Respiratory Rate During the First 24 Hours of Life in Healthy Term Infants

Lars Tveiten, MD,[a,b] Lien My Diep, MSc,[c] Thomas Halvorsen, MD, PhD,[b] Trond Markestad, MD, PhD[a,b]

abstract

BACKGROUND AND OBJECTIVE: Abnormal respiratory rate (RR) is a key symptom of disease in the newborn. The aim of this study was to establish the reference range for RR during the first 24 hours of life in healthy infants born at term.

METHODS: Infants were included at the hospital postnatal ward when time permitted. During sleep or a defined quiet state, RR was counted at 2, 4, 8, 16, and 24 hours by placing the bell of a stethoscope in front of the nostrils and mouth for 60 seconds. Data on maternal health, pregnancies, and births were obtained from medical records and the Medical Birth Registry of Norway.

RESULTS: The study included 953 infants. Median RRs were 46 breaths/minute at 2 hours, thereafter 42 to 44 breaths/minute. The 95th percentile was 65 breaths/minute at 2 hours, thereafter 58 to 60 breaths/minute. The fifth percentile was 30 to 32 breaths/minute. Within these limits, the intraindividual variation was wide. The overall mean RR was 5.2 (95% confidence interval [CI], 4.7 to 5.7, $P < .001$) breaths/minute higher while awake than during sleep, 3.1 (95% CI, 1.5 to 4.8, $P < .001$) breaths/minute higher after heavy meconium staining of the amniotic fluid, and 1.6 (95% CI, 0.8 to 2.4, $P < .001$) breaths/minute higher in boys than girls. RR did not differ for infants born after vaginal versus cesarean deliveries.

CONCLUSIONS: The RR percentiles established from this study allow for a scientifically based use of RR when assessing newborn infants born at term.

[a]Department of Pediatrics, Innlandet Hospital Trust, Elverum, Norway; [b]Department of Clinical Science, University of Bergen, Bergen, Norway; and [c]Oslo Centre for Biostatistics and Epidemiology, Oslo University Hospital, Oslo, Norway

Dr Tveiten conceptualized and designed the study, supervised data collection, carried out the initial analyses, and drafted the initial manuscript; Dr Markestad conceptualized and designed the study, participated in analysis and interpretation of results, and critically reviewed and revised the manuscript; Ms Diep participated in the analysis and presentation of the data, created the percentile figures, and reviewed and revised the manuscript; Dr Halvorsen participated in the analysis and presentation of the data and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

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Address correspondence to Lars Tveiten, MD, Department of Pediatrics, Innlandet Hospital Trust, Kirkeveien 31, N-2418 Elverum, Norway. E-mail: lars.tveiten@sykehuset-innlandet.no

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WHAT'S KNOWN ON THIS SUBJECT: It is commonly taught that a respiratory rate >60 breaths/minute may be a cause for concern, but a normal range has not been scientifically established in healthy term newborn infants.

WHAT THIS STUDY ADDS: This study provides percentiles and individual variation in respiratory rate and the effects of sleep, meconium staining of amniotic fluid, and gender during the first 24 hours of life in healthy term infant.

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Although prematurely born newborns are closely monitored because disease and complications are expected, low-risk infants born at term usually undergo a minimum of standardized observations as long as they appear well.[1,2] However, unexpected diseases in the term neonate are common and may rapidly become life-threatening shortly after birth[3]; for example, >70% of early group B streptococcal infections in the United States occur in newborns born at term.[4] Even severe diseases tend to evolve insidiously, and early detection depends on a systematic approach to identify risk factors and clinical signs of possible illness. Tachypnea, and more rarely irregular or low respiratory rates (RR), are important symptoms of disease in the immediate neonatal period, but after searching the literature, it seems that recommendations for concern provided in authoritative textbooks are reiterations rather than being based on appropriate scientific studies.

The aims of the current study were to determine the reference range and variation in RR during the first 24 hours of life in healthy infants born at term and to assess the influence of common clinical situations.

