CLINICAL GUIDELINES FOR RECENTLY ARRIVED IMMIGRANT CHILDREN

Newly arrived immigrant children come to this country with varied medical needs, some simple and some complex. The Division of Global Migration and Quarantine of the CDC (https://www.cdc.gov/ncezid/dgmq/index.html) provides the Department of State (DOS) and the U.S. Citizenship and Immigration Services (USCIS) with medical screening guidelines for all examining physicians, and outlines in detail the scope of the medical examination.

We outline here the elements of the initial medical evaluation for newly arrived immigrant children, identified by the CDC, supplemented with recommendations based on published evidence.

1) Comprehensive History and Physical Examination

History

- Obtain and review pre-departure treatment and medical evaluations, if available.
- Encourage sharing of personal narrative (i.e., ask about country of origin, countries of transit, time in refugee camp, history of torture, "How did you come to this country?")
- If available: birth history, developmental history.
- Perform a review of systems, focusing on infectious diseases and mental health.
- Ask about use of traditional medications or healing practices.
- Apply age appropriate developmental and behavioral screening tools and social determinant of health screening tools.

Immunizations

- Follow CDC guidelines for vaccination schedules and catch-ups.
- Vaccinations given in other countries are acceptable if original vaccination records are available and the vaccinations conform to appropriate intervals and age guidelines.
- Health care providers need to assess each patient based on age and risk factors to decide whether immunity testing is appropriate. For children, rely on documented immunization records, not antibody titers, for evidence of previous vaccination. In adults, laboratory evidence of immunity is available for measles, mumps, rubella, hepatitis A, hepatitis B, polio, and varicella.

Physical exam

In addition to the essential components of the physical exam, pay attention to:

- Blood pressure. To all children but particularly those ≥ 3 years old.
- Body mass index.
- Head circumference in children < 2 years.
- Hearing screening in children > 4 years and in any child with speech delay.
- Eyes: undiagnosed vision problems.
- Vision screening: photo screening -if available- in > 1 year olds, visual acuity in > 4 year olds.
- Infectious disease: pallor, splenomegaly, jaundice.
- Skin: burns, scars, or other signs of trauma or ritual scarification.
- Genitourinary: female circumcision.
- Dental condition: caries, missing teeth, gingivitis, betel nut use.

2) Initial laboratory evaluation

- CBC with differential. Pay attention to the following:
    1. White blood cell count for infection (WBC high, eosinophilia, neutropenia, etc).
    2. Eosinophilia (absolute eosinophil count >400 warrants further investigation - possible parasitic infection).
    3. Hemoglobin/Hematocrit for anemia.
    4. RBC indices for potential hemoglobinopathies (ie. Thalassemia or Sickle Cell Trait).
- Basic metabolic panel (adults only)
- IGRA testing (or TST if <2 y old) *(a)*
- Ova and parasite and stool culture *(b)*
- Hepatitis B serology (HBsAg, HBsAb, HBcAb), hepatitis A, and hepatitis C serology if history is unknown or any high risks
- HIV 1 and 2 antibodies *(c)*
- Lead (if ≤16 y old) *(d)*
- Syphilis testing. RPR recommended for all recent immigrants unless maternal status clearly known and child has had no high risk activity (ie. did not travel unaccompanied to the US and no possible sexual abuse)
- Titers (adults only): varicella, MMR, hepatitis B
- Lipid screening for all children between 9 and 11, and 17 and 21 years old
- Optional:
    1. Urinalysis (if concern for *Schistosomiasis*).
    2. Thick-and-thin blood smear (if concern for malaria). Malaria should be ruled out in any international traveler from malaria endemic regions who has fever in the 6 to 12 months following arrival.
    3. Chlamydia/Gonorrhea testing. Consider in all patients, especially in those that emigrated as unaccompanied minor and/or have been sexually abused.
    4. Zika viral RNA on urine or serum RT-PCR, Zika virus IgM (+) *(e).*

(a) Use tuberculin skin testing alone or in conjunction with interferon-gamma release assay (IGRA) to screen children younger than 2 years for tuberculosis. IGRA is preferred when patient has a history of BCG administration (TB vaccine)

(b) Include 2 evaluations for ova and parasites plus a complete blood count with differential when screening refugees for parasitic infections.

