Pyrexia of Unknown Origin

- ❑Introduction
- ❑Fever vs Hyperthermia
- ❑Physiology review
- ❑PUO classification and definitions
- ❑Causes of PUO
- ❑Patterns of Fever
- ❑Diagnostic approaches
- ❑Management
- ❑Prognosis

- According to the International Union of Physiological Sciences Commission for Thermal Physiology, fever is :

“a state of elevated core temperature, which is often, but not necessarily, part of the defensive responses of multicellular organisms (host) to the invasion of live (microorganisms) or inanimate matter recognized as pathogenic or alien by the host.”

- The active rise in body temperature during fever is to be distinguished from that occurring during episodes of passive hyperthermia.
- During the rising phase of fever, thermoregulation works to increase body temperature by:

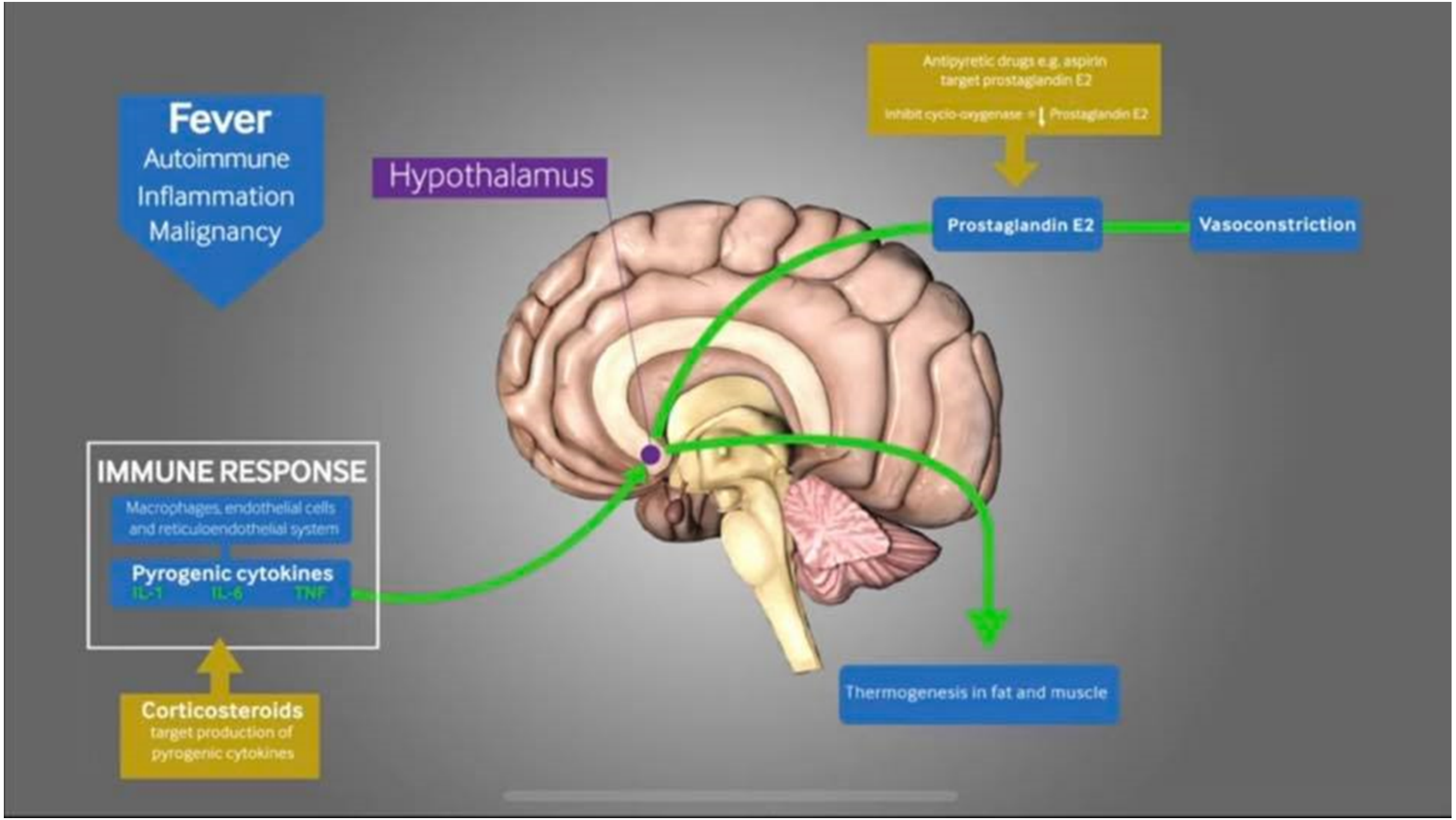
➢ increasing heat production (e.g., by shivering).

➢ decreasing heat loss (e.g., by cutaneous vasoconstriction).

- In contrast, during hyperthermia the thermoregulation system works to decrease body temperature by increasing heat loss (e.g., by sweating), and the fact that body temperature nevertheless increases equates to the system's failure.

Definition according to CDC

- Fever is considered when a measured temperature of 100.4 °F [38 °C] or greater, or feels warm to the touch, or gives a history of feeling feverish.
- it is not always possible to take a person's temperature. In certain situations, other methods of detecting a possible fever should be considered: self-reported history of feeling feverish when a thermometer is not available or the ill person has taken medication that would lower the measured temperature.
- the person feels warm to the touch appearance of a flushed face, glassy eyes, or chills if it is not feasible to touch the person or if the person does not report feeling feverish.


Fever
Autoimmune
Inflammation
Malignancy
Hypothalamus
Antipyretic drugs e.g. aspirin
target prostaglandin E2
Inhibit cyclo-oxygenase → ↓ Prostaglandin E2
Prostaglandin E2
Vasoconstriction
IMMUNE RESPONSE
Macrophages, endothelial cells
and reticuloendothelial system
Pyrogenic cytokines
IL-1 IL-6 TNF
Corticosteroids
target production of
pyrogenic cytokines
Thermogenesis in fat and muscle

- Body temperature is regulated by the CNS at the level of the hypothalamus.
- Fever is a normal physiologic phenomenon caused by the release of either exogenous or endogenous pyrogens (any substance that causes fever).
- When a fever occurs, the hypothalamic thermoregulatory center shifts its set-point upward.
- This upward shift is due to ↑ prostaglandin E2 (PGE2) in the preoptic area of the hypothalamus (increased PGE2 is caused by circulating pyrogens).

