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## Review

## Chronic meningococcal disease: Systematic literature review

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## ABSTRACT

**Background:** Chronic meningococcal disease is a rare and under-recognized manifestation of *Neisseria meningitidis* infection. Unlike acute meningococcal infections, its presentation is insidious, leading to diagnostic delays. We conducted a systematic review to better characterize its clinical, microbiological, and epidemiological profile.

**Methods:** A systematic review was performed in accordance with PRISMA 2020 guidelines and registered in PROSPERO (CRD42024608035). We searched Excerpta Medica, National Library of Medicine, Web of Science, Google Scholar, and bibliographies for cases reported since 1960 using the terms "chronic meningococemia" or "chronic meningococcal disease." Eligible cases involved previously apparently healthy individuals with *N. meningitidis* isolated from a normally sterile site. Two reviewers independently extracted data on demographics, clinical features, diagnostics, microbiology, treatment, and outcomes.

**Results:** A total of 126 cases from 97 reports were included. Most patients (median age: 21 years) presented with recurrent fever (98%), non-blanching skin lesions (95%), and musculoskeletal symptoms (90%) over a period of  $\geq 10$  days. In over two-thirds of cases, symptoms followed a relapsing-remitting pattern, with alternating episodes of fever, rash, and joint involvement. Diagnosis was delayed longer in adults than in children ( $P < 0.0001$ ). Blood cultures were positive in 77% of cases; molecular testing and skin biopsy improved diagnostic yield. *N. meningitidis* serogroup B (58%) and C (31%) were most common. Meningeal signs were largely absent (94%). Antimicrobial therapy led to complete recovery without sequelae in all patients. Testing for inherited susceptibility was conducted in 52 cases and revealed abnormalities – primarily complement deficiencies – in 13 (23%) of them.

**Conclusions:** Chronic meningococcal disease should be considered in individuals with relapsing fever, vasculitic skin lesions, and joint involvement, especially when cultures are negative or symptoms mimic viral or autoimmune conditions. Early use of molecular diagnostics and awareness of characteristic patterns may improve recognition. The term "relapsing-remitting meningococcal disease" may better reflect its clinical nature.

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