

# What Factors Affect Intrapartum Maternal Temperature? A Prospective Cohort Study

## Maternal Intrapartum Temperature

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### ABSTRACT

**Background:** In recent years, several reports have indicated that maternal temperature elevations during labor may also be observed in the absence of an infection. Presumed noninfectious causes of maternal temperature elevations include epidural analgesia, endogenous heat production generated by the contracting uterus, and delivery in an overheated room. To investigate the potential causes of noninfectious maternal temperature changes during labor, we conducted a prospective cohort study in women scheduled for labor induction.

**Methods:** We recorded hourly oral temperatures from admission to delivery. We calculated whether temperature changed during labor in 81 women. We then determined if body mass index, and duration of labor, or time from rupture of amniotic sac to delivery, or oxytocin dose, would affect maternal temperature. To evaluate the possible role of epidural analgesia, we compared the temperature slope before and after starting epidural analgesia.

**Results:** We observed an overall significant linear trend of temperature over time with an estimated temperature slope of  $+0.017^{\circ}\text{C}/\text{h}$  ( $P = 0.0093$ ). Patients with a positive temperature trend had also a significantly longer time from rupture of membranes to delivery ( $P = 0.0077$ ) and a higher body mass index ( $P = 0.0067$ ). Epidural analgesia had no effect on the temperature trend.

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### What We Already Know about This Topic

- Maternal temperature increases in some women during labor in the absence of evidence for infection and has been speculated to result in unnecessary fetal evaluation for sepsis.
- Whether epidural analgesia increases the risk of fever during pregnancy is unclear.

### What This Article Tells Us That Is New

- Maternal temperatures were recorded in 81 women with induced labor. Slightly more than half of the women showed a small positive temperature trend.
- Increasing body weight and the duration of rupture of membranes were associated with increasing temperature, but epidural analgesia had no effect on maternal temperature.

**Conclusions:** In our cohort of patients, there was an overall significant linear trend of temperature over time after correcting for heterogeneity among patients. Temperature increase was associated with higher body mass index values and longer time from rupture of membranes to delivery. Epidural analgesia had no effect on maternal temperature.

ALTHOUGH maternal infections are recognized as the foremost cause for fever during childbirth, other causes have been investigated. In more recent years, an association of temperature increase during childbirth and epidural analgesia has been described.<sup>1-3</sup> More importantly, it has also been postulated that maternal intrapartum fever may be associated with poor neonatal outcome.<sup>4-7</sup> Whereas some investigators implied that epidural analgesia might be the cause for maternal fever,<sup>8-10</sup> others asserted that the observed associations are noncausal, noting that women who request epidural analgesia tend to have longer labors, and thus a higher chance of developing chorioamnionitis.<sup>8,11</sup> The discussion about the potential role of epidural analgesia in maternal fever has stimulated a broader conversation about whether maternal temperature elevation during labor is a real phenomenon and whether it could have a noninfectious etiology.<sup>12</sup>

In general, fever occurs when the hypothalamic thermoregulatory center is reset at a higher temperature by “endog-

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enous pyrogens” produced by specific host cells in response to infection, inflammation, injury, or an antigenic challenge.<sup>13–15</sup> Some noninfectious reasons for maternal fever are anticholinergic drugs such as atropine, which raise core temperature by inhibiting sweating or vasodilatation without changing the normal hypothalamic set point. Other noninfectious causes may include endogenous heat production generated by the contracting uterus and maternal expulsive efforts with delivery in an overheated room. Theories to explain the association of maternal intrapartum fever and epidural analgesia are based on the concept that epidural analgesia may suppress heat-dissipating mechanisms such as pain-associated hyperventilation, or that epidural analgesia may facilitate a placental inflammatory process that in turn triggers maternal intrapartum fever.<sup>10,13,16–20</sup>

These theories on the causation of maternal intrapartum fever by epidural analgesia are not very convincing. From a physiologic perspective, the sympathetic blockade caused by epidural analgesia should result in hypothermia from the redistribution of heat from the core to the periphery, and thus a net heat loss to the environment.<sup>21</sup> Most of the existing publications focus on large temperature changes and compare the relative proportion of febrile patients based on type of labor analgesia rather than evaluating small changes in temperature. We designed our study to evaluate subtle changes in maternal temperature and to determine the possible effect of several intrapartum factors, including epidural analgesia, on maternal temperature. Because oxytocin induces uterine contractions and associated endogenous heat production, we studied patients scheduled for labor induction.

