Acute rheumatic fever (ARF) is primarily the result of a bacterial infection with potentially serious consequences for the heart. ARF develops from contact with a specific bacterium called *Group A Streptococcus* (GAS). After exposure, the body generates antibodies to help destroy the bacteria. However, because of close structural similarity between certain parts of the bacterial cell wall and heart tissue, these antibodies may also act against the person’s own heart valves (which separate the different chambers of the heart). This leads to valve damage in the form of narrowed (stenotic) or leaky (regurgitant) valves. Over time, there is progressive damage (rheumatic heart disease, RHD) that may lead to heart failure, stroke, infection of the valves (infective endocarditis), and death.

This disease has been almost eradicated in Western countries, but remains a major health problem in developing countries and among indigenous populations in wealthy countries. RHD is related to overcrowding, inadequate hygiene, poor access to healthcare, and low awareness. Recent estimates suggest that disability related to RHD alone equals more than a quarter of all cancers put together. Globally, RHD remains the leading cause of heart failure in children and young adults, accounting for at least 250,000 deaths annually.

**Natural History of ARF and RHD**

ARF usually occurs a few weeks after sore throat caused by GAS and may affect the joints, skin, brain, and heart. Involvement of the heart (occurring in more than half of the cases) results in the most severe manifestations, both acute and long term (Table 1). Although the first ARF episode can sometimes lead to persistent heart valve damage, RHD is most often the result of cumulative valve damage attributable to recurrent episodes of ARF that may sometimes even be silent (without clinical symptoms). This makes identification of the disease challenging.

RHD almost always affects left-sided heart valves. Although right-sided valves are rarely damaged directly, they are usually affected as a consequence of malfunction of the left sided valves. The most common manifestation in the early stages is leakiness of a left-sided (mitral) valve, which allows blood to leak back from the lower chamber (ventricle) to the upper chamber (atrium). This can remain silent for several years as the heart enlarges to compensate before it finally fails. Narrowing of the mitral valve can also develop, which results in obstruction of blood flow (Figure 1). The resulting back pressure can be reflected to the right side, responsible for leakiness of the right sided valves and enlargement of the right chambers.

Symptoms of RHD include features of heart failure such as shortness of breath, ankle swelling, fatigue, and rapid heartbeat (attributable to abnormal rhythms resulting from dilated heart chambers). Stagnation of blood in enlarged chambers can result in clot formation, which can then break off and obstruct blood flow to different parts of the body, resulting for example, in a stroke. Very often, the diagnosis is made late in the course of the...
disease, through complications such as these or signs of heart failure.

Diagnosis by the physician is mainly dependent on identifying abnormal heart murmurs generated from the diseased valves and may be of limited accuracy, especially in early stages of the disease. Scanning the heart using ultrasound (called echocardiography) helps in earlier diagnosis and in identifying the affected valve(s), which are typically thickened and in advanced stages, structurally distorted.2

Open-heart valve surgery or other invasive procedures (such as balloon dilatation of the narrowed valve) are usually required for advanced disease. These sometimes carry significant risk, are expensive, and are often not readily available in the developing world. Hence, prevention and early identification are valuable.

**Different Levels of Prevention for RHD**

*Primordial prevention* essentially focuses on socio-economic development as it directly impacts on hygiene, access to medical care, and living conditions (such as avoidance of overcrowding). Decline in ARF in the Western countries started before the antibiotic era and has been attributed to better living conditions.

Ideally, prevention should avoid the first ARF attack. Thus, *primary prevention* aims to achieve this by treating all GAS sore throat by oral or injectable penicillin (Table 2). Although not all sore throat leads to ARF, it is important that parents are educated to take their children to the doctor if they have symptoms of a sore throat (Figure 2). The doctor can identify whether the sore throat is attributable to the GAS bacterium by taking a swab and then treating with antibiotics. An even simpler approach where all sore throat is treated using penicillin without costly tests to identify the infecting agent could be especially relevant in resource-limited settings.3 Another potential path to *primary prevention* is the development of a vaccine targeting the bacterium responsible. However, lack of interest from industry and the presence of different strains of bacteria worldwide pose a major challenge.

