious diseases • advice to primary health care provider about follow-up controls and immunisations

Table 1: Suggested collaboration for the testing and follow-up of infectious diseases in refugee children and adolescents.

	Primary vaccinations (intervals, in months from 0)				DTPa/dTpa booster vaccinations (age, as per routine vaccination schedule)		
Age[1]	0	1	2	8	4-7 y	11-15 y	25 y
6-11 mo[2, 3]	DTP_a-IPV-Hib-HBV	DTP_a-IPV-Hib-HBV[4]		DTP_a-IPV-Hib-HBV	DTP_a-IPV	dTp_a-IPV	dTp_a
12 mo-3 y[2, 3]	DTP_a-IPV-Hib-HBV MMR[5]		DTP_a-IPV-Hib-HBV MMR[5]	DTP_a-IPV HBV	DTP_a-IPV	dTp_a-IPV	dTp_a
4-7 y[2, 3]	DTP_a-IPV-Hib-HBV MMR[5]		DTP_a-IPV MMR[5] HBV	DTP_a-IPV HBV		dTp_a-IPV	dTp_a
8-10 y[6, 7]	dTp_a-IPV MMR[5] HBV		dTp_a-IPV MMR[5] HBV	dT-IPV HBV		dTp_a-IPV	dTp_a
11-15 y	dTp_a-IPV MMR + VZV[8] HBV[9]		dT-IPV MMR[5] + VZV	dT-IPV HBV[9]			dTp_a
≥ 16 y	dTp_a-IPV MMR[5] + VZV		dT-IPV MMR[5] + VZV	dT-IPV			dTp_a
HPV[10]	11–14 y old girls 15–19 y old women	2 doses at 0, 4–6 mo 3 doses at 0, 1–2, 6 mo					

Table 2: Vaccination schedule of previously unimmunised children and adolescents

1) For clarification of the age groups, e.g. 4–7 years means from the 4th birthday until the day before the child turns 8.
2) In infants and children up to 7 years of age, 1 or more doses of hepatitis B vaccination can be given using a hexavalent vaccine.
3) In this age group, children can be vaccinated against hepatitis B with a 3-dose-schedule either using the hexavalent (0, 2, 8 mo) or the monovalent vaccine (0, 1, 6 mo).
4) Interval of 1 mo for early protection
5) Two doses of MMR vaccine are usually given 2 mo apart or with an interval of at least 1 mo between doses. MMR vaccination should optimally be administered before the age of 2 y although it can be given at any age.
6) Because of potentially severe local reactions, a vaccine containing reduced doses of diphtheria toxoid (d) and pertussis (pa) is used in children age 8 years of age and older
7) For children incompletely vaccinated against diphtheria and tetanus who haven't received any pertussis vaccine see table 3.
8) Vaccination against varicella is recommended for children aged 11–15 y without a history of chickenpox. A catch-up is recommended for adolescents and adults <40 y of age without a history of chickenpox.
9) For this age group, a 2-dose-schedule (4–6 mo apart) can be used but only for HBV vaccines that are approved for this schedule.
10) This vaccine is recommended for female adolescents between 11–14 y of age and is given as a 2-dose-schedule. Unvaccinated young women 15–19 y of age should be given the vaccine using a 3-dose-schedule.

Immunisations

Immunisation recommendations vary substantially across countries. Country specific recommendations can be found on the WHO website http://apps.who.int/immunisation_monitoring/globalsummary/schedules and may serve as an orientation as to which immunisations are routinely given in various countries. However, one should not generally assume that recommended immunisations had been administered if documentation is lacking. Unfortunately, children and adolescents frequently immigrate without any immunisation records and history of received immunisation may not be reliable. Since December 2013 children <5 years of age admitted at EVZ/CEP are recommended to be immunised against poliomyelitis if they have not received prior polio immunisations according to the Swiss recommendation (personal communication V. Masserey, 16/11/2015). The rational for this is the re-emergence of poliomyelitis in the Middle East with the risk of asymptomatic shedders arriving and subsequently spreading poliomyelits to unimmunised refugees. The FOPH recommends that the poliomyelitis vaccine is given in this situation as part of a combination vaccine (DTPa-IPV-Hib) according to the Swiss immunisation schedule (SIS)[6].

