The Journal of Infectious Diseases

CORRIGENDUM

In the 1 September 2016 issue of the *Journal*, in the article by Khoury et al (Khoury DS, Cromer D, Möhrle JJ, McCarthy JS, Davenport MP. Defining the effectiveness of antimalarial chemotherapy: investigation of the lag in parasite clearance following drug administration. J Infect Dis 2016; 214:753–61), the authors stated on page 755 that "Two subjects were excluded [from analyses in the subsection "Timing of Treatment Affects Parasite Kinetics in the Lag Phase After Therapy"] because they were treated in the afternoon…." However, 2 errors were made by the authors subsequently in the article. First, although both subjects were excluded from the analysis in this subsection, they were included in analyses summarized in subsequent subsections of Results. Second, 11 other subjects were mistakenly classified as having been treated in the morning despite having been treated in the afternoon. Accordingly, the 11 subjects should have been excluded from analyses, for consistency.

These exclusions have no impact on the overall conclusions of the study. They have very minor impacts on the study findings (almost exclusively altering values in the last significant figure), summarized as follows. First, originally, 96 individuals treated with 8 different drugs were included in the analysis. However, removing those individuals treated in the afternoon leaves 85 individuals in our analysis, treated with 6 different drug regimens (artemether/lumefantrine and atovaquone/proguanil are now excluded from our analysis because investigators in the studies using these drugs treated all subjects in the afternoon). Second, we previously showed a correlation between rises in parasite numbers after treatment and the day of treatment. However, after the appropriate exclusions, we had only 1 subject treated on an odd day (day 7) who also received a slow-acting regimen; hence, it is not possible to confirm that individuals treated with a slow-acting drug on an odd day were not at risk of a rise in parasite concentration (Figure 3*B* and 3*D*). Third, we previously found evidence for a correlation between growth rates before treatment and after treatment with a slow-acting drug. However, after the exclusion of individuals treated in the afternoon, less statistical power has resulted in this relationship being only marginally significant ($P = .054$).

Details of all changes in the main text of the article are presented below in Supplementary Table 1.

The authors regret these errors.

The Journal of Infectious Diseases® 2019;219:1852–3

DOI: 10.1093/infdis/jiy729

Table 1. Itemization of Changes to the Article After Excluding Individuals Treated in the Afternoon

