ATEŞ NEDENİNİ BULAMADIM!

Prof. Dr. Ergin ÇİFTÇİ

Ankara Üniversitesi Tıp Fakültesi
Çocuk Enfeksiyon Hastalıkları Bilim Dalı

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7 Ekim 2025

ODAĞI BİLİNMEYEN AKUT ATEŞ

Odak Neresi?

ODAĞI BİLİNMEYEN AKUT ATEŞ

Odak Neresi?

Fever Without A Focus
Fever Without A Source
Fever Without Apparent Source
Fever Without Localizing Signs

GROUP	MANAGEMENT
Any toxic-appearing child 0-36 mo and temperature ≥38°C (100.4°F)	Hospitalize, broad cultures plus other tests,* parenteral antibiotics
Child <1 mo and temperature ≥38°C (100.4°F)	Hospitalize, broad cultures plus other tests,* parenteral antibiotics
Child 1-3 mo and temperature ≥38°C (100.4°F)	Two-step process 1. Determine risk based on history, physical examination, and laboratory studies. Low risk: • Uncomplicated medical history • Normal physical examination • Normal laboratory studies • Urine: negative leukocyte esterase, nitrite and <10 WBC/HPF • Peripheral blood: 5,000-15,000 WBC/mm^3; <1,500 bands or band: total neutrophil ratio <0.2 • Stool studies if diarrhea (no RBC and <5 WBC/HPF) • CSF cell count (<8 WBC/μL) and negative Gram stain • Chest radiograph without infiltrate 2. If child fulfills all low-risk criteria, administer no antibiotics, ensure follow-up in 24 hr and access to emergency care if child deteriorates. Daily follow-up should occur until blood, urine, and CSF cultures are final. If any cultures are positive, child returns for further evaluation and treatment. If child does not fulfill all low-risk criteria, hospitalize and administer parenteral antibiotics until all cultures are final and definitive diagnosis determined and treated
Child 3-36 mo and temperature 38-39°C (100.4-102.2°F)	Reassurance that diagnosis is likely self-limiting viral infection, but advise return with persistence of fever, temperatures >39°C (102.2°F), and new signs and symptoms
Child 3-36 mo and temperature >39°C (102.2°F)	Two-step process: 1. Determine immunization status 2. If received conjugate pneumococcal and *Haemophilus influenzae* type b vaccines, obtain urine studies (urine WBC, leukocyte esterase, nitrite, and culture) for all girls, all boys <6 mo old, all uncircumcised boys <2 yr, all children with recurrent urinary tract infections If did not receive conjugate pneumococcal and *H. influenzae* type b vaccines, manage according to the 1993 Guidelines (see Baraff et al. *Ann Emerg Med* 22:1198-1210, 1993.)

*Other tests may include chest radiograph, stool studies, herpes simplex polymerase chain reaction.
CSF, cerebrospinal fluid; HPF, high-powered field; RBC, red blood cell; WBC, white blood cell.

GROUP	MANAGEMENT
Any toxic-appearing child 0-36 mo and temperature ≥38°C (100.4°F)	Hospitalize, broad cultures plus other tests,* parenteral antibiotics
Child <1 mo and temperature ≥38°C (100.4°F)	Hospitalize, broad cultures plus other tests,* parenteral antibiotics
Child 1-3 mo and temperature ≥38°C (100.4°F)	Two-step process 1. Determine risk based on history, physical examination, and laboratory studies. Low risk: • Uncomplicated medical history • Normal physical examination • Normal laboratory studies • Urine: negative leukocyte esterase, nitrite and <10 WBC/HPF • Peripheral blood: 5,000-15,000 WBC/mm^3; <1,500 bands or band: total neutrophil ratio <0.2 • Stool studies if diarrhea (no RBC and <5 WBC/HPF) • CSF cell count (<8 WBC/μL) and negative Gram stain • Chest radiograph without infiltrate 2. If child fulfills all low-risk criteria, administer no antibiotics, ensure follow-up in 24 hr and access to emergency care if child deteriorates. Daily follow-up should occur until blood, urine, and CSF cultures are final. If any cultures are positive, child returns for further evaluation and treatment. If child does not fulfill all low-risk criteria, hospitalize and administer parenteral antibiotics until all cultures are final and definitive diagnosis determined and treated
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CSF, cerebrospinal fluid; HPF, high-powered field; RBC, red blood cell; WBC, white blood cell.

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*Other tests may include chest radiograph, stool studies, herpes simplex polymerase chain reaction.
CSF, cerebrospinal fluid; HPF, high-powered field; RBC, red blood cell; WBC, white blood cell.

CLINICAL PRACTICE GUIDELINE

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old

Robert H. Pantell, MD, FAAP,[a] Kenneth B. Roberts, MD, FAAP,[b] William G. Adams, MD, FAAP,[c] Benard P. Dreyer, MD, FAAP,[d] Nathan Kuppermann, MD, MPH, FAAP, FACEP,[e] Sean T. O'Leary, MD, MPH, FAAP,[f] Kymika Okechukwu, MPA,[g] Charles R. Woods Jr, MD, MS, FAAP[h] SUBCOMMITTEE ON FEBRILE INFANTS

To cite: Pantell RH, Roberts KB, Adams WG, et al. Clinical Practice Guideline: Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old. *Pediatrics*. 2021;148(2):e2021052228