(c) Screen all adolescent and adult refugees for human immunodeficiency virus infection.

(d) Check blood lead levels in all children 6 months to 16 years of age on arrival in the United States and 6 months later.

(e) Confirm a Zika IgM (+) test with serum plaque reduction neutralizing test (PRNT). The IgM test for Zika cross-reacts with other flaviviruses, including dengue and yellow fever, but the PRNT confirms which viral illness is present. Of note: RT-PCR may be negative after in-utero infection.

3) Other

a) Tuberculosis screening

Newly arrived children are a higher risk of **latent tuberculosis infection** (**LTBI**) and **active TB** than the general US population. Since 2002, more than 50% of all people diagnosed with TB in the United States have been born outside the country. Tuberculosis is much more likely to progress to active TB in infants,

young children, and people co-infected with HIV (10 % per year) than in otherwise healthy adults (10 % life-time risk).

All newly arrived immigrant children need to be screened for TB and treated appropriately.

- Screen for **active TB** with a chest radiograph and possibly a sputum analysis during the Overseas Medical Examination (OME).
- Screen for **LTBI** consist of PPD if age is less than 2 years old and Interferon-gamma release assay (**IGRA**) if age is ≥ 2 and history of BCG vaccine.
- Although the BCG vaccination can reduce the incidence of TB meningitis and disseminated TB in children, it can cause false positives PPDs and does not protect adults against primary infection or reactivation of TB.
- PPD can be placed same day as live-virus vaccines, but should wait 6 weeks if placing after live-virus vaccine already given.
- If PPD is negative, consider repeating it in 6 months in patients with chronic illnesses or malnourish (not a concern with IGRA testing since the control test results will tell you if the patient is anergic).
- Because the IGRA is a blood test, it eliminates interpretation errors associated with tuberculin skin testing and is not affected by BCG vaccination or anergy.
- If either test is positive, obtain a chest X-ray to rule out pulmonary TB, then begin treatment for latent TB if no other signs/symptoms for active TB (cough, fever, night-sweats, weight loss, lymphadenopathy).
- Perform serial sputum evaluation whenever the chest radiograph indicates potential active TB.

Tuberculosis treatment

Everyone with latent (LTB) or active TB must be treated according to CDC http://www.cdc.gov/tb/topic/treatment/ltbi.htm or your local TB treatment center. Patients may receive TB treatment from either individual medical providers or city or state health departments, depending on local capacity.

At the time of this writing (April 2019), the current TB treatment consist of:

- For **LTBI:**
    1. In adults and children ≥ 5 year old: **INH** + **RIF** for 12 doses once weekly
    2. In children ≤ 2 year old: RIF for 4 months daily dose *or* INH + RIF for 12 doses once weekly
    3. for those 2 to 5 year old consider treating as those ≥ 5 year old.

  The **INH** dose is:
    1. In adults (≥ 18 years of age) 5 mg/kg per day orally to a maximum daily dose of 300 mg.
    2. Children should receive 10 to 20 mg/kg per day orally to a maximum daily dose of 300 mg. Twice weekly therapy schedules are also an alternative, commonly used for children who receive treatment in school.
       Pyridoxine (vitamin B6) supplementation to aid in preventing peripheral neuropathy in patients taking isoniazid is not needed except in the following cases: pregnancy, breastfeeding, patients of all ages suffering from diabetes, renal failure, alcoholism, malnutrition, HIV, or a seizure disorder. The adult oral dose of Pyridoxine is 25 to 50 mg/d, and the pediatric oral dose is 6.25 mg/d.

