



Figure. Bottle of artemisinin, available over-the-counter as an herbal supplement.

of artemisinin or its derivatives as monotherapies could potentially lead to progressively increasing resistance in *P. falciparum* malaria (3). Studies in western Cambodia, where artemisinin monotherapy has been available for many years, have revealed in vivo artesunate resistance, with markedly decreased parasite clearance times (3). Progressive spread of artemisinin resistance could have disastrous consequences for the global control of malaria. Thus, minimally regulated use of potent compounds in dietary supplements has the potential for major public health implications.

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Yersinia pestis DNA Sequences in Late Medieval Skeletal Finds, Bavaria

To the Editor: We read with interest the report by Wiechmann et al. that, in the investigation of late medieval plague, partial sequencing of the *Yersinia pestis* pPCP1 plasmid yielded the observation of a 3-T homopolymeric tract which differed from the 5-T homopolymeric tract of the Orientalis *Y. pestis* CO92 type strain (1). This observation was unexpected because previous data from multispacer sequence typing and *glp* D gene sequencing yielded only the Orientalis biotype in cases of ancient plague (2).

Using suicide PCR (3), we therefore further investigated pPCP1 in 10 negative control dental pulp specimens and 60 specimens collected from 1 Justinian Orientalis plague site (2), 2 Black Death Orientalis sites, and 2 additional medieval plague sites. All negative controls remained negative; 14 (23%) of 60 plague specimens yielded a PCR product, and 7 interpretable sequences yielded a 3-T homopolymeric tract in all cases.

We further tested a *Y. pestis* isolate collection comprising 2 Antiqua, 6 Medievalis, and 4 Orientalis strains. No amplification was obtained in DNA-free PCR mix and 5 *Y. enterocolitica*-negative control isolates, whereas sequencing yielded a 3-T homopolymeric tract in all 12 *Y. pestis* isolates.

BLAST analysis (<http://blast.ncbi.nlm.nih.gov/blast.cgi>) indicated that the 5-T homopolymeric tract has been found only once in the *Y. pestis* CO92 strain (4) and in none of 22 modern and 11 ancient sequences (Table). This 5-T homopolymeric tract is therefore CO92 strain specific and not a marker for the Orientalis biotype. This pPCP1 plasmid sequence, located into a noncoding region of the 3' extremity of the plasmid, is characterized by several homopolymeric tracts of poly (A) and poly (T), including the 1 herein investigated. Instability of the T-stretches has been reported in bacterial genomes (5) as being hot spots for mutations (5).

Therefore, in our assessment, the data reported for the late medieval Bavaria burial (1) do not support that deaths of persons buried in this site resulted from a non-Orientalis plague. Typing modern or ancient *Y. pestis* strains should not rely on poly (A) and poly (T) homopolymeric tracts sequencing.

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Table. Alignment of pPCP1 *Yersinia pestis* modern and ancient sequences

Source and <i>Y. pestis</i> strain	GenBank accession no.	Sequence, 5' → 3'
Complete sequence		
<i>Y. pestis</i> CO92 plasmid pPCP1	AL109969.1	8488_TATATTTTCAAGAAAAGCTGGCTATTTAACAT AACGGCAATTTTGTACGCACCACTGAA_8547
<i>Y. pestis</i> KIM plasmid pPCP1	AF053945.1	8488_TATATTTTCAAGAAAAGCTGGCTATTTAACAT AACGGCAATTT..GTACGCACCACTGAAAT_8547
<i>Y. pestis</i> biovar <i>Microtus</i> str. 91001 plasmid pPCP1	AE017046.1	8487_TATATTTTCAAGAAAAGCTGGCTATTTAACAT AACGGCAATTT..GTACGCACCACTGAAAT_8546
<i>Y. pestis</i> Nepal516 plasmid pPCP	CP000307.1	9650_TATATTTTCAAGAAAAGCTGGCTATTTAACAT AACGGCAATTT..GTACGCACCACTGAAAT_9709
<i>Y. pestis</i> Antiqua plasmid pPCP	CP000310.1	9661_TATATTTTCAAGAAAAGCTGGCTATTTAACAT AACGGCAATTT..GTACGCACCACTGAAAT_9720
<i>Y. pestis</i> D182038 plasmid pPCP1	CP001592.1	8486_TATATTTTCAAGAAAAGCTGGCTATTTAACAT AACGGCAATTT..GTACGCACCACTGAAAT_8545
<i>Y. pestis</i> Z176003 plasmid pPCP1	CP001596.1	8487_TATATTTTCAAGAAAAGCTGGCTATTTAACAT AACGGCAATTT..GTACGCACCACTGAAAT_8546
Modern isolate		
103813 <i>Y. pestis</i> Nairobi rattus Antiqua	HQ542863	61_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_120
103814 <i>Y. pestis</i> JHUPRI Antiqua	HQ542864	61_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_120
103815 <i>Y. pestis</i> 14–47 Medievalis	HQ542865	61_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_120
103817 <i>Y. pestis</i> 5G5 Medievalis	HQ542866	61_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_120
103818 <i>Y. pestis</i> 5F1 Medievalis	HQ542867	61_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_120
103819 <i>Y. pestis</i> 6B4 Medievalis	HQ542868	61_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_120
103820 <i>Y. pestis</i> 8B7 Medievalis	HQ542869	61_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_120
103821 <i>Y. pestis</i> 9F11 Medievalis	HQ542870	61_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_120
103822 <i>Y. pestis</i> 6/69M Orientalis	HQ542871	61_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_120
103823 <i>Y. pestis</i> EV-76 Orientalis	HQ542872	61_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_120
103824 <i>Y. pestis</i> algeria 1 Orientalis	HQ542873	64_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAA_123
103825 <i>Y. pestis</i> algeria 2 Orientalis	HQ542874	61_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_120
Ancient strain detected from teeth		
Tooth no. 107 (excavated from Lariey site, France, 17th century)	HQ542875	62_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAATGC_123
Tooth no. 515 (excavated from Venice site, Italy, 14th–16th centuries)	HQ542876	60_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAATGC_121
Tooth no. 1183 (excavated from Bondy site, France, 11th–15th centuries)	HQ542877	62_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_121
Tooth no. 1184 (excavated from Bondy site, France, 11th–15th centuries)	HQ542878	61_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_121
Tooth no. 1190 (excavated from Bondy site, France, 11th–15th centuries)	HQ542879	61_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_120
Tooth no. 254 (excavated from Venice site, Italy, 14th–16th centuries)	HQ542880	61_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_120
Tooth no. 1180 (excavated from Bondy site, France, 11th–15th centuries)	HQ542881	61_TATATTTTCAAGAAAAGCTGGCTATTTAACATAA CGGCAATTT..GTACGCACCACTGAAAT_120

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In Response: We thank Tran et al. for their interest in our article

(*I*). In it, we described the detection of several *Yersinia pestis*-specific plasmid pPCP1 DNA sequences in skeletal remains from a late medieval mass burial in Bavaria, Germany. In 1 of these sequence sections, we found a deviation from the reference sequence used (*Y. pestis* strain CO92 plasmid sequence AL109969.1). We did not further interpret this result because we agree with Tran et al. that typing of *Y. pestis* strains should not rely on poly (A) and poly (T) homopolymeric tract sequencing (2). As we have stated (*I*), further analyses of our material, including chromosomal markers (3,4) will be conducted to obtain clues as to the specific *Y. pestis* strain.

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