Original	Corrected
Timing of Treatment Affects Parasite Kinetics in the Lag Phase After Therapy	
"Two subjects were excluded because they were treated in the afternoon; also, cohorts that received noncurative doses were excluded, leaving 96 of 112 subjects available for analysis."	"Thirteen subjects were excluded because they were treated in the afternoon; also, cohorts that received noncurative doses were excluded, leaving 85 of 112 subjects available for analysis."
"Of the 96 subjects, 90 had a 12-hour (posttreatment) sample available for analysis."	"Of the 85 subjects, 79 had a 12-hour (posttreatment) sample available for analysis."
Volunteers treated on an odd day (peak) showed a decline (−3.7/day; 95% CI, −4.3 to −3.1) in parasite numbers (Figure 3A). These dynamics occurred regardless of whether a fast-acting or slow-acting antimalarial was used (Figure 3B).	Volunteers treated on an odd day (peak) showed a decline (−3.9/day; 95% CI, −4.7 to −3.2) in parasite numbers (Figure 3A). Rises in parasite concentrations occurred regardless of whether a fast-acting or slow-acting antimalarial was used (Figure 3B).
Before Treatment, Current Parasite Growth Is Predicted by Parasite Growth 36 Hours Ago	
"We observed a significant correlation between the parasite growth rates 12 hours before treatment (growth rate from −12 hours to 0 hour) and 36 hours earlier (from −48 hours to −36 hours) in our volunteers before treatment (r = 0.68; $P < .0001$). Fitting these data, we estimated a slope of 0.86 (95% CI, .59–1.1) (Figure 4A [black dashed line]), similar to the expected 1:1 relationship."	"We observed a significant correlation between the parasite growth rates 12 hours before treatment (growth rate from −12 hours to 0 hour) and 36 hours earlier (from −48 hours to −36 hours) in our volunteers before treatment (r = 0.72; $P < .0001$). Fitting these data, we estimated a slope of 0.87 (95% CI, .62–1.1) (Figure 4A [black dashed line]), similar to the expected 1:1 relationship."
Parasite Kinetics Immediately After Treatment Are Predicted by What Was Expected With No Treatment	
(Figure 4A), we found a strong correlation (r = 0.73; $P < .0001$).	(Figure 4A), we found a strong correlation (r = 0.69; $P < .0001$).
Fitting this relationship with a linear model by using Deming regression revealed that the slope was significantly <1 (0.74; 95% CI, .55–.92) but not significantly different from the slope for the pretreatment data (0.86; 95% CI, .59–1.1; $P = .32$). However, when we kept the slopes equal for the 2 groups, the intercept of the line fitted to the treatment data (−1.1/day; 95% CI, −1.7 to −.57) was significantly lower than the intercept of the line fitted to pretreatment data (−0.078/day; 95% CI, −.60–.45; $P = .0052$).	Fitting this relationship with a linear model by using Deming regression revealed that the slope was not significantly <1 (0.89; 95% CI, .57–1.2) and not significantly different from the slope for the pretreatment data (0.87; 95% CI, .62–1.1; $P = .91$). However, when we kept the slopes equal for the 2 groups, the intercept of the line fitted to the treatment data (−1.7/day; 95% CI, −2.5 to −.89) was significantly lower than the intercept of the line fitted to pretreatment data (−0.53/day; 95% CI, −1.1–.07; $P = .010$).
Fast-Acting Drugs Show Higher Effectiveness Early After Treatment Commences	
We observed a significant positive correlation between the growth rate 36 hours before treatment and the growth rate in the first 12 hours after treatment for both fast-acting and slow-acting drugs (r = 0.69 and r = 0.75; $P < .0001$ and $P < .0001$, respectively; Figure 4A). We found no significant difference between the regression lines for fast-acting drugs and slow-acting drugs (slopes, 0.80 [95% CI, .48–1.1] and 0.63 [95% CI, .40–.86], respectively [$P = .54$]; intercepts, −1.2/day [95% CI, −2.1 to −.34] and −0.64/day [95% CI, −1.2 to −.071], respectively). However, both slow-acting and fast-acting drugs showed significantly lower intercepts, compared with the pretreatment data ($P = .035$ and $P = .25$, respectively).	We observed a significant positive correlation between the growth rate 36 hours before treatment and the growth rate in the first 12 hours after treatment for fast-acting (r = 0.69 ; $P < .0001$; Figure 4A), and weak evidence of a positive correlation for slow acting drugs (r = 0.39; $P = 0.054$). We found no significant difference between the regression lines for fast-acting drugs and slow-acting drugs (slopes, 0.94 [95% CI, .49–1.4] and 0.70 [95% CI, -.48 to 1.9], respectively [$P = .76$]; intercepts, −1.7/day [95% CI, −2.8 to −.56] and −0.96/day [95% CI, −5.6 to 3.7], respectively). However, both slow-acting and fast-acting drugs showed significantly lower intercepts, compared with the pretreatment data ($P = .044$ and $P = .048$, respectively).
We once again found a significant positive correlation between expected and observed growth in volunteers treated with slow-acting drugs (r = 0.52; $P < .002$; Figure 4B), indicating that parasite growth in the first day after treatment with slow-acting drugs was still dependent on parasite growth before treatment. The estimated slope for slow-acting drugs (1.00; 95% CI, .43–1.6) was not significantly different from the estimated slope in the pretreatment data (0.93; 95% CI, .47–1.4; $P = .78$; Figure 4B [blue vs black dashed lines]). However, when we kept the slope equal for the 2 groups, the estimated intercept of the linear fit of the slow-acting drugs was significantly less than the intercept estimated for the pretreatment data (−2.0/day [95% CI, −3.0 to −1.1] and 0.18/day [95% CI, −.52–.87], respectively; $P < .0001$), indicating that slow-acting drugs were boosting the natural killing rate. In contrast, when considering volunteers treated with fast-acting drugs, we found no significant correlation between expected and observed growth in parasitemia level (r = −0.025; $P = .88$; Figure 4B), showing that, over the first 24 hours, fast-acting drugs acted independently of the stage of the parasite growth cycle at which they were administered. The mean growth rate over the first 24 hours after treatment with a fast-acting drug was −2.7/day (95% CI, −3.3 to −2.2).	We once again found a significant positive correlation between expected and observed growth in volunteers treated with slow-acting drugs (r = 0.73; $P < .0001$; Figure 4B), indicating that parasite growth in the first day after treatment with slow-acting drugs was still dependent on parasite growth before treatment. The estimated slope for slow-acting drugs (.68; 95% CI, .42–.95) was not significantly different from the estimated slope in the pretreatment data (0.49; 95% CI, .10–.88; $P = .27$; Figure 4B [blue vs black dashed lines]). However, when we kept the slope equal for the 2 groups, the estimated intercept of the linear fit of the slow-acting drugs was significantly less than the intercept estimated for the pretreatment data (−.79/day [95% CI, −1.4 to −.18] and 0.35/day [95% CI, −.17–.86], respectively; $P < .0004$), indicating that slow-acting drugs were boosting the natural killing rate. In contrast, when considering volunteers treated with fast-acting drugs, we found no significant correlation between expected and observed growth in parasitemia level (r = −0.036; $P = .84$; Figure 4B), showing that, over the first 24 hours, fast-acting drugs acted independently of the stage of the parasite growth cycle at which they were administered. The mean growth rate over the first 24 hours after treatment witha fast-acting drug was −2.6/day (95% CI, −3.2 to −2.0).