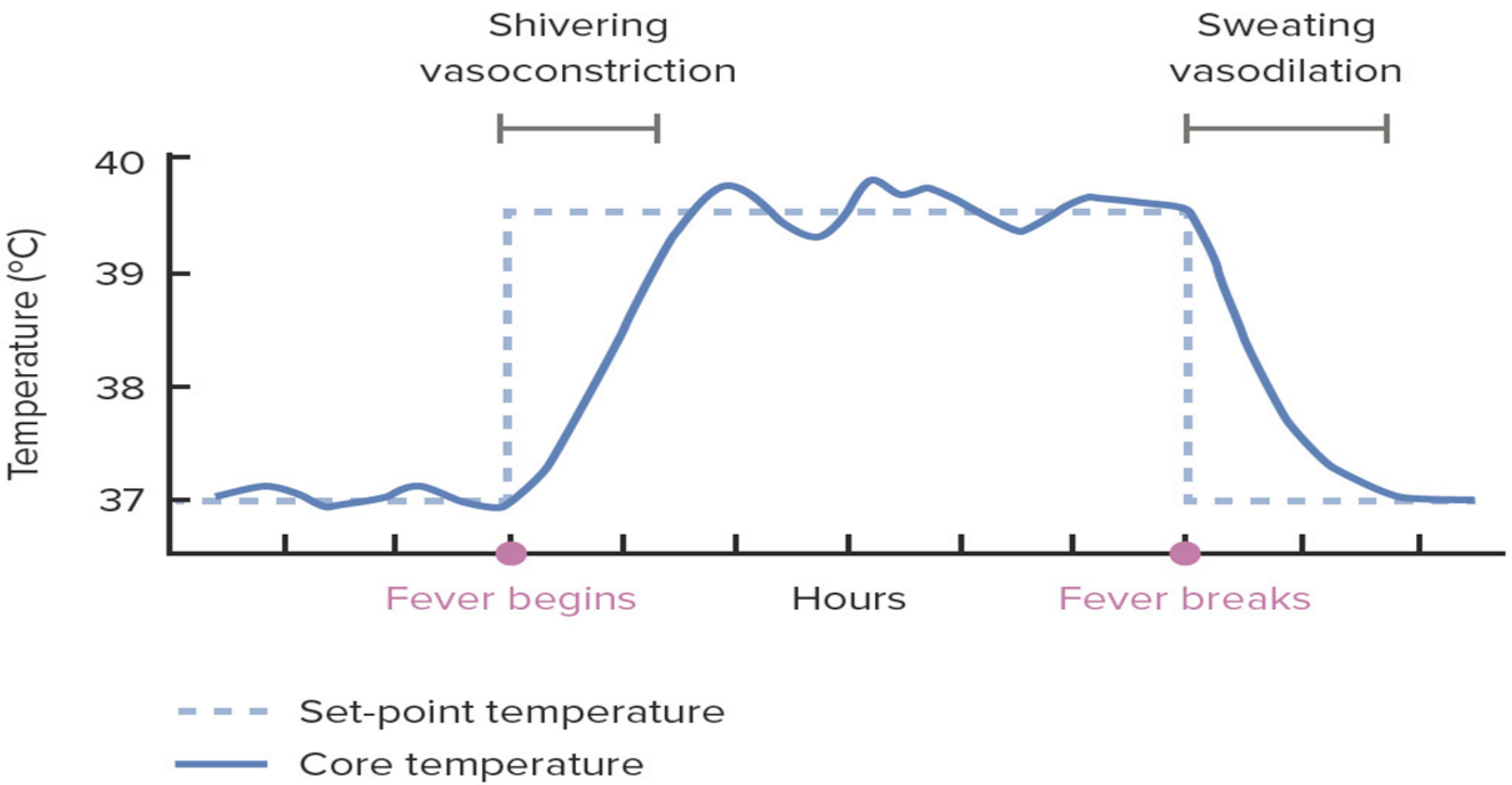
❑Endogenous pyrogens:

- Produced by inflammation, trauma, or antigen-antibody complexes
- Interleukin-1 (IL-1) , IL-6 , TNF-α and Interferon-γ
- Activates the arachidonic acid pathway, which releases PGE2 → activates the preoptic area of the hypothalamus → increases temperature set-point

❑ Exogenous pyrogens:

- Primarily from microbes.
- Lipopolysaccharides (LPS) of gram-negative bacteria
- Endotoxins
- Exotoxins

Time course of typical fever



Physiologic effects of fever

- Heat conservation: vasoconstriction.
- Increases heat production in the periphery.
- Causes a subjective cold sensation in the hands and feet as blood is shunted from the periphery to internal organs .
- Heat production: thermogenesis of muscle and adipose tissue
- Increased core temperature by release of (ATP)
- Muscle heat production → shivering

** Once the hypothalamic set-point is reset downward, heat loss occurs through: *Vasodilation, sweating, and behavior changes; may be due to a reduction in pyrogenic cytokines or the use of antipyretics*

PYREXIA OF UNKNOWN ORIGIN

Terminology and definitions

- The first formal definition of FUO to gain broad acceptance was proposed by *Petersdorf and Beeson nearly six decades ago*:

"fever higher than 38.3°C (100.9°F) on several occasions, persisting without diagnosis for at least 3 weeks in spite of at least 1 week's investigation in hospital."

- Later investigators have modified and extended this classic definition to reflect evolutionary changes in clinical practice.
- These changes include the conduct of most diagnostic tests in the outpatient setting.
- rather than in the hospital, the increasing number of immunocompromised patients (especially those with neutropenia), the proliferation of increasingly complex surgical and intensive care treatment protocols, and the advent of human immunodeficiency virus (HIV) infection leading to the acquired immunodeficiency syndrome (AIDS).

Updated….

- *Durack and Street,7 in 1991*, proposed a revised definition in which cases of FUO require 3 days of investigation and must be codified into four distinct subclasses of the disorder:

1. Classic FUO.
2. Nosocomial (health care–associated) FUO .
3. Neutropenic (immunedeficient) FUO.
4. HIV-related FUO.

Summary of Definitions and Major Features of the Four Subtypes of Fever of UnknownOrigin (FUO)

	CLASSIC FUO	NOSOCOMIAL (HEALTH CARE–ASSOCIATED) FUO	NEUTROPENIC (IMMUNE-DEFICIENT) FUO	HIV-RELATED FUO
Definition	>38.3° C (100.9° F), >3 wk, >2 visits or 3 days in hospital	>38.3° C (100.9° F), >3 days, not present or incubating on admission	>38.3° C (100.9° F), >3 days, negative cultures after 48 hr	>38.3° C (100.9° F), >3 wk for outpatients, >3 days for inpatients, HIV infection confirmed
Patient Location	Community, clinic, or hospital	Acute care hospital	Hospital or clinic	Community, clinic, or hospital
Leading Causes	Cancer, infections, inflammatory conditions, undiagnosed, habitual hyperthermia	Health care–associated infections, postoperative complications, drug fever	Majority due to infections, but cause documented in only 40%-60%	HIV (primary infection), typical and atypical mycobacteria, CMV, lymphomas, toxoplasmosis, cryptococcosis, IRIS
History Emphasis	Travel, contacts, animal and insect exposure, medications, immunizations, family history, cardiac valve disorder	Operations and procedures, devices, anatomic considerations, drug treatment	Stage of chemotherapy, drugs administered, underlying immunosuppressive disorder	Drugs, exposures, risk factors, travel, contacts, stage of HIV infection
Examination Emphasis	Fundi, oropharynx, temporal artery, abdomen, lymph nodes, spleen, joints, skin, nails, genitalia, rectum or prostate, lower limb deep veins	Wounds, drains, devices, sinuses, urine	Skin folds, IV sites, lungs, perianal area	Mouth, sinuses, skin, lymph nodes, eyes, lungs, perianal area
Investigation Emphasis	Imaging, biopsies, sedimentation rate, skin tests	Imaging, bacterial cultures	CXR, bacterial cultures	Blood and lymphocyte count; serologic tests; CXR; stool examination; biopsies of lung, bone marrow, and liver for cultures and cytologic tests; brain imaging
Management	Observation, outpatient temperature chart, investigations, avoidance of empirical drug treatments	Depends on situation	Antimicrobial treatment protocols	Antiviral and antimicrobial protocols, vaccines, revision of treatment regimens, good nutrition
Time Course of Disease	Months	Weeks	Days	Weeks to months
Tempo of Investigation	Weeks	Days	Hours	Days to weeks

Classic FUO

“Fever of unknown origin (FUO) is defined as fever at or above 101°F (38.3°C) for 3 weeks or more that remains undiagnosed after 3 days of in-hospital testing or during two or more outpatient visits.”

T > 38.3°c (100.9 F) on several occasions.

>3 weeks & more in duration.

>2 outpatient visits or 3 days in hospital without diagnosis.

Nosocomial (health care–associated) FUO

- Fever >38.3°C develops on several occasions in a hospitalized patient who is receiving acute care and in whom infection was not manifest on admission.
- 3 days of investigation and including at least 2 days' incubation of cultures.

Neutropenic (immune deficient) FUO

- Temperature >38.3°C ,Neutrophil count <500/ml , 3 days of investigation .
- 2 days' incubation of cultures (negative cultures after 48 hours) .