  The **Rifampin** dose is:
    1. For patients ≥ 16 years of age is 10 mg/kg per day orally to a maximum daily dose of 600 mg.

2. Patients ≤ 15 years of age is 10 to 20 mg/kg per mouth per day, also to a maximum daily dose of 600 mg.

- For patients with **active TB**, treatment is more complex and based on the patient's overall health. Please refer to the CDC recommendation for the treatment of active TB (http://www.cdc.gov/tb/topic/treatment/tbdisease.htm) or contact your local TB treatment center.

b) Diagnose and treat Parasites.

All children should be either screened or empirically treated for common parasitic infection. **Common pathogens** in untreated immigrants are hookworms (*Ancylostoma duodenale* and *Necator americanus*), *Schistosoma* species, *Strongyloides stercoralis*, whipworm *Trichuris trichiura*, and *Giardia lamblia*. Although sustained domestic transmission is unlikely, these parasites may cause growth delay, anemia, hyper-infestation syndrome and disseminated infection (*A. lumbricoides* and *S. stercoralis*), and increased cancer risk (*Schistosoma hematobium*). Transmission of *Ascaris* and whipworm occurs via ingestion of soil contaminated with these helminths in human feces, and infection with hookworm occurs primarily through direct contact between skin (such as bare feet) and contaminated soil. Infections may be asymptomatic or may cause abdominal pain, diarrhea, nausea/vomiting, or anemia due to malabsorption or blood loss. Treatment of choice is albendazole; however clinicians should confirm that patients do not have a history of seizures or other neurologic deficits (which may be indicative of other parasitic infections, i.e. neuro cysticercosis) prior to treatment.

Screening mostly consist of stool ova and parasite collection (2-3 samples, each more than 24 hours apart due to low sensitivity of single test) and Strongyloides serology.
New, more sensitive and specific assays have been developed for many parasites, including *Cryptosporidium parvum*, *Entamoeba histolytica*, *Giardia lamblia*, *Stronyloides stercoralis*, and *Schistosoma* species, but these specialized tests are not recommended unless the provider strongly suspects a specific parasite based on history and physical exam or persistent eosinophilia. Serology for IgG antibodies against *Strongyloides* is the testing of choice for diagnosis. Ivermectin is the preferred drug but should not be used in patients from *Loa loa*-endemic regions unless co-infection has been ruled out.

All newly arrived immigrant should have a complete blood count with differential to help identify occult parasitemia. In line with CDC guidelines, failure to identify a cause of eosinophilia in a newly arrived immigrant should prompt referral to an infectious disease specialist and further work-up. Re-testing for ova and parasites in stool (2 samples), should be performed in those with suspected treatment failure after antibiotic treatment of any parasite, and in immunocompromised patients.

Empiric treatment is simple and generally safe, with few contraindications.
The immigrant region of origin orient us towards what organism(s) therapy should focus. If their origin is Middle East, South Asia, or Southeast Asia, *Strongyloides stercoralis* and other roundworms predominate (Albendazole and Ivermectin are drugs of choice). In Africa other parasites are more prominent: *Schistosoma* species, and *S. stercoralis* and other roundworms. Consider presumptive treatment with Praziquantel for all immigrants from Sub-Saharan Africa per CDC guidelines (be aware of contraindications to treatment).

