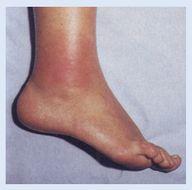
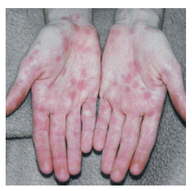
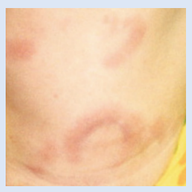
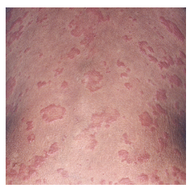
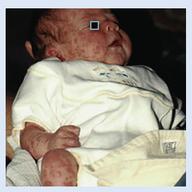
AUTOINFLAMMATORY ANSWERS

DIFFERENTIATING MONOGENIC PERIODIC FEVER SYNDROMES

	Predominant ethnic distribution[1]	Worldwide prevalence or number of cases[2-4]	Gene mutation[2,5]	Typical age at onset[2,5,6]	Delay in Diagnosis[7-10]	Duration of attacks[1,11,12]	Frequency of attacks[12-16]	Cutaneous findings[16-21]		Other select clinical features[1,5,18,21,22]	
FMF	Turkish, Armenian, Arab, Jewish, Italian	1 to 5 in 10,000	MEFV, autosomal recessive inheritance	<20 years, with 60% appearing <10 years	Mean delay in diagnosis can be 10 years	12 hours to 3 days	Irregular; once per week to once every 5 to 10 years		• Erysipelas-like erythema • Characterized by red, warm, and swollen areas • Lesions are tender to the touch, can be 10 cm to 15 cm in diameter, and usually occur below the knee on the anterior leg or top of foot	• Abdominal pain • Peritonitis • Constipation > diarrhea • Chest pain • Arthritis/monoarthritis • Myalgia	
HIDS/MKD	Dutch or Northern European	>180	MVK, autosomal recessive inheritance	<1 year	Median delay in diagnosis can be 10 years†	3 to 7 days	Irregular; 2- to 8-week intervals		• Diffuse maculopapular eruption extending to the palms and soles, or nodular, urticarial, or morbilliform • Erythematous macules that are sometimes painful can occur	• Abdominal pain • Vomiting • Diarrhea > constipation • Cervical lymphadenopathy • Aphthous ulcers • Rarely peritonitis • Arthralgia/polyarthritis	
TRAPS	All ethnicities	>1000	TNFRSF1A, autosomal dominant inheritance	Varies; <3 years to <20 years	Median delay can be >10 years†	7 to 28 days; nearly continuous in one-third of patients	Irregular; 5 weeks to months or years		• Erythematous, migratory rash • Often overlies an area of myalgia and migrates together in a centrifugal pattern • Often found on the torso or extremity	• Abdominal pain • Arthralgia • Arthritis in large joints • Peritonitis • Diarrhea	• Constipation • Musculoskeletal pain • Eye manifestations, such as periorbital edema • Migratory myalgia and erythema
CAPS: FCAS	Mostly European	<1 in 1,000,000*	NLRP3, autosomal dominant inheritance	<1 year	Median delay in diagnosis can be >10 years (FCAS & MWS)†	12 to 24 hours	Variable; triggered by generalized cold exposure		• Urticaria-like appearance • Typically raised, erythematous, maculopapular, usually nonpruritic • Described by patients as feeling painful, tight, and/or warm • Severity worsening in the evening • Usually appears on the trunk and limbs with individual migratory lesions	• Headache • Arthralgia • Fatigue	• Myalgia • Conjunctivitis • Nausea
CAPS: MWS				<20 years		2 to 3 days	Variable; triggered by cold, fatigue, and stress			• Occasional abdominal pain • Headache • Arthralgia	• Fatigue • Conjunctivitis • Sensorineural hearing loss
CAPS: NOMID	All ethnicities	<1 in 1,000,000*	NLRP3, autosomal dominant inheritance	<1 year	Median delay in diagnosis can be 2 years†	Periodicity of the attacks is lost, and, instead, there is a low-level continuous disease activity, with an occasional flare-up			• Neutrophilic urticarial skin lesions	• Most severe end of CAPS spectrum • Neurological involvement is a diagnostic feature; chronic aseptic neutrophilic meningitis with chronic irritability, headache, and seizures • Sensorineural hearing loss • Progressive vision loss • Conjunctivitis • "Typical facies" with frontal bossing, large cephalic perimeter, and the appearance of a "saddleback nose" in patients with hydrocephalus • Chronic aseptic meningitis • Cognitive delay	

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*Prevalence includes patients with FCAS, MWS, and NOMID.
†Delay in diagnosis based off of a study.

CAPS=cryopyrin-associated periodic syndromes; CRP=C-reactive protein; ESR=erythrocyte sedimentation rate; FCAS=familial cold autoinflammatory syndrome; FMF=familial Mediterranean fever; HIDS=hyperimmunoglobulin D syndrome; IgD=immunoglobulin D; MKD=mevalonate kinase deficiency; MWS=Muckle-Wells syndrome; NOMID=neonatal-onset multisystem inflammatory disease; PFS=periodic fever syndromes; SAA=serum amyloid A; TRAPS=tumor necrosis factor receptor–associated periodic syndrome.

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