HIV-associated FUO

- Fever >38.3°C
- >3 weeks for outpatients or >3 days for hospitalized patients and appropriate investigations were done over 3 days, including 2 days' incubation of cultures (negative cultures after 48 hours).
- HIV infection is confirmed

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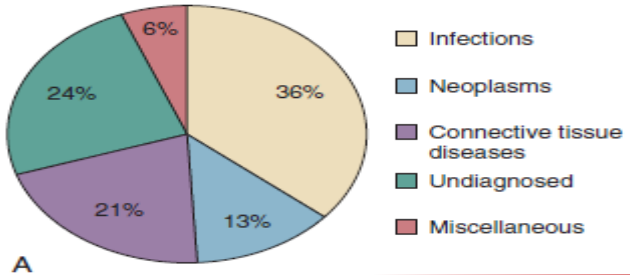
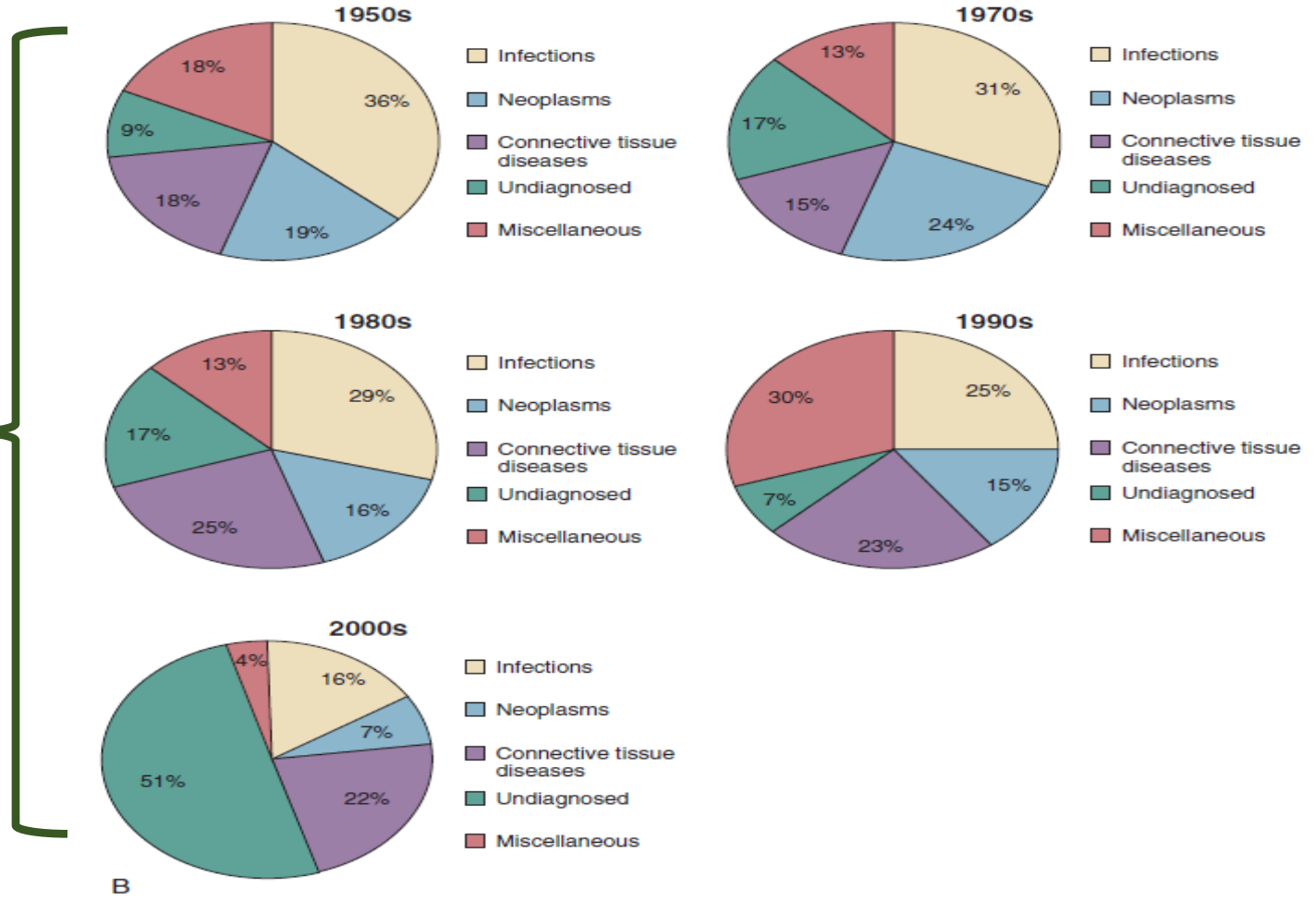
Main causes



A

By decades



B

FIG. 56.1 (A) Frequency of the five main etiologic categories of fever of unknown origin. (B) Frequency of the five main etiologic categ of fever of unknown origin by decade. *(A from Hayakawa K, Ramasamy B, Chandrasekar PH. Fever of unknown origin: an evidence-based re* Am J Med Sci. *2012;344:307–316; B from Mourad O, Palda V, Detsky AS. A comprehensive evidence-based approach to fever of unknown origin.* Intern Med. *2003;163:545–551.)*

TABLE 56.3 Final Diagnosis in Elderly Compared With Younger Patients With Fever of Unknown Origin From Patient Series Pre-1990

DIAGNOSIS	<65 YEARS (*N* = 152)	>65 YEARS (*N* = 201)
Infections	33 (21%)	72 (35%)
Abscess	6	25
Endocarditis	2	14
Tuberculosis	4	20
Viral infections	8	1
Tumors	8 (5%)	37 (19%)
Hematologic	3	19
Solid	5	18
Multisystem diseases[a]	27 (17%)	57 (28%)
Miscellaneous[b]	39 (26%)	17 (8%)
Other	13	12
No diagnosis	45 (29%)	18 (9%)

[a]Rheumatic diseases, connective tissue disorders, vasculitis (including temporal arteritis), polymyalgia rheumatica, and sarcoidosis.
[b]Includes factitious fever (seven cases), habitual hyperthermia (five cases), and drug-induced fever (three cases).
Modified from Iikuni Y, Okada J, Kondo H, et al. Current fever of unknown origin 1982–1992. Intern Med. *1994;33:67–73; and Knockaert DC, Vanneste LJ, Bobbaers HJ. Fever of unknown origin in elderly patients.* J Am Geriatr Soc. *1993;41:1187–1192.*

- As duration of fever increases, infectious etiology decreases.

- Malignancy and factitious fevers are more common in patients with prolonged FUO.

Fever of Unknown Origin

Infection	Malignancy	Non-infectious Inflammatory Diseases (e.g. autoimmune)	Miscellaneous
Extrapulmonary tuberculosis*	Hematologic malignancies	Lupus	Drug fever
Abscess*	• Lymphoma*	Rheumatoid arthritis	Factitious fever
Endocarditis*	• Leukemia	Vasculitis (Temporal arteritis is prob the most common vasculitis to cause FUO)	Hypothalamic dysfunction
Osteomyelitis / Discitis	• Multiple myeloma	Sarcoidosis	Castleman disease
Infected hardware	Solid tumors	Adult onset Still's disease	Kikuchi disease
Infected thrombosis (e.g. Lemierre's syndrome)	• Renal cell carcinoma	Familial Mediterranean fever	Idiopathic*
Malaria	• Pancreatic adenocarcinoma		
Brucellosis	• Hepatocellular carcinoma		
Q fever			
EBV, CMV			

* (Probably) Most common etiologies of FUO worldwide

Factitious Fever

- Underlying psychiatric Condition
- Defined as fever caused by the patient himself by manipulating thermometer to obtain medical care
- Typically seen in young females who work in medical professions.
- Examples of manipulation include dipping the thermometer in hot drinks to fake a fever

11.3 Clues to the diagnosis of factitious fever

- A patient who looks well
- Bizarre temperature chart with absence of diurnal variation and/or temperature-related changes in pulse rate
- Temperature >41°C
- Absence of sweating during defervescence
- Normal erythrocyte sedimentation rate and C-reactive protein despite high fever
- Evidence of self-injection or self-harm
- Normal temperature during supervised (observed) measurement
- Infection with multiple commensal organisms (e.g. enteric or mouth flora)