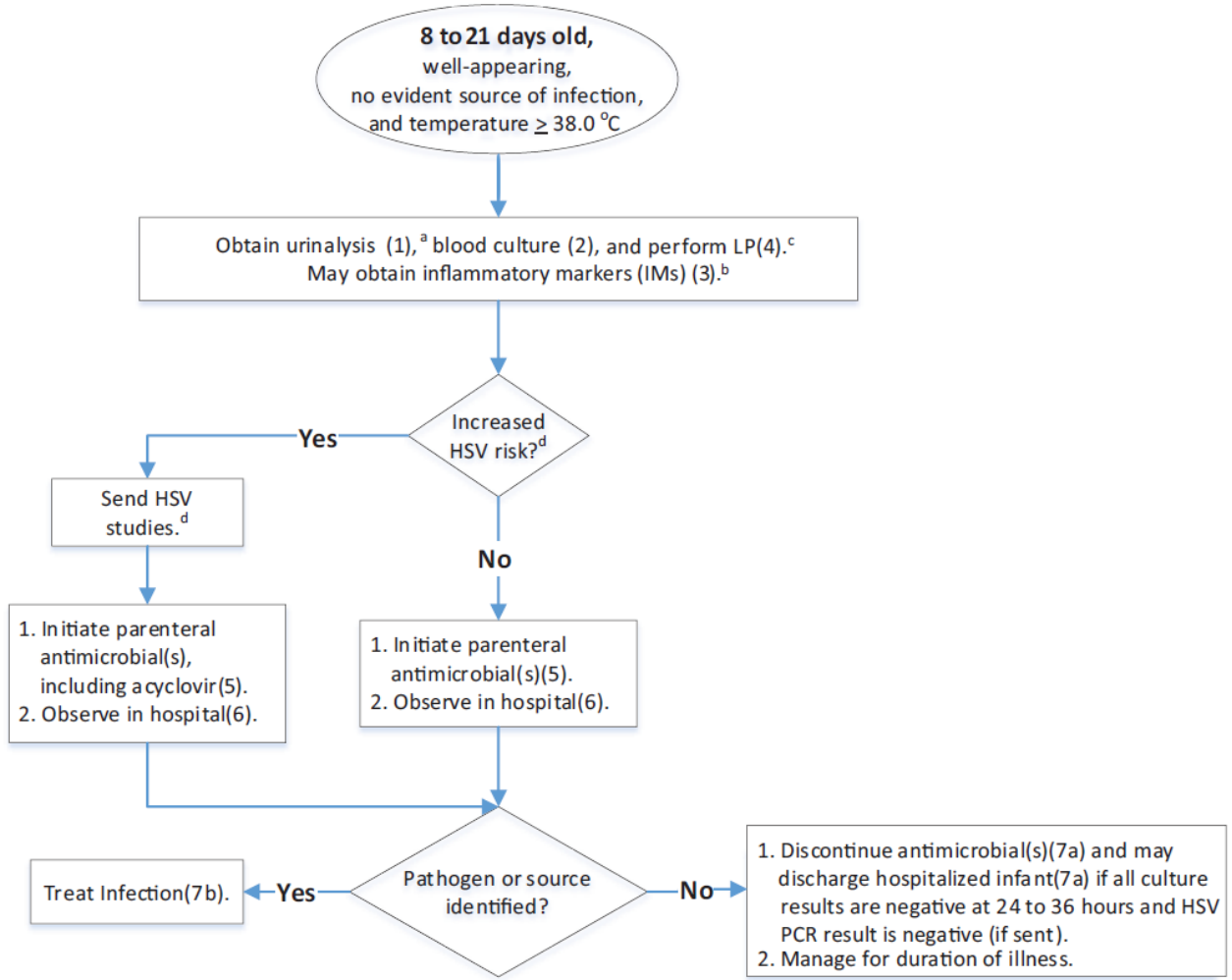
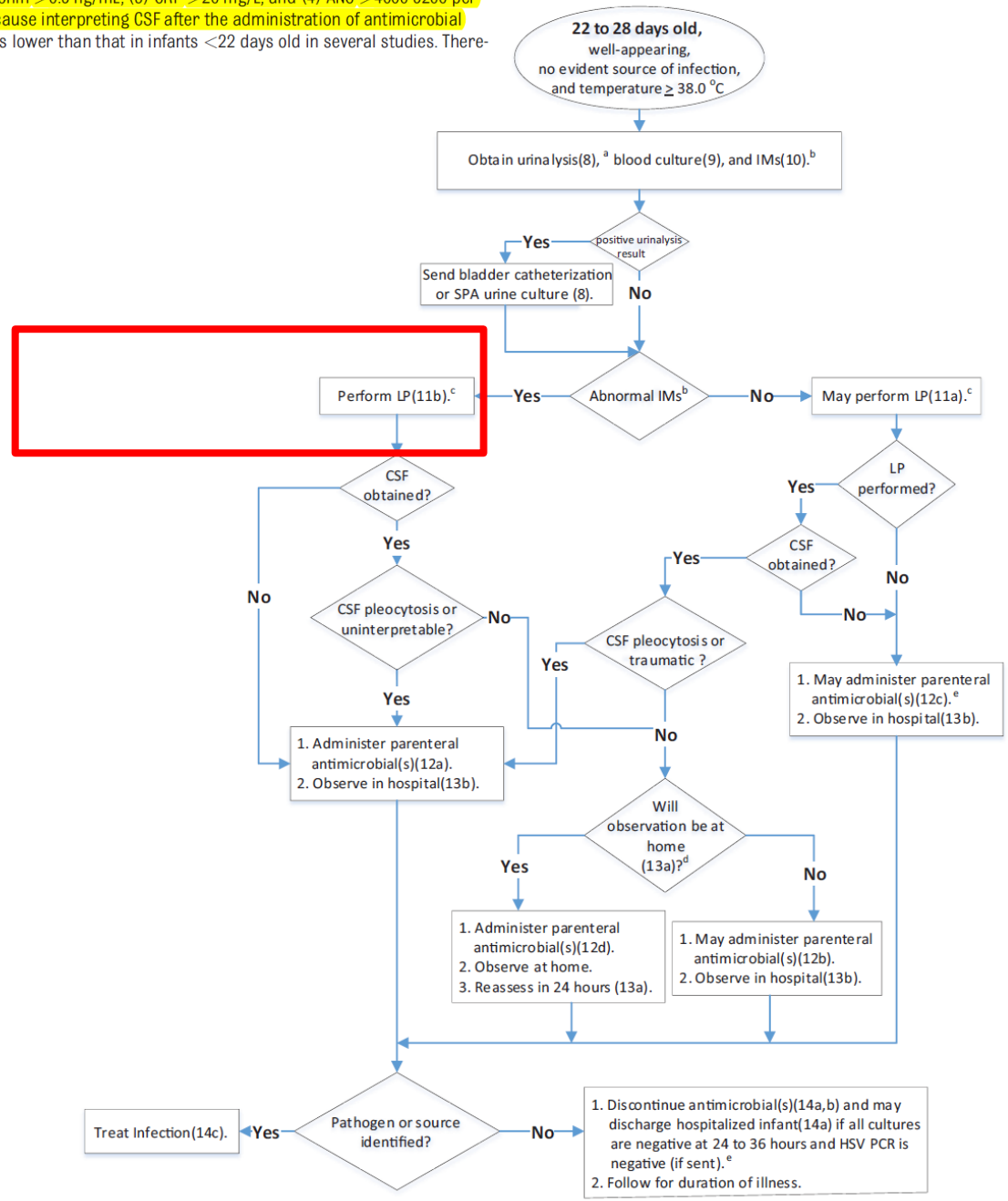


