

Fetal Heart Rate after Epidural Lidocaine and Bupivacaine for Elective Cesarean Section

John R. Loftus, M.D.,* R. Hal Holbrook, M.D.,† Sheila E. Cohen, M.B.Ch.B., F.F.A.R.C.S‡

This prospective double-blind study was designed to determine whether the fetal heart rate (FHR) changes that have been reported after epidural administration of bupivacaine and lidocaine during labor are present when larger doses of these drugs are given during elective cesarean section. Prior to inserting an epidural catheter, FHR and maternal vital signs were monitored during a control period in 60 healthy term parturients. Patients were randomly assigned to receive either 0.5% bupivacaine with 0.1 mEq sodium bicarbonate added to each 20 ml (n = 30) or 2% lidocaine with 1:300,000 epinephrine (n = 30). A 3-ml test dose of the study solution was injected *via* the catheter and was followed by an additional 17 ml, in increments; additional doses were administered as necessary to obtain surgical anesthesia. FHR and maternal vital signs were monitored for at least 20 min and the characteristics of the anesthetic block noted. At delivery, neonatal status was evaluated, and maternal and cord blood samples were obtained for local anesthetic assays and neonatal blood gases. The groups were similar with respect to maternal characteristics, onset of surgical anesthesia, time to delivery, and uterine incision-delivery interval. Maternal blood pressure decreased from control values in both groups ($P < 0.05$), but there was no difference between the groups in either the incidence of hypotension or ephedrine requirements. Analysis of FHR tracings by a perinatologist blinded to the study group revealed no changes after anesthesia and no significant differences between the groups at any time in basal FHR, short- or long-term variability, or the incidence of accelerations or decelerations. More infants in the lidocaine group had Apgar scores < 7 at 1 min ($P < 0.05$), but at 5 min all neonates had scores > 7 . Cord blood gases were similar in both groups. Local anesthetic umbilical vein/maternal vein ratios were 0.29 ± 0.04 and 0.48 ± 0.03 for bupivacaine and lidocaine, respectively. Our results suggest that epidural anesthesia performed for cesarean section in the nonlaboring patient does not appreciably affect the heart rate pattern of the healthy fetus. It is possible that the fetus may be minimally affected by epidurally administered local anesthetics during both labor and cesarean delivery yet manifest FHR changes only when factors associated with labor unmask or potentiate such an effect. (Key words: Anesthesia: obstetric. Anesthetic techniques: epidural. Anesthetics, local: lidocaine; bupivacaine. Monitoring: fetal heart rate.)

EPIDURAL LIDOCAINE and bupivacaine are used routinely to provide analgesia during labor and cesarean delivery.¹⁻⁵ However, in addition to their analgesic properties, local anesthetics alter myocardial electrophysiology

and contractility.⁶⁻¹² Reports of bupivacaine cardiotoxicity have focused attention on the cardiovascular effects of local anesthetic agents in the parturient. Whether these also have implications for the fetus is unknown. Electronic fetal heart rate (FHR) monitoring is commonly used to evaluate fetal condition before delivery. Previous studies of epidural analgesia during labor have demonstrated changes in FHR variability after lidocaine^{13,14} and bupivacaine¹⁵ and an increased incidence of decelerations after bupivacaine.¹⁵⁻¹⁷ Even more significant changes might be anticipated during cesarean section, when much larger doses of local anesthetic are administered and hemodynamic changes are greater. Reports of FHR during cesarean delivery performed with general and regional anesthesia have concentrated on the relationship of deceleration patterns to specific surgical events, such as sterile skin preparation, skin incision, uterine incision, and delivery of the fetal head.¹⁸⁻²⁰ In the studies in which epidural anesthesia was used, most patients were in labor, and little information is provided about the anesthetic or the condition of the neonate.^{18,20} The goal of the current study was to compare the effects on FHR patterns of bupivacaine and lidocaine administered epidurally for elective cesarean section.

Materials and Methods

After the Human Subjects Committee had approved the study protocol, written informed consent was obtained from 60 healthy, term parturients scheduled for elective cesarean section. All subjects had previously selected epidural anesthesia for their delivery; none had ruptured membranes or were in labor. Prior to epidural catheter placement an initial FHR tracing was obtained for a minimum of 20 min using a Hewlett Packard 8040A external monitor. During this period maternal blood pressure and heart rate were monitored at 5-min intervals, and 1500-2000 ml Lactated Ringer's solution was infused intravenously.

