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# Neonatal procedural pain exposure and pain management in ventilated preterm infants during the first 14 days of life

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## Summary

**Objectives:** Ventilated preterm infants are at high risk for procedural pain exposure. In Switzerland there is a lack of knowledge about the pain management in this highly vulnerable patient population. The aims of this study were to describe the type and frequency of procedures and to determine the amount of analgesia given to this patient group in two Swiss neonatal intensive care units.

**Method:** A retrospective cohort study was performed examining procedural exposure and pain management of a convenience sample of 120 ventilated preterm infants (mean age = 29.7 weeks of gestation) during the first 14 days of life after delivery and born between May 1st 2004 and March 31st 2006.

**Results:** The total number of procedures all the infants underwent was 38,626 indicating a mean of 22.9 general procedures performed per child and day. Overall, 75.6% of these procedures are considered to be painful. The most frequently performed procedure is manipulation on the CPAP prongs. Pain measurements were per-

formed four to seven times per day. In all, 99.2% of the infants received either non-pharmacological and/or pharmacological agents and 70.8% received orally administered glucose as pre-emptive analgesia. Morphine was the most commonly used pharmacological agent.

**Discussion:** The number of procedures ventilated preterm infants are exposed to is disconcerting. Iatrogenic pain is a serious problem, particularly in preterm infants of low gestational age. The fact that nurses assessed pain on average four to seven times daily per infant indicates a commitment to exploring a painful state in a highly vulnerable patient population. In general, pharmacological pain management and the administration of oral glucose as a non-pharmacological pain relieving intervention appear to be adequate, but there may be deficiencies, particularly for extremely low birth weight infants born <28 weeks of gestation.

**Key words:** preterm infants; procedural exposure; pain management; pain assessment

## Introduction

Pain exposure in a neonatal intensive care unit (NICU) is considered a major source of distress for children and their families [1-4]. The most frequently described painful procedures include endotracheal and naso-pharyngeal suctioning [5, 6] and the heel lance [7-9]. The removal of adhesive tape and the application of an intra-

venous cannula are also frequently performed painful procedures [10]. The number of such procedures to which a neonate is exposed varies from 2 to 14 per day [5, 6, 8, 10].

Pain treatment is viewed as inadequate in the context of acute diagnostic and therapeutic procedures in NICUs, in contrast to the postoperative

routine medication with opioids [11]. Recent findings suggest that neonates' exposure to pain tends to be exceedingly high during their hospitalisation, because pain relieving methods are not adequately applied [6, 10, 12-14]. This is particularly true in infants at high risk of neurological impairment [10]. At present, there is a lack of data on how frequently neonate pain is assessed by a pain measurement tool in the daily clinical setting. Specifications on the use of such a tool are usually restricted to studies of interventions and have no applicability to the daily routine. Preterm infants needing mechanical ventilation are subjected to highly sophisticated neonatal intensive care treatment due to their general immaturity, which is connected with a high risk for neurological impairment.

In Switzerland there is a general lack of knowledge about the frequency of procedural ex-

posure and management of pain in ventilated preterm infants. This knowledge could provide evidence for comparison with international studies and could form the basis for improvement of the quality of care of a highly vulnerable population.

Therefore, the aims of the present study were a) to explore both the number of procedures and the extent of pain exposure of ventilated preterm neonates during the first 14 days of life, b) to describe how often neonatal nurses use pain assessment tools in the context of routine clinical care, and c) to explore the type and frequency of analgesia (pharmacological and non-pharmacological) use in mechanically ventilated preterm neonates during their first 14 days of life in two NICUs in Switzerland. All aims also focussed on possible differences related to the gestational age of the infants.

## Methods

A retrospective cohort study was conducted examining procedural exposure and pain management of a convenience sample of 120 ventilated preterm infants (mean age = 29.7 weeks of gestation) during the first 14 days of life after delivery. They were all born between May 1st 2004 and March 31st 2006.

### Patients

A convenience sample of 120 neonates born at between  $\geq 24$  0/7 and 37 0/7 weeks of gestation based on early ultrasound and hospitalised in the NICU for at least 14 days, needing intubation and mechanical ventilation in the first 48 hours of life due to respiratory distress, were eligible for the study independently of their health/illness status. Only preterm infants needing a transfer into another clinic during the first 14 days of life were excluded from the analysis. The sample was recruited from two tertiary level NICUs in two different university hospitals in Switzerland with 32 (site 1) and 19 (site2) beds respectively. The NICUs were comparable in their function and in the basic educational level of their staff. All the preterm neonates were born in the period between 1.5.2004 and 31.3.2006.