Our primary research aim was to study the time-course of maternal temperature individually and as a group. Our secondary research aims were to investigate whether duration of labor, epidural analgesia, oxytocin dose, or length of time from rupture of membranes to delivery would be associated with a maternal temperature increase.

## Materials and Methods

### Design

The Institutional Review Board of the University of Alabama at Birmingham (Birmingham, Alabama) approved this study. After obtaining written informed consent, 90 women were recruited at University of Alabama at Birmingham’s Women and Infants Center from November 2008 to September 2010 scheduled for induction of labor. Upon admission to the labor and delivery unit, patients were screened to determine study eligibility. We excluded patients with medical conditions that would affect temperature regulation or the normal course of labor, particularly chorioamnionitis. Patients who received medications known to affect body temperature (acetaminophen, prostaglandin, or ibuprofen), and patients with active cardiac, pulmonary, or neurologic disease were also ineligible. The diagnosis of chorioamnionitis was based on a combination of fever (temperature more than 38.0°C) or a combination of at least two of the following findings: significant maternal tachycardia (more than 120 beats per minute [bpm]), fetal tachycardia (more than

160 bpm), purulent or foul-smelling amniotic fluid or vaginal discharge, uterine tenderness, or maternal leukocytosis (total blood leukocyte count more than 18,000 cells/ $\mu$ l). Obstetrical indications for labor inductions included multiparity and a gestational age of at least 39 weeks, postterm for women with gestational age of more than 40 weeks, and fetal conditions such as suspected fetal growth retardation.

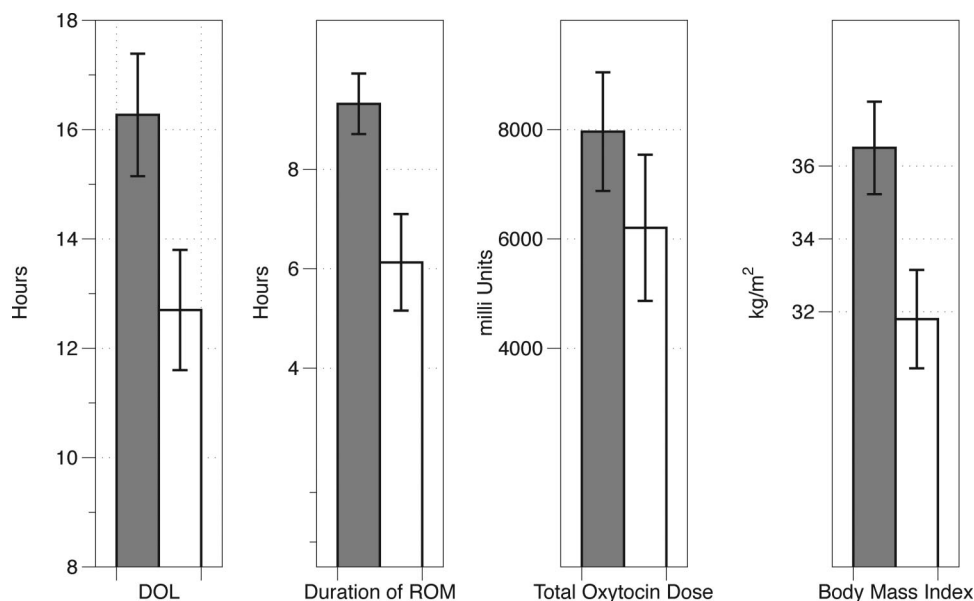
Once enrolled, we recorded a set of baseline study parameters about the patient. This consisted of date and time of admission to the labor and delivery unit, date of birth, admissions weight, height, ethnicity (white, African-American, Hispanic, Asian-American, or other), parity (number of full-term deliveries, preterm deliveries, abortions, and living children), group B streptococcal (GBS) status (positive, negative, or unknown), and leukocyte count on admission. After delivery, the following supplemental information was documented: time and date of initiation of epidural analgesia, rupture of membranes (ROM) and delivery, diagnosis of chorioamnionitis (yes/no), acetaminophen administration intrapartum (yes/no), and prostaglandin administration (yes/no). Epidural analgesia, consisting of bupivacaine 0.1% with 2  $\mu$ g/ml fentanyl, was delivered as patient-controlled analgesia using a basal rate of 8 ml/h and a demand bolus of 4 ml every 20 min. During the course of labor, nurses recorded the following information each hour: cervical dilation of the last vaginal examination, contraction intensity, oxytocin dose, and maternal temperature.