Recommendations

- Available immunisation records should be evaluated for all refugee children and adolescents by comparison with age appropriate national recommendations (SIS[6]) established by the FOPH in collaboration with the Swiss national immunisation technical advisory committee EKIF[6].
- Anamnestic reports by parents or other caregivers about previous immunisations are frequently not helpful and vaccinations are generally only considered valid if there is written documentation of administration.
- Missing immunisations should be completed by use of algorithms for incomplete immunisations in children and adolescents, where all documented previous immunisations will be taken into consideration, irrespective of complete or incomplete primary series *(Tables 2 and 3)*.
- Serological investigations to determine specific immunity should not be used routinely since their accuracy is usually not high enough to warrant the expenses.
- As an exception, for tetanus catch-up, anti-tetanus toxin antibody levels may be determined 4 weeks after a dose of a tetanus toxoid-containing immunisation to investigate for the need of further catch-up immunisations. If anti-tetanus toxin antibody levels are measured the need for further doses is based on the following:
  - ≥ 1000 IU/l: no further tetanus immunisation is needed
  - ≥ 500 and <1000 IU/L: single additional dose 6 months after the first one
  - < 500 IU/L: two further doses 2 and 6 months after the first one[7]
- Anti-tetanus toxin antibody levels are also a marker for sufficient priming with diphtheria and pertussis vaccines as they are almost always given in combination.
- Alternatively, individuals can be considered as unimmunised and given a full course of catch-up immunisation.
- If tetanus catch-up is given without determination of anti-tetanus toxin antibody levels, significant local reactions following tetanus toxoid-containing vaccines may prompt determination of anti-tetanus toxin antibody levels to investigate for over-immunisation, followed by termination of the catch-up immunisation series if levels are high (>1000 IU/l).
- As a general principle, missing immunisations targeted against diphtheria, tetanus, pertussis, poliomyelitis, measles, mumps and rubella should be completed in children and adolescents regardless of age.
- In contrast, the following basic immunisations in Switzerland are age-dependent and usually only need to be given within the specified age ranges: *Haemophilus influenzae* type b (Hib) vaccine: <5 years of age,

	Number of previously received doses of DTP_a-IPV(-Hib)[1] [schedule with intervals between doses in months]				
Age	**1**	**2**	**3**	**4**	**5**
6–11 mo	2 doses DTP_a-IPV-Hib [0, 6]	1 dose DTP_a-IPV-Hib			
12–14 mo	1 dose DTP_a-IPV-Hib, 1 dose DTP_a-IPV [0,7]	1 dose DTP_a-IPV			
15 mo-3 y	3 doses DTP_a-IPV [0, 2, 8]	2 doses DTP_a-IPV [0, 6]	1 dose DTP_a-IPV		
4–7 y 1st dose <6 mo 1st dose ≥6 mo	 3 doses DTP_a –IPV[2] / DT + IPV [0, 2, 8] 3 doses DTP_a –IPV[2] / DT + IPV [0, 2, 8]	 3 doses DTP_a –IPV[2] / DT + IPV [0, 2, 8] 2 doses DTP_a-IPV [0, 6]	 2 doses DTP_a-IPV [0, 6] 1 dose DTP_a-IPV	 1 dose DTP_a-IPV –	
8–10 y 1st dose <6 mo 1st dose 6–12 mo 1st dose ≥ 1 y	 3 doses dT(p_a[2])-IPV [0, 2, 8] 3 doses dT(p_a[2])-IPV [0, 2, 8] 2 doses dT(p_a[2])-IPV [0, 6]	 3 doses dT(p_a[2])-IPV [0, 2, 8] 2 doses dT(p_a[2])-IPV [0, 6] 1 dose dTp_a-IPV	 2 doses dTp_a-IPV [0, 6] 1 dose dTp_a-IPV –	 1 dose dTpa-IPV – –	
11–15 y 1st dose <6 mo 1st dose 6–11 mo 1st dose 1–3 y 1st dose ≥4 y	 3 doses dT(p_a[2])-IPV [0, 2, 8] 3 doses dT(p_a[2])-IPV [0, 2, 8] 3 doses dT(p_a[2])-IPV [0, 2, 8] 2 doses dT(p_a[2])-IPV [0, 6]	 3 doses dT(p_a[3])-IPV [0, 2, 8] 3 doses dT(p_a[3])-IPV [0, 2, 8] 2 doses dT(p_a[3])-IPV [0, 6] 1 dose dTp_a-IPV	 3 doses dT(p_a[3])-IPV [0, 2, 8] 2 doses dT(p_a[3])-IPV [0, 6] 1 dose dTp_a-IPV	 2 doses dT(p_a[3])-IPV [0, 6] 1 dose dTp_a-IPV –	 1 dose dTp_a-IPV – – –