METHODS

This single-center observational study was conducted at the obstetric unit at Innlandet Hospital Trust, Elverum, Norway. Mother-infant dyads were recruited at the time of birth and at all hours dependent only on the workload in the maternity ward, by using convenience sampling. Inclusion criteria were as follows: gestational age ≥37 weeks, 5-minute Apgar score >7, no birth defects, congenital syndromes, or suspected neurologic diseases, and no maternal substance abuse. We planned to recruit 1000 mother-infant dyads, but because of an error in registration of numbers, they were recruited during 2 time periods: February 19, 2008, to March 3, 2010 (n = 754), and December 21, 2010, to January 2, 2012 (n = 199).

Gestational age was based on ultrasound scanning at 17 to 18 weeks' gestation (99%) or on the first day of the last menstrual period if ultrasound scanning was not performed. Apgar scores were assessed by a midwife 1 and 5 minutes after birth. The umbilical cord was clamped within 1 minute, and blood samples from a clamped part were obtained for arterial and venous blood gases. Vitamin K was given intramuscularly in the delivery room.

The newborn infant was positioned prone or on the side on the mother's chest with the face close to the nipple, and the mother was assisted in initiating breastfeeding within a half hour of birth in accordance with the recommendations of the World Health Organization and the United Nations Children's Fund.[5] The mother and child were generally not disturbed for at least 1 hour to facilitate bonding. The general routines differed somewhat in cases of birth complications or if the mother had received general anesthesia. Newborns at risk for hypoglycemia (ie, birth weights >5000 g or <2500 g or born to mothers with diabetes or gestational diabetes) had blood glucose monitoring during at least the first 2 to 6 hours after birth.

Twenty nurse assistants and midwives collected the clinical data. Data on maternal health and habits and characteristics of pregnancy, birth, and the newborn were registered according to the requirements of the Medical Birth Registry of Norway, supplemented with relevant clinical and laboratory data from the hospital medical records.

We decided to count RR by stethoscopic auscultation at the mouth/nose because it can be easily performed without disturbing the infant. To validate this method with those of previous published studies on RR in early infancy (ie, auscultation of the chest[6–8] and visual observation of respiratory movements[6,9–12]), different health care personnel counted RR simultaneously and independently with all 3 methods in a separate study. On 102 observations (6 separate observations on 17 infants with rotating personnel), there were no significant differences between auscultation at the nose/mouth and auscultation of the chest (mean difference 1.2; 95% confidence interval [CI], –0.3 to 2.8 breaths/minute, paired t test) or visual observation (mean difference –0.4; 95% CI, –1.6 to 0.8 breaths/minute). The infants were undressed and touched by a stethoscope during this procedure.

The mother or both parents gave written informed consent, and the study was approved by the Regional Committee for Medical and Health Research Ethics, South East Norway (1.2007.1138 and S-07287d).

Measurements

Participating midwives and nurse assistants were trained in the procedures by the principal investigator (LT), and their skills were reassessed to make sure that all observations were as accurate and standardized as possible. Before each assessment, the infant was in a quiet state and was not handled for at least 10 minutes before counting RR. At 2 hours, the RR was counted while positioned on the mother's chest or supine in a cot. From 4 hours on, RR, rectal temperatures, and room temperature were recorded while the infant was positioned on the mother's chest or supine in a cot in a quiet environment.

First, we recorded whether the infant was awake or asleep. Second, the number of breaths

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was counted manually for 60 seconds by positioning the bell of a stethoscope close to, but not touching, the nostrils and mouth. Finally, the rectal temperature was obtained by inserting a rectal thermometer (Digitemp MT 1671, Microlife AG, Widnau, Switzerland) ∼2 to 3 cm into the rectum. The temperature was recorded when the thermometer gave an audible signal after ∼1 minute. The same rectal thermometer was used for all rectal temperatures in the same infant. The thermometer was rinsed in Alkotip (isopropyl alcohol 70%) after each measurement and soaked in Perasafe (Antec International Limited, Sudbury, United Kingdom) for 10 minutes for full disinfection between infants. We did not make further observations on participants who were transferred to the NICU but had access to subsequent NICU observations and diagnoses.

