Rheumatic fever was first described in the nineteenth century. Though potentially preventable, it continues to be a major health problem and is still a major cause of mortality from heart disease during the first 50 years of life.

The incidence of rheumatic fever in the western world began to decline long before the introduction of antibiotic treatment. In Denmark, for example, the incidence of the disease decreased from 250 per 100,000 population in 1862 to 100 per 100,000 in 1962 [1]. This trend was rapidly accelerated with the introduction of antibiotics, and the incidence reported in 1980 was less than 2 per 100,000.

In developing countries, however, the incidence is still high and is up to 13.4 per 100,000 hospitalized children [2]. According to current estimates, 10–20 million new cases per year are expected in these countries [3]. Nevertheless, the sudden reappearance of focal epidemics in the United States in the mid-1980s reminded us that the disease still poses a threat worldwide [4].

A better understanding of the pathogenesis of RF is needed to explain its changing incidence. Despite the expanding epidemiological and immunological evidence linking group A Streptococcus infection to RF, many unanswered questions remain. Studies have shown that not all group A streptococcal strains are rheumatogenic. It is known that pyoderma and soft tissue infections never cause rheumatic fever. Furthermore, even though the pharynx is the site of the antecedent rheumatic infection, not all group A streptococcal pharyngeal infections lead to RF.

Though opinions vary regarding the rheumatogenicity of certain streptococcal strains [3], several factors do support their existence, namely:

- Some of the 80 distinct streptococcal A serotypes, defined by their M protein molecule, have been associated with epidemics of RF.
- The Streptococcus A that causes RF is distinct from the one that causes glomerulonephritis.
- Certain M serotypes of group A streptococci, once so prevalent in RF epidemics, have made a recent reappearance.
- There is no association between RF and invasive streptococcal infections such as toxic shock syndrome.

The rheumatogenic strains are associated with certain characteristics [5]. They are highly contagious. They possess the M protein and large hyaluronate capsules, both responsible for the striking resistance to phagocytosis and virulence. Their most important property, however, is the inclusion in the large M protein molecules of epitopes that cross-react with cardiac and other host tissues.

Another important factor in the pathogenesis of RF is the site of the streptococcal infection in the pharynx, where the large repository of lymph tissue may be important in the initiation of the abnormal immune response [3].

The concept of a genetic predisposition to RF has long intrigued researchers [6]. Several studies have reported a genetic association with RF, some related to the major histocompatibility complex, others not. Patarroyo and colleagues [7] described a B cell alloantigen in several diverse populations with RF that was not MHC related. More recently, studies using monoclonal antibodies against B cells from patients with RF found that this B cell antigen is expressed in 100% of RF patients compared with only 10% of healthy individuals [8]. Thus, this antigen may serve as a marker of RF susceptibility. At the same time, other investigators have described an increased frequency of different HLA types in different populations with RF [9–11]. These conflicting results have led to the speculation that the reported association might be of genes located close to but not identical with the RF susceptibility gene, or that susceptibility to RF is polygenic.

Hence, RF represents an autoimmune response in genetically and environmentally predisposed individuals to an untreated rheumatogenic strain of group A streptococcal pharyngitis.

In this issue of IMAJ, Habib and colleagues [12] present important information about the incidence of RF during the last decade in the Nazareth area of Israel. They report a mean annual incidence of 5 per 100,000 population, with a peak in 1990 of 13.4 per 100,000. These numbers are astonishingly high compared to other developed countries.
between these two studies. The figures of Habib and colleagues [12] fall
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between these two studies.

Regarding the clinical picture, Habib’s team [12] noted
that the arthritis was migratory in only half their cases.
The term “migratory” is often used to describe the poly-arthritis of RF and is not meant to signify that in-
flammation necessarily disappears in one joint when it
appears in another. Rather, the various locations usually
overlap in time, and it is the onset that “migrates” from
joint to joint [3].

The rate of carditis in the article (34%) was surpris-
ingly low compared to other reports (65% to 91%) [14,15]. The reason for the discrepancy may lie in the authors’
diagnosis of carditis on the basis of clinical and radiological
findings, without echocardiographic screening of all their
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However, it should be emphasized, as the authors also
noted, that they are representative only of a subpopulation
living in Arab villages under very low socioeconomic
conditions and cannot be extrapolated to all of Israel or to
other areas of the country.

It is surprising that in Israel, where RF is relatively
common, there are no accurate data regarding the extent
of its morbidity. To the best of our knowledge, this is only
the second published report on the incidence of RF in
Israel. The first was conducted by Bitton and Joseph [13]
and included 222 cases of RF in southern Israel from 1974
to 1983. This area is populated mainly by Jews from Arab
countries and Bedouins and has a low socioeconomic
rating. According to this study, the mean annual incidence
of RF was 12–16 per 100,000, and it did not change
significantly during the 10 year follow-up. In a third, un-
published, study of 144 cases of RF in central Israel from 1977 to 1987, a higher incidence of the disease was noted
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