Participating delivery nurses were educated on the purpose of the study and the particular requirements and received the same information as checklist as part of the study data entry forms used. We particularly emphasized the importance of obtaining accurate hourly temperature readings. Labor and delivery nursing protocols at the University of Alabama at Birmingham specify that body temperatures should not be obtained immediately after the patient had received ice chips. Oral temperature, given the latter restriction, most accurately reflects core body temperature when compared with skin, tympanic, or axillary temperature.<sup>22</sup> After ROM, an intrauterine pressure catheter was inserted to measure labor intensity in Montevideo units. These units were calculated as uterine pressure above baseline tone multiplied by the number of contractions in a 10-min period. Oxytocin dose was then adjusted by the nurse, according to protocol, to induce and maintain adequate labor, defined as at least 200 Montevideo units using the peak contraction pressure values obtained from the intrauterine pressure catheter.

### Statistical Analysis

**Analysis 1: Does Temperature Change Over Time?** We used a mixed linear model with a random intercept and slope. This model is ideally suited for this type of repeated measures data because it estimates a common intercept and slope and also accounts for individual baseline temperatures and individual temperature slopes. The statistical model can be expressed as

$$Y_{ij} = \beta_0 + \beta_1 t_{ij} + b_{0i} + b_{1i} t_{ij} + \varepsilon_{ij}, \quad (1)$$



**Fig. 1.** Differences between patients with positive and negative slope. Patients with a positive temperature slope (gray bars) differed from patients with a negative temperature slope (white bars) with respect to the duration of labor, the time from rupture of membranes to delivery (duration of ROM), total oxytocin dose, and body mass index. Error bars represent the SEM. DOL = duration of labor; ROM = rupture of membranes.

where the Greek letters  $\beta_0$  and  $\beta_1$  denote estimates for the common intercept and slope and the Latin letters  $b_{0i}$  and  $b_{1i}$  denote estimates for the  $i^{\text{th}}$  subject intercepts and slope.

We also tested higher-order polynomial models for temperature.

**Analysis 2: Do Covariates Have an Effect on Temperature Trend?** We tested the effects of covariates on temperature with a regression analysis where individual temperature slopes from Analysis 1 were used as outcome variables and duration of labor, total oxytocin dose, time from ROM to delivery, and body mass index (BMI), and the interaction of duration of labor and BMI as explanatory variables. To illustrate the effect of individual covariates, we also arranged participants into patients with a positive temperature slope more than 0 ( $N = 44$ ) and patients with a negative temperature slope less than 0 ( $N = 37$ ) and compared groups with a Student  $t$  test (fig. 1).

**Analysis 3: Effect of Epidural Analgesia on Temperature Slope?** To test whether epidural analgesia had an effect on temperature, we calculated temperature slopes before and after initiation of epidural analgesia and then tested whether the change of slope was different from zero. We used a paired Student  $t$  test assuming unequal variances for this analysis. We required that each subject used for this analysis be observed for at least 4 h prior and after the initiation of epidural analgesia. The resulting sample size for this paired Student  $t$  test was  $n = 39$ .

### Statistical Power

We calculated a minimum sample size of  $n = 23$  to detect a slope change of  $0.025^\circ\text{C}/\text{h}$  assuming a SD of temperature slopes of  $0.035^\circ\text{C}/\text{h}$ , an  $\alpha$  level of 0.05, and 90% power. We

expected that we could only use a proportion of the total sample for the comparison of slopes before and after initiation of epidural analgesia (Analysis 3) because many patients might not have enough data points to obtain stable estimates for the comparison of slopes before and after initiation of epidural analgesia (Analysis 3). Therefore, we estimated that we would need 3 or 4 times the sample size required for Analysis 1 to carry out all analyses with adequate power.

