Fever: When it is not Malaria

Gina Oladokun
College of Medicine, University of Ibadan
&
University College hospital, Ibadan

Outline

- Introduction
- Epidemiology of fever
- Causes of Non-Malarial Fever (Overview)
  - Bacterial, viral Causes
  - Non-Infectious Causes
- Clinical clues suggesting non-malarial fever
- Diagnostic approach for Fever with negative malaria tests
- Management Principles

Case Study 1:

- 7-year-old boy presented with fever x 5 days, persistent abdominal pain, frequent stools, loss of appetite, no chills, no rigors, no headache
- PMHx: No chronic illness, immunisations up to date
- Initial Diagnosis – Malaria: Presumed as a result of fever and child lives in a malaria-endemic area
- Treatment - Artemether-lumefantrine; No improvement
- Investigations: Malaria Rapid Diagnostic Test (RDT): Negative; FBC- ↑WBC; Blood culture: *Salmonella typhi*
- Final Diagnosis: Enteric fever (Typhoid fever), not malaria.
- Management: IV Ceftriaxone with good outcome

Case study 2:

- 15 month old girl with fever x 2weeks referred to UCH having been admitted for 1wk in a private hospital; received IV ceftriaxone, genticin x7/7. Contact & travel -nil of note; immunisation- complete
- Playing intermittently
- RDT- Negative, BF for MP- Neg
- Diagnosis: “Sepsis” (No specific systemic focus).
- FBC: WBC- 19,180 (N-38%, L-51%, M-9.8%), Plat-480,000, HCT 25%
- Peripheral film: No blasts; Blood culture sterile
- Paed ID Review: Monitor off antibiotics.
  - Fever subsides after 2 days of observation. Discharged

Introduction

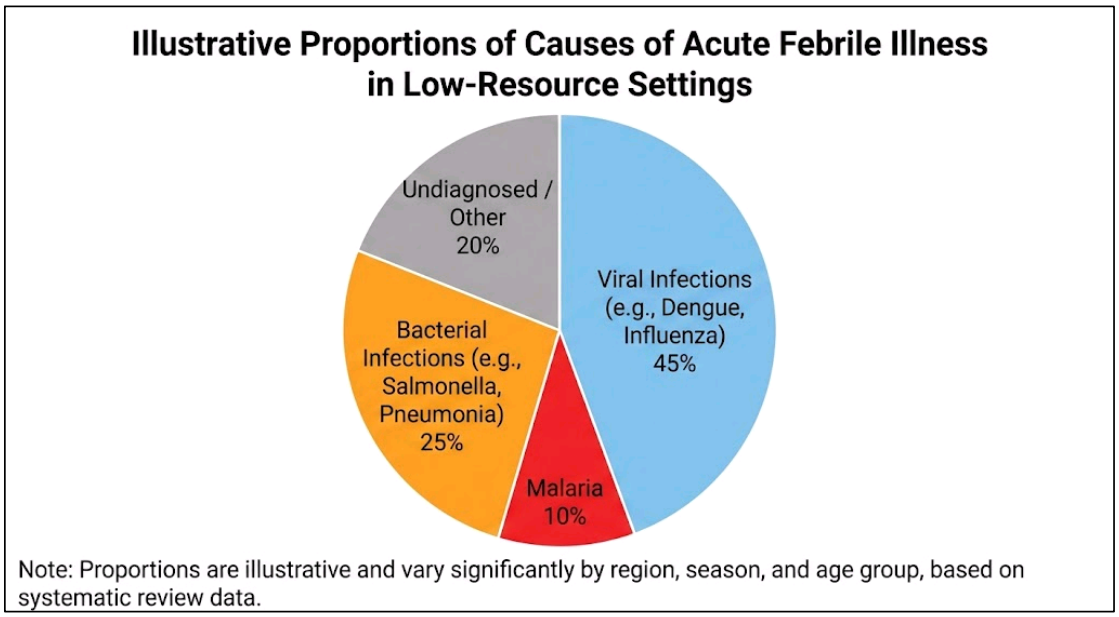
- Fever is a common presenting symptom in children- at least 1/3
- Fever is a symptom of underlying pathology, not a diagnosis in itself
- In malaria-endemic regions, malaria has historically been the leading cause of fever
- Malaria is over-diagnosed; presumptive treatment still widely practiced
- Incidence of malaria has reduced and other febrile illnesses are increasingly common
- RDT available; Malaria RDTs are highly sensitive (≥ 95%)
    - Negative malaria tests often ignored