For further details consult the CDC: Immigrant and Refugee Health: Domestic Intestinal Parasite Guidelines. Available at: https://www.cdc.govimmigrantrefugeehealth/guidelines.

c) Watch for ubiquitous hepatitis infection

In accordance with CDC vaccination guidelines and American Academy of Pediatrics Bright Futures recommendations, we endorse hepatitis A serology testing with re-vaccination unless immunity is documented for newly arrived children 1 to 18 years of age.
A third of the world's population shows serologic evidence of past infection with hepatitis B virus (HBV); high rates occur in Southeast Asia and sub-Saharan Africa, where most infections are transmitted perinatally.
A study of Minnesota refugees found 7% to be positive for hepatitis B surface antigen (HBs Ag), with a higher prevalence among refugees from sub-Saharan Africa. Most screening protocols test for HBs Ag and antibody to hepatitis B surface antigen (HBs Ab); it is reasonable to add a screen for antibody to hepatitis B core antigen (HBc Ab total and IgM). Screening for HBV infection using HBs Ag, HBs Ab, and HBc Ab minimizes under-diagnosis in this high-risk population. Encourage immunization, especially for patients with hepatitis or cirrhosis from any cause.

Hepatitis C screening should follow CDC guidelines for the general population, focusing on migrants from countries with high prevalence of hepatitis C and high-risk groups such as injection drug users, victims of sexual violence, people with multiple sexual partners, recipients of blood transfusions, and people with any other type of hepatitis.

d) Malaria

Many immigrants come to the United States from areas where malaria is endemic. In 2007, the CDC instituted empiric treatment before arrival in the United States for all refugees from sub-Saharan Africa. Immigrants from other areas do not routinely need to be screened unless they exhibit symptoms.
Malarial vectors are present throughout much of the United States; malaria (specifically *Plasmodium falciparum*) can cause significant morbidity and mortality. Relapsing fevers, unexplained malaise or fatigue, pallor, thrombocytopenia, or splenomegaly should trigger testing with thick- and thin-blood smears for trophozoites (3 separate samples drawn at 12- to 24-hour intervals) and rapid antigen detection testing.
Immigrants from sub-Saharan Africa should receive presumptive treatment for malaria unless there is written confirmation of pre-departure treatment. Treatment for malaria is outlined in https://www.cdc.gov/malaria/diagnosis_treatment/index.html.

e) Screen for HIV

By consensus among specialists in infectious diseases in the USA the current recommendation is to perform HIV screening at the time of first encounter in all health care settings for everyone 13 to 64 years of age and any patient with recent potential exposure or who engage in high risk activity, has other risk factors, and those who requests it. The CDC recommends 4th generation testing with antigen/antibody to not miss acute infection window before seroconversion.

f) Zika virus

Zika can be transmitted via a mosquito bite, sexual transmission from male partner, by blood transfusion and in utero mother to fetus. Symptoms are usually mild and self-limited, lasting up to a week; the classic tetrad consist of fever, rash, conjunctivitis and arthralgia in a person with travel to an affected area within the past 14 days. The in-utero infection can cause microcephaly. There are no known abnormalities from

Zika acquired around time of delivery. There are no reported cases of transmission through breastfeeding; the CDC encourages infected mothers and mothers in endemic areas to breastfeed.

Overall indications for testing include infants with microcephaly or intracranial calcifications and a positive maternal travel history (should be tested within 48 hours of birth), and infants with mothers with positive or inconclusive Zika serum tests. Infants without abnormalities do not need to be tested if the mother was negative. Placenta and umbilical cord tissue can also be tested for Zika. More specific circumstances as per the Children's National Medical Center are:

- Any woman that was pregnant during their last potential Zika exposure (travel or sexual), or who became pregnant within 8 weeks of their last potential exposure.
- Any pregnant woman who has had a miscarriage or fetal demise with a potential Zika exposure while pregnant or in the 8 weeks prior to their pregnancy.
- During the first month of life, any infant with a potential Zika exposure during pregnancy or around the time of birth, with or without birth defects.
- Any person with concern for Zika virus infection and complicated illness (Guillian-Barre Syndrome, neurologic manifestations, fetal anomaly).
- Any person where it is highly suspected they are infected with Zika virus but have no known exposure history (i.e., concern for local transmission, transfusion or laboratory exposure).