Table 3: Vaccination schedule for *incompletely* immunised children and adolescents

1) HBV doses to be added as necessary for completion of a 2, 3 or 4-dose schedule (age-dependent).
2) Only 2 (first and third) of these doses should contain the pertussis component.
3) Only 1 (first) of these doses should contain the pertussis component.

human papilloma virus (HPV) vaccine: females, 11–14 years of age *(for males see Table 4)*.
- With regards to specific indications, all recommended immunisations also apply to immigrant children and adolescents. Specifically, from 11 years of age onwards, individuals with a negative or uncertain history of varicella should receive 2 doses of varicella vaccine (monovalent or, consider if indicated and <13 years of age, in combination with measles, mumps and rubella as MMRV vaccine. Note that the combination vaccine is not reimbursed by health insurances as of Dec 2015).
- In addition to basic immunisations, so-called complementary immunisations should be offered according to the SIS[6] as catch-up to all immigrant children and adolescents if missing *(Table 4)*. Further to this, additional risk-based immunisations are to be offered in particular to those with specific risks. Thus, indications e.g. for hepatitis B (see below), influenza, meningococcal, pneumococcal and other risk-based immunisations should also be checked systematically[6].

Tuberculosis

After inhalation of *Mycobacterium tuberculosis*, individuals can be infected but many remain asymptomatic (latent tuberculosis). The risk of tuberculosis (TB) transmission is influenced by many factors including the infectiousness of the index case, duration of exposure and the age of the exposed individual[8), 9)]. After infection the risk of developing TB disease is also dependent on several factors including the immunity and age of the host and is generally estimated to be around 10% over a lifetime[10)]. Importantly, in children the risk of developing TB disease after infection is considerably increased: 33% of children <5 years of age and 19% aged 5 to 14 years with TB infection developed TB disease within 5 years in a recent study in Amsterdam[11)]. The highest risk for progression to active TB is generally in the first two to three years but in children is usually in the first 6 months after infection[10), 11)]. In addition, young children exposed are at particular high risk to develop severe forms of TB such as miliary TB and TB meningitis[8)]. TB is primarily transmitted by adults with pulmonary TB disease living in the same household. Transmission by children and adolescents with TB is described in only few cases because childhood TB is rarely sputum positive[12)].

TB is a rare disease in Switzerland with a yearly incidence of 1–2/100000 children (14 to 31 cases per year between 1996 and 2011) with over 80% occurring in children and adolescents of foreign origin[13)]. TB incidence in Switzerland is in dramatic contrast to many of the countries where refugees originate from, in which TB incidence rates in children and adolescents are estimated to be > 100/100000[14), 15)]. In addition, the risk of TB exposure may be increased in those living in refugee camps or exposed to crises caused by armed conflict, forced population displacement, or natural disasters suggested by a recent systematic review showing at least a two fold increase of TB incidence in these settings[16)].