### Procedures

Retrospective data collection from nursing and medical charts covering the first 14 days of life was gathered. Data were collected by two trained study nurses. A standardised document listing 27 routine procedures was used to record the number of procedures, the number of failed procedures (the documentation of failed procedures is an integral part of the routine documentation in nursing charts), the number of documented pain scores and the number and type of pharmacological and non-pharmacological interventions that were used throughout the first 14 days of routine care.

The standardised list of NICU procedures was developed on the basis of a literature search highlighting the number of procedures neonates are exposed to most frequently [6-8]. The list was further supplemented by expert opinion in Switzerland (clinical nurse specialists and the medical heads of the neonatological units) and was also used in a survey of 431 neonatal NICU health care providers to test for subjective pain intensity assessment

and to establish a pain intensity ranking for each mentioned routine procedure. According to the survey results, the majority (70.3%) of the routine procedures were considered to be painful based on a mean pain value of  $\geq 4$  points on the visual analogue scale [15].

For the purpose of the current study, two study nurses used the standardised list of NICU procedures mentioned to review the chart of each neonatal subject in order to document each procedure performed and its daily frequency. The two nurses reviewed all charts independently and their findings were compared. Discrepancies were rated ( $<1.0\%$ ) and resolved by going back to the chart. Both completed and failed procedures (e.g. unsuccessful venipuncture attempts) were counted. For all study sites, there was standardised extensive chart documentation of all procedures, even non-painful procedures such as nappy changes.

### Pain assessment

According to existing clinical standard operating procedures (SOPs) at both sites, pain needs to be measured on a regular daily basis in order to detect a possible painful status of the preterm infant. These measurements need to be made independently of acutely painful procedures. The guidelines specify a pain assessment after each nursing shift change (related to the control of routine vital signs). Furthermore, measures of pain need to be made at least once per shift according the needs of the child (e.g. changing behavioural patterns). The guidelines require at least four pain assessments per day/child and for this to be done separately from any painful procedure. The documented pain ratings were scored by using two validated pain scores: the "Bernese Pain Scale for Neonates" (BPSN) [15] at site 1 and the "Neonatal Infants Pain Scale" (NIPS) [16] at site 2. We examined the frequency and timing of the pain assessments in the two NICUs and the reported scores.

### Pain relieving interventions

This study also examined the use of pharmacological agents as well as the non-pharmacological agent, oral glucose, in the management of preterm neonatal pain. Oral glucose is administered in the same way at both clinics (in infants  $<1000$  g; 0.1 ml/kg; in infants  $>1000$  g; 0.5 ml/kg).

The administration of glucose (similar to sucrose) has been the most frequently studied non-pharmacological intervention for the pain relief of procedural pain in neonates and has an established effectiveness in the relief of an acute painful stimulus [17–20].

### Data analysis

The data were entered into an Excel database and then transferred to SPSS (version 14.01) and SAS (version 9.1). Descriptive statistics (mean, standard deviation, percentages) were computed, depending on measurement level and distribution. For inferential analysis, we used general linear models and controlled for the variable “hospital” in every analysis. Longitudinal tests were conducted using a random-intercepts analysis involving gen-

eralised estimating equations. The first calendar day (first day of life) was excluded because it did not consist of an entire day of 24 hours for every study subject. Nonlinearities in the occurrence of the outcome variable were modelled by entering a quadratic function of time into the model.

### Ethical approval

Approval for retrospective data collection from existing nursing and medical data was given by the medical director for research of the University of Berne and the ethical boards of the Canton of Berne and Zurich according to the general ethical approval practices for retrospective data.

## Results

During the study period data from the medical and nursing records of 120 preterm neonates were collected (85 from site 1 and 35 from site 2) (see fig. 1). As shown in table 1, the mean gestational age of the study sample was 29.7 weeks.

Most of the preterm infants included ( $n = 49$ ) had a low gestational age of between 24 0/7 and 28 0/7 weeks. The mean ventilation time for the whole cohort was 94.8 hours (SD 122.28).