FIGURE 1 Algorithm for 8- to 21-day-old infants. [a] KAS references are shown in parentheses. [b] Laboratory values of inflammation are considered elevated at the following levels: (1) procalcitonin >0.5 ng/mL, (2) CRP >20 mg/L, and (3) ANC >4000 to 5200 per mm^3. Although we recommend all infants in this age group have a complete sepsis workup, receive parenteral antimicrobial agents, and be monitored in a hospital, knowing IM results can potentially guide ongoing clinical decisions. [c] Send CSF for cell count, Gram stain, glucose, protein, bacterial culture, and enterovirus PCR (if available) if pleocytosis is present and during periods of increased local enterovirus prevalence. [d] HSV should be considered when there is a maternal history of genital HSV lesions or fevers from 48 hours before to 48 hours after delivery and in infants with vesicles, seizures, hypothermia, mucous membrane ulcers, CSF pleocytosis in the absence of a positive Gram stain result, leukopenia, thrombocytopenia, or elevated alanine aminotransferase levels. For further discussion, see the current *Red Book*. Recommended HSV studies are CSF PCR; HSV surface swabs of the mouth, nasopharynx, conjunctivae, and anus for an HSV culture (if available) or PCR assay; alanine aminotransferase; and blood PCR.

FIGURE 2 Algorithm for 22- to 28-day-old infants. [a] KAS references are shown in parentheses. [b] If available, procalcitonin should be obtained along with ANC or CRP. If procalcitonin is unavailable, both ANC and CRP should be obtained, and a temperature >38.5°C is considered abnormal. IMs are considered abnormal at the following levels: (1) temperature >38.5°C, (2) procalcitonin >0.5 ng/mL, (3) CRP >20 mg/L, and (4) ANC >4000 5200 per mm^3. [c] LP is recommended before administration of antimicrobial agents because interpreting CSF after the administration of antimicrobial agents is difficult. However, the risk of meningitis in 22- to 28-day-old infants is lower than that in infants <22 days old in several studies. There-



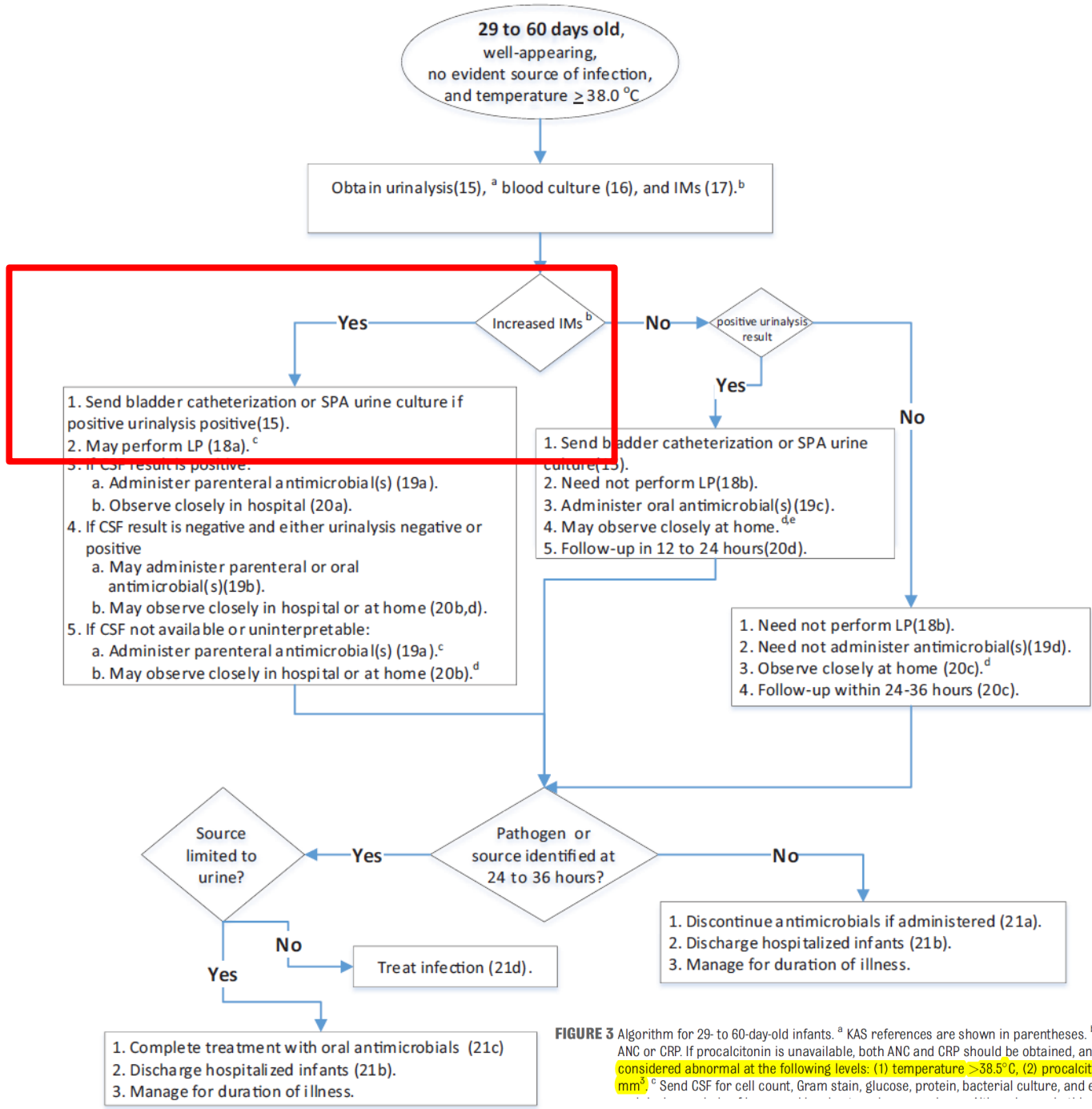


FIGURE 3 Algorithm for 29- to 60-day-old infants. [a] KAS references are shown in parentheses. [b] If available, procalcitonin should be obtained along with ANC or CRP. If procalcitonin is unavailable, both ANC and CRP should be obtained, and a temperature >38.5°C is considered abnormal. IMs are considered abnormal at the following levels: (1) temperature >38.5°C, (2) procalcitonin >0.5 ng/mL, (3) CRP >20 mg/L, (4) ANC >4000 to 5200/mm^3. [c] Send CSF for cell count, Gram stain, glucose, protein, bacterial culture, and enterovirus PCR (if available) if CSF pleocytosis is present