Diagnostic Anchoring- Bias for malaria

- Clinicians default to assuming fever equals malaria, even with negative tests

- Missed diagnosis
  - Delayed diagnosis & treatment for life- threatening conditions (Meningitis, Sepsis, Pneumonia)
  - Poor patient outcomes
- Public Health impact
  - Unnecessary use of antimalarials and antibiotics → AMR

Epidemiology of febrile illness



Majority of febrile illness cases in many regions are now due to non-malarial causes

Figure: Illustrative proportions of fever aetiology in low-resource settings. Adapted from "Etiology of Severe Febrile Illness in Low- and Middle-Income Countries: A Systematic Review," by N. Prasad et al., 2015, *PLoS ONE*, 10(6), e0127962.

Causes of Non-Malarial Fever

- Major Categories
  - Bacterial
  - Viral
  - Parasitic & fungal
    - Fungal infections (in immunocompromised patients)
  - Non-infectious

Common bacterial infections

- Typhoid and other enteric fevers
- Urinary tract infections
- Pneumonia
- Sepsis
- Tuberculosis
- Meningitis

Common viral causes

- Viral hepatitis
- RSV, influenza
- EBV- Infectious mononucleosis
- Acute HIV infection
- Rickettsial infections
- Dengue fever
- Chikungunya
- Yellow fever
- COVID-19

Non-Infectious Causes of Fever

Malignancies (Leukaemia & Lymphoma)

- Suspect in cases of: Prolonged fever, weight loss, pallor, generalised lymphadenopathy, bone pain.
- Investigation: Complete Blood Count and peripheral
- blood smear.

Drug-Induced Fever

- Diagnosis of exclusion.
- Pattern: Fever persists without an infectious source. Resolves upon stopping the drug.
- Common culprits: Antibiotics, anticonvulsants

