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[Home](#) | [Skin signs of systemic disease](#)

PAPA syndrome

PAPA syndrome is an acronym for **P**rogenic **A**rthritis, **P**oderma gangrenosum and **A**cne. It is a rare genetic disorder characterised by its effects on skin and joints.

PAPA syndrome is inherited in an autosomal dominant fashion, which means that there is a 50% chance that a child will inherit the disease from an affected parent. It usually begins with arthritis at a young age, with the skin changes more prominent from the time of puberty.

Recently the responsible gene has been identified on Chromosome 15. Two mutations have been found in a protein called CD2 binding protein 1 (CD2BP1). This protein is part of an inflammatory pathway associated with other autoinflammatory diseases such as familial Mediterranean fever, hyper IgG and periodic fever syndrome, Muckle Wells syndrome, neonatal onset multisystem inflammatory disease and familial cold autoinflammatory syndrome. The exact mechanism of how the mutated gene causes the disease is still being investigated.

How is it diagnosed?

The clinical features along with the familial tendency may be enough to make a diagnosis, though gene testing may be available at some centres.

Clinical Features

The arthritis is the predominant feature, noted by its juvenile onset and destructive course. Individuals often recall episodes of arthritis precipitated by a traumatic event. With repeated episodes the joints become damaged with multiple joint replacements required. Hopefully with improved treatment options the damage will be limited in new cases.

[Pyoderma gangrenosum](#) is variably expressed, which means that it is not always present in all individuals with the disease. It presents as poorly healing ulcers with undermined edges. Pathergy is an important feature (this term refers to the tendency of ulcers to arise at points of injury). There are reports of lesions developing at the site of a joint replacement wound, central venous line and intravenous drip insertion.

[Acne](#) affects most individuals with PAPA syndrome but to a variable degree. It is usually of a severe [nodulocystic type](#) which if untreated results in [scarring](#).

Skin biopsy

Prominent inflammation is seen in affected tissues, with a predominance of neutrophil white blood cells within a synovial biopsy (joint tissue) and [skin biopsy](#). Biopsies of pyoderma gangrenosum show superficial ulceration as well as neutrophilic inflammation.

Treatment

[Acne treatment](#) may require oral [tetracycline antibiotics](#) or [isotretinoin](#).

Developments in the treatment of the arthritis and pyoderma gangrenosum are largely in the area of [biological response modifiers](#). These are drugs directed at particular inflammatory proteins (cytokines), and have shown success in the treatment of other inflammatory conditions like [rheumatoid arthritis](#) and [psoriasis](#).

Treatments directed at tumour necrosis factor (TNF) ([infliximab](#), [etanercept](#)) and interleukin 1 (anakinra) have shown a good response in resistant arthritis and pyoderma gangrenosum.

Related information

References:

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- [Skin signs of systemic disease](#)
- [Pyoderma gangrenosum](#)
- [Nodulocystic acne](#)

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- [Acne conglobata](#) – emedicine, the online textbook of dermatology

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