Patients were randomly assigned to receive either 0.5% bupivacaine with 0.1 ml 8.4% sodium bicarbonate added to 20 ml local anesthetic solution (bupivacaine group; n = 30) or 2% lidocaine with 1:300,000 epinephrine (lidocaine group; n = 30). The study solutions were freshly prepared by an anesthesiologist not involved in data collection. Epidural catheters were inserted using a standardized technique *via* either the L2-L3 or L3-L4 interspace. A 3-ml test dose of the study drug was followed

* Fellow in Obstetric Anesthesia.

† Assistant Professor of Obstetrics and Gynecology.

‡ Professor of Anesthesia.

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Address reprint requests to Dr. Cohen: Department of Anesthesia, Stanford University School of Medicine, Stanford, California 94305.

by an additional 17 ml injected in increments over 3–5 min. Patients were carefully questioned regarding symptoms of possible intravascular or intrathecal injection. FHR monitoring was resumed immediately after completion of the injection and was continued for a minimum of 20 min or until adequate surgical anesthesia was obtained. Patients were positioned to avoid aortocaval compression throughout the study. Supplemental oxygen was administered by a nonbreathing mask until delivery.

Data were obtained by an investigator blinded to the treatment. Sensory blockade to pinprick was assessed bilaterally using a 25-G needle at 2-min intervals for 10 min and then at 5-min intervals until surgical anesthesia (a T4–S5 block) was established. Maternal heart rate and blood pressure were monitored using an automated, non-invasive monitor at 1- to 2-min intervals and recorded for study purposes every 5 min. Hypotension, defined as a systolic blood pressure less than 100 mmHg or a decrease of 20% below baseline, was treated by rapid infusion of lactated Ringer's solution and intravenous ephedrine. Additional doses of the study solution were administered as needed to obtain adequate surgical anesthesia.

At the time of delivery, umbilical arterial and venous blood was obtained from a doubly clamped segment of umbilical cord for blood gas analyses and determination of local anesthetic concentrations. Maternal blood also was obtained from an antecubital vein for the latter purpose. Blood was centrifuged and the plasma frozen for subsequent local anesthetic assay with gas chromatography; the lowest detection limit was 10 ng/ml for both drugs.²¹ Apgar scores at 1 and 5 min were assigned by a pediatrician blinded to the treatment.

After completion of the study all FHR tracings were analyzed by a perinatologist unaware of the patient's clinical course or the identity of the study drug. Variability was assessed using a modification of the template method described by Hon.²² Short-term variability (STV) was ranked on a scale of 0–4 based on the beat-to-beat change in FHR (0 = absent, 1 = minimal, 2 = average, 3 = moderate, and 4 = marked variability). Each long-term variability (LTV) event was defined as a change in FHR for three or more consecutive beats in the same direction, followed by a matching change in the opposite direction.

TABLE 1. Ranking of Long-term Variability

Score	Changes in FHR for ≥3 Consecutive Beats per 20 min
4	≥5
3	4–5
2	3
1	1–2
0	0

TABLE 2. Maternal Characteristics

	Bupivacaine (n = 30)	Lidocaine (n = 30)
Age (yr)	31 ± 0.8	31 ± 0.7
Height (cm)	163 ± 1.4	164 ± 1.4
Weight (kg)	75 ± 2.3	80 ± 2.5
Preepidural anesthesia iv fluid (ml)	1,710 ± 49	1,628 ± 48
Parity		
Nulliparous	5	7
Parous	25	23

No significant differences.

The number of these events in 20 min was counted and used to determine the score for LTV (table 1). For each tracing, variability rankings were assigned for the periods preceding (control) and after drug administration. In addition, both STV and LTV were classified in each post-epidural tracing as either "increased" or "decreased" compared with control. Mean basal FHR was determined for the pre- and postepidural monitoring period, and the number of accelerations and decelerations occurring during each period was noted. Accelerations were defined as a maximum increase in FHR of 15 beats per min above baseline, sustained for 15 s or longer. Mild decelerations were defined as a decrease in FHR of 15% from baseline for 15 s or longer or a decrease to ≤90 beats per min lasting 15–60 s. Moderate decelerations were defined as a decrease in FHR to between 60 and 90 beats per min lasting more than 60 s. Severe decelerations were defined as a decrease to ≤60 beats per min lasting 1 min or longer.