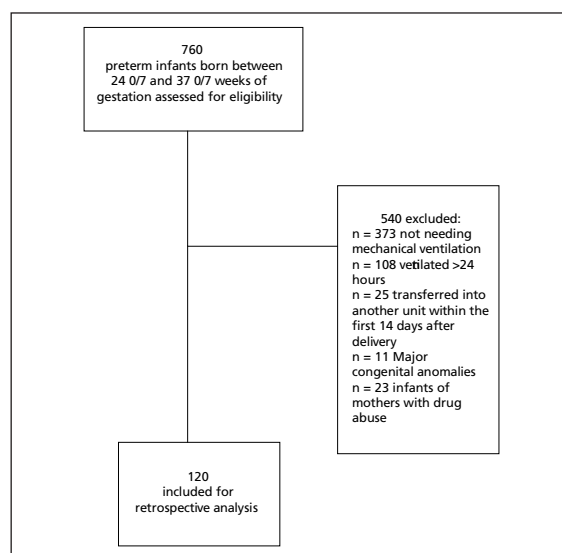
### Procedural pain exposure during the first 14 days of life

#### Number of procedures

A total number of 38,626 procedures were performed on the entire sample during the first 14 days after birth, averaging at 22.9 general procedures performed per child and day. Preterm infants of the lowest gestational age ( $\geq 24$ –28 weeks of gestation) were exposed to the highest number of general procedures ( $p < .0001$ ) (fig. 2; table 2). The same holds true for the analysis of painful procedures only ( $p < .0001$ ), but not for non-painful interventions ( $p = 0.45$ ). The average number of interventions was highest in the first days after birth and decreased non-linearly over time (fig. 2;  $p < .0001$ ). The rate at which the number of interventions decreased differed be-

**Figure 1**

Flow chart of included and excluded infants.



**Table 1**

Neonatal characteristics of study sample.

	Total sample	Gestational group		
	Mean (std)	1 Mean (std)	2 Mean (std)	3 Mean (std)
Gestational age	29.7 (3.5)	26.2 (1.2)	29.7 (1.8)	33.7 (1.5)
Birth weight	1334.0 (635.6)	795.7 (208.9)	1256.0 (347.6)	2107.8 (541.2)
Intubation time in hours	94.8 (122.3)	137.2 (162.8)	60.9 (74.1)	70.5 (69.4)
Gender	n (%)	n (%)	n (%)	n (%)
Male	65 (45.8%)	25 (51.0%)	23 (62.2%)	17 (50%)
Female	55 (54.2%)	24 (49.0%)	14 (37.8%)	17 (50%)
Mortality				
Deaths	13 (10.8%)	10 (20.4%)	1 (2.7%)	2 (5.9%)
Delivery mode				
Spontaneous labour	80 (67.0%)	/	/	/
C-Section	40 (33.0%)	/	/	/
Single birth (# of children)	101 (84.1%)	/	/	/
Twin birth (# of children)	16 (13.3%)	/	/	/
Triplet birth (# of children)	3 (2.5%)	/	/	/

**Table 2**

Number of procedures in study sample during the first 14 days.

Parameter	Estimate	Standard Error	Confidence limits	p-value
<b>Total procedures<sup>a</sup></b>				
Intercept	752.11	106.67	(450.85; 963.36)	<.0001
Gestational age	-17.05	3.21	(-23.41; -10.71)	<.0001
Hospital	107.91	25.11	(58.19; 157.65)	<.0001
<b>Total painful procedures</b>				
Intercept	674.35	96.42	(483.39; 865.31)	<.0001
Gestational age	-16.61	2.90	(-22.35; -10.87)	<.0001
Hospital	88.26	22.70	(43.31; 133.21)	<.0001
<b>Total non painful procedures</b>				
Intercept	77.76	19.76	(38.63; 116.89)	<.0001
Gestational age	-0.45	0.59	(-1.63; 0.73)	0.45
Hospital	19.66	4.65	(10.45; 28.87)	<.0001
<b>Total procedures<sup>b</sup></b>				
Intercept	38.49	2.39	(33.74; 43.24)	<.0001
Day (2 to 14)	-4.36	0.49	(-5.32; -3.40)	<.0001
Day * Day	0.14	0.02	(0.09; 0.19)	<.0001
Hospital	8.24	2.24	(3.85; 12.64)	<.0002
Day * Hospital	0.59	0.22	(0.16; 1.02)	0.007