We used the statistical software SAS (SAS Institute, Cary, NC) version 9.2 (modules PROC MIXED, PROC TTEST, and PROC UNIVARIATE) for our statistical analysis.

## Results

### Subject Characteristics

Out of 90 patients enrolled in the study, four were excluded because they received acetaminophen for intrapartum pain, whereas one patient was excluded based on the clinical diagnosis of chorioamnionitis. From the 85 eligible participants, we excluded another four from analysis who were not observed for at least 4 h. Their inclusion does eliminate patients with faster labor but would possibly result in unreliable estimates of temperature slopes. Therefore, 81 patients were included in Analyses 1 and 2. Summary data on the patient baseline characteristics leukocyte count, parity, and cervical dilation are provided in table 1.

Summary statistics of the 81 patients included in the analysis are provided in table 2. The average duration of labor was 11 h and 41 min. Our patient population included similar proportions of white (48%) and African-American (45%) women with an average BMI of  $34.4 \text{ kg}/\text{m}^2$  and a leukocyte count of  $9.4 \pm 2.7/\text{l}$  on admission.

**Table 1.** Parity, Leukocyte Count, and Cervical Dilation By Slope Categories

Parity	0	1	2	3	4	5	6
Positive Temp. Trend	16	13	5	1	3	0	0
Negative Temp. Trend	18	13	10	3	0	1	2
		Mean		SD			
<b>Leukocyte Count</b>							
Positive Temp. Trend		9.32		2.87			
Negative Temp. Trend		9.48		2.39			
<b>Cervical Dilation</b>							
Positive Temp. Trend		1.85		0.20			
Negative Temp. Trend		2.15		0.21			

Included are patient baseline characteristics not included in the analysis. Patients who had a positive temperature trend did not differ significantly from patients who had a negative temperature trend with respect to race, cervical dilation on admission, and leukocyte count.

**Results for Analysis 1**

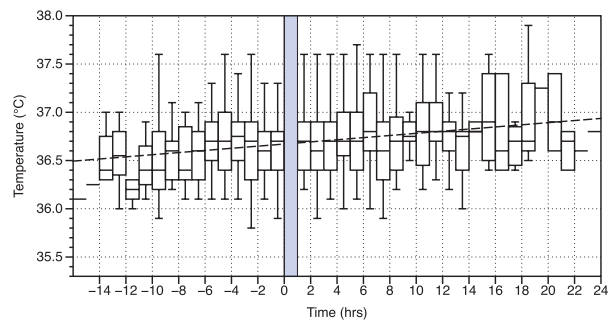
The population slope in the linear mixed model was estimated to be 0.017°C/h with 95% CI = [0.0044, 0.0302], significantly different from zero ( $P = 0.0093$ ), indicating that there was a significant linear trend of temperature. Higher-order polynomial models did not improve the fit.

**Table 2.** Descriptive Statistics of Observed Variables

Variable	Median (Proportion)	Mean	SD (Range)
Labor duration (min)	701	838.8	423.5
Total oxytocin dose (μU)	4,298	6,510	6,659
Length ROM to delivery (min)	387	479	335
Body mass index (kg/m <sup>2</sup> )	—	34.6	9
Admission Cervical Dilation (cm)	—	2	(0–5)
Leukocyte count (WBC)	—	9.4	2.6
Race	—	—	—
African American	(40.0%)	—	—
Asian American	(4.7%)	—	—
Hispanic	(4.7%)	—	—
White	(47.1%)	—	—
Other	(2.4%)	—	—
Parity	—	—	—
0	(40%)	—	—
1	(31%)	—	—
2	(17%)	—	—
3	(5%)	—	—
4	(4%)	—	—
5	(1%)	—	—
6	(2%)	—	—
GBS status	—	—	—
Positive	(21.7%)	—	—
Negative	(55.8%)	—	—
Unknown	(22.6%)	—	—

Continuous variables are described in terms of their mean and standard deviation. Categorical variables are described as median and proportions, where appropriate.

GBS = group B streptococcus; ROM = rupture of membranes.



**Fig. 2.** All temperature data centered around the time of epidural anesthesia initiation (marked by vertical blue line). For each hour the temperature values are summarized as boxplots. There are fewer observation points toward both ends of the graph because fewer patients with longer times to epidural anesthesia and from epidural anesthesia to delivery were observed. The horizontal line shows the median temperature for each hour across all participants. The bottom and top of the box show the 25th and 75th percentiles, respectively. The dotted line represents the linear temperature trend.