Table 220.2 Management of Fever Without Source in Infants 0-36 Months Old

GROUP	MANAGEMENT
Any toxic-appearing child 0–36 mo and temperature ≥38°C (100.4°F)	Hospitalize, cultures (blood, urine, CSF) plus other tests*, parenteral antibiotics
WELL-APPEARING CHILD	
Child <22 days and temperature ≥38°C (100.4°F)	Hospitalize, cultures (blood, urine, CSF) plus other tests*, parenteral antibiotics
Child 22–60 days and temperature ≥38°C (100.4°F)	**Three-Step Process** 1. Determine risk based on history, physical examination, and laboratory studies. Low risk: • Uncomplicated medical history • Well-appearing physical examination • Normal laboratory studies • Urine: negative leukocyte esterase and nitrite, ≤5 WBC/hpf centrifuged and <10 WBC/hpf uncentrifuged • Inflammatory markers: temperature ≤38.5°C, procalcitonin ≤0.5 ng/mL, CRP ≤20 mg/L, absolute neutrophil count ≤4,000-5,200/mm^3 • Stool studies if diarrhea (no RBC and <5 WBC/hpf) 2. If child *fulfills all low-risk criteria*, use age to determine need for LP, parenteral antimicrobials, and hospital observation. • **Age 22-28 days**: Obtain UA, blood culture, inflammatory markers. May perform LP. May administer parenteral antimicrobials. Observe in hospital. • **Age 29-60 days old**: Obtain UA, blood culture, inflammatory markers. Need not perform LP. Need not administer antimicrobials. Observe closely at home with follow-up within 24-36 hr. 3. If child does not fulfill all low-risk criteria, use age and lab results to determine need for LP, antimicrobials, and hospital observation. • **Age 22-28 days** with abnormal UA and normal inflammatory markers: May perform LP. Administer parenteral antimicrobials. Observe in hospital. • **Age 22-28 days** with abnormal inflammatory markers: Perform LP. If CSF pleocytosis, CSF uninterpretable, or abnormal UA, administer parenteral antimicrobials and observe in hospital. If CSF and UA are normal, may observe at home after parenteral antimicrobials or observe in the hospital with or without parenteral antimicrobials. • **Age 29-60 days** with abnormal UA and normal inflammatory markers: Administer oral antimicrobials. May observe closely at home with follow-up in 12-24 hr. • **Age 29-60 days** with abnormal inflammatory markers: May perform LP. If CSF pleocytosis, administer parenteral antimicrobials and observe in hospital. If CSF is normal, may administer parenteral or oral antimicrobials and may observe closely in hospital or at home. If CSF is not available or uninterpretable, administer parenteral antimicrobials and may observe closely in hospital or at home.
Child 2-36 mo and temperature 38–39°C (100.4–102.2°F)	Reassurance that diagnosis is likely self-limited viral infection, but advise return with persistence of fever, temperatures >39°C (102.2°F), and/or new signs and symptoms.
Child 2-36 mo and temperature >39°C (102.2°F)	**Two-Step Process** 1. Determine immunization status. 2. If received conjugate pneumococcal and *Haemophilus influenzae* type b vaccines, obtain urine studies (urine WBC, leukocyte esterase, nitrite, and culture) for all females, all males <6 mo old, all uncircumcised males <2 yr, and all children with recurrent urinary tract infections. If did not receive conjugate pneumococcal and *H. influenzae* type b vaccines, manage according to the 1993 Guidelines (see Baraff et al. *Ann Emerg Med.* 1993;22:1198–1210).

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NEDENİ BİLİNMEYEN UZAMIŞ ATEŞ

Nedeni Nedir?

Fever of Unknown Origin
Pyrexia of Unknown Origin

İlk kez 1961 yılında Petersdorf ve Beeson

1. En az üç hafta süren
2. Bir hafta süreyle hastanede yapılan incelemelere karşın nedeni belirlenemeyen
3. Belgelenmiş 38.3°C üzerinde ateş

NEDENİ BİLİNMEYEN UZAMIŞ ATEŞ

Çocuklarda Nedenler

ÇOCUKLARDA NEDENLER					
YAZAR HASTA SAYISI	**ENFEKSİYONLAR**	**MALİGNİTE**	**KVH/ OTOİMMÜN**	**DİĞER**	**TANI KONULAMAYAN**
Pizzo 100	%52	%6	%20	%10	%12
McLung 99	%29	%8	%11	%19	%33
Lohr 54	%33	%13	%20	%15	%8
Mouaket 221	%78	%2	%3	%0	%15
Steele 109	%22	%2	%6	%3	%67
Çiftçi 102	%44.2	%11.7	%6.8	%24.5	%12.8

Annals of Tropical Paediatrics (2003) 23, 259–263

Pyrexia of unknown origin in children: a review of 102 patients from Turkey

ERGİN ÇİFTÇİ, ERDAL İNCE & ÜLKER DOĞRU

Department of Paediatric Infectious Diseases, University of Ankara Medical School, Ankara, Turkey

(Accepted July 2003)

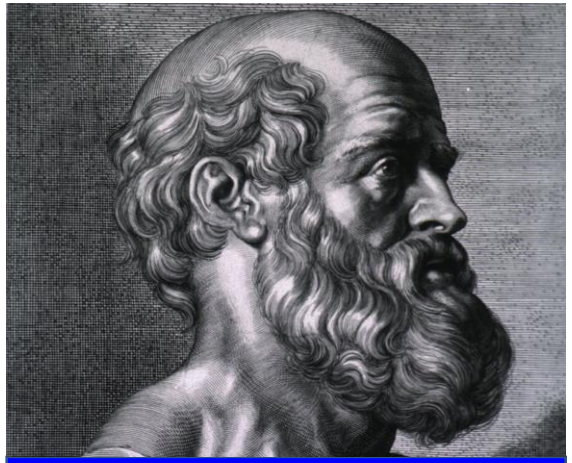
Summary Pyrexia of unknown origin (PUO) has not been appropriately investigated in Turkish children and therefore a study was undertaken to determine the causes of PUO and to evaluate which clinical procedures are useful in establishing a diagnosis. A total of 102 children fitting the classical PUO criteria seen in our clinic between 1995 and 2002 were investigated retrospectively. Infections, collagen vascular disorders, malignancy and miscellaneous conditions constituted 44.2%, 6.8%, 11.7% and 24.5% of cases, respectively, while 12.8% of the cases remained undiagnosed. Enteric fever, brucellosis and respiratory tract infections were the most commonly encountered infections, whereas familial Mediterranean fever was the commonest non-infectious disorder. Biopsy, aspiration, serology, bacteriology, radiology and observation of the clinical course were the most useful diagnostic procedures.