<sup>a</sup> General linear models

<sup>b</sup> Random-intercept model

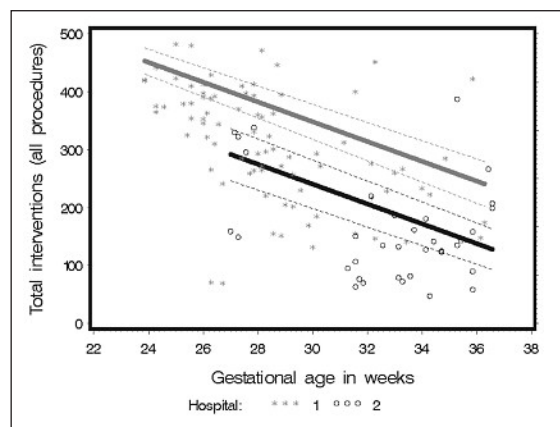
tween the two different hospitals, with a larger decline in the hospital that applied the lowest number of interventions at baseline ( $p < .0001$ ).

*Type and frequency of procedures*

The most prevalent procedure was the manipulation with CPAP (prongs insertion/reinsertion), which represented 24.27% of all procedures. Further ranking of procedures is provided in table 3.

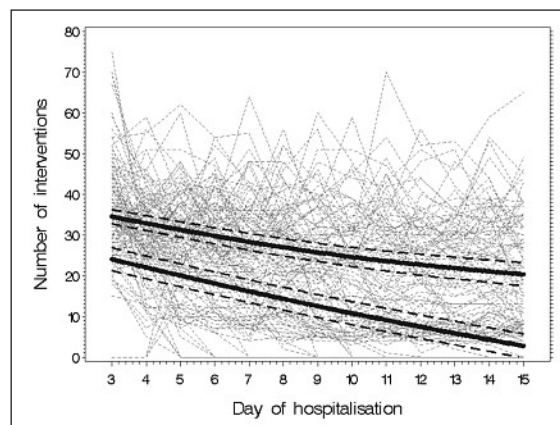
**Figure 2**

Number of procedures according to gestational age.



**Figure 3**

Number of procedures per child during the first 14 days of life and average trend over all children.



**Pain management**

*Pain assessment in the clinical routine*

At site 1, nurses used the BPSN a total of 4,820 times on 85 infants during the first 14 days of life, resulting in an average of 4.05 measurements per day/child. All infants were subjected to at least one pain assessment per day. The instrument was completed as part of the routine evaluation of the neonates' clinical status and most often at the time of shift change. The scores ranged from 0 to 22 (mean = 9.8, SD = 4.32). When scores were examined according to gestational age, they revealed a significantly higher number of measurements performed on infants with the lowest gestational age (mean 65.28; SD 24.97;  $F_{5.573} p 0.005$ ). In total, 93.7% of the measured BPSN scores indicated a non-painful state (<11 points). We found significantly more BPSN scores in the non painful range in the group of infants with the lowest gestational age ( $F_{7.042} p 0.002$ ).

At site 2, NIPS was completed a total of 3,510 times for 35 infants during the first 14 days of life, resulting in an average of 7.1 measurements per day/child. Again, pain was assessed for each child at least once per day. NIPS scores ranged from 0 to 7 (mean = 2.33, SD = 1.8). When assessments were categorised according to gestational group, the results are similar to those based on BPSN. A significantly higher number of measurements were performed on infants with the lowest gestational age (mean 181.17; SD68.78;  $F_{6.039} p 0.006$ ). In total, 83.6% of the measured NIPS scores indicated a non-painful state (<2 points). Again, we found significantly more NIPS scores in the non painful range (<2 points) in the group of infants with the lowest gestational age again ( $F_{7.937} p 0.002$ ).



