Not all diseases are as common as others; doctors are often taught to think of horses when they hear hooves not zebras. But sometimes you need to distinguish the plains zebras from the mountain zebra or Grévy's zebra! Here's how to distinguish the causes for culture-negative endocarditis:

1. **Repeat blood cultures off antibiotics and prolong the incubation to at least 14 days**
2. **Investigate 1st line infective serology**
   - *Coxiella burnetii* (Q fever) and *Bartonella* spp. (cause between 25-50% of cases of culture-negative endocarditis)
   - *Brucella* spp. if risk of exposure identified in history e.g. dietary (drinking unpasteurised milk), occupational (veterinarians, dairy farmers, abattoir workers and Microbiologists!) or travel history (Africa, the Middle East, Latin America and the Caribbean)
3. **Investigate non-infective serology**
   - Rheumatoid factor and antinuclear antibodies

4. **Request specific PCR on EDTA blood samples (if available) for *Bartonella* spp. and *T. whipplei***

5. **Investigate 2nd line infective serology**
   - *Mycoplasma* spp., *Chlamydia* spp. *Legionella* spp. these should not be performed routinely as very rare <1% of cases of culture-negative endocarditis (if a positive result is obtained it is more likely to be a false positive rather than the cause of infection). If positive repeat the serology but start treatment until results known

6. **If the heart valve has been surgically removed**
   - Molecular testing of the heart valve using 16s RNA can identify any bacteria, and 18sRNA for fungi, by finding fragments of their genetic material
   - Histopathological examination of valve tissue for non-infective causes