NEDENİ BİLİNMEYEN UZAMIŞ ATEŞ

Nedeni Nedir?

İlk kez 1961 yılında Petersdorf ve Beeson

1. En az üç hafta süren
2. Bir hafta süreyle hastanede yapılan incelemelere karşın nedeni belirlenemeyen
3. Belgelenmiş 38.3°C üzerinde ateş



Hipokrat

NEDENİ BİLİNMEYEN UZAMIŞ ATEŞ

Tanım

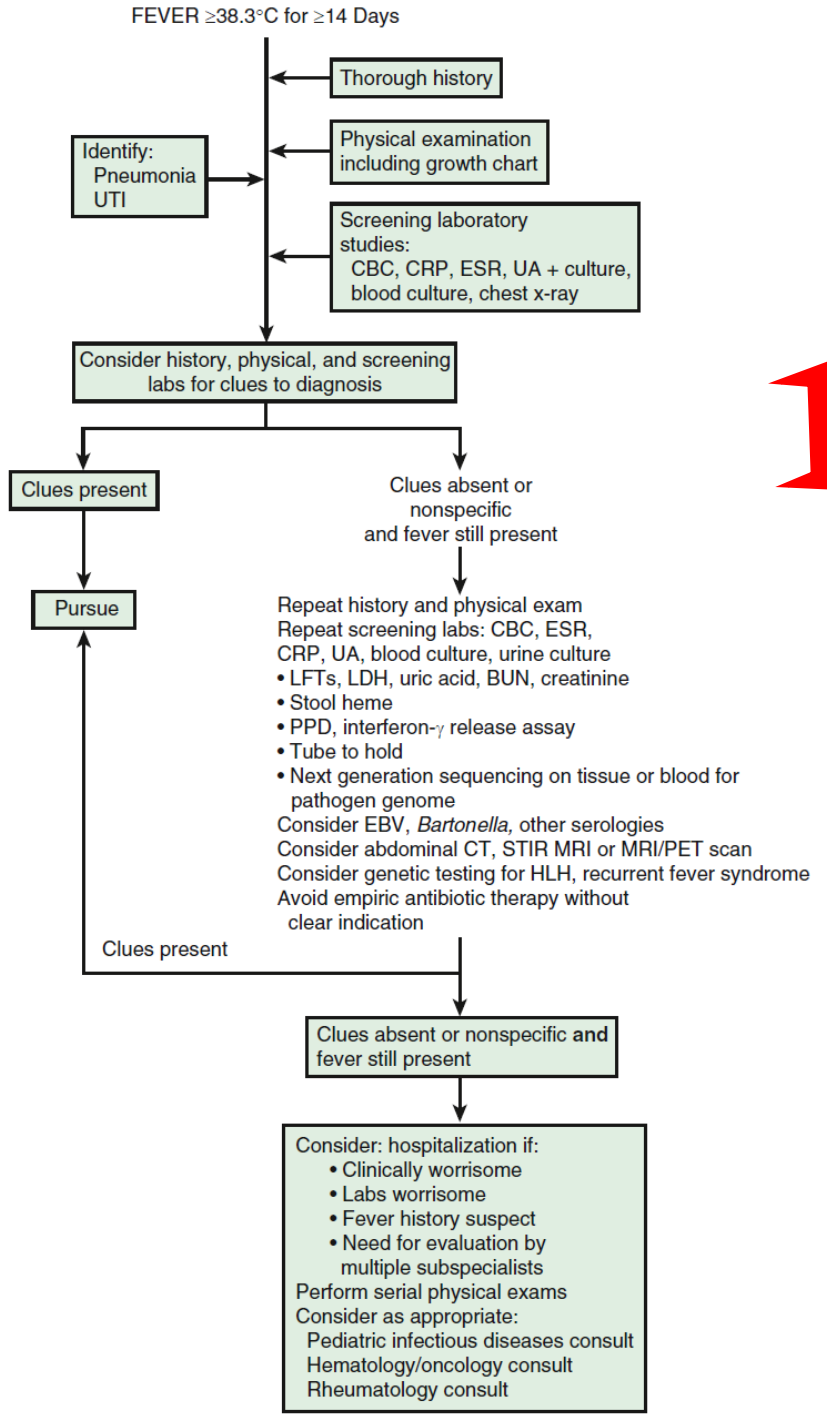
TABLE 56-1 Summary of Definitions and Major Features of the Four Subtypes of Fever of Unknown Origin (FUO)