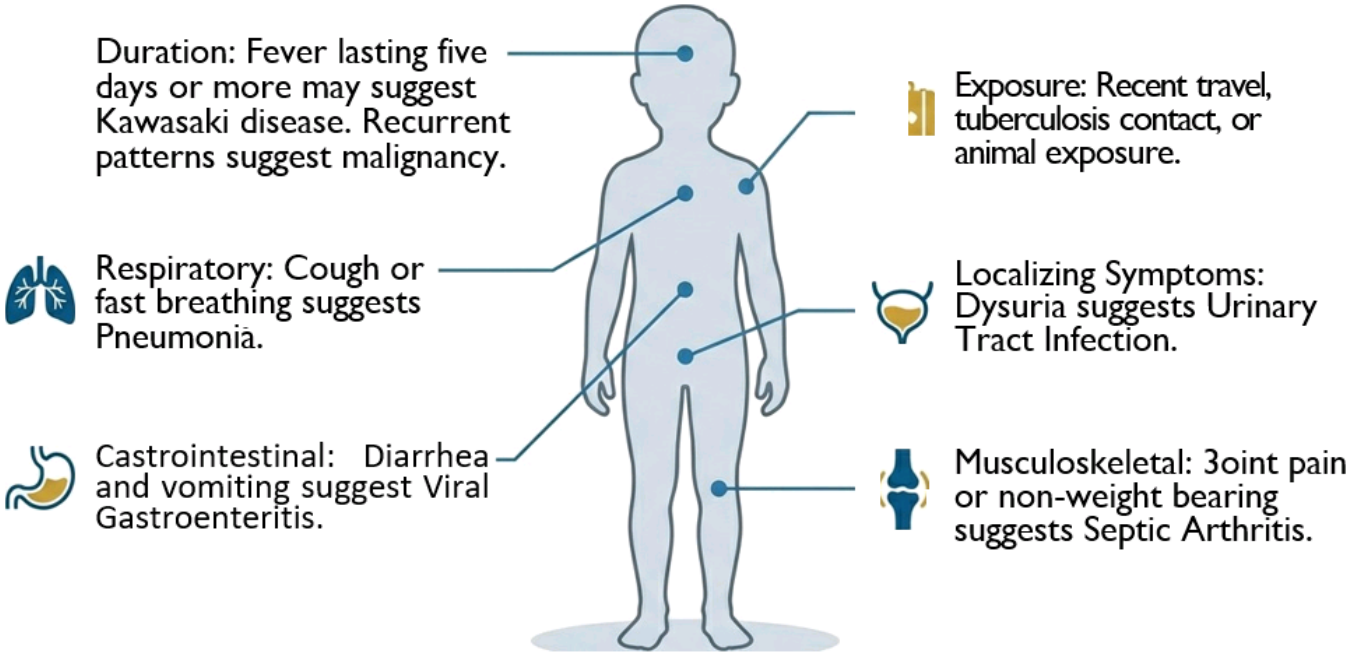
Autoimmune disorders

- SLE
- JIA
- Rheumatic fever

Clinical clues suggesting fever is not malaria

- Negative malaria RDT or blood smear microscopy
- Persistent or worsening fever despite antimalarials
- Localising symptoms or signs
  - Cough, sore throat, chest pain → suggest respiratory infection: Pneumonia, PTB
  - Urinary symptoms: dysuria, frequency → urinary tract infection
  - Skin rash or joint pain → viral exanthems, dengue, chikungunya, SLE
  - Gastrointestinal symptoms: abdominal pain, diarrhoea → typhoid, gastroenteritis
  - Neck stiffness, headache, seizures, altered sensorium → meningitis
- Prolonged fever (>7 days)
- Weight loss

The Initial Clinical Approach: History Taking



VIRAL HEMORRHAGIC FEVERS (VHF)

- Group of severe viral illnesses presenting with acute fever and systemic involvement
- Common in West Africa: Lassa fever, Ebola, Yellow fever*
    - Often mimics malaria in early stages

Clinical Features of VHF

General Signs:
•**Early (non-specific stage)** :
Fever, headache, malaise, myalgia, vomiting/diarrhea
•**Severe:**
Bleeding (epistaxis, gum bleeding, petechiae), facial edema, shock, neurological symptoms
⚠ Bleeding may be absent early

INDICATORS OF VHF

•Persistent fever despite treatment
•Unexplained bleeding or bruising
•Contact with suspected case or outbreak exposure

Why It Is Missed as Malaria:
- Occurs in malaria-endemic regions
- Similar early symptoms
- Poor response to antimalarial therapy

DIAGNOSIS
- High index of suspicion
- PCR confirmation (where available)
- Thrombocytopenia, leukopenia, raised liver enzymes

MANAGEMENT PRINCIPLES
- Immediate isolation and infection control*
- Supportive care ± specific antivirals (e.g. Ribavirin for Lassa)

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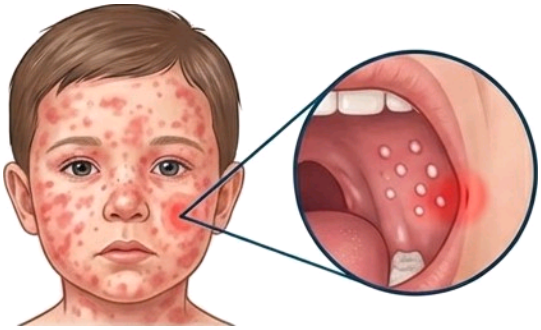
SLE