Comparisons of FHR patterns between groups and before and after epidural anesthesia were made using unpaired and paired Student's *t* tests, the Mann-Whitney U test, chi-squared analysis, and Wilcoxon's signed-rank tests as appropriate. One- or two-factor repeated-measures analysis of variance was used to compare blood pressure and pulse changes during the study, with Fisher's progressive least squares difference test used to investigate differences further. Pearson's coefficient was used to evaluate correlation between variables. Data are expressed as the mean ± standard error of the mean. *P* < 0.05 was considered statistically significant.

Results

The groups were similar with respect to maternal age, height, weight, parity, and the volume of intravenous fluid administered prior to the block (table 2). There were no differences between the groups with respect to FHR patterns at any time during the study (tables 3 and 4). Baseline FHR was normal (usual range 110–160 beats per min) before and after local anesthetic administration, and there

TABLE 3. Fetal Heart Rate Data

FHR	Bupivacaine (n = 30)		Lidocaine (n = 30)	
	Preepidural	Postepidural	Preepidural	Postepidural
Baseline (beats per min)	139 ± 2	140 ± 2	138 ± 2	138 ± 1
Accelerations (number per 20 min)				
0-4	15	16	21	17
5-10	14	12	8	10
≥10	1	2	1	3
Decelerations (number per 20 min)				
0	28	28	25	28
1-2	2	2	5	2

For accelerations and decelerations, values in table represent numbers of patients.

FHR = fetal heart rate.
No significant differences.

was no change in the incidence of accelerations or decelerations in either group (table 3). Although occasional decelerations occurred during the study, all were classified as mild. The distribution of rankings for STV and LTV were unchanged after anesthesia, again with no differences between the groups (table 4). For simplicity, rankings in table 4 are grouped together as "average or greater" (2-4) and "absent or minimal" (0-1), these categories representing healthy and possibly stressed patterns, respectively. STV was average or above average in the majority of tracings; no fetus demonstrated absent STV. Similar numbers of tracings in both groups were classified as having increased or decreased variability after the epidural block. LTV remained unchanged throughout the study (table 4).

The characteristics of sensory blockade were similar after both local anesthetics (table 5). Mean arterial pressure decreased significantly from baseline values in both groups 10, 15, 20, 25, and 30 min after initiation of anesthesia ($P < 0.05$ vs. control; fig. 1A). However, the incidence and severity of hypotension and ephedrine requirements were similar in both groups (table 5). All episodes of hypotension lasted less than 2 min. Maternal heart rate remained unchanged in the bupivacaine group

but increased significantly in the lidocaine group at 5, 10, 15, and 20 min ($P < 0.05$ vs. control; fig. 1B).

Delivery and newborn characteristics are shown in table 6. The groups did not differ with respect to the time from uterine incision to delivery, gestational age, and infant length, weight, and sex. Four newborns in the lidocaine group, in contrast to none in the bupivacaine group, had 1-min Apgar scores of 6 or less ($P = 0.04$). We were unable to detect any significant correlation between low 1-min Apgar scores and time from uterine incision to delivery, incidence of hypotension, infant weight, incidence of decelerations before or after epidural anesthesia, and maternal or fetal drug concentrations. All newborns had Apgar scores greater than 7 at 5 min. Umbilical cord blood gases were satisfactory and similar in both groups (table 7). Maternal venous, umbilical venous, and umbilical arterial plasma local anesthetic concentrations are shown in table 8.

Discussion

Electronic monitoring of the FHR is widely used to evaluate fetal condition. Accelerations and the presence of STV (beat-to-beat variability) and LTV in FHR are regarded as reassuring, since they imply normal cerebral oxygen uptake and physiologic integrity of the entire

TABLE 4. Short- and Long-term Variability in Fetal Heart Rate

	Bupivacaine (n = 30)		Lidocaine (n = 30)	
	Preepidural	Postepidural	Preepidural	Postepidural
STV rank				
0-1	0	2	6	4
2-4	30	28	24	26
LTV rank				
0-1	1	2	3	4
2-4	29	28	27	26

Values represent number of tracings.
STV = short-term variability; LTV = long-term variability.
No significant differences.