In all EVZ/CEP an interview-based screening system for TB has been in place for all refuges since 2006, which is performed within the 5 first days after arrival, with the aim of early detection of contagious pulmonary TB[17)]. This system has been developed and evaluated for adults only[17)]. An interview based-screening system is of limited value to detect TB disease in children and adolescents because they are more commonly asymptomatic or have non-specific clinical features compared to adults[18), 19)]. However contagious disease is very rare particularly in young children and in those who are asymptomatic. A TB screening based on chest radiography is also of limited value particularly in younger children. Sensitivity of a chest x-ray is reported to be 28% in children < 2 years increasing to 63% in older children and highest with 78% in adolescents > 12 years[19)–21)]. In addition, children and adolescents are more sensitive to the effects of ionising radiation and therefore radiological investigations should be kept to a minimum. Immunodiagnostic testing (with either a tuberculin skin test (TST) or an interferon-γ release assay (IGRA)) has the highest sensitivity and specificity for detection of TB diseases in children and adolescents ranging from 60% to 80%[22), 23)]. Moreover, in younger children in contrast to adults a positive immunodiagnostic test result correlates with primary and recent infection. Screening refugee children and adolescents for TB is mandatory in the majority of OECD countries and in 56% of the countries this includes at least an immunodiagnostic test such as a tuberculin skin test (TST)[24)]. Demographic characteristics for selection of screening such as age or TB-incidence in the country of origin are highly variable across Europe[24)]. One option for a targeted TB screening is to base this on TB-incidence in the country of origin. (Current global TB incidence rates are available from the WHO TB country profiles see: http://www.who.int/tb/country/data/profiles/en/.) In summary, refugee children have a higher risk of recent infection as a result of originating from a TB high risk country or acquiring TB during escape and have an age-associated vulnerability for progression to TB disease and for severe disease. Therefore targeted TB screening for young immigrant children who consult a physician is justified because these are high risk populations in which early recognition of disease is needed, in accordance with the national TB strategy[25)].

	Primary vaccinations (intervals, in months from 0)			
Age	**0**	**1**	**2**	**8**
6–11 mo	PCV-13[1, 2]	PCV-13		PCV-13
12–23 mo	PCV-13[2] MCV-C[3]		PCV-13	
2–4 y	PCV-13[2] MCV-C[3]			
5–19 y	MCV-C[3]			
>11 y (males)	HPV		(HPV)[4]	HPV[4]

Table 4: Recommended complementary immunisations

1) 13-valent pneumococcal conjugate vaccine (PCV-13)
2) Children who have already received doses of the 7-valent pneumococcal conjugate vaccine (PCV-7), can be switched to a PCV-13 schedule at any age. Children ≥ 12 mo who are partially immunised with PCV-7 only need a single dose of PCV-13 for optimal protection.
3) Group C meningococcal conjugate vaccine (MCV-C)
4) (4-) 6 months after the first dose; those > 15 years of age should receive 3 doses (0-2-6 month schedule)

Recommendation for testing and follow-up

- The rationale for a TB screening is identification of those children needing further evaluation for TB disease.
- All refugee children and adolescents known to be recently exposed to an index case with TB disease or who have an immunodeficiency should be screened.
- All refugee children < 5 years of age regardless of their country of origin should be screened.
- In children ≥ 5 years of age testing for TB should be done if there is any of the following: persistent cough (>2 weeks), unremitting cough, weight loss/failure to thrive, persistent (>1 week) unexplained fever (>38°C), persistent, unexplained lethargy or reduced playfulness: activity reported by the parent/caregiver.
- A tuberculin skin test (TST) should preferably be used for screening in children < 5 years of age regardless of Bacillus Calmette-Guérin (BCG) vaccination status. In cases of shortage of PPD an IGRA may be used in children < 5 years of age.
- In children and adolescents ≥ 5 years TST or IGRA may be used for testing.
- The TST should only be applied and read by trained personnel. A dose of 0.1 mL of PPD RT23 tuberculin (containing 2 tuberculin units) is injected intradermally to the volar aspect of the forearm using a short-bevel needle (26 G).
- An induration ≥5 mm measured 48–72 hours after injection is considered a positive test result[10].
- All children and adolescents with positive TST or IGRA results should be referred to paediatric infectious disease or paediatric respiratory medicine specialist for further evaluation and treatment of TB infection and disease, respectively.