Measles

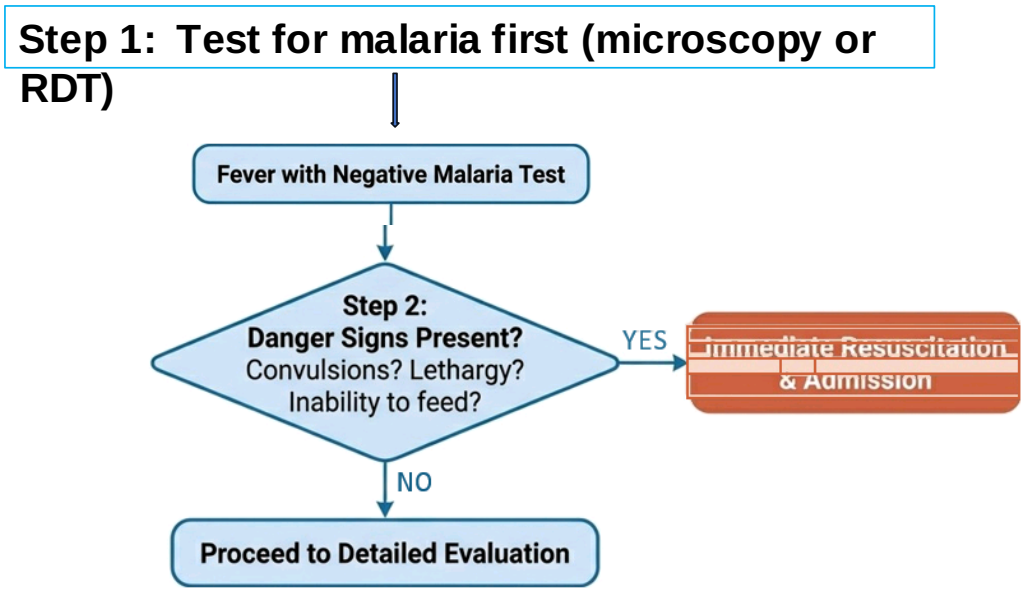


- Signs: High fever, cough, coryza, conjunctivitis
- Pothognomonic: Koplik spots on buccal mucosa