Statistical Analysis

Data were entered into EpiInfo version 3.5.1 data entry (EpiInfo, Centers for Disease Control and Prevention, Atlanta, GA) and validated by using check code in EpiInfo and by double entry using the datacompare application in EpiInfo. We estimated the required number of newborns to be 300 for creating percentile charts[13] of RR, presuming a mean RR of 45 breaths/minute with a precision of 8 breaths/minute[12] for a 2-sided reference interval. One thousand newborns were included to increase the precision of the key estimates.

Differences in characteristics between participants and nonparticipants were tested by a χ^2 test or 2 independent samples *t* test depending on the distribution of data.

To construct the percentile curves, the Generalized Additive Model for Location, Scale and Shape algorithm for normal distribution (as the GAMLSS package[14] in R[15]) was fitted to log-transformed RR, and the percentiles from its embedded smoothing function were then antilogged. We used 3 degrees of freedom for smoothing the curves.

Estimations of differences in RR according to age, gender, and awake/asleep status were examined by using linear mixed effect models with RR as dependent variable. Newborn identifiers were treated as random intercept and age as random slope with unstructured variance-covariance matrix to fit 5 measurements of RR per newborn. Age, awake or sleep state, and gender were defined as fixed effects in the linear mixed model.

To estimate the within-newborn variation in RR compared with the total variation, we estimated intraclass correlation coefficients (ICC) type 3 by using Stata (Stata Corp, College Station, TX).[16] To adjust for awake/asleep status in the estimation of ICC, the between-subject variability in relation to the sum of within-subject and between-subject variabilities was assessed by using the estat icc post-estimation command in Stata after including awake/asleep status and fitting the mixed model. The value of ICC lies between 0 and 1. A small estimate of ICC reflects that the within-subject variability is large.

RESULTS

Of 1021 recruited infants, 21 were not assessed because of heavy workload (*n* = 16) or early NICU transfer (*n* = 5). Of 1000 infants studied according to the protocol, 33 were ineligible due to prematurity (*n* = 28), unknown gestational age (*n* = 2), 5-minute Apgar score <8 (*n* = 2), or a verified syndrome (*n* = 1), and 14 infants were excluded because of acute disease, including infections (*n* = 8), hypoglycemia (*n* = 4), fracture of the clavicle (*n* = 1), or hyperbilirubinemia (*n* = 1), leaving 953 (93%) of recruited infants in the study.

Four of the 953 infants who appeared healthy at their first assessments were transferred to the NICU during the study at 8 to 24 hours of age, and 5 after 24 hours, because of clinical symptoms suggestive of infection. The mean RR of the altogether 9 NICU transfers was 13 (95% CI, 8.6 to 17, $P < .001$) breaths/minute higher than the mean RR of those not transferred, and 4 had RR >60 breaths/minute at least once. Five of the transferred infants were treated with intravenous antibiotics, but blood cultures were negative and C-reactive protein remained low.

Arterial or venous umbilical cord base excess was below –10 mmol/L in 57 of 953 infants, and arterial or venous umbilical cord pH was below 7.1 in 14 of these. All appeared healthy. Umbilical cord blood gases were missing for 161 of the 953 healthy infants (arterial for 371 and venous for 199).

There were no significant differences in prepregnancy, pregnancy, or newborn baseline characteristics between participants and eligible nonparticipants who were not included because of heavy workload in the maternity unit, except a higher rate of stained amniotic fluid and a lower transfer rate to the NICU for the participants (Table 1).

Due to work shifts, each infant was usually assessed by 3 or 4 observers. Of the 953 included infants, 260 (27%) were born during the night shift from 10 PM to 7 AM, 423 (44%) during the day shift between 7 AM and 3 PM, and 270 (28%) from 3 PM to 10 PM.

The median (interquartile range) ages at assessment were 2 (0.1), 4 (0.1), 8 (0.1), 16 (0.07), and 24 (0.05) hours. RR was missing for 138 (2.9%) of planned observations, and 25 (0.5%) observations were not included in the analyses because they were recorded before 1 or after 26 hours of age.

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The 50th percentile for RR was 46 breaths/minute at 2 hours and later ~43 breaths/minute. The 95th percentile was 65 breaths/minute at 2 hours, thereafter ~60 breaths/minute, and the fifth percentile was from 30 to 32 breaths/minute (Tables 2 and 3; Figs 1 and 2).