	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

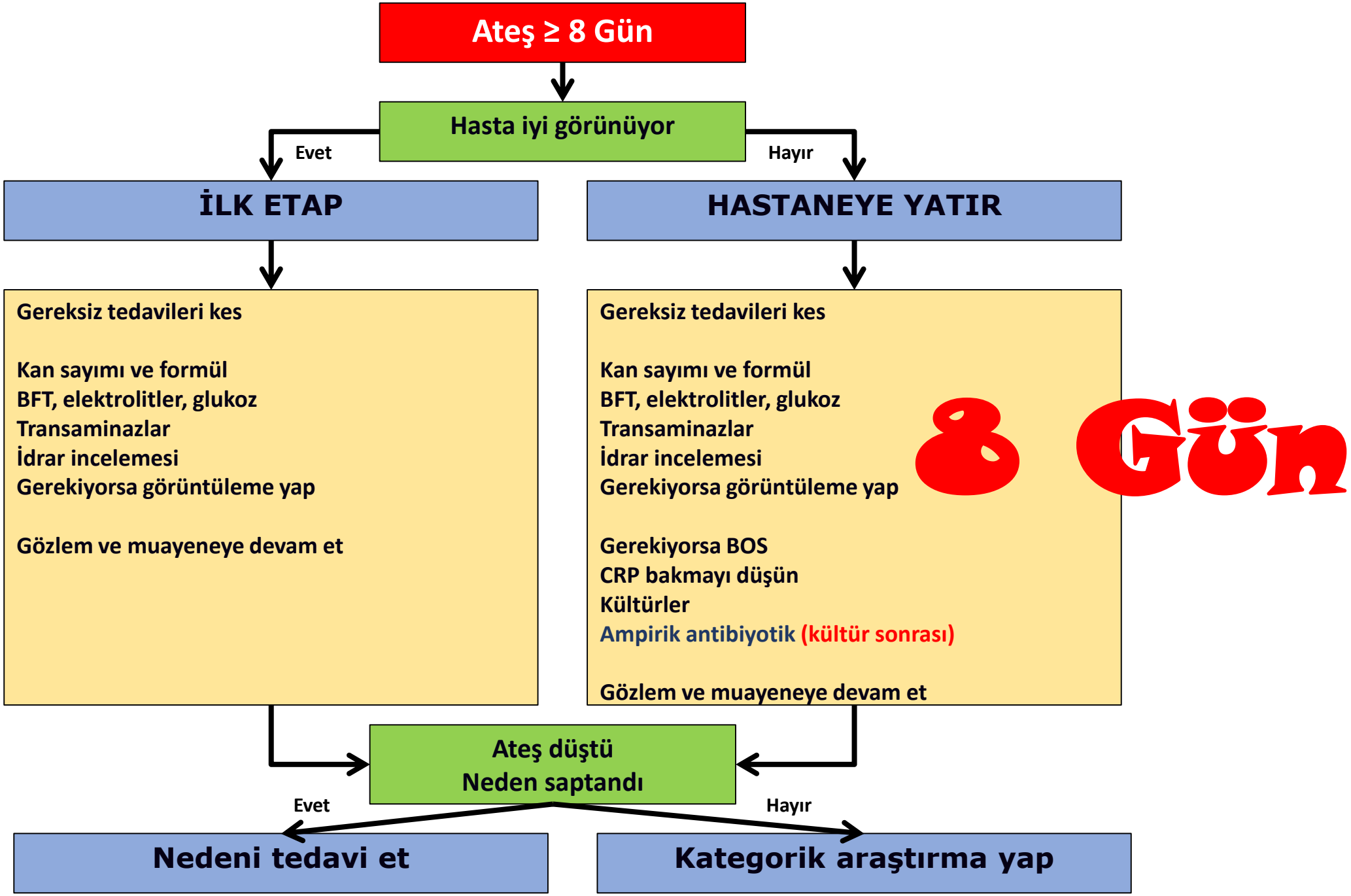
Table 177-4 Summary of Definitions and Major Features of the 4 Subtypes of Fever of Unknown Origin

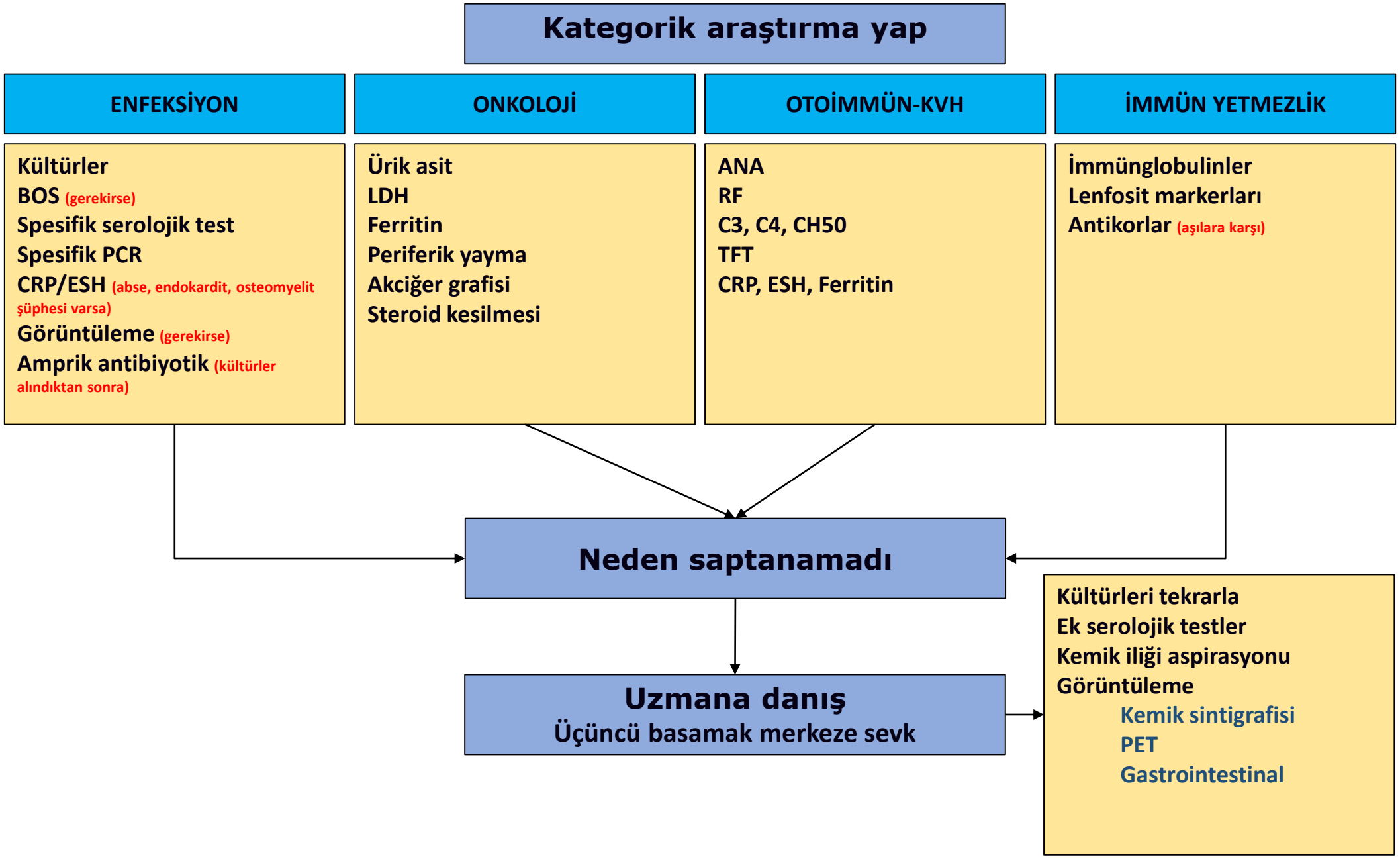
FEATURE	CLASSIC FUO	HEALTHCARE-ASSOCIATED FUO	IMMUNE-DEFICIENT FUO	HIV-RELATED FUO
Definition	>38°C (100.4°F), >3 wk, >2 visits or 1 wk in hospital	≥38°C (100.4°F), >1 wk, not present or incubating on admission	≥38°C (100.4°F), >1 wk, negative cultures after 48 hr	≥38°C (100.4°F), >3 wk for outpatients, >1 wk for inpatients, HIV infection confirmed