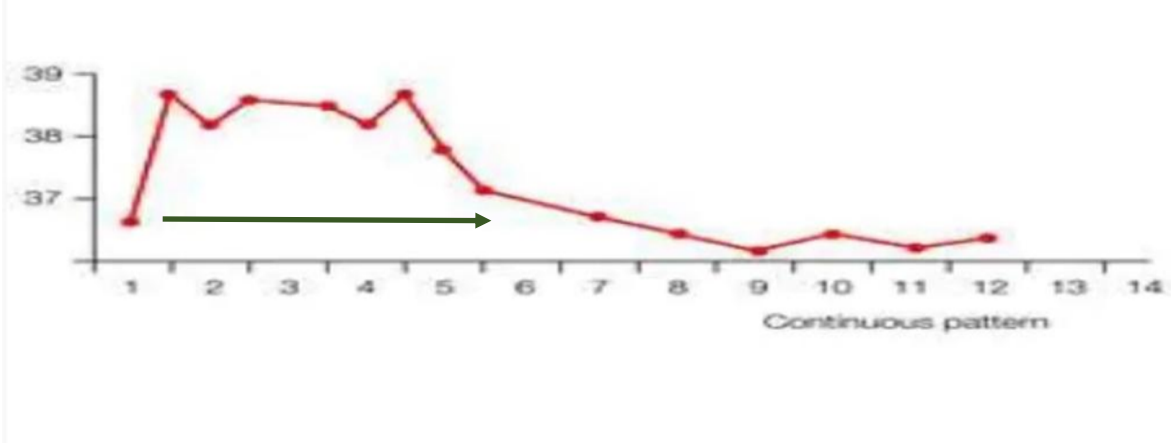
Types of fever patterns

Pattern type	Description	Associated diseases
Continuous fever	 Temperature continuously remains above normal, with daily fluctuations < 1°C.	- Typhus - Viral pneumonia
Remittent fever	 Temperature continuously remains above normal, with daily fluctuations ≥ 1°C.	- Typhus - Sepsis - Tuberculosis - Rheumatic fever
Intermittent fever	 Temperature remains above normal only for a certain period, later returning back to normal.	- Pleuritis - Sepsis
Biphasic fever	 Fever that breaks and returns twice a day	- Yellow fever - Dengue - Malaria - Typhoid - Leptospirosis
Undulant fever	 Temperature continuously remains above normal, with daily fluctuations ≥ 1°C.	- Brucellosis
Recurrent fever	 **Relapsing fever:** Days of fever followed by an afebrile period of several days and then a relapse into additional days of fever, usually after 14–21 days. **Pel-Ebstein fever:** Fever lasting 1–2 weeks followed by 1–2 weeks of an afebrile period **Periodic fever:** Fever that recurs over months or years; associated with the absence of infection of malignancy	- Pleuritis - Sepsis

Continuous fever :

Fever that never touches the baseline in 24 hours and fluctuates by less than 1 degree C in a day.

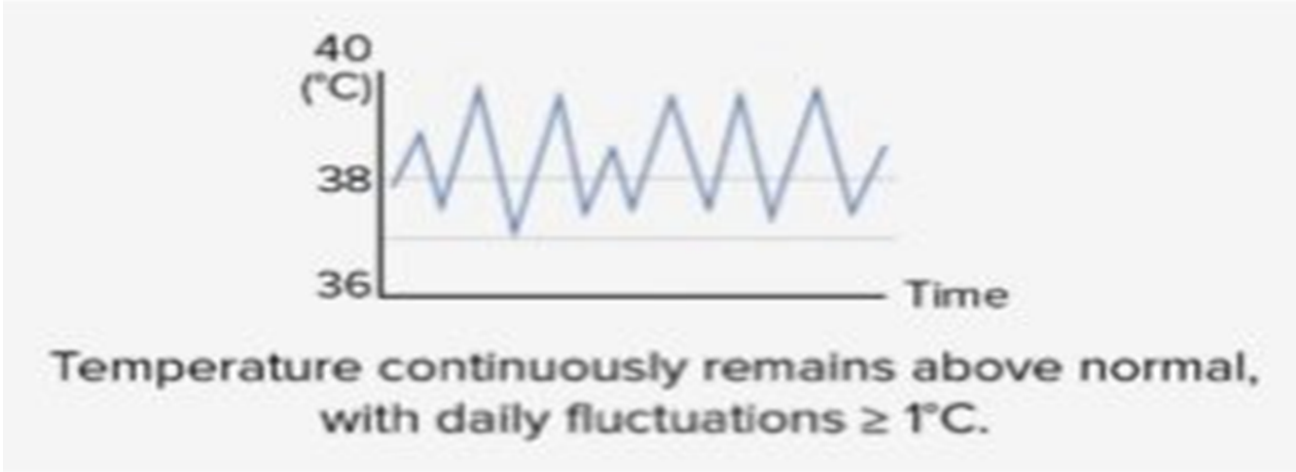
Seen in **enteric fever , lobar pneumonia ,brucellosis , typhus.**



Remittent fever :

Fever that fluctuates by more than 1 degree C but never touches the baseline in 24 hours

Seen in **infective endocarditis**



Intermittent fever:

Fever that touches the baseline for a few hours during the day.

High spikes and rapidly declining

Seen in **malaria, acute pyelonephritis, sepsis**

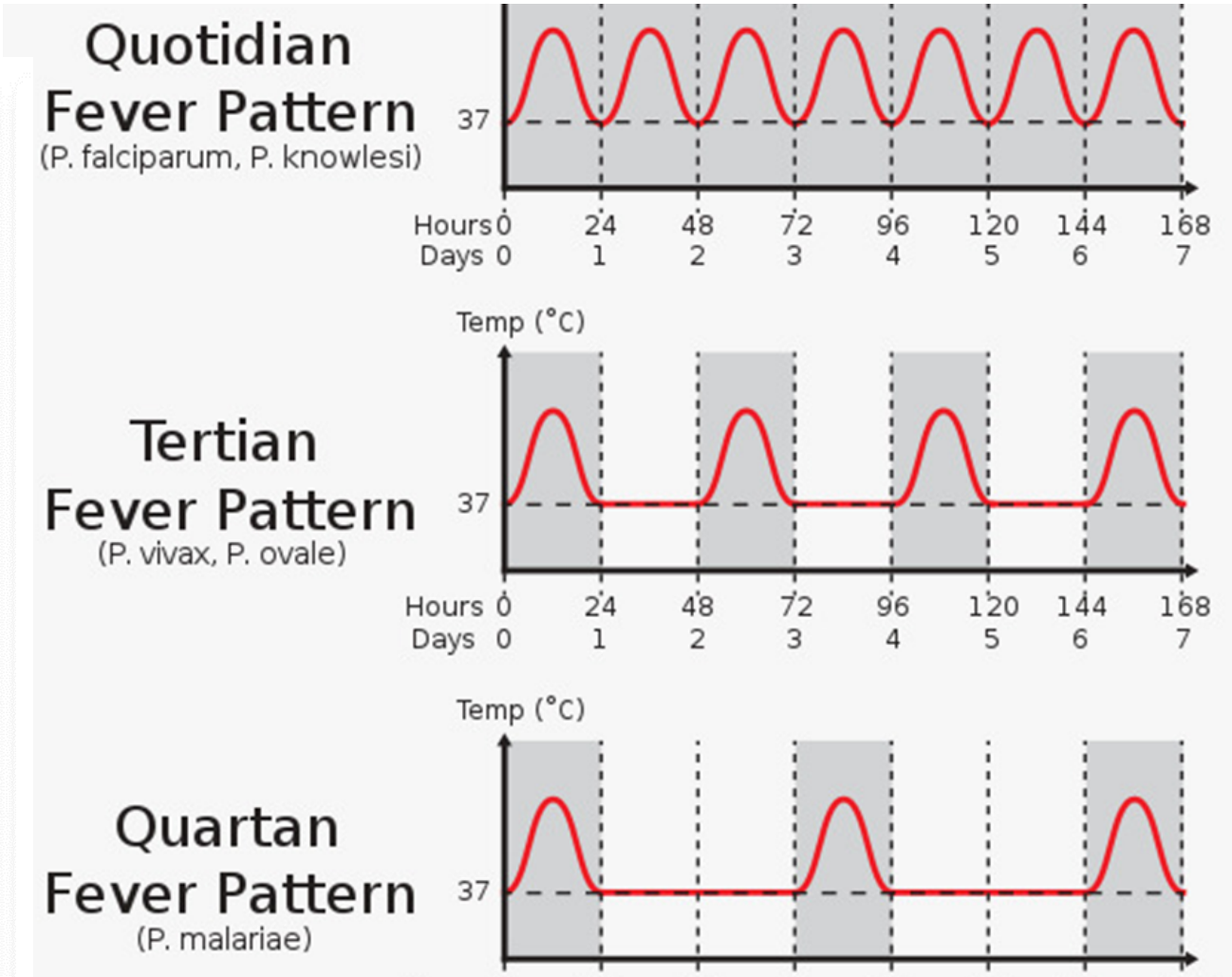
Malaria

- Types of intermittent fever :

