Lessons from Practice

Syphilis has become a rare disease, although peaks of syphilis notifications occurred in Australia in the mid 1970s to mid 1980s and again more recently. Clinicians need to be aware of the manifestations of syphilis, and to consider the diagnosis outside the groups considered at risk of this infection in the modern era, such as men who have unprotected sex with other men. The five patients in our series ranged in age from 40 to 77 years. Notably, all were born overseas, and none belonged to a group considered at high risk of syphilis in the contemporary Australian context. Serology was consistent with acquisition of infection in the distant past in four of the five patients.

Among patients with untreated syphilis, aortitis occurs in up to 70%–80%, and the clinically apparent manifestations of aortic regurgitation, coronary ostial stenosis and aortic aneurysms are seen in 10%–15%. Although aortic regurgitation is rarely caused by syphilis, it occurs in 20%–30% of patients with syphilitic aortitis. Coronary ostial lesions may be seen in 20%–25% of patients with syphilitic aortitis, but it is uncommon for such
coronary ostial lesions to lead to acute myocardial infarction. In contrast, ostial lesions are only seen in 0.1% of patients with coronary artery disease, and bilateral lesions are even less common. The high plasma reagin titre seen in Patient 2 is also unusual for people with aortic regurgitation, especially those with risk factors, including birth in a country where syphilis has been or continues to be common. Although rates of neurosyphilis are low in patients with cardiovascular syphilis, a cerebrospinal fluid examination is recommended to exclude neurosyphilis. In addition, screening for other sexually transmitted infections, including HIV, should be considered, and appropriate contact tracing instituted. Sexual transmission of syphilis occurs only when mucocutaneous lesions are present, but long-term sexual partners of patients with late latent or tertiary syphilis should be screened serologically.

The duration and route of penicillin therapy for cardiovascular syphilis are controversial. Each of our five patients received a different therapy. Penicillin has never been formally evaluated as treatment for cardiovascular syphilis, but a study from the 1950s showed that few patients had progressive disease after penicillin therapy, and up to 60% reported symptomatic relief. The

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**Table: Cardiovascular syphilis: one proven and four presumptive cases**

<table>
<thead>
<tr>
<th>Age, sex and country of origin</th>
<th>Syphilis serology and cardiovascular risk factors</th>
<th>Management and follow-up</th>
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<tbody>
<tr>
<td>75 years, female, Greece</td>
<td>RPR: 1:2, TPPA: reactive Hypertension</td>
<td>Aortic valve and aortic root replacement. Histological confirmation of syphilitic aortitis.</td>
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<tr>
<td><strong>Aortic regurgitation; dilated aortic root</strong></td>
<td></td>
<td>Treated for cardiovascular syphilis with intravenous ceftriaxone 1 g daily for 3 weeks. No evidence of a Jarisch–Herxheimer reaction.</td>
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<tr>
<td><strong>Acute myocardial infarction; bilateral ostial lesions and no visible disease in the right coronary artery</strong></td>
<td>RPR: 1:64, TPPA: reactive Smoker</td>
<td>Lumbar puncture not performed. Follow-up 15 months after therapy: mild exertional shortness of breath. Follow-up syphilis serology has not been requested.</td>
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<tr>
<td>56 years, female, Vietnam</td>
<td>RPR: 1:1, TPPA: reactive Type 2 diabetes mellitus Hypercholesterolaemia</td>
<td>Ostial lesions were not sufficiently severe to require revascularisation procedures, so no biopsies were taken of the aortic wall or coronary arteries. Presumptively treated for cardiovascular syphilis with intramuscular procaine penicillin 1 g daily for 15 days. No evidence of a Jarisch–Herxheimer reaction. CSF normal (lumbar puncture performed after treatment completed). Follow-up 1 year after therapy: symptom-free with RPR 1:1. Cardiovascular MRI revealed no further evidence of ostial coronary disease.</td>
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<tr>
<td><strong>Angina; bilateral ostial lesions; minor irregularities of the left circumflex artery, but no visible disease in the left anterior descending and right coronary arteries</strong></td>
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<tr>
<td>77 years, male, Hong Kong</td>
<td>RPR: 1:2, TPPA: reactive Hypertension Type 2 diabetes mellitus</td>
<td>Aortic regurgitation was not sufficiently severe to warrant valve replacement, so no aortic wall biopsy was obtained. Presumptively treated for cardiovascular syphilis with intramuscular benzathine penicillin 2.4 g weekly for 3 doses. No evidence of a Jarisch–Herxheimer reaction. CSF normal. Follow-up: returned to Hong Kong and lost to follow-up. Follow-up syphilis serology has not been requested.</td>
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<tr>
<td><strong>Aortic regurgitation; dilated aortic root</strong></td>
<td></td>
<td></td>
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<tr>
<td>72 years, male, Timor</td>
<td>RPR: Non-reactive TPPA: reactive No cardiovascular risk factors present</td>
<td>Aortic regurgitation was not sufficiently severe to warrant valve replacement, so no aortic wall biopsy was obtained. Presumptively treated for cardiovascular syphilis with intravenous penicillin 1.8 g 4 hourly for 14 days. Intravenous hydrocortisone 50 mg four times a day given for 48 hours because of concern about a Jarisch–Herxheimer reaction when atrial fibrillation occurred on antibiotic therapy. No other manifestations of a possible Jarisch–Herxheimer reaction. Atrial fibrillation reverted to sinus rhythm with amiodarone and sotalol therapy. CSF normal. Follow-up: ongoing medical management for cardiac failure. Repeat syphilis serology 3 years after therapy, showed RPR non-reactive.</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass graft. CSF = cerebrospinal fluid. MRI = magnetic resonance imaging. RPR = rapid plasma reagin titre. TPPA = Treponema pallidum particle agglutination test.
Australian Therapeutic guidelines: antibiotic suggest intravenous benzylpenicillin for 15 days,10 the Australian National management guidelines for sexually transmissible infections suggest intramuscular procaine penicillin for 20 days,11 and the World Health Organization, European and United States guidelines suggest intramuscular benzathine penicillin 2.4 million units once weekly for three doses.12-14 These variations reflect the paucity of good clinical data comparing the different regimens. Although definitive evidence of the efficacy of benzathine penicillin is lacking, there is also no evidence to the contrary. There is little evidence that Jarisch–Herxheimer reactions complicate treatment of cardiovascular syphilis.8,9,15

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