**Table 3**  
Procedures performed in 120 preterm neonates categorised by pain-intensity and frequency.

Pain-intensity	Procedure	Frequency of procedures (120 neonates)	Mean procedure per neonate	Proportion %
Very painful (VAS: 7 – 10 points)	Endotracheal suctioning	3263	27.19	8.45%
	Heelstick	2007	16.73	5.20%
	Venipuncture	1998	16.65	5.17%
	Insertion of intravenous cannula	777	6.48	2.01%
	Intubation	192	1.6	0.50%
	Bladder puncture	55	0.46	0.14%
	Injections im/sc	44	0.37	0.11%
	Thoracal drain with suction	30	0.25	0.08%
	Insertion chest tube	30	0.25	0.08%
	Eye Examination	21	0.18	0.05%
	Removal chest tube	17	0.14	0.04%
	Lumbar puncture	5	0.04	0.01%
Painful (VAS: 4 – 6 points)	CPAP prongs insertion / reinsertion	9376	78.13	24.27%
	Naso-pharyngeal suctioning	4339	36.16	11.23%
	Transcutaneous O2 tape removal	3366	28.05	8.71%
	Tape removal	2845	23.71	7.37%
	Insertion of nasogastric tube	681	5.68	1.76%
	Extubation	155	1.29	0.40%
	Insertion bladder catheter	27	0.23	0.07%
	Not painful (VAS: 0 – 3 points)	Changing diaper	7071	58.93
Removal of nasogastric tube		549	4.58	1.42%
X-Ray		470	3.92	1.22%
Removal intravenous cannula		394	3.28	1.02%
Cranial ultrasound		377	3.14	0.98%
Removal EKG stickers		340	2.83	0.88%
Insertion umbilical line		100	0.83	0.26%
Removal umbilical line		97	0.81	0.25%
	<b>All procedures</b>	<b>38626</b>	<b>321.88</b>	<b>100%</b>

### 3.2.2 Non-pharmacological and pharmacological analgesia

Of all the preterm infants, 99.2% had one or more analgesic treatments. Only one infant of the cohort was not given an analgesic during the first 14 days of life. Overall, 70.8% of the infants received preemptive analgesia with glucose before a painful procedure, but only 9.2% of them were given orally administered glucose before a procedure every day.

As a pharmacological agent the most frequently used was an intermittent bolus of morphine (65.8%). Morphine was followed by pethidine

(25%) and fentanyl (15.8%). Regarding the total amount of pharmacological pain relief there is a significant difference according to gestational age ( $F_{8,308}$   $p < 0.001$ ). The group of infants of the lowest gestational age (up to 28 weeks;  $n = 49$ ) received a mean total of 6.53ml analgesics, the group of 28–32 weeks of gestation ( $n = 37$ ) a total of 45.56 ml, and infants of 32–37 weeks gestation ( $n = 34$ ) a total of 138.97 ml during the first 14 days after delivery. The two sites did not differ significantly in the administration of pharmacological agents ( $F_{0,25}$   $p 0.62$ ).

## Discussion

This study aimed at investigating type and frequency of procedures and pain management in ventilated preterm infants during the first 14 days of life in two NICUs in Switzerland. The results show an exposure to almost 39,000 procedures in this patient population, of which 75% are considered to be painful [13]. Furthermore, study findings indicate that pain assessment in preterm infants using vali-

dated pain tools is performed systematically in daily practice and that analgesia was given to 99.2% of all neonates under investigation.

The results of our study confirm that iatrogenic pain exposure is a serious problem, particularly in preterm infants of low gestational age. The mean frequency of 22.9 general procedures and 17.3 painful procedures per infant per day that we found

is a substantially higher number of procedures than reported in previous studies [5, 6, 8, 10, 14]. In interpreting the data, however, it should be noted that the highest frequency was documented for the procedure manipulation on CPAP (prongs insertion/reinsertion), which is hardly described as a procedure in other studies. A further explanation for the high number could be that other procedures, such as the insertion and removal of a nasogastric tube and the removal of tapes have probably not been evaluated in the same systematic way as in the present study. Failed procedures (i.e. number of attempts) were also part of our analysis. This could have led to the considerably higher number of procedures in comparison with other studies. Furthermore, the lower mean of gestational age, 29.7 weeks, of the whole sample compared with 32 weeks of gestation in previous study samples [6, 8] could be an explanation for the higher number of procedures in this study. It was also noted that the two participating hospitals differ in the number of procedures they perform. This might be due to the fact that one site hospitalised infants with a gestational age of lower than 26 weeks of gestation who consequently needed highly invasive intensive care for survival for a longer period, while the other site hospitalised infants upwards of 26 weeks only. This difference between the sites might be explained by the much larger geographical recruitment area of one of the participating Swiss hospitals.