- Quotidian fever, with a periodicity of 24 hours, typical of *Plasmodium falciparum*

- Tertian fever,with a 48 hour periodicity,typical of *Plasmodium vivax* or *Plasmodium ovale*

-Quartan fever,with a 72 hour periodicity,typical of *Plasmodium malariae*

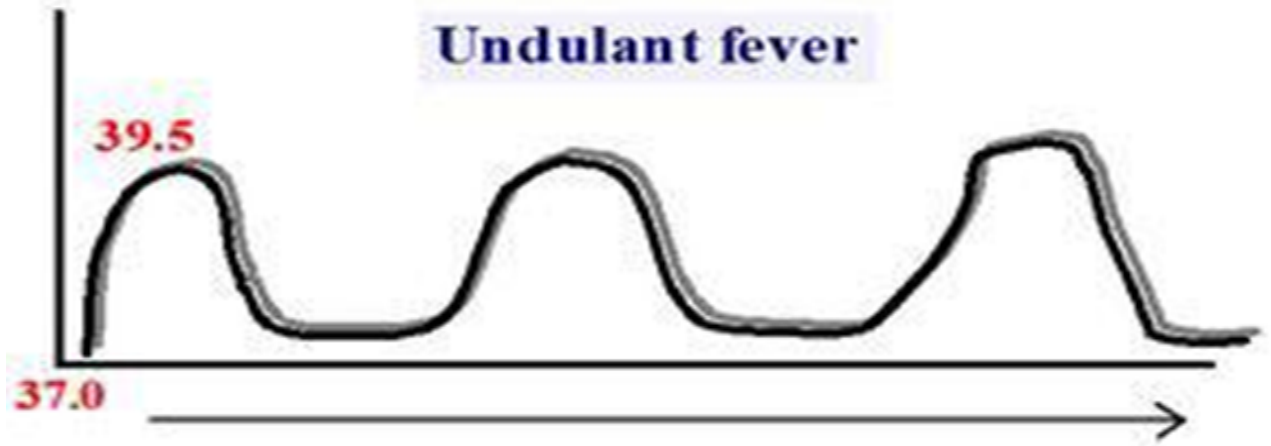


Undulant fever :

Temperature rises gradually and falls (like a wave) over days to weeks.

Raising and falling in wave

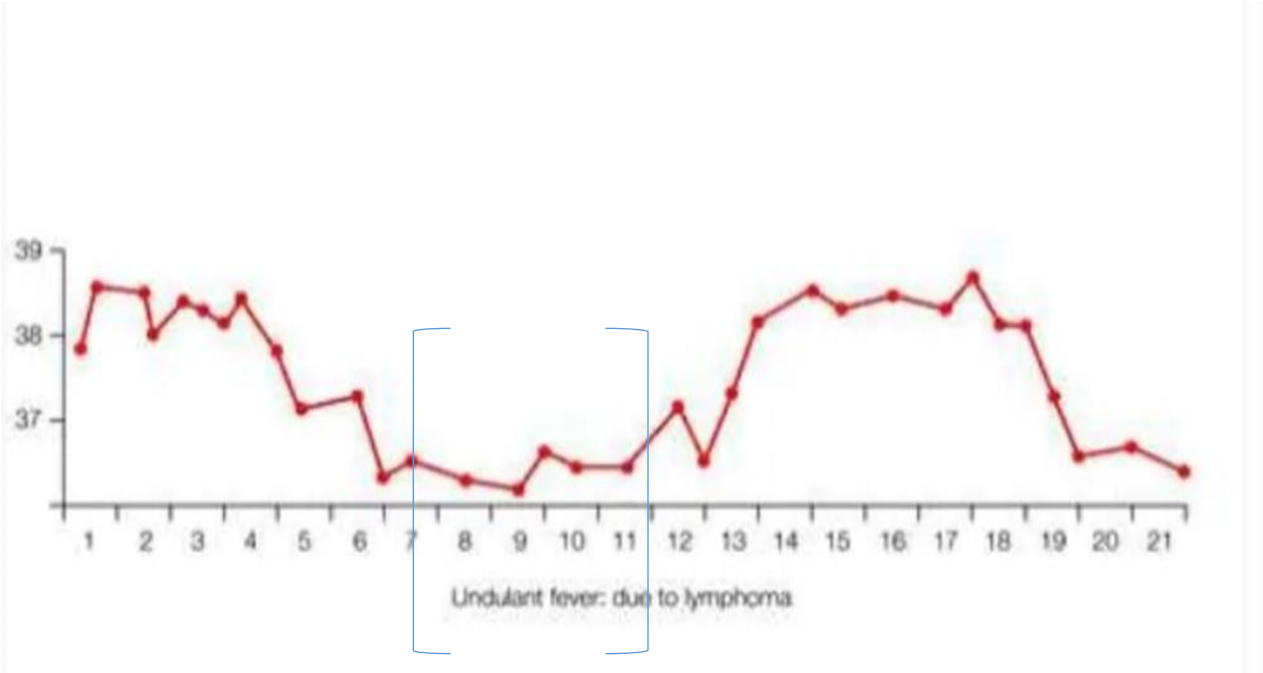
seen in **brucellosis**



Recurrent /Relapsing fever:

Relapsing fever: Days of fever followed by an afebrile period of several days and then a relapse into additional days of fever, usually after 14–21 days