TABLE 5. Epidural Anesthetic Data

	Bupivacaine (n = 30)	Lidocaine (n = 30)
Total dose (ml)	24 ± 0.8	24 ± 0.7
Time from injection to T4-S5 sensory block (min)	20 ± 1.7	19 ± 1.1
Time from injection to delivery (min)	38 ± 2.3	38 ± 2.2
Hypotension (number of patients)	7	8
Ephedrine administration (number of patients)	5	8
Ephedrine dose (mg)	11 ± 2.4	10 ± 2.2

No significant differences.

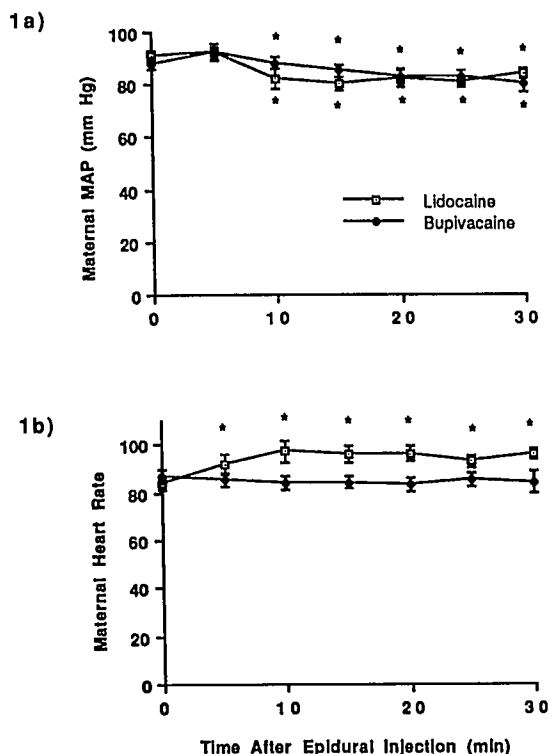


FIG. 1. Changes in maternal mean arterial pressure (A) and pulse rate (B) after epidural anesthesia with bupivacaine or lidocaine with epinephrine. Values are means \pm SEM. * $P < 0.05$ versus control values.

pathway involving the fetal cerebral cortex, the cardiac integratory center in the medulla oblongata, the vagus nerve, and the cardiac conduction system.²³ Decreases in fetal cerebral or myocardial oxygenation thus may result in absence of normal FHR variability. Decelerations of the FHR from baseline usually are of concern and may indicate umbilical cord compression, decreased uteroplacental gas exchange, myocardial ischemia, or abnormalities in cardiac conduction.

Epidural administration of local anesthetics, with or without epinephrine, potentially can affect FHR by a number of mechanisms, including direct drug effect on the fetal myocardium or central nervous system, maternal hypotension, constriction of uterine or umbilical vessels, and increases in uterine tone.²⁴ Local anesthetics exert significant cardiovascular effects; bupivacaine is of particular concern in this respect. For example, in an animal model, bupivacaine in the toxic dose range was 16 times more potent than lidocaine in inducing cardiac arrhythmias and caused altered conduction for a significantly longer period of time.¹⁰ The fetus and neonate may be even more susceptible to these effects than is the adult. In studies in guinea pigs, Bosnjak *et al.*²⁵ found that the sinoatrial node of neonates was more sensitive than that of the adult to the depressant effects of bupivacaine and

lidocaine; bupivacaine was 4–5 times more potent in this respect.

Local anesthetics also are myocardial depressants; bupivacaine, again, exhibits more pronounced depression than does lidocaine.¹² Such data suggest that fetal cardiac conduction or contractility might be affected by bupivacaine in the dose range associated with epidural anesthesia. In support of this, Fleming *et al.*²⁶ demonstrated small but significant decreases in heart rate in fetal lambs exposed to bupivacaine concentrations comparable to those accompanying routine epidural anesthesia. It was unclear whether these changes were due to a direct effect of bupivacaine on the myocardium, a central neurologic effect, or the minimal increase in umbilical artery resistance observed during the study. Amide local anesthetics also are known to cause uterine artery constriction and uterine hypertonus, although only in concentrations markedly higher than those associated with uncomplicated epidural anesthesia.²⁷ In a recent retrospective study of laboring patients, Steiger and Nageotte²⁸ found an association between prolonged FHR decelerations and uterine hypertonia in patients who had received bupivacaine epidural anesthesia. Although it was suggested that increased uterine activity was related to the epidural block, a causal relationship could not be ascertained.