*Secondary prevention* is based on regular penicillin administration after an initial attack of ARF to avoid reinfection, thus preventing subsequent episodes and thereby disease progression. Three to 4 weekly intramuscular injections of benzathine penicillin is the treatment of choice. Oral antibiotics may be more convenient but carry higher rates of relapse. The duration of secondary prophylaxis (usually a minimum of 5–10 years) depends on the presence and severity of valvular damage and the patient’s age. This could be needed lifelong in those with significant valve damage.

### Table 1. Key Facts About Rheumatic Fever and RHD

| Rheumatic fever results from a specific infection (bacterial sore throat) |
| Structural similarity between the bacterial cell wall and heart valve tissue results in damage to the valves from the body’s own immune system |
| Recurrent episodes of ARF result in cumulative damage leading to RHD |
| Infection by the culprit organism is favored by poor living conditions and overcrowding |
| ARF and RHD cause significant disability, especially in the young |
| Surgery or catheter based interventional procedures are palliative and often scarce in resource-poor settings |
| Effective prevention is possible through early detection, public education and antibiotic prophylaxis using penicillin |

### Table 2. Different Preventions of RHD

<table>
<thead>
<tr>
<th>Type of Prevention</th>
<th>Aim (What?)</th>
<th>Modality (How?)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primordial</strong></td>
<td>Eliminate factors conducive for infection through developmental measures at the population level</td>
<td>Socio-economic development: avoidance of overcrowding, improved hygiene.</td>
</tr>
<tr>
<td><strong>Primary</strong></td>
<td>Eliminate infection early to prevent the first episode of ARF</td>
<td>Prompt treatment of all sore throat by penicillin in endemic areas</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
<td>Eliminate recurrence of acute rheumatic fever to prevent cumulative damage leading to rheumatic heart disease</td>
<td>Regular antibiotic prophylaxis (monthly injection of long-acting penicillin), sometimes lifelong, after a first episode of acute rheumatic fever or diagnosed rheumatic heart disease</td>
</tr>
</tbody>
</table>

*Figure 1. Rheumatic mitral stenosis. Cross-sectional view of the base of the heart showing the 4 valves. The mitral valve (a left-sided heart valve; identified by arrows) has 2 leaflets around an orifice through which it allows blood flow from the upper chamber (atrium) to the lower chamber (ventricle). On the left-hand side is a normal mitral valve with normal leaflets, whereas on the right-hand side a mitral valve narrowed as a result of rheumatic heart disease is depicted. Note how the orifice is severely narrowed as a result of abnormal thickening and fusion of the valve leaflets. Obstruction to blood flow through the narrowed orifice results in symptoms as heart failure or stroke. Reproduced with permission from A.D.A.M. Inc.*
Ways to Achieve Eradication of RHD

Comprehensive programs including education and awareness, followed by strict implementation of primary and secondary prevention, should enable eradication of the disease. Early diagnosis through ultrasound screening of children may also help (Figure 3). However, such strategies require sustainability, because prevention runs through several decades of life. Efforts from the World Heart Federation, the RhEACH initiative as well as the Global Heart Network to connect stakeholders to resources that provide vital cardiac care should enable access to information on how to build such programs and optimize patients’ care.5,6

In conclusion, RHD is caused by a bacterial infection, with potentially devastating effects on the heart. This disease has been eradicated from the Western world but remains endemic in emerging nations. Prevention, in its different forms, and targeted public education to raise awareness, have the potential to reduce disease burden.

Sources of Funding

This work was supported by the French Institute of Health and Medical Research and the French Federation of Cardiology.

Disclosures

None.

References

Prevention of Acute Rheumatic Fever and Rheumatic Heart Disease
Mariana Mirabel, Kumar Narayanan, Xavier Jouven and Eloi Marijon

Circulation. 2014;130:e35-e37
doi: 10.1161/CIRCULATIONAHA.113.007855

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/130/5/e35

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/