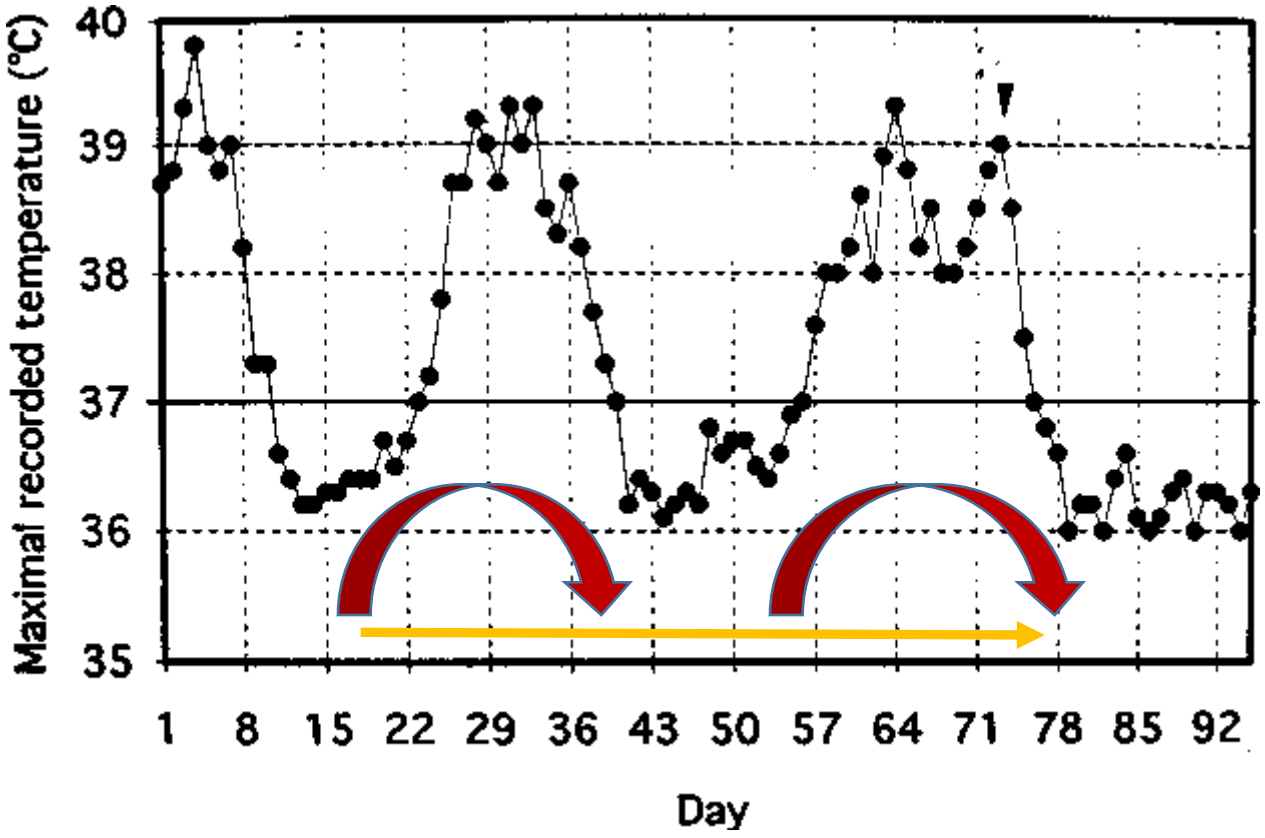
seen in **borreliosis** , **brucellosis**



Pel-ebstein fever

Fever lasting 1-2 wks followed by afebrile period of 1-2 wks.

Seen in **Hodgkin lymphoma**



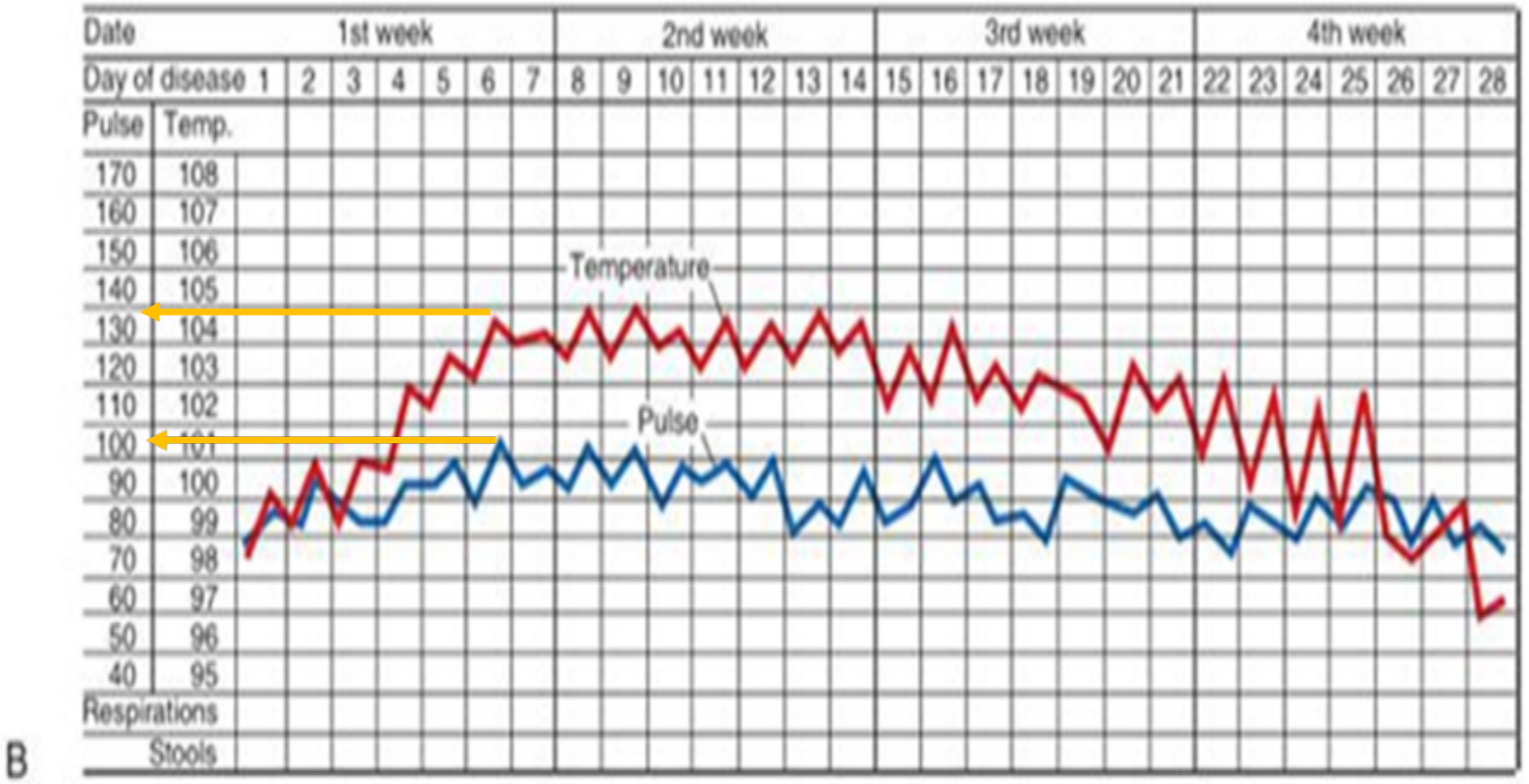
Relative Bradycardia

- Physiologically, for each 1 °F rise in body temperature, there is a commensurate increase in the heart rate of 10 beats/min . When temperature elevations are not accompanied by a physiologic increase in the pulse, the patient is said to have a pulse-temperature deficit.

- However, the term ‘relative bradycardia’ should only be applied to patients with temperatures in excess of 102 ° F since the difference between pulse and temperature readings of ≤ 102 ° F is insufficient to discern pulse temperature abnormalities.

Faget sign — sometimes called pulse temperature dissociation — is the unusual pairing of fever with bradycardia (slow pulse).

102-104 exp rise 20 b/min--→100->130



Diagnosis of Relative Bradycardia

➢Criteria for using relative bradycardia in clinical diagnosis:

- Age of patient >= 13 years
- Temperature >= 102°F and <= 106°F
- The pulse is taken simultaneously with the temperature.
- The patient has normal sinus rhythm with no arrhythmias, second or third degree heart block, or pacemaker.
- The patient must not be taking beta-blockers.

