This seminar covers the causes of fever other than malaria. At first glance of the IMCI guidelines, management of fever appears to be restricted to the management of malaria. In reality, the guidelines for managing fever identify most of the common causes of fever. In some countries, other conditions must be considered, but these will be discussed separately.

Many of the infectious diseases assessed, classified and treated using the IMCI guidelines have fever as a secondary cause. For example, many children with a upper respiratory tract infection, pneumonia or ear infection will have fever. Children with dysentery and diarrhea may also have fever. In these patients, the cause of the fever is treated and fever is not used in decision making. While these conditions all cause fever, the management of the condition itself results in the management of the fever. Hence, no separate guidelines were derived for these conditions.

Severe illnesses associated with danger signs are also associated with fever, such as sepsis septicemia and meningitis. The danger signs lead to appropriate referral for the illness.

Fever is also associated with malaria, but since there are no other clinical signs that reliably distinguish malaria from other common causes of infection without extensive clinical examination and laboratory testing, the IMCI guidelines concentrate on the management of malaria,. This is discussed in another seminar.

In other non-obvious causes of fever, the danger signs associated with them would identify a seriously ill child who needs to be referred and managed at the referral facility. For instance, a child with a peritonsillar abscess or intra-cranial abscess may have persistent vomiting or a stiff neck. A child
with typhoid fever without any other localizing signs may be lethargic and abnormally sleepy, as may a child with relapsing fever. A child with dengue shock syndrome may have fever and be unconscious.

In all these conditions, non-localizing signs do not allow for distinction at a first-level health facility. However, because they have a danger sign, they are appropriately referred to a referral facility that has diagnostic and therapeutic capacity to investigate them further.

**SLIDES 5 & 6  Fever after Seven Days - Referral**

In the IMCI guidelines, a child with a duration of fever more than seven days is referred to a referral hospital for further assessment. This strategy is used to differentiate between children with simple viral fevers, which usually subside by five to seven days, and other diseases where the only presenting symptom is fever.

For conditions that are not immediately life threatening, referral can lead to more diagnostic and therapeutic intervention. For instance, tuberculosis, HIV, urinary tract infections, relapsing fever, typhoid fever, bone and joint infections, and multiple other abscesses, such as perirectal abscess or intracranial abscess, may be detected.

Non-infectious etiologies of fever would also be detected encompassing such conditions as malignancies, and the rarer rheumatologic diseases. All these conditions require assessment and management that cannot be done at a first-level health facility.

Most of these conditions also will not have any obvious simple clinical sign to help localize infection, such as TB, UTI, relapsing fever, or will need invasive interventions such as those needed for septic arthritis and malignancies.

Furthermore, the relative prevalence of these conditions being low, it is not possible to include specific signs and symptoms for all these conditions. However, they all have one feature in common and that is a duration of fever of greater
than seven days. Thus, in effect, **most common causes of fever are managed using the IMCI algorithm.**

**SLIDE 7  Relapsing Fever - Borreliosis — Overview**

Relapsing fever is characterized by **recurrent attacks of fever lasting three to five days that relapse and remit.** It is caused by a spirochete of the *Borrelia* species (1) and is **transmitted by lice and soft body ticks.** It usually occurs in parts of the world with poor sanitation or catastrophic situations such as war, famine, and refugee camps (2).

The clinical picture consists of a sudden onset of fevers with chills, severe muscle pain, headache, joint pain, petechiae, stiff neck, and jaundice. Hepatosplenomegaly and abdominal tenderness are common (3). There may be mucocutaneous bleeding with a petechial rash and bleeding from gums and nose. **Symptoms are usually harder to detect in children under age 5 years.**

After three to five days, the fever subsides by lysis with profuse sweating followed by three to six days of an afebrile and asymptomatic state. Relapsing can occur up to five or six times and if untreated, can result in a **mortality of up to 70 percent.** If treated, the mortality is 5 percent or less and then usually associated with a Jarisch-Herxheimer Reaction (JHR) (4).

**SLIDE 9  Relapsing Fever — Jarisch-Herxheimer Reaction**

**Treatment of relapsing fever is relatively simple** — penicillin or tetracycline work very well. **Most of the mortality in treated patients arises due to the Jarisch-Herxheimer Reaction or JHR.** This can occur with treatment of any spirochetal infection but is especially common in relapsing fever.

The **JHR occurs within the first one or two hours after the first antibiotic dose** and is caused by the release of TNF and cytokines caused by lysis of the spirochete (5). It is characterized by high fever chills and aggravation of existing symptoms, tachypnea, vasoconstriction and high blood pressure.
pressure, followed later by shock (6). Thus, any child treated for relapsing fever should be observed for several hours after being given the first dose of antibiotic.