In view of the above, it is perhaps surprising that in the current study FHR remained unchanged after significant doses of either lidocaine or bupivacaine. In previous studies in which epidural bupivacaine was administered for cesarean section, Taylor²⁰ similarly found no FHR abnormalities, whereas Petrikovsky *et al.*¹⁸ reported moderate or severe decelerations coincident with vigorous manipulation of the uterus during abdominal preparation in 15% of patients. However, these studies included only small numbers of patients, and the reports provide only minimal information regarding epidural anesthesia or resultant hemodynamic changes; local anesthetic concentrations were not measured. In both studies internal FHR monitoring was continued during surgery, and deceler-

TABLE 6. Delivery and Newborn Characteristics

	Bupivacaine (n = 30)	Lidocaine (n = 30)
Uterine incision–delivery time (s)	87 \pm 8.4	91 \pm 7.3
Gestational age (weeks)	39 \pm 0.2	39 \pm 0.2
Length (cm)	51 \pm 0.6	50 \pm 1.3
Weight (g)	3,627 \pm 104	3,746 \pm 91
Sex		
Male (number of infants)	20	17
Female (number of infants)	10	13
Apgar <7 at 1 min	0	4*
Apgar <7 at 5 min	0	0

* $P = 0.04$.

TABLE 7. Umbilical Cord Blood Gases

	pH	P _{CO₂}	P _{O₂}	HCO ₃
Umbilical artery				
Bupivacaine (n = 28)	7.30 ± 0.01	57.7 ± 0.9	15.0 ± 0.9	27.5 ± 0.5
Lidocaine (n = 29)	7.29 ± 0.01	58.4 ± 1.4	16.3 ± 0.7	27.7 ± 0.3
Umbilical vein				
Bupivacaine (n = 28)	7.37 ± 0.01	44.4 ± 0.8	28.5 ± 1.0	25.5 ± 0.4
Lidocaine (n = 29)	7.36 ± 0.01	44.3 ± 1.1	29.7 ± 1.2	24.6 ± 0.3

No significant differences.

ations were reported in association with myometrial incision and delivery of the fetal head.

Our results contrast markedly with those of previous studies in which epidural anesthesia was used to provide labor analgesia.¹³⁻¹⁷ Hehre and associates¹⁴ noted transient decreases in FHR variability beginning 6 min after a 7-ml dose of 2% lidocaine with 1:200,000 epinephrine and lasting 4 min. Similarly, in 64% of cases, Boehm *et al.*¹³ observed diminished FHR variability occurring within 5 min of injection of 1-2% lidocaine with epinephrine (mean dose 142 mg) and persisting for 9 min; changes were less frequent with plain lidocaine. Increased variability was observed by Lavin *et al.*¹⁵ shortly after epidural injection of bupivacaine during labor. In two studies, Abboud *et al.*^{16,17} compared bupivacaine, lidocaine, and chloroprocaine for labor analgesia and reported normal FHR variability but a high incidence of late or variable decelerations. In one study in which an intermittent dosing regimen was used, decelerations occurred in 24% of cases after 0.5% bupivacaine, in 17% after 1.5% lidocaine, and in 6% after 2% chloroprocaine.¹⁶ In a second study in which continuous infusions (and larger cumulative doses) were used, these incidences were 59, 17, and 10% after the three drugs, respectively.¹⁷ Neonatal status in all of these labor studies was good, as evidenced by high 5-min Apgar scores,¹³⁻¹⁷ normal acid-base status, and normal neurobehavioral examinations.^{16,17} Fetal stress, if any, therefore appears to have been transient and minor in degree.