Causes of relative bradycardia

a. Infectious:

➢ *Flavivirus:*

- Dengue fever
- Yellow fever

➢ *Bacteria:*

- Salmonella typhi, Salmonella paratyphi
- Leptospira
- Brucella
- Chlamydia psitacci , Chlamydia pneumoniae
- Ricketssia prowazeki (epidemic typhus)
- Coxiella burnetti (Q fever)
- Legionella

➢ *Parasites:* Malaria

b. Non-infectious:

- Rise in ICP (Cushing's reflex):
- Brain abscess
- Meningitis
- Brain tumors
- Pontine hemorrhage
- Other: Lymphoma, Drug fevers
- Factitious fever

Aids to Diagnosis

- Pneumonia + Relative bradycardia = Think of Atypical pneumonia (Legionella, Q fever, Chlamydia pneumoniae)
- Hospitalization + Multiple drugs for treatment + Other causes of fever excluded + Relative bradycardia = Think of Drug fever
- Rashes + Relative bradycardia = Think of Typhus
- Hemorrhagic rash + Systemic toxemia + Relative bradycardia = Think of viral hemorrhagic fever
- Headache + Constipation/Diarrhea + Cough + Relative bradycardia = Think of 1st week of enteric fever

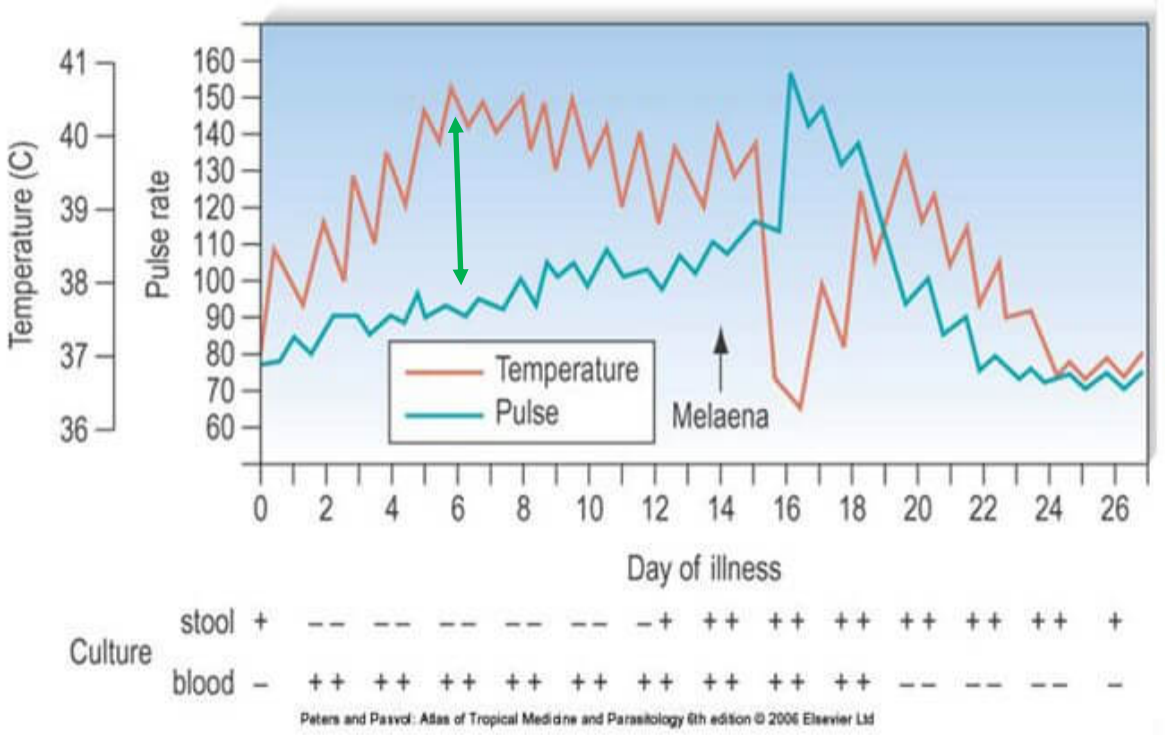
Clinical Presentation of Enteric Fever

Enteric Fever:

- Relative bradycardia at the *peak of the fever in the first week* of illness is an indicator of typhoid fever, although this finding is not universal.

- The fever may progress in a stepwise manner to become persistent and high grade by the end of second week. *It can last up to 4 weeks if left untreated*, followed by return to a normal temperature.

Temperature chart of untreated typhoid fever



Fever is almost invariable
Relative bradycardia only first week

DIAGNOSTIC APPROACH AND CLINICAL PERSPECTIVE

- diagnostic approach to the FUO patient is often extensive consisting of three phases:

- **1. Initial evaluation** should include relevant FUO history as well as physical examination that look particularly for diagnostic finding relevant to FUO
- Initial nonspecific laboratory tests provide clues pointing toward a particular diagnosis while simultaneously eliminating other diagnosis.

2. Second phase of FUO evaluation consists of a focused history and comprehensive physical examination with additional relevant lab tests.

3. Third phase of FUO work-up is the definitive diagnostic testing including specific lab tests and biopsy to confirm the diagnosis.

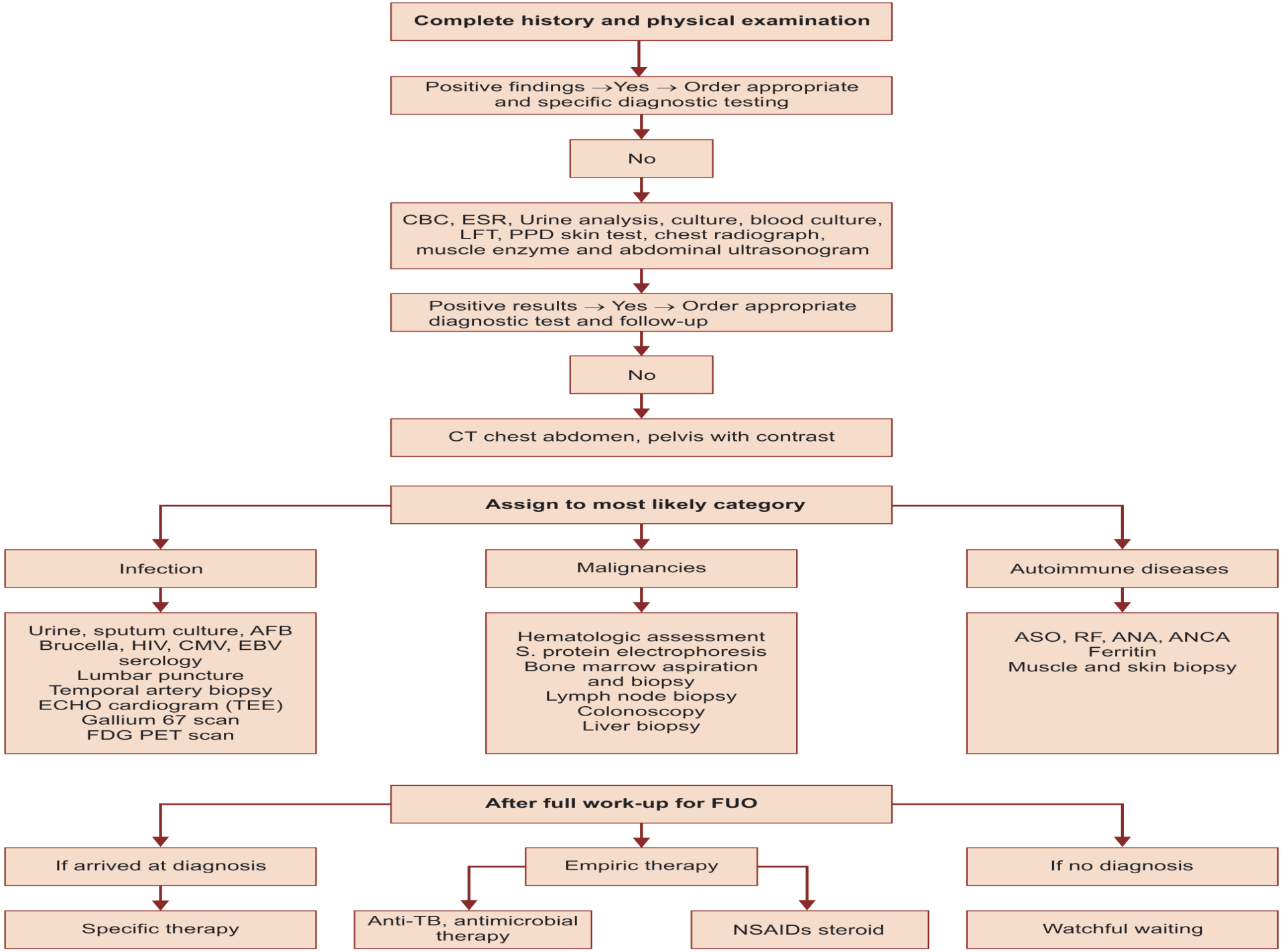

Complete history and physical examination
Positive findings → Yes → Order appropriate and specific diagnostic testing
No
CBC, ESR, Urine analysis, culture, blood culture, LFT, PPD skin test, chest radiograph, muscle enzyme and abdominal ultrasonogram
Positive results → Yes → Order appropriate diagnostic test and follow-up
No
CT chest abdomen, pelvis with contrast
Assign to most likely category
Infection
Urine, sputum culture, AFB
Brucella, HIV, CMV, EBV serology
Lumbar puncture
Temporal artery biopsy
ECHO cardiogram (TEE)
Gallium 67 scan
FDG PET scan
Malignancies
Hematologic assessment
S. protein electrophoresis
Bone marrow aspiration and biopsy
Lymph node biopsy
Colonoscopy
Liver biopsy
Autoimmune diseases
ASO, RF, ANA, ANCA
Ferritin
Muscle and skin biopsy
After full work-up for FUO
If arrived at diagnosis
Specific therapy
Empiric therapy
Anti-TB, antimicrobial therapy
NSAIDs steroid
If no diagnosis
Watchful waiting