Viral infections
Hepatitis B

Hepatitis B infection is caused by the hepatitis B virus (HBV) and may result in a liver disease that can be acute or chronic. HBV transmission occurs by mother-to-child transmission, percutaneous or mucosal contact with infected blood or other body fluids mainly through sexual contact or unsafe medical practices. Chronic infection with HBV is a major public health problem throughout the world. The majority of individuals chronically infected are not aware of their infection status although infection is associated with cirrhosis, chronic liver failure, and hepatocellular carcinoma in 15–40% of affected individuals. Worldwide, an estimated 2 billion people have serologic evidence of HBV infection, 350 million are chronically infected, and 621,000 people die from HBV-related liver disease each year[26), 27)]. The prevalence of chronic HBV infection in the general Swiss population is estimated to be 0.3%[28)]. In children, the seroprevalence is unknown but likely to be very low. In the adult immigrant population the seroprevalence of chronic HBV infection is higher in certain populations particularly originating from East Asia, Sub-Saharan Africa and Eastern Europe[26)]. In countries of high endemicity, transmission is mainly perinatal but in early childhood it may also occur through contact with chronic carriers and unsafe medical practices. In areas of intermediate endemicity, transmission is either perinatal or horizontal. In countries of low endemicity, most HBV infections are acquired by horizontal transmission in adolescent or early adult life, mainly through sexual activities. For HBV infection, the risk of developing chronic infection varies inversely with age, being about 90% in infants infected at birth, 20% to 50% in children younger than 5 years, and 1% to 10% in persons infected at a later age[28)]. HBV vaccination coverage has been expanding worldwide since the year 2000 according to the WHO, and it is estimated that between 72% and 91% of children < 12 months have received 3 doses of HBV vaccine in 2012[29)].

Recommendation for testing and follow-up

- The rationale for testing is to identify children and adolescents with current HBV infection; this will allow a close monitoring and their close contacts will be offered HBV immunisation to prevent further transmission.
- Screening for HBV infection should include anti-HBc and HBsAg.
- In infants and newborns, if available, the records of the mother should be evaluated for her HBV status. If the mother has a negative serology no further testing is needed for the infant.
- In addition, HBV immunisation status should be assessed.
- Measurement of anti-HBs in children with unknown immunisation history is not advised as correlates of protection in this setting (i.e. unclear how many doses have been given) are not established.
- Children and adolescents not infected (HBs-Ag and anti-HBc negative) and not previously immunised should be immunised *(see management depending on serology results Table 5)*.
- If they originate from a country with higher prevalence of HBV infections, HBV immunisation is recommended before adolescence.
- Measurement of anti-HBs after a full course of immunisation to confirm immunity should not be done unless the child or adolescent belongs to a risk group (such as children from mothers with a positive HBs-Ag, patients with immunodeficiencies or on hemodialysis).
- In case of diagnosis of an acute or chronic HBV infection the patient should be referred to a pediatric gastroenterologist and/or infectious diseases specialist.

Human immunodeficiency virus

Human immunodeficiency virus (HIV) infection results from infection with HIV-1 or HIV-2 by mother-to-child transmission, contact with infected blood or vaginal, anal or orogenital sexual contact. In 2013 an estimated 35 million people were living with HIV of which 3.2 million were children <15 years. In children younger than 15 years new HIV in-fections occurred in an estimated 240000 (210000–280000) in 2013[30), 32), 34)]. The vast

HBs-Ag	Anti-HBc IgG/IgM	Interpretation	Action
neg	neg	not infected	complete immunisation series if previously unimmunised
pos	pos or neg	acute or chronic HBV	please refer to a paediatric infectious disease or gastroenterology specialist
neg	pos	uncertain or past infection	

Table 5: Interpretation and recommendations of hepatitis B serology and consecutive management in refugee children and adolescents without a full course of HBV immunisation.

majority of these children are infected through mother-to-child transmission and mostly during delivery. In Switzerland the prevalence of HIV in recently arrived refugee children and adolescents is unknown but estimated to be low. Worldwide 1.5 million people died due to the acquired immune deficiency syndrome (AIDS) in 2013, of which 190 000 were younger than 15 years. The risk of dying from HIV-associated complications is considerably higher in infants and adolescents (10–19 years) compared to older patients and early initiation of treatment has been shown to reduce mortality[33]. The majority of infected children are asymptomatic particularly in the first year after infection.

Recommendation for testing and follow-up

- The rationale for HIV testing is early identification of those infected to limit short term morbidity and mortality and maximise long-term outcomes and quality of life in all children. In sexually active adolescents HIV testing is needed to minimise the risk of onward transmission[33].
- If available the records of the mother should be evaluated for her HIV status. If the mother is HIV negative a screening should not be done unless there is suggestive history or clinical presentation.
- Screening for HIV infection should be offered to all refugee children and adolescents.
- Screening should be done by HIV-1 and HIV-2 antibody testing and all positive tests should be confirmed by a second sample test.
- In children <18 months of age with a positive serology for HIV-1 or HIV-2 antibodies a polymerase chain reaction (PCR) test for HIV DNA should be done as anti-HIV antibodies may be of maternal origin.
- All children and adolescents with positive HIV antibody or PCR tests should be referred to a paediatric infectious disease specialist as soon as possible for counselling and management.