The root mean square error remained at 0.433. The overall temperature course over time is illustrated in figure 2;  $N = 37$  participants had a slope less than 0 and  $n = 44$  participants had a slope more than 0.

**Results for Analysis 2**

The interaction term of the time of ROM to delivery and BMI was significant ( $P = 0.0475$ ). Therefore, as weight increased the effect of the duration of ROM on maternal temperature (positive temperature slope) was more pronounced. The results of our supplemental analysis of covariates by slope category are depicted in figure 1. As we observed in our regression model, in this categorical analysis, patients with a positive temperature trend had a significantly longer time from rupture of membranes to delivery ( $P = 0.0077$ ) and a higher body mass index ( $P = 0.0067$ ). To adjust for multiple comparisons in the latter analysis, a  $P$  value of  $0.05/4 = 0.0125$  was considered statistically significant (Bonferroni correction).

**Results for Analysis 3**

All but three patients included in the study received epidural analgesia. The median duration and interquartile range of epidural analgesia was 7.9 (4.3, 12.1) hrs. To study whether epidural analgesia had an effect on temperature, we compared temperature slopes before initiating epidural analgesia (admission to epidural) with temperature slopes after initiating epidural analgesia (epidural to delivery). The parameter estimate and 95% CI for the mean difference of the slope before versus after initiation of epidural analgesia was  $-0.0068, 0.00338$ . This indicates that in our study group epidural analgesia had no effect on the temperatures slope.

**Discussion**

Several investigators have reported maternal temperature elevations in women whom received epidural analge-



sia.<sup>9,10,13,14,17–19,22–26</sup> This observation received widespread attention by anesthesiologists, obstetricians, and the media when Liebermann *et al.* suggested that neonatal sepsis evaluations were attributable to the use of epidural analgesia.<sup>10</sup> The study on which this opinion was based, as well as other retrospective studies, have several important limitations<sup>9,17,19,22</sup>, because the investigators had no control of the quality of temperature recordings and frequency at which these measures were obtained and investigators could not reliably rule out that some patients may have received medications that either increase temperature such as prostaglandins or lower an increased temperature (antipyretics).

There are few prospective randomized controlled trials that also describe an association of maternal temperature increases and epidural analgesia in the context of placental inflammation,<sup>13–15</sup> neonatal sepsis work-up,<sup>18</sup> pregnancy-induced hypertension,<sup>23</sup> or labor progress and mode of delivery.<sup>24,25,27</sup> Philip *et al.*<sup>28</sup> investigated the incidence of maternal fever, defined as temperature more than 38.0°C, as primary outcome. They also found a higher proportion of patients with longer labor in the epidural group. Because we were interested in the noninfectious etiology of maternal intrapartum fever, we purposefully excluded patients with maternal fever at the beginning of our study and excluded women with clinical evidence for infection. We evaluated the temperature trend of all patients, regardless of whether they met a pre-defined temperature cutoff or not.

It is not surprising that the average temperature trend is very small, a temperature increase of approximately 0.2 of a degree over 10 h of labor. It is well established that mild fluctuations in temperature (0.25°C) are observed as physiologic variations of the female menstrual cycle and studies in animals have shown that estrogen and progesterone can act directly on specific sex steroid-binding neurons in the preoptic/anterior hypothalamus.<sup>29,30</sup> However, because the mechanisms of temperature variation during labor are different than those associated with diurnal or menstrual changes, even a subtle change that would otherwise be considered inconsequential may be important because it may be indicative of an inflammatory process that is potentially harmful to the neonate. Segal<sup>12</sup> pointed out that the observed maternal temperature change, summarized across treatment groups in the randomized clinical trials, could be an “averaging artifact,” a suspicion that we can confirm. Using the mixed model analysis, we learned that only 54% of individuals had a temperature slope greater than or equal to zero and the remaining 46% had a temperature slope less than zero.

