

Appendix 1 (as supplied by the authors): Detailed Methods

A research assistant not involved in assignment or care of the trial patients generated the randomization sequence with a computerized random number generator. The assistant concealed the allocation sequence from the investigators, who enrolled the participants by putting the assigned treatments in sequentially numbered, opaque, sealed envelopes. These were opened sequentially only after an eligible participant had been found and informed consent obtained, after which a study nurse attached a self-fastening slip of paper containing the patient's name to the official study logbook.

The study notebook included written instructions for their general practitioner about the study and information on the need for examining and recording the ear, throat and nose status thoroughly and taking the blood and culture samples and an illustration on how to obtain the culture sample. In addition, the patients were given a package containing laboratory stickers for blood samples, equipment for taking a throat swab specimen (Transpocult, Orion Diagnostica, Helsinki, Finland) and prepaid microbiological postal package. The doctors were informed to send these samples to Oulu University Hospital laboratories for analysis and to advise the patient to visit the study laboratory for the second blood sample three days later.

The culture sample was obtained from the surface of both tonsils or tonsillar fossae and from the posterior pharyngeal wall.

Serum C reactive protein concentrations were measured at assignment and at acute visits using an automated turbidometric immunoassay (ADVIA Immunoassay System, Siemens Healthcare Diagnostics, Tarrytown, USA).

When analyzing bacteriological cultures, we plated the swab on sheep blood agar, selecting the growth of streptococci, and incubated them at 35 °C for 18–24 hours before reading. The plates were examined again at 48 hours. We used latex agglutination tests (streptococcal grouping kit, Oxoid, Unipath, Hampshire) to differentiate group A streptococcus from the other β haemolytic streptococci. To identify streptococcal carriers, we obtained throat cultures at assignment when the patients were asymptomatic.