Helminths and protozoa other than malaria

Children of all ages can be infected or infested by intestinal and extra-intestinal parasites. Individuals with poor personal hygiene, low quality of clean drinking water supply are at high risk for parasitic infections. Many parasitic infections are asymptomatic and self-limited but long term sequelae may occur. Chronic parasitic infections can result in impaired physical and mental development such as iron deficiency, anemia, micronutrient deficiencies, malnutrition, growth and cognitive retardation, and malabsorption[35]. Some parasites may persist for years and cause severe long term complications such as bladder cancer and portal hypertension (schistosomiasis) or life-threatening hyperinfection (immunosuppressed patients with chronic strongyloidiasis)[36), 37]. It is estimated that more than one billion people are infected with soil-transmitted helminthes, 200 million with *Schistosoma spp.*, and 100 million with *Strongyloides spp.*[36]. Globally, among intestinal protozoa, the most frequently found pathogenic parasites are *Giardia lamblia* (10.8%), followed by *Entamoeba spp.* (4.3%), and *Cryptosporidia* (4.0%)[37].

Recommendation for testing and follow-up

- The rationale for testing for helminth and protozoan infections is identification of those needing further evaluation and treatment to prevent long-term complications.
- All refugee children and adolescents should have three stool probes sent for microscopic parasitic examination. Three microscopic exams increase sensitivity for parasites detection[38)-40)].
- Alternatively: presumptive treatment of asymptomatic individuals (> 2 years and > 10 kg) may be done using a single dose of albendazole (400 mg)[41].
- Schistosomiasis serology is recommended for refugee children and adolescents from all African and Middle Eastern countries as well as from Brazil, Venezuela, the Caribbean, Surinam, China, Indonesia, the Philippines, the Lao People's Democratic Republic and Cambodia (up-to-date country maps can be found at http://www.who.int/mediacentre/factsheets/fs115/en/)[36), 42].
- Strongyloides serology is recommended for refugee children and adolescents from highly endemic countries (Southeast Asia and Africa)[36), 42]. In case of immunosuppression, screening for strongyloides should be done regardless of the patient origin.

Malaria

Malaria is caused by an infection with different *Plasmodium spp.*, transmitted by female Anopheles mosquitos. Approximately half of the global population lives in a malaria-endemic region. Malaria is a life-threatening condition and therefore it should be ruled out in any febrile patient from an endemic area. The WHO World Malaria Report stated that malaria is endemic in 97 countries worldwide, with the highest burden in the African Region[43]. An estimated 3.2 billion people are at risk and in 2013 almost two million cases of malaria occurred globally. Malaria led to over half a million deaths, particularly in the African Region and in children < 5 years of age, who account for 78% of all deaths (for endemic countries see http://worldmalariareport.org/library). Among all parasitic infections, malaria has the highest mortality globally with more than 400000 deaths in children younger than 5 years of age in 2012[44]. Malaria should be considered in any child presenting with fever with or without other clinical signs and symptoms and who has lived in or travelled to an endemic region in the last 6–12 months. Incubation period is usually 7–15 days but may be up to several years in rare cases. Additional symptoms may occur including nausea, vomiting, headache, chills and arthralgia/myalgia. Clinical examination may reveal hepatomegaly, splenomegaly and jaundice.

Recommendation for testing and follow-up

- Routine screening for malaria for refugee children and adolescents is not recommended.
- Malaria should be managed by experienced clinicians and urgent referral of patients with suspected malaria to a paediatric infectious disease or tropical medicine specialist is important.