SLIDE 9 & 10  Relapsing Fever — Jarisch-Herxheimer Reaction (continued)

While tetracycline is very efficacious, it is unfortunately associated with almost a 45 percent rate of JHR resulting in the case fatality rate of 5 percent (7). Slightly lower rates are found with higher dosages of procaine penicillin (400,000 IU). On the other hand, low dose procaine penicillin results in a 5 percent JHR rate with no case fatality but a high rate of relapses. Each of the subsequent relapses, however, is less severe and can be retreated with a single low dose of IM procaine penicillin (8).

It should be remembered that antimicrobial treatment alone is not sufficient and identification of a case of relapsing fever should be combined with a delousing program targeted to all members of the family, the boiling of all personal clothes, burning of blankets (as these are impossible to delouse) and shaving of the head, if possible. Spraying of the dwelling is also necessary (9).

SLIDE 11 & 12  Relapsing Fever — Adaptation

In endemic malarial areas, relapsing fever should be suspected in all children with persistent fever or fever that follows a pattern of remission and relapses. In areas with no or low malaria risk, which are also endemic for relapsing fever, children who have not traveled to a high malaria area should be suspected of having relapsing fever if there are other cases occurring in the neighborhood (10). The treatment should be with a single low dose of procaine penicillin.

Health workers should also be advised to counsel mothers about personal hygiene and delousing the whole family and dwelling. This adaptation would be necessary in the “counsel mother section” of the guidelines. A new drug box could be added for procaine penicillin, as well.
SLIDE 13  Sore Throat - Overview

Streptococcal sore throat and rheumatic fever affect school-age children older than 5 predominantly. Since the generic IMCI guidelines do not address the older child, sore throat was not included in the guidelines. Furthermore, in most countries, streptococcal sore throat is very uncommon in children under 5.

The main reason to treat a streptococcal sore throat is for the prevention of rheumatic fever and subsequently rheumatic heart disease (11). In some countries such as Egypt (12) and India, rheumatic fever does occur in children less than 5 years of age, and juvenile mitral stenosis occurs by the age of 10 years (13). Clearly, in these children, streptococcal sore throat occurs in children under the age of 5.

The global burden of disease study has estimated that rheumatic heart disease accounts for 1.1 percent of deaths in developing countries. In a study from Ghana, RHD ranked 32, accounting for 1 percent of healthy days lost. In comparison, malaria, measles and pneumonia ranked first, second and third, accounting for 10.2, 7.3 and 5.5 percent of healthy days lost, respectively (14).

SLIDE 14  Sore Throat - Prevention

WHO recommends the secondary prevention of rheumatic heart disease by giving prophylactic benzathine penicillin every 3 to 4 weeks to children who have had rheumatic fever (15). This is called secondary prevention because it does not prevent the development of rheumatic fever, but rather prevents the progression once it has occurred.

The primary prevention of rheumatic fever entails treating children with streptococcal pharyngitis with penicillin. However, the strategy is expensive, which limits its use in developing countries. And because the strategy is usually directed at school age children, primary prevention is of limited use in children under the age of 5.
**SLIDE 15  Sore Throat — Management Issues**

The management of sore throat is complicated by many factors. A major problem is that even if every sore throat were correctly treated, 30-50 percent of rheumatic fever occurs following unapparent infection (15).

In the older child, one-fifth to one-sixth of sore throats are caused by group A strep and, therefore, reliable signs are required to prevent over-treatment.

The selection of signs continues to remain problematic especially in the younger child less than 3 years who most often has non-specific signs such as fever and crusts around the nose, and Group A streptococcal (GAS) infections are rare in those under 2 years of age (16).

**SLIDE 16 & 17  Sore Throat — Management Issues (continued)**

Treating a common disease such as sore throat where only a fifth to a sixth of children with a sore throat have group A strep, is problematic because sensitivity and specificity tend to move in opposite directions. For instance, while a history of fever in a child with a sore throat is fairly sensitive, it is very non-specific (17). On the contrary, while a child with an exudate and a large and tender lymph node is fairly specific for GAS, it is not very common in these children and, therefore, the sensitivity is very low.

Requiring only one of these signs, such as a large cervical node or throat exudate, raises the sensitivity to 84 percent. However, there is a significant reduction in specificity to 40 percent. Thus, this table illustrates the difficulty in making a clinical diagnosis of GAS infection without the help either of a rapid diagnostic test or routine culture.

However, for different countries, the prevalence of RHD may be used to decide upon management guideline. For instance, in Egypt where the prevalence of RHF and RHD are high, a choice of signs and symptoms with a high sensitivity would be more appropriate. Conversely in countries with low levels of
RHD, the combination of signs and symptoms should be more specific where a loss of sensitivity is acceptable in order to prevent gross over-treatment of patients.