Specific questions related to Zika testing can be directed to the Children's National Medical Center through email (doh.epi@dc.gov) or speaking with an Infectious Disease Physician Infectious Disease attending (call hospital operator at 202-476-5000 and ask for the ID attending on-call).
Follow up for infants with positive or inconclusive Zika virus test are:

- Hearing screen at 6 months.
- Head circumference and developmental milestones through age 1 year.
- Refer for abnormalities (neurology, developmental pediatrics, physical or speech therapy).

g) Malnutrition

Newly arrived immigrant children from developing countries maybe at high risk for iron deficiency, and should be evaluated for this deficit according to AAP guidelines. Also consider vitamin D deficiency and rickets, particularly people with darker skin and women who wear veils. CDC guidelines recommend a multivitamin with iron for children 6 to 59 months of age.

Height, weight, and BMI must be followed over time to ensure appropriate acclimation to the US diet.

h) Evaluate dental health

All newly arrived immigrant children should have their dentition evaluated. Formal dental examination should follow in all patients, giving priority to those with clear evidence of active disease. Data on pediatric refugees in the United States have shown dental caries to be common, with prevalence between 16.7% and 42%, with marked difference based on region of origin. In the Southeast Asian community is noted heavy use of betel nut leading to significant dental disease.

i) Mental Health

Most immigrant children are well adjusted and should be treated as all children in the pediatric medical home. However, newly arrived immigrant children might have been exposed to trauma, including war, torture and family separation, increasing their risk for mental illness. Mental health and developmental screening tools that are normed to the general population in the US are useful for immigrant children, however they have not been validated in all immigrant or refugee populations and should be used with caution.

Mental health care for newly arrived immigrant children is complicated by language and cultural barriers, adjustment disorders, access to psychiatric services, and uncertainty about elective treatments in refugee populations. Children who are victims of torture should be referred to experienced mental health practitioners. After ruling out acute psychosis and destructive behaviors, it is recommended to postpone an exhaustive mental health screening post until several months after arrival.

Some Mental Health/Trauma screening tools are:

1. Anxiety/PTSD/Depression
    - Child PTSD Symptom Scale (CPSS)
    - Trauma Symptom Checklist for Children and Trauma Symptom Checklist for Young Children (TSCC and TSCYC)
    - Adverse Childhood Experience (ACE) Questionnaire
    - Univ. of California at Los Angeles Posttraumatic Stress Disorder Reaction Index (UCLA-PTSDRI)
    - Patient health questionnaire (PHQ-9)

2. Relational, emotional and behavioral development in pre-school children:
    - Strengths and Difficulties Questionnaire (SDQ) in many languages
    - Ages & Stages Questionnaires®: Social Emotional (ASQ:SE)
    - The Survey of Well-being of Young Children (SWYC)
    - Pediatric Symptom Checklist in many languages

j) Identify and address chronic disease

Hypertension, diabetes, smoking are also highly prevalent in immigrant populations. These patients require close follow-up to minimize sequelae from chronic conditions. Multidisciplinary teams may provide an opportunity to promptly address chronic health conditions that can have severe short-term consequences if not adequately managed (i.e, insulin dosage adjustment based on diet in patients with diabetes).

Since many newly arrived immigrant children have never had any health screening, we recommend a comprehensive medical history and evaluation for chronic disease.

k) Newborn Metabolic Screening

Kentucky's Newborn Screening Program uses a metabolic panel screening for 53 disorders which includes: congenital hypothyroidism, cystic fibrosis, abnormalities in hemoglobin i.e. sickle cell, and disorders in the metabolism of carbohydrates, amino acid, organic acids, fatty acids, and lysosomes (https://chfs.ky.gov/agencies/dph/dmch/ecdb/Pages/newbornscreening.aspx). Even if a baby is not born in a hospital, it is critical that they be tested within the first 24- 48 hours after birth. There are states where the maximum age of screen up to 6 months old **(**MD, VA), and in DC there is no maximum age but need to interpret in context of age).