Repeated measurements showed that RR varied considerably for each infant during the first 24 hours (ICC = 0.31 [95% CI, 0.28 to 0.34] at ages 2 to 24 hours and ICC = 0.38 [95% CI, 0.34 to 0.42] at ages 8 to 24 hours). Differences between being awake or asleep only accounted for part of this variation, and after adjusting for awake or asleep status, ICC was 0.46 (95% CI, 0.42 to 0.51).

The mean RR was 1.6 (95% CI, 0.8 to 2.4, $P < .001$) breaths/minute higher for boys than girls, and the difference did not vary with age at assessment. Awake versus asleep state was recorded for 91% of the observations; 44% of the counts were done during sleep, and this rate did not differ between the ages of assessment. The mean RR was 5.2 (95% CI, 4.7 to 5.7, $P < .001$) breaths/minute higher when awake than asleep, but 4.3 breaths/minute higher (95% CI, 3.8 to 4.8, $P < .001$) after adjusting for rectal temperature. The mean RR was 1.1 (95% CI, 0.4 to 1.9, $P = .003$) breaths/minute lower when the infants were observed in the cot (86% of the assessments; 47% at 2 hours, 89%–94% later) than with the mother (13%), or the father (1%), usually on their chests. The mean RR of infants exposed to heavy meconium-stained amniotic fluid but without clinically significant symptoms of meconium aspiration syndrome ($n = 56$) was 3.1 (95% CI, 1.5 to 4.8, $P < .001$) breaths/minute higher than for those with clear or lightly stained fluid. There was no difference in RR between infants delivered by caesarean delivery ($n = 156$) and vaginally (mean difference −0.1; 95% CI, −1.2 to 0.96 breaths/minute) or between infants born to mothers of non-Caucasian ($n = 62$) and Caucasian ethnicity (1.0; 95% CI, −0.6 to 2.6 breaths/minute).

Several sensitivity analyses were carried out to estimate the effects of removing various subgroups from the sample, including removing the last sampled group ($n = 199$), the transfers, and the group with meconium-stained amniotic fluid, none of which changed the 95th percentile by more than −1 to +2 breaths/minute.

TABLE 1 Maternal, Pregnancy, and Infant Characteristics of Participants and Potentially Eligible Infants Who Were Not Recruited[a]

	Participants ($n = 953$)	Not Recruited ($n = 1754$)	P[b]
Maternal characteristics, n (%)			
Married/cohabitating	889 (93.3)	1606 (91.6)	.10
Daily smoker (during early pregnancy)[c]	134 (15.1)	256 (15.8)	.76
Nullipara	370 (38.8)	726 (41.4)	.14
Pregnancy characteristics, n (%)			
Oligohydramnion	30 (3.1)	73 (4.2)	.20
Preeclampsia	10 (1.0)	36 (2.1)	.08
Delivery characteristics, n (%)			
Epidural anesthesia	227 (23.8)	487 (27.8)	.03
Spinal anesthesia	123 (12.9)	231 (13.2)	.70
Amniotic fluid, stained	203 (21.3)	273 (15.6)	<.001
Cesarean delivery	156 (16.4)	304 (17.3)	.36
Rupture of membranes 12–24 h	22 (2.3)	40 (2.3)	.98
Rupture of membranes >24 h	27 (2.8)	55 (3.1)	.60
Infant characteristics			
Male gender, n (%)	488 (51.2)	920 (52.5)	.84
Birth wt, mean (SD), g	3594 (483)	3542 (502)	.006
Head circumference, mean (SD), cm	35.1 (1.5)	35.0 (1.5)	.006
Gestational age at birth, mean (SD), d	280 (8.6)	280 (8.9)	.99
Apgar score at 1 min, <8, n (%)	39 (4.1)	96 (5.5)	.19
Transferred to the neonatal ward, n (%)	9 (0.9)	112 (6.4)	<.001

[a] Based on data from the Medical Birth Registry of Norway. Patients not recruited due to heavy work load in the obstetrics department.
[b] P value for the difference in characteristics between participants and nonrecruited infants. χ^2 or Student t tests as appropriate.
[c] Missing for 63 (6.6%) of participants and 137 (7.6%) of nonrecruited infants ($P = .39$).