TABLE 56.7 Examples of Subtle Physical Findings Having Special Significance in Patients With Fever of Unknown Origin

BODY SITE	PHYSICAL FINDING	DIAGNOSIS
Head	Sinus tenderness	Sinusitis
Temporal artery	Nodules, reduced pulsations	Temporal arteritis
Oropharynx	Ulceration; tender tooth	Disseminated histoplasmosis periapical abscess
Fundi or conjunctivae	Choroid tubercle, petechiae, Roth spot	Disseminated granulomatosis,[a] endocarditis
Thyroid	Enlargement, tenderness	Thyroiditis
Heart	Murmur	Infective or marantic endocarditis
Abdomen	Enlarged iliac crest lymph nodes, splenomegaly	Lymphoma,[b] endocarditis, disseminated granulomatosis[a]
Rectum	Perirectal fluctuance, tenderness	Abscess
	Prostatic tenderness, fluctuance	Abscess
Genitalia	Testicular nodule	Periarteritis nodosa
	Epididymal nodule	Disseminated granulomatos
Lower extremities	Deep venous tenderness	Thrombosis or thrombophlebitis
Skin and nails	Petechiae, splinter hemorrhages, subcutaneous nodules, clubbing	Vasculitis, endocarditis

Investigations

- Laboratory Investigations
- Imaging Studies
- Invasive Diagnostic Procedures
- Molecular Genetic Testing

Diagnostic testing — A wide variety of diagnostic tests may be useful in FUO.

- Erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)
- Serum lactate dehydrogenase
- Tuberculin skin test or interferon-gamma release assay
- HIV immunoassay and HIV viral load for patients at high risk
- Three routine blood cultures drawn from different sites over a period of at least several hours without administering antibiotics, if not already performed
- Rheumatoid factor
- Creatine phosphokinase
- Antibody test in children and young adults
- Antinuclear antibodies
- Serum protein electrophoresis
- Computed tomography (CT) scan of abdomen and chest
- Thyroid function test

Acute Phase Reactants

ESR

- If elevated → significant inflammatory process
- Greatest use in establishing a serious underlying disease, esp. if v. high → ESR > 100 mm/h …

Tuberculosis … temporal arteritis

- ↑ High ESR → lacks specificity:

Drug Reaction

Thrombophlebitis (may cause very high ESR)

Nephrotic Syndrome

CRP-closely associated with inflammatory process due to bacterial infx and cancers.

- *Usually does not go up with viral infection.*

* ESR & CRP is elevated in:

- Bacterial Infection
- Neoplasm
- Immunological-mediated inflammatory states
- Tissue infarction

- **CT scan chest**

Mediastinal mass → Tuberculosis/Lymphoma/ Sarcoidosis

Dorsal Spine → Spondylitis and disc space disease

- **CT Scan Abdomen** → very effective to visualize all types of abscesses ,Retroperitoneal tumor, lymph node or hematoma.

➢ The finding of abdominal lymphadenopathy can be a clue to lymphoma or a granulomatous process.

- **Culture:**

❖Sputum for mycobacteria

❖ Cerebrospinal fluid (CSF)

❖ Gastric aspirate for mycobacteria • Stool

❖ Swabs

Additional investigations in PUO

❖**Serological tests for connective tissue disorders**:

- Autoantibody screen
- Complement levels
- Immunoglobulins
- Cryoglobulins

❖ **Echocardiography**

❖ Ultrasound of abdomen

❖CT/MRI of thorax, abdomen and/or brain

❖Imaging of the skeletal system (skeletal survey)

- Plain X-rays (osteomyelitis)
- CT/MRI spine (pott's diseases (TB in spine) , brucellosis).

- Biopsy

- Bronchoscopy and lavage ± transbronchial biopsy
- Lymph node aspirate or biopsy for possible malignancy, especially lymphoma, or infections such as cat-scratch disease Caseating Granulomatous disease (Tuberculosis).
- Biopsy of radiological accessable lesions.
- Biopsy of liver for possible miliary tuberculosis (disseminated), granulomatous hepatitis, or other granulomatous diseases such as sarcoidosis

- Bone marrow aspirate and biopsy

Aplastic Cells → Leukemia

Leishmania Bodies → Kala-Azar

Atypical Cells → Lymphoma

Atypical Plasma Cells → M. myeloma

- Laparoscopy and biopsy
- Temporal artery biopsy to look for giant cell arteritis or biopsy of an affected tissue to diagnose a vasculitic process such as polyarteritis nodosa

THERAPY

- Therapeutic Trials
- Management

- therapeutic trials, even when successful in reducing fever, may delay the correct diagnosis and thus the appropriate treatment of FUO.

- Therefore empirical therapeutic trials should be reserved for those very few patients in whom all other approaches have failed or those so seriously ill that therapy cannot be withheld for a further period of observation, or both. In practice, this occurs most often in the case of suspected tuberculosis.

➢Limitation and risk of empirical therapeutic trials:

- Rarely specific
- Underlying disease may remit spontaneously false impression of success.
- Disease may respond partially and this may lead to delay in specific diagnosis.
- Side effect of the drugs can be misleading.

❖**Antimicrobial Trials:**

Expected to suppress, but not cure, an infectious process such as abscess →many infectious processes such as an occult abscess ,and adjunctive drainage would usually be required.

- Failure to have quick response → does not mean wrong diagnosis

patients with FUO <u>should not</u> have empiric antibiotics started <u>solely</u> to treat fever.

❖A therapeutic trial of **glucocorticoids** for an inflammatory process **<u>should not replace</u>** relevant biopsies for steroid-responsive disease such as sarcoidosis, other granulomatous diseases, or vasculitis.

A careful evaluation for infection should precede such a trial.

Empiric Drug:

Culture-negative Endocarditis

Vasculitis … Temporal Arteritis

Empiric drug trial for suspected culture

(-ve) Endocarditis:

Patient with new or changing murmur or peripheral signs of endocarditis.

Vancomycin or ampicillin + Gentamycin, may be used.

Empiric drug trials for suspected Vasculitis:

- Elderly with weight loss and any symptoms suggestive (headache, visual disturbance, jaw claudication) and ↑ ESR > 50 mm/hr → Prednisolone 60 PO
- Patient above 50 yrs who is c/o muscle pain and stiffness around hip and shoulder with ↑ ESR → Prednisolone 20 mg PO

Prognosis

- The outcome of patients with an FUO depends upon the underlying diagnosis.
- Generally poor in elderly and Neoplasm.

- Diagnostic delay has adverse effect in:
  - Intra Abdominal Infection
  - Miliary Tuberculosis
  - Recurrent Pulmonary Emboli
  - Disseminated Fungal Infection
  - Temporal Arteritis

5 – 15% of cases → The diagnosis remain obscure.

Most adults who remain undiagnosed after an extensive evaluation also have a good prognosis

- The overall mortality of PUO is 30–40%, mainly attributable
- to malignancy in older patients. If no cause is found,
- the long-term mortality is low and fever often settles spontaneously.

Thank You