Chagas disease

Chagas disease is caused by protozoan *Trypanosoma cruzi* and is transmitted by triatomine insects, which are also known as «cone-nosed or kissing bugs». Vector-borne transmission occurs exclusively in the Americas, where millions of people are infected. Transmission can also occur through blood products, organ transplantation and vertically with a risk of mother-to-child transmission of 5%[45]. An estimated 5 to 6 million people are chronically infected worldwide, with more than 50 000 new cases per year. Imported Chagas disease is not rare in Europe. A recent estimate based on number of immigrants from Chagas-endemic countries suggest that between 1500 to 4000 individuals with Chagas disease live

in Switzerland[46]. In a study conducted in Geneva, 1012 immigrants from Latin America were screened using serology of which 12.8% where positive; the majority originating from Bolivia[47].

Acute Chagas infection is usually asymptomatic, regardless of the point of entry. Acute infection is followed by an indeterminate phase which is also asymptomatic and can last for life. However, a third of all patients will develop chronic cardiac or gastrointestinal disease, during life time, generally decades after acute infection. Gastrointestinal dysfunction (mainly mega-oesophagus, megacolon, or both) are found in about 10–15% of chronically infected individuals. The cardiac form develops in 20–30% of patients and leads to abnormalities of the conduction system, apical aneurysms, cardiac failure and sudden death. Chagas disease reactivation in immunosuppressed patients is a life threatening condition leading to myocarditis and neurological compromised.

Recommendation for testing and follow-up

- The rationale for testing for Chagas infections is identification of those needing treatment to prevent long-term complications.
- Screening for Chagas infection is recommended for refugee children and adolescents from Central and South America and in particular from Bolivia should be screened for Chagas infection by serology.
- Screening should be done by a serological test.
- All children older than 9 months from mothers originating from Central and South America should be screened by a serological test if the mothers' serological test is unknown or positive.
- Children and adolescents with a positive Chagas serology should be referred to a paediatric infectious disease specialist for treatment.
- Children and adolescents with a suspicion or clinical signs of Chagas disease should be referred to a paediatric infectious diseases specialist for testing.

Sexually transmitted infections

Sexually transmitted infections (STI) can be transmitted from mother to child during pregnancy and thereby play an important role in children. For refugee children and adolescents syphilis is the most important STI as it may have been acquired congenitally and is often asymptomatic in its presentation. All other STI are acquired in sexually active individuals or in children and adolescents that have been sexually abused. The seroprevalence of syphilis is highest in the African Region, with 3–4% of individuals affected, lower in the American and South-East Asian Region with 1–2% and below 1% in the Eastern Mediterranean, European and the Western Pacific Regions of WHO[48].

Recommendation for testing and follow-up

- The rationale for syphilis testing is identification of congenitally infected infants and those with sexually transmitted syphilis with the intention to treat, prevent complications and limit further transmission.
- Screening for syphilis is recommended for refugee children < 2 years of age, adolescents (from 12–15 years onwards) and at any age if there is a history of sexual abuse.
- Screening should be done using a T. *pallidum* particle agglutination (TPPA) assay, a treponemal enzyme immunoassays (EIA) or a chemiluminescent immunoassay (CLIA).
- If any of these tests are positive the patient should be referred to a paediatric infectious disease specialist.
- Screening for other STIs should be based on a history of sexual intercourse or abuse and/or clinical findings. *C. trachomatis* and *N. gonorrhoeae* culture and/or PCR must be done from a conjunctival, urethral, vaginal swab or on a first-void urine. *T. vaginalis* culture and/or PCR for must be done from vaginal discharge or urine.

Summary of recommendations

Table 6 provides a checklist for infectious disease check-up for healthy-looking refugee children and adolescents.

Specimen	Test recommended for all refugee children and adolescents	Test recommended based on age, risk factors and epidemiology
Blood	HBsAg, anti-HBc HIV-1/HIV-2 antibody +/- tetanus antibody (1 month after booster)	Chagas serology Interferon-γ release assay (IGRA) Schistosomiasis serology Strongyloides serology Syphilis serology (TPPA or similar)
Stool	3 x for parasites	
Other	TST (< 5 years of age)	TST

Table 6: Checklist for recommended investigations

Conclusion

This guidance is intended to improve or maintain health in immigrant children and adolescents and their families. Early recognition and treatment of a variety of infectious diseases which are more prevalent in the immigrant population is a responsibility of all primary care physicians and paediatricians in Switzerland. Consistent and rapid catch-up immunisations in all immigrant children and adolescents are equally important and may prevent outbreaks of contagious illnesses and therefore protect the resident population as well.

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