TABLE 2 RR Percentiles[a] During the First 24 Hours of Life

RR Percentile[a]	RR (Breaths/Minute)				
	Age (Hours)				
	2 ($n = 931$)	4 ($n = 928$)	8 ($n = 931$)	16 ($n = 914$)	24 ($n = 898$)
99th	82	73	69	73	70
95th	65	58	60	60	59
90th	60	54	55	56	56
75th	52	48	48	50	50
50th	46	42	42	44	44
25th	40	38	38	40	40
10th	36	32	33	34	35
5th	32	30	30	31	31
1st	28	24	26	25	28
Mean	47.3	43.1	43.2	44.7	44.8
SD	10.5	9.6	8.8	9.2	8.6
CV	0.22	0.22	0.20	0.21	0.19

CV, coefficient of variation.
[a] Raw data, unsmoothed.

DISCUSSION

To our knowledge, this is the first large and systematic study of RR

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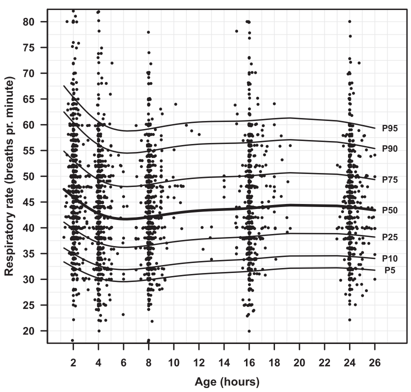

FIGURE 1
Individual observations and smoothed percentiles (P) of RRs based on observations at ~2, 4, 8, 16, and 24 hours of age in 953 healthy term infants.

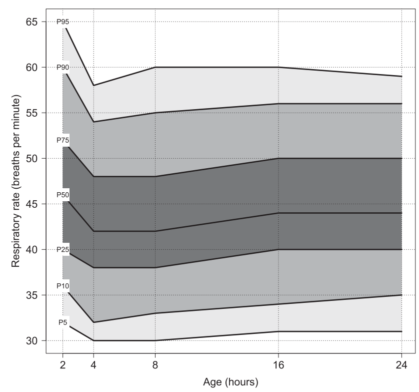

FIGURE 2
Unsmoothed percentiles (P) of RRs based on observations at ~2, 4, 8, 16, and 24 hours in 953 infants.

in healthy infants during the early neonatal period, and the only study paying careful attention to clinical characteristics that potentially may affect RR. RRs were slightly higher at 2 hours than later during the first 24 hours of life, but still remarkably consistent in the cross-sectional analyses with a median at 40 to 45 breaths/minute, fifth percentile at 30 to 32, and 95th percentile at ~60 breaths/minute. On average, RRs were ~5 breaths/minute higher when quietly awake than when asleep, and 3 breaths/minute higher after heavy meconium staining of the amniotic fluid compared with no or minimal staining. Cesarean delivery, gender, and being on the mother's chest as opposed to in a cot had no or minimal clinical significance. However, for each infant, the RR varied significantly within these normal limits.

The strengths of this study were the large number, adherence to standardized conditions, and consistent inclusion of information that could be important modifiers of RR. A limitation of the study was the potential for selection bias. However, the minute differences in baseline characteristics between those who were or were not included and the similar results in the various sensitivity analyses suggest that the results were valid.

Some papers published before the 1960s reported RR in newborns

TABLE 3 RR Percentiles[a] For Subgroups (Awake Versus Asleep, Male Versus Female, Heavily Stained Versus Unstained or Lightly Stained Amniotic Fluid)