21 Gün


FEVER ≥38.3°C for ≥14 Days
Thorough history
Physical examination including growth chart
Identify: Pneumonia UTI
Screening laboratory studies: CBC, CRP, ESR, UA + culture, blood culture, chest x-ray
Consider history, physical, and screening labs for clues to diagnosis
Clues present
Clues absent or nonspecific and fever still present
Pursue
Repeat history and physical exam
Repeat screening labs: CBC, ESR, CRP, UA, blood culture, urine culture
• LFTs, LDH, uric acid, BUN, creatinine
• Stool heme
• PPD, interferon-γ release assay
• Tube to hold
• Next generation sequencing on tissue or blood for pathogen genome
Consider EBV, Bartonella, other serologies
Consider abdominal CT, STIR MRI or MRI/PET scan
Consider genetic testing for HLH, recurrent fever syndrome
Avoid empiric antibiotic therapy without clear indication
Clues present
Clues absent or nonspecific and fever still present
Consider: hospitalization if:
• Clinically worrisome
• Labs worrisome
• Fever history suspect
• Need for evaluation by multiple subspecialists
Perform serial physical exams
Consider as appropriate:
Pediatric infectious diseases consult
Hematology/oncology consult
Rheumatology consult

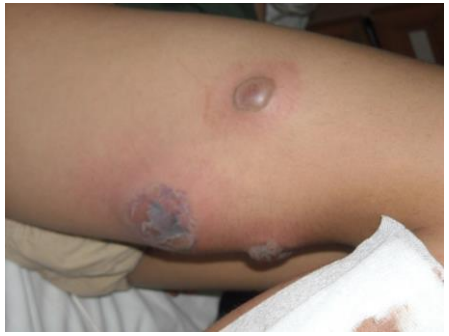
14 Gün

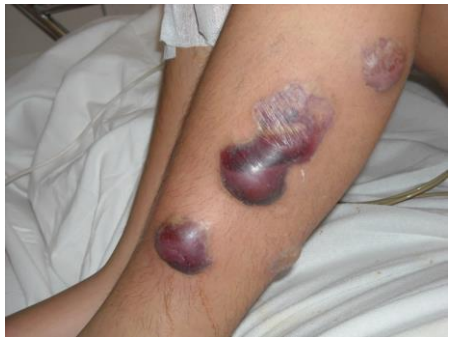

Ateş ≥ 8 Gün
Hasta iyi görünüyor
Evet
Hayır
İLK ETAP
HASTANEYE YATIR
Gereksiz tedavileri kes
Kan sayımı ve formül
BFT, elektrolitler, glukoz
Transaminazlar
İdrar incelemesi
Gerekiyorsa görüntüleme yap
Gözlem ve muayeneye devam et
Gereksiz tedavileri kes
Kan sayımı ve formül
BFT, elektrolitler, glukoz
Transaminazlar
İdrar incelemesi
Gerekiyorsa görüntüleme yap
Gerekiyorsa BOS
CRP bakmayı düşün
Kültürler
Ampirik antibiyotik (kültür sonrası)
Gözlem ve muayeneye devam et
8 Gün
Ateş düştü
Neden saptandı
Evet
Hayır
Nedeni tedavi et
Kategorik araştırma yap

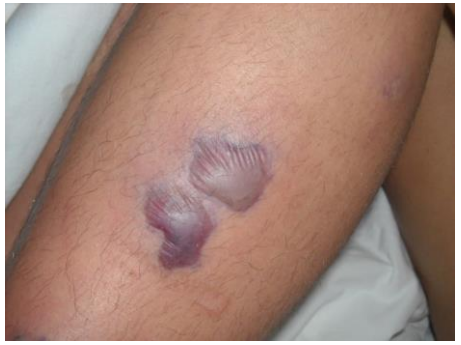

Kategorik araştırma yap
ENFEKSİYON
ONKOLOJİ
OTOİMMÜN-KVH
İMMÜN YETMEZLİK
Kültürler
BOS (gerekirse)
Spesifik serolojik test
Spesifik PCR
CRP/ESH (abse, endokardit, osteomyelit şüphesi varsa)
Görüntüleme (gerekirse)
Amprik antibiyotik (kültürler alındıktan sonra)
Ürik asit
LDH
Ferritin
Periferik yayma
Akciğer grafisi
Steroid kesilmesi
ANA
RF
C3, C4, CH50
TFT
CRP, ESH, Ferritin
İmmünglobulinler
Lenfosit markerları
Antikorlar (aşılara karşı)
Neden saptanamadı
Uzmana danış
Üçüncü basamak merkeze sevk
Kültürleri tekrarla
Ek serolojik testler
Kemik iliği aspirasyonu
Görüntüleme
Kemik sintigrafisi
PET
Gastrointestinal