A very important question from the anesthesiologist’s perspective is whether epidural analgesia is indeed associated with maternal temperature changes during labor as suggested by some authors.<sup>16,31</sup> Most researchers would argue that the best way to address this question is to randomly assign patients to

either receive intravenous or epidural analgesia. However, withholding epidural analgesia would probably be considered unethical in current practice. Moreover, even past studies where investigators attempted such a design were flawed with a relatively low recruitment rate and high crossover from intravenous to epidural analgesia. We therefore took a different approach. One of the important early studies on the topic by Camann *et al.*<sup>3</sup> compared patients receiving epidural analgesia with patients who received parenteral opioids for labor pain relief. With this design it is possible that patient groups, apart from the obvious treatment allocation, were dissimilar. For example, the parenteral opioid group might have received acetaminophen. It is also possible that parenteral opioids by themselves may have a mitigating effect on temperature elevation during labor as opposed to epidural analgesia having a thermogenic effect. To avoid this ambiguity, we designed our study such that patients acted as their own control. We used a mixed model to estimate individual temperature slopes (random effects) and then compared individual temperature slopes before and after epidural anesthesia with a paired Student *t* test. With each individual patient serving as her own control, we compared the temperature slope before initiation of epidural analgesia with the slope after starting epidural analgesia. Using a paired Student *t* test, we found no difference. This observation indicates that epidural analgesia had no discernable impact on maternal temperature.

Noteworthy is also the absence of a temperature drop following the first 4 h after initiation of epidural anesthesia because of blood flow redistribution as described by Holdcroft *et al.*<sup>21</sup> Given the low local anesthetic concentration of 0.1% used in our study when compared with 0.5% for surgical anesthesia in Holdcroft’s study, the absence of a temperature reduction is not surprising. One might expect that more advanced labor might produce a greater amount of metabolic heat and thus a greater degree of temperature elevation. The absence of such an effect is best explained by our practice of maintaining labor at an adequate pattern with oxytocin based on calculated Montevideo units (uterine activity).

A variety of potential theories on noninfectious factors affecting maternal temperature have been proposed. Fusi *et al.*<sup>2</sup> proposed the theory of high ambient temperatures in the delivery room. An alternative theory is based on an imbalance of metabolic heat production and heat-dissipation during labor. Compensatory mechanisms such as sweating and pain-related hyperventilation may be attenuated by epidural analgesia.<sup>32–34</sup> Others argue that intravenous  $\mu$ -receptor agonist narcotics such as fentanyl may have a modest effect in preventing maternal temperature elevations.<sup>35,36</sup> Probably the best-supported and most plausible theory is based on the systemic effect of thermogenic inflammatory mediators, such as interleukin-6, released from the placental-myometrial interface into the maternal circulation.<sup>13,16,20,37</sup> In our study, we recorded oxytocin dose and contraction strength to evaluate the possible fever-producing

effect of the contracting uterus, the duration of labor, time from ROM to delivery, and BMI information possibly related to inflammatory processes.

Among those variables, the time from rupture of membrane (ROM) to delivery and BMI showed a significant positive association with temperature, and duration of labor and total oxytocin dose showed a notable positive trend. Long labor, prolonged uterine activity, or a long time from ROM to delivery may sustain an inflammatory process that may result in the temperature elevation in those patients. The same mechanism may be responsible for the observed association of obesity and a positive temperature slope since the link of obesity to inflammation has been well established.<sup>38</sup>

Summarizing the key findings of our study, we conclude that induced labor is associated with a small temperature increase. We found an overall significant linear trend of temperature over time after correcting for heterogeneity among patients. Patients with higher BMI and longer duration from ROM to delivery are more likely to increase their body temperature during labor. In our study of women scheduled for induction of labor, epidural analgesia had no effect on maternal temperature.

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## ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

### Albert Schweitzer's Favorite Anesthetist, His Wife Helene



Helene  
Schweitzer  
(1879 - 1957)

During the early years in Lambaréné, Gabon, medical missionary Albert Schweitzer (1875–1965) conducted surgery as his wife Helene (1879–1957) administered anesthetics. Of the agents available there in the African jungle, Helene's favorites for clinical use were chloroform and papaveretum. The latter was a mixture of noscapine with the hydrochlorides of morphine, papaverine, and codeine. Her health compromised by protracted jungle exposures and by her imprisonment during World War I, Helene Schweitzer died 5 years after Albert received his 1952 Nobel Peace Prize. (Copyright © the American Society of Anesthesiologists, Inc.)

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