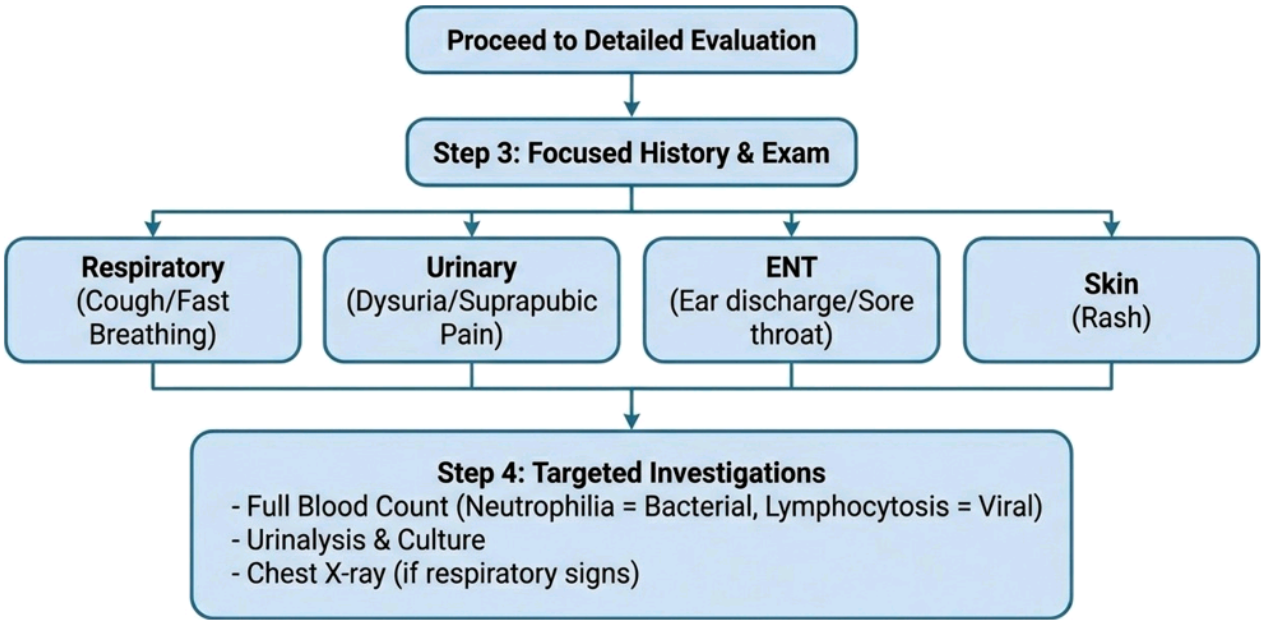
Practical Approach for Clinicians

- Yes, malaria endemic: Always test for malaria first (microscopy or RDT)
  - If negative, broaden differential diagnosis based on symptoms and local epidemiology.
- Use targeted investigations: blood cultures, chest X-ray, urinalysis, serology, PCR
- Consider co-infections: malaria can coexist with typhoid or pneumonia.
- Avoid presumptive treatment unless diagnostic capacity is absent and patient is critically ill.

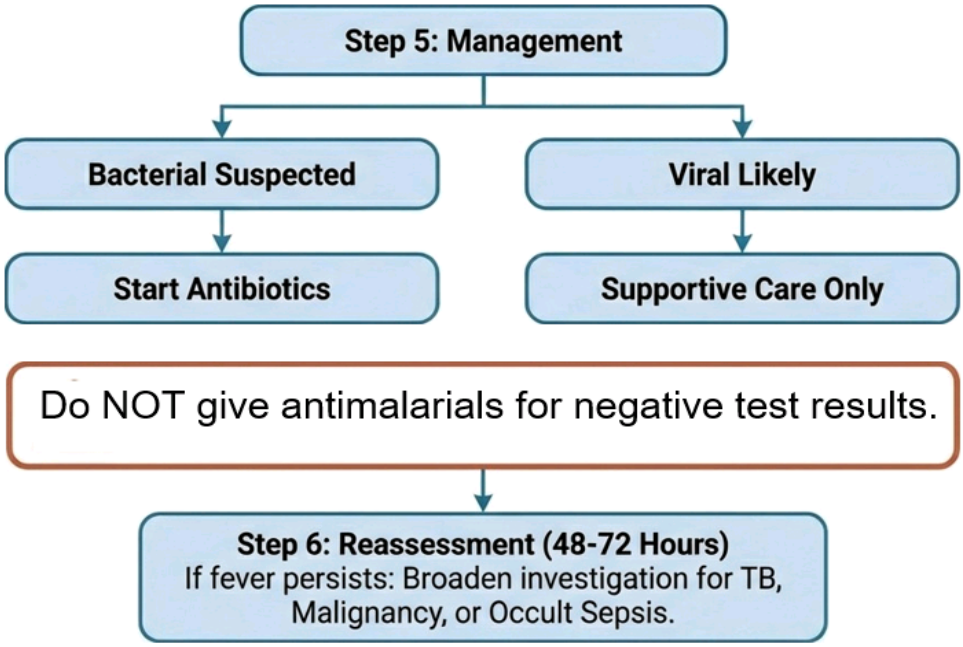
DIAGNOSTIC ALGORITHM FOR A CHILD WITH FEVER



DIAGNOSTIC ALGORITHM: NON MALARIAL FEVER



DIAGNOSTIC ALGORITHM: MANAGEMENT AND REASSESSMENT



Conclusion

- Recognise that fever is not a diagnosis but a symptom requiring careful evaluation.
- Fever in endemic areas is not always malaria
    - Avoid inappropriate antimalarial use when malaria test is negative
- Apply a systematic approach to febrile patients to identify common causes of non-malarial fever

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THANK YOU