**SLIDE 18  Sore Throat — Treatment Options**

The main reason for administration of penicillin to a child with GAS sore throat is the reduction of rheumatic fever and rheumatic heart disease. But studies have shown that treatment does reduce the duration of symptoms and signs, and anorexia, as well.

The treatment of choice remains a single dose of IM benzathine penicillin since the levels of penicillin in the throat remain elevated for up to 10 days. This therapy can also prevent a sore throat developing for up to 21 days later. The danger with administering benzathine penicillin is that it is very painful and, if given incorrectly, can cause sterile abscesses as well as sciatic nerve injury. Penicillin V or amoxicillin are acceptable alternatives, however, compliance with a 10-day regimen is poor and more expensive.

**SLIDE 19 & 20  Sore Throat — Adaptation**

While GAS sore throat is common, it is not a major cause of mortality. Thus, this condition could absorb considerable resources because the treatment of choice is an injection of benzathine penicillin. Because of a lack of reliable clinical signs, almost inevitably there will be over-treatment of sore throat, resulting in unnecessary injections to many children.

If sore throat is to be included in an adaptation, it should be considered depending on the sensitivity and specificity of the signs and symptoms being considered and the prevalence of GAS sore throat in children 3-5 years of age. One possibility is to use the acute respiratory infection (ARI) box ‘as is’ and accept low sensitivity. However, it should not be used for younger children.
SLIDE 21  Dengue Fever — Overview

Dengue fever has become increasingly important in Asia and is becoming a significant problem in Latin American and east Africa (18).

Dengue hemorrhagic fever is frightening because it presents as shock or bleeding and because it occurs in epidemics every 3 to 4 years (19). Politically, it is an important cause of morbidity in these countries. Dengue fever most commonly occurs in children 5 to 15 years of age, and is uncommon in children under 5.

Left untreated, the mortality can be up to 10 percent, however, in centers where DHF is managed correctly, the mortality can be as low as 0.5 percent (20).

SLIDE 22  Dengue Fever — Overview (continued)

First-level treatment usually comprises management of shock and referral based on the major clinical manifestations of dengue fever, which are:

- shock — DSS or dengue shock syndrome;
- hemorrhage — dengue hemorrhagic fever or DHF;
- fever (dengue fever) with or without hepatomegaly that is tender (19).

Until recently, there have been no studies that have tried to assess the sensitivity and specificity of various signs and symptoms in relationship to DHF. Thus, countries with DHF have selected various signs for inclusion of the algorithm dependent on the recognition of the signs, the feasibility and prevalence for each of the different signs seen in the different stages identified above, and treatment options.

SLIDE 23  Dengue Fever — Referral

A comparison of algorithms from Indonesia, Philippines and Vietnam (21) shows the distribution of countries that have used various signs or symptoms to identify children needing referral. You can see the great variation in signs, as well as
the number of different signs and symptoms that are used in each algorithm.

As you can see, **three countries** used cold clammy extremities, severe bleeding from nose or gums and black vomit or stools. **Two countries** included weak or undetectable radial pulse, skin petechiae, frequent vomiting and abdominal pain. **Only one country** included a capillary refill time of greater than 3 seconds, lethargy or restlessness, right upper abdominal tenderness, a positive tourniquet test, and petechiae plus a positive tourniquet test.

**SLIDE 24  Dengue Fever — Referral (continued)**

Most algorithms have erred on the side of safety, and children with any sign of DHF or DSS are immediately referred to the hospital.

**Non-specific signs** such as abdominal pain, restlessness isolated skin petechiae or high continuous fever have been identified as signs requiring observation of the child on frequent returns to the first-level facilities.

In a study from Indonesia and Vietnam (21), the only signs that were found to be useful with sensitivities and specificities greater than 80 percent were shock and mucocutaneous bleeding. Abdominal pain, hepatomegaly, and the tourniquet test were too low in prevalence and added considerably to the complexity of the algorithm without adding substantially to the sensitivity. Children with fever and vomiting alone should be called back for reassessment.

**SLIDE 25  Dengue Fever — Treatment Plan and Adaptation**

Treatment plans include management of shock and potential fluid losses. Children with shock or DHF should be started on Plan C and referred immediately to the nearest referral level health facility.
It is well known that the major cause of death is capillary leak due to the release of cytokines from the endothelial cells lining the blood vessels. For children with vomiting and fever alone, fluid plan A for the management of potential fluid loss may prevent progression to more severe forms of dengue and is necessary to manage fluid losses incurred by vomiting.

This treatment plan fits the needs of most national guidelines. A potential problem with adaptations is that there has not been adequate analysis of the best signs and symptoms to include in a treatment algorithm.
REFERENCES