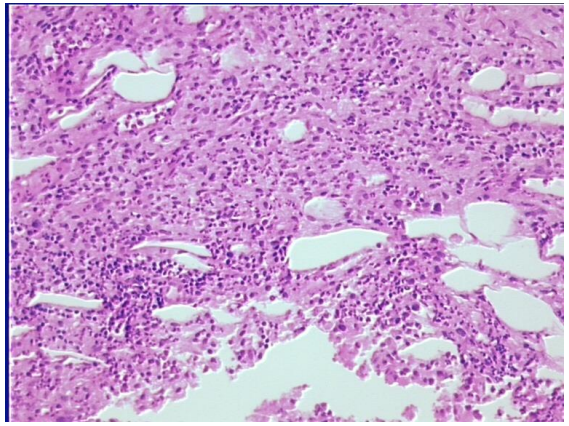
NEDENİ BİLİNMEYEN UZAMIŞ ATEŞ

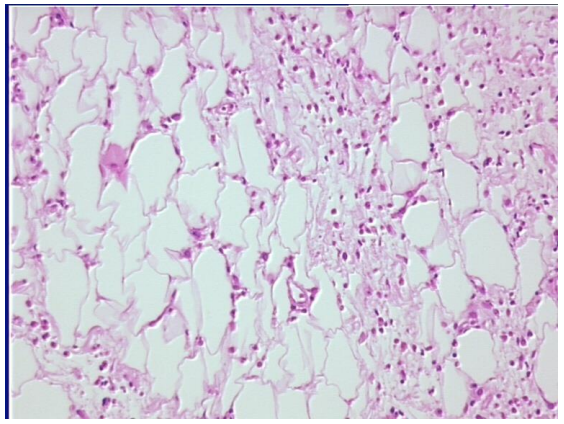
Biyopsi



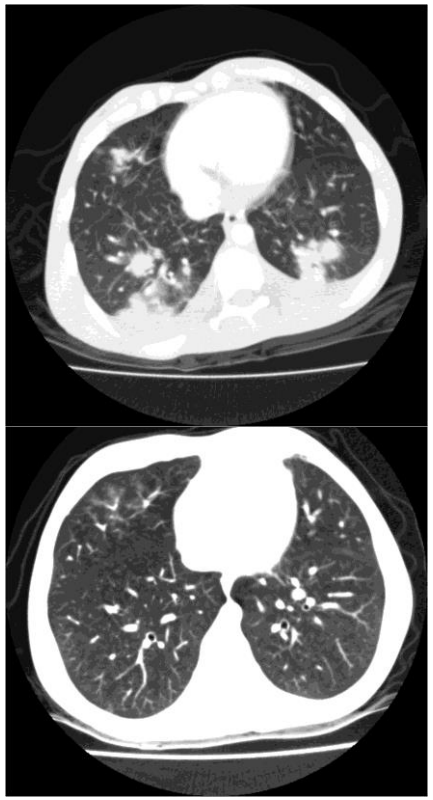








Cilt Biyopsisi



Sweet Sendromu

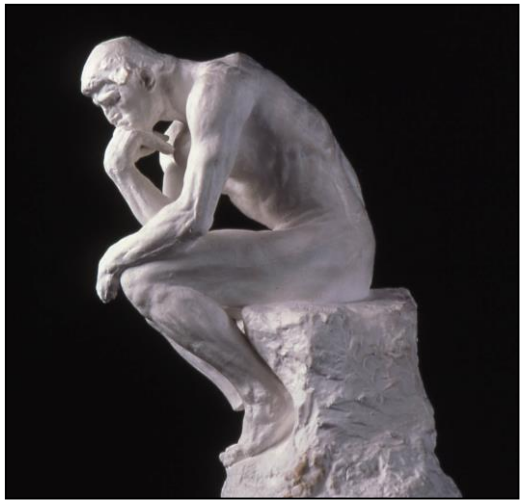
NEDENİ BİLİNMEYEN UZAMIŞ ATEŞ

Tanıya Giden Yol

- Hastanın başvuru yakınmaları ve bulguları
- Eşlik eden semptomlar
- Coğrafi bölge
- Çevresel maruziyet
- Deneyimli bir hekim değerlendirmesi
- Mevcut test olanaklarının kullanılması

NEDENİ BİLİNMEYEN UZAMIŞ ATEŞ

Tanıya Giden Yol



Common Causes of Pediatric FUO

Infectious

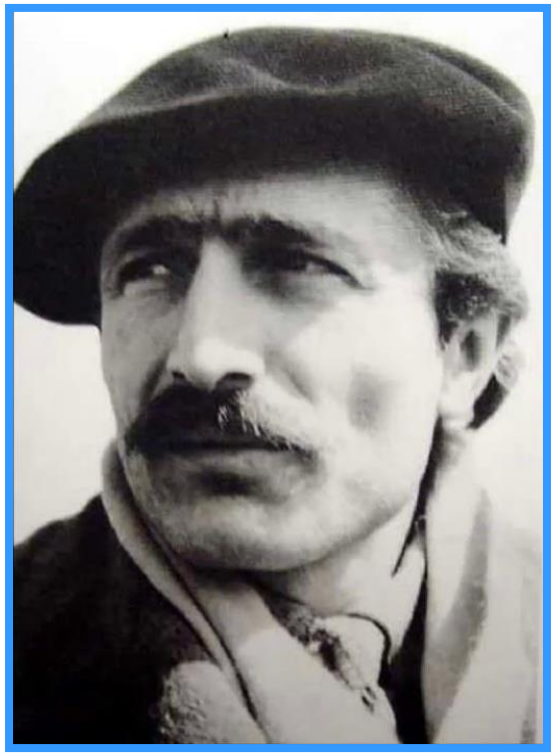
Bacterial	*Viral*	*Other*
Abscess	Adenovirus	Blastomycosis
Bartonella	Arbovirus	Cryptosporidium
Brucellosis	Cytomegalovirus	Ehrlichiosis
Leptospirosis	Enterovirus	Histoplasmosis
Mastoiditis	Epstein-Barr Virus	Leishmaniasis
Mycoplasma	Hepatitis Viruses	Lymphogranuloma Venereum
Osteomyelitis	Herpes Simplex Virus	Malaria
Pyelonephritis	Human Immunodefiency Virus	Psittacosis
Rat Bite Fever	Picornavirus	Q Fever
Salmonellosis		Rocky Mountain Spotted Fever
Sinusitis		Toxoplasmosis
Tuberculosis		Visceral larva migrans
Tularemia		
Non-Tuberulous Mycobacteria		

Non-Infectious

Oncologic	*Autoimmune*	*Other*
Leukemia	Behcet Disease	Diabetes Insipidus
Lymphoma	Inflammatory Bowel Disease	Drug Fever
Langerhans Cell Histiocytosis	Hyperthyroidism	Factitious Fever
Neuroblastoma	Granulomatosis (with polyangitis)	Familial Dysautonomia
Hemophagocytic Lymphohistiocytosis	Juvenile Idiopathic Arthritis	Periodic Fever Syndromes
	Kawasaki Disease	Pancreatitis
	Polyarteritis Nodosa	Serum Sickness
	Sarcoidosis	Cyclic neutropenia
	Systemic Lupus Erythematous	Kikuchi-Fujimoto Disease
	Antiphospholipid Antibody Syndrome	
	Subacute thyroiditis	

NEDENİ BİLİNMEYEN UZAMIŞ ATEŞ

Tanıya Giden Yol



Damla kendini tamamlayınca damlar.

ÖZDEMİR ASAF