How can we explain the disparity between the current results and those involving laboring patients? Although the umbilical venous/maternal venous local anesthetic ratios in the current study were similar to those reported

by Abboud *et al.*^{16,17} after labor epidural anesthesia, umbilical vein bupivacaine concentrations were higher in our study. Direct fetal cardiac or central nervous system depression by the local anesthetic thus appears unlikely as the cause of the abnormal FHR patterns observed during labor. However, this etiology cannot be excluded completely, since the timing of delivery relative to drug administration is considerably longer during labor compared to cesarean section, allowing greater placental transfer and fetal drug exposure. Moreover, tissue concentrations, particularly of a highly lipid-soluble agent such as bupivacaine, may be considerably higher than plasma concentrations.

Differences in the onset and extent of anesthetic blockade and consequent hemodynamic changes also may affect the incidence of FHR changes. We attempted to produce similar onset of block and thus similar hemodynamic profiles with the agents by adding sodium bicarbonate to bupivacaine to shorten its latency period.²⁹ Although we succeeded in this respect, hypotension occurred in 23 and 27% of patients with bupivacaine and lidocaine, respectively. Since this incidence is higher than that reported during epidural analgesia performed for labor,^{16,17} a greater rather than a lesser effect on FHR is expected during cesarean section. The absence of FHR changes in our patients confirms that brief periods of hypotension are well tolerated by the healthy fetus and suggests that factors other than hypotension must be considered to explain the abnormalities in laboring patients. Although oxygen was administered to all patients in the current study but seldom is administered to laboring patients, we do not believe that this factor is sufficient to explain the marked differences between our findings and those resulting from studies of patients in labor.

The remaining variable to be considered is the labor process itself. That patients in the current study were not in labor suggests that this may be the most relevant factor in the etiology of the FHR changes after labor epidural anesthesia. Considerable physiologic fluctuations are associated with contractions, perhaps explaining the 6% incidence of FHR decelerations that occur during normal labor without epidural analgesia.³⁰ In a recent study of the effects of epidural fentanyl on FHR variability, Vis-

TABLE 8. Local Anesthetic Concentrations

	Bupivacaine	Lidocaine
MV (µg/ml)	1.04 ± 0.09	2.61 ± 0.09
UV (µg/ml)	0.27 ± 0.06	1.17 ± 0.06
UA (µg/ml)	0.15 ± 0.01	0.79 ± 0.05
UV/MV ratio	0.29 ± 0.04	0.48 ± 0.03

MV = maternal vein; UV = umbilical vein; UA = umbilical artery.

comi *et al.*³¹ noted a progressive decrease in variability and in the frequency of accelerations as labor progressed, independent of opioid administration. They speculated that this decrease was due either to the effect of the epidural lidocaine administered to all patients or "to some other factor associated with labor."³¹ Conceivably, the fetus may be minimally affected by epidurally administered local anesthetics both during cesarean and vaginal delivery yet manifest FHR changes only when subjected to the added stresses of labor. The association between uterine hypertonia and an increased incidence of FHR decelerations²⁸ suggests that increased uterine activity in labor, perhaps potentiated by the local anesthetic, may unmask an effect of epidural anesthesia not apparent during elective cesarean section when uterine contractions are absent.

Although neither local anesthetic adversely affected FHR, more neonates in the lidocaine group had Apgar scores of less than 7 at 1 min. This brief depression, also found by Norton *et al.*¹ after lidocaine with epinephrine, may reflect the transient impairment of neuromotor tone attributed by Scanlon's group to a high concentration of lidocaine in the neonate.³² However, in more recent studies of epidural lidocaine, several groups of investigators^{2,5,16,17} have failed to confirm Scanlon *et al.*'s findings. An alternative explanation is that the addition of epinephrine to lidocaine may adversely affect the fetus by causing placental vasoconstriction. Although the increase in maternal heart rate in the lidocaine group suggests that some systemic absorption of epinephrine occurs, previous studies indicate that low concentrations of epinephrine are not detrimental to the fetus.^{4,33} We elected not to use plain lidocaine since it has been associated with unsatisfactory surgical anesthesia.^{2,4,5}

In conclusion, abnormal FHR patterns were absent after the administration of epidural bupivacaine or lidocaine with epinephrine for elective cesarean section. These agents provided similar anesthesia with respect to onset of sensory blockade and effects on maternal hemodynamics. Although significantly more neonates in the lidocaine group had low 1-min Apgar scores, 5-min scores and cord blood gas analyses did not indicate neonatal depression. We conclude that factors associated with labor must account for the high incidence of FHR changes observed after epidural anesthesia during labor.

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