As expected, infants with the lowest gestational age (24 to 28 weeks of gestation) were subjected to the greatest number of procedures during their first 14 days of life. It is known that these infants are at high risk for neurological impairment. This higher procedural exposure can be explained by the general immaturity of these infants, requiring a higher degree of intensive care interventions as underlined by the significantly longer ventilation time also confirmed by this study. However it should also be noted that these infants may suffer more pain than other neonates due to misconceptions in the assessment of their pain by caregivers [21].

Manipulation on the CPAP prongs (insertion/reinsertion) was the most prevalent procedure with a frequency of 24.3% among the 27 documented procedures. It should be mentioned that in the sites participating in this study removal and insertion of CPAP prongs is a standard procedure after each change of position for the neonate and is needed for naso-pharyngeal suctioning. The second most frequent painful procedure in the ranking was naso-pharyngeal suctioning, followed by transcutaneous O<sub>2</sub> tape removal. Endotracheal suctioning and heel lance, which are usually considered to be procedures with the highest frequency in other studies [5-9] only ranked in places 5 and 7, respectively, in the present study.

It is encouraging that for both sites the two pain assessment tools BPSN and NIPS are used with a mean frequency of between 4.05 and 7.1 times per day/child. Because of their limited energy reserves infants of low gestational age cannot sus-

tain the ability to express pain via behavioural and physiological patterns [22]. Thus, there is a high risk that a painful state will be underestimated in this group of patients [8, 21, 23]. It is therefore particularly commendable that pain assessment was performed most frequently in preterm infants of low gestational age in the present study. Most of the measurements performed at both sites showed a "non painful" state. The frequency of a "non-painful" state as a measurement outcome might appear to contradict the high amount of procedural exposure described in this study. It should however be noted that the ability to express pain can be influenced by the general immaturity of preterm infants, particularly if they are ventilated, since facial expression is reduced due to respiration devices. This phenomenon is underlined by the result of this study, which shows the highest number of non-painful scores described in the group of infants with the lowest gestational age.

We found that 70.8% of the preterm infants received glucose as a preventive intervention on a daily basis before a procedure. Although this is a higher amount of pain prevention than described in earlier studies [6, 8] this result clearly indicates that despite the growing body of literature on the efficacy of sucrose as an analgesic, nurses do not administer it before painful procedures in a standardised way, as only 9.2% of all infants receiving glucose received it every day. As a pharmacological agent an intermittent bolus of morphine is the most commonly used analgesic (65.8%). At both sites opioids are given only for procedures with an assumed high pain potential (e.g. intubation) and not for minor procedures. Due to the significant side effects of pharmacological agents on the immature organic system it is not surprising that infants with the lowest gestational age had in total the lowest amount of pharmacological pain relief during the time under investigation.

The fact that only one child had no analgesia at all indicates more appropriate pain management than reported in previous studies [6, 8, 12], where the absence of non-pharmacological and pharmacological analgesia was much more common. As several studies in neonates show, repeated and sustained pain can have direct and long term consequences on neurological and behaviour oriented development [22, 24-32].

The interpretation of these results should acknowledge several limitations. Firstly, this is an observational study describing a phenomenon without allowing conclusions or generalisations about pain management in NICUs in Switzerland. Secondly, these results are based on retrospective chart analysis of a convenience sample in two clinics. As there was no electronic documentation at the time the study took place, the analysis of the paper charts might be biased by missing or illegible documentation. Although the documentation of procedures and analgesia, particularly failed attempts, are part of standardised operating procedures in both clinics, we cannot exclude the possibility that some de-

tails such as analgesia use, particularly the use of glucose, or the number of attempts recorded in real time were inaccurate. Thirdly, only two comparable NICUs at tertiary level have been included in the study. Increasing the number of participating institutions and thus the number of infants would have increased our ability to make generalisations.

We believe, however, that our results give preliminary information about pain management in a highly vulnerable patient population in Switzerland. Our results are thus important for improving the situation in the clinical setting by reducing exposure to pain and improving pain relieving interventions for most preterm infants.

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