RR Percentile[a]	RR (Breaths/Minute)									
	Age (Hours)					Age (Hours)				
	2	4	8	16	24	2	4	8	16	24
			Awake					Asleep		
	n = 407	*n* = 377	*n* = 465	*n* = 532	*n* = 545	*n* = 181	*n* = 527	*n* = 444	*n* = 363	*n* = 343
95th	72	60	61	60	60	58	56	54	57	58
90th	63	58	58	58	56	56	52	50	52	55
75th	56	51	50	51	50	48	46	44	48	48
50th	48	45	44	45.5	46	42	40	40	40	42
25th	42	40	40	40	40	38	35	36	37	38
10th	38	35	36	37	37	33	30	31	32	32
5th	35	32	35	34	33	30	27	28	30	30
			Male					Female		
	n = 480	*n* = 477	*n* = 476	*n* = 467	*n* = 457	*n* = 451	*n* = 451	*n* = 455	*n* = 447	*n* = 441
95th	65	59	60	62	60	63	58	58	58	58
90th	60	55	56	58	57	60	54	54	55	54
75th	54	49	48	50	50	52	48	48	49	49
50th	47	43	42	44	45	46	40	42	43	43
25th	42	38	38	40	40	40	36	38	38	40
10th	36	32	34	34	35	35	31	32	34	33
5th	32.5	30	32	31	32	32	28	30	32	30
			Heavily Stained					Unstained or Lightly Stained		
	n = 55	*n* = 56	*n* = 55	*n* = 52	*n* = 51	*n* = 871	*n* = 867	*n* = 871	*n* = 857	*n* = 842
95th	68	60	60	60	63	65	58	59	60	58
90th	61	58	60	58	59	60	54	54	56	55
75th	58	52.5	51	51.5	55	52	48	48	50	50
50th	50	46	44	45.5	48	46	42	42	44	44
25th	42	40	40	40	41	40	38	38	40	40
10th	36	38	36	36	38	36	32	33	34	34
5th	33	32	33	35	36	32	30	30	31	31

[a] Raw data, unsmoothed.

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but usually as part of pioneering studies on lung mechanics using body plethysmography. The numbers of included infants were small, recruitments were haphazard during the first few weeks of life, and the study conditions (eg, wake versus sleep state when counted by observation)[12] were not registered. Few observations were made during the first 24 hours of life, which in our view is an important age because of the transition from fetal life and because this is the time when life-threatening conditions often emerge. One exception was a study that included 76 healthy term infants as a control group in which an average RR of 41 to 42 breaths/minute was found during the first 3 days of life.[12] In another study of 54 term infants, the highest mean (SD) RR during the first 24 hours was 48 (6) breaths/minute at age 3 hours, when obtained from a special recording device.[17] As far as we know, only 1 percentile chart that includes RR of newborn infants has been published.[18] It covers all ages until 18 years and is based on several studies performed at different ages. For the first day of life, the figures seem to be based on only 1 study of 84 infants during quiet sleep, and RR was registered from a pressure-sensitive mattress.[19] Their median RR at birth was 44, and median RR (1st and 99th percentiles) at 0 to 3 months of age was 43 (25–66) breaths/minute.

To our knowledge, the method of counting RR by placing the bell or membrane of the stethoscope in front of the nostrils/mouth has not been reported in scientific studies of infants or children, although it is our impression that it is commonly used. This method has several advantages: the infant is not disturbed, breaths are easy to identify, no expensive equipment is required, and there is no reason to believe that it is less accurate than other manual methods, an assumption confirmed by data from the separate method comparison study. In previous studies of newborns, respiration has been recorded by visual observation[10,12] or by using special recording devices,[19–23] whereas auscultation of the chest has been used in older infants.[6–8] Counting by visual observation is difficult and unreliable in postnatal quiet sleep without removing covers and undressing the infant, and methods involving touching affect RR by disturbing the infant.[17,21] We counted RR for 60 seconds, according to the recommendations by the American Academy of Pediatrics[1] and the World Health Organization.[24,25] No specific recommendations on duration of counting are given in the UK National Institute of Health and Care Excellence clinical guideline.[26] Continuous counting for 60 seconds gives a higher repeatability and lower RRs compared with 30 seconds or repeated periods of <60 seconds.[8,11,21]

CONCLUSIONS

RR is acknowledged as an important clinical parameter of health and disease in the newborn. The current study provides reference data for healthy term infants during the first day of life. RR can be easily monitored in any setting, and in future studies, the significance of abnormal RR as a diagnostic tool for various diseases in the newborn period should be explored.

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ABBREVIATIONS

CI: confidence interval
ICC: intraclass correlation coefficient
RR: respiratory rate

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