CASE REPORT

Procalcitonin Read Outside Its Derivation Population and an Antibiotic Course Ended by the Calendar: A Late Preterm Neonate with Transient Tachypnoea of the Newborn Managed as Probable Early-Onset Sepsis

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ABSTRACT

Background: Respiratory distress in a late preterm neonate forces an early choice between transient tachypnoea of the newborn and pneumonia with early-onset sepsis, usually before any confirmatory result exists.

Objective: To audit how biomarkers and an antibiotic stop rule were interpreted in a late preterm neonate managed as probable early-onset sepsis.

Methods: This CARE-guided case report reviewed the de-identified clinical record, re-read each test against its derivation population, and recomputed clinical, respiratory, bilirubin, fluid, nutrition, and dosing quantities.

Results: A 36-week male neonate weighing 3,000 g was born after prolonged preterm premature rupture of membranes with oligohydramnios and grunted from birth. Continuous positive airway pressure began at one minute; oxygen returned to room air by five minutes and support ended on day 3. The full blood count was normal for age, C-reactive protein fell from 28 to 11 mg/L, and a bacterial polymerase chain reaction was negative, yet a five-day antibiotic course was completed. Procalcitonin of 6.8 ng/mL was interpreted outside the population from which its reference interval was derived, and the stop rule depended on a culture result that never arrived.

Conclusion: Neonatal biomarkers should be interpreted against age- and physiology-matched populations, and antibiotic stop rules should execute after a defined interval unless the culture signals. A twelve-item minimum data set is proposed.

1. Introduction

Respiratory distress is the commonest reason a newborn infant is admitted to intensive care, and in the first hours of life the clinical picture rarely separates its causes. Among 560 moderate and late preterm infants with early neonatal respiratory failure enrolled prospectively across 46 French neonatal units, transient tachypnoea of the newborn accounted for 57.3% of diagnoses and respiratory distress syndrome for 39.8%, with continuous positive airway pressure used in 82.9% of those born at 34 to 36 weeks and invasive ventilation in 13.2%.[1] The distinction matters because the two commonest explanations for the same set of signs – delayed clearance of fetal lung fluid on one hand, and pneumonia with early-onset sepsis on the other – carry opposite management consequences. The first resolves with supportive respiratory care within 24 to 72 hours and requires no antibiotic. The second, untreated, is among the few neonatal emergencies in which hours of delay change outcome.

The asymmetry of those consequences is the reason empirical antibiotics are started before any confirmatory result exists, and it is also the reason they are so often continued after the results that would stop them have arrived. Across 13 hospital-based and population-based networks in 11 countries, 21,703 of 757,979 late preterm and term neonates (2.86%, 95% confidence interval 2.83 to 2.90) received intravenous antibiotics in the first postnatal week, at a median of 4 days (interquartile range 3 to 6) in those without early-onset sepsis; the incidence of early-onset sepsis itself was 0.49 cases per 1,000 livebirths, so 58 neonates were started on antibiotics and 273 antibiotic days were administered for every case.[2] A subsequent analysis of the same population separated the treated infants by duration and found that culture-negative sepsis treated for five days or more accounted for 7,996 of 21,703 treated infants (37%), an incidence of 10.6 per 1,000 livebirths (95% confidence interval 10.3 to 10.8) – 21-fold more frequent than culture-proven early-onset sepsis.[3] In Indonesia, a cross-sectional study of 2,509 neonates admitted within 72 hours of life to three neonatal units found 242 suspected cases (9.6%) and 83 culture-proven cases, with median antibiotic durations of 9 days in the culture-negative group and 19 days in the culture-proven group.[4]

Each of the tests brought to bear on this question carries a reference frame that is easily separated from the number itself. C-reactive protein rises physiologically after birth: in 145 infants of at least 34 weeks screened for presumed early-onset sepsis who did not receive antibiotics, the concentration peaked at 24 hours, and the study reports the centiles at that hour separately for its two arms – in the 109 term infants a 90th centile of 10.80 mg/L and a 97th of 12.00 mg/L, and in the 36 preterm infants a 90th centile of 7.60 mg/L and a 97th of 8.00 mg/L.[5] Its discriminating power depends on when it is drawn: within four hours of the blood culture, a cut-off of 10 mg/L gave a sensitivity of 41.7%, a

specificity of 89.9% and a positive likelihood ratio of 4.12 among 10,134 admitted infants, whereas a sample taken 24 to 72 hours after the culture raised sensitivity to 89.5% but dropped specificity to 55.7% and the likelihood ratio to 2.02.[6] Procalcitonin has a steeper physiological surge still. Among 315 uninfected very low birth weight preterm neonates contributing 1,015 determinations, the average value peaked at 15.12 ng/mL at about 36 hours of life.[7] The most widely used neonatal reference interval – a median of 1.05 ng/mL with a 95% range of 0.14 to 4.39 in 143 term samples and 1.01 ng/mL with a range of 0.15 to 4.44 in 95 preterm samples at 12 to 36 hours – was derived after deliberately excluding neonates with respiratory failure, and the same study reports separately that the median in neonates who did have respiratory failure without bacterial infection was 6.83 ng/mL in term and 9.56 ng/mL in preterm infants, against 49.82 ng/mL in preterm infants with bacterial infection.[8]

Blood culture, which decides everything, has a well described latency. Among 594 cultures growing a pathogen and obtained within 72 hours of birth at 19 hospitals, the median time to positivity was 21.0 hours (interquartile range 17.1 to 25.3), with 68% positive by 24 hours, 94% by 36 hours and 97% by 48 hours; neither maternal intrapartum antibiotic prophylaxis nor gestation below 35 weeks altered the median.[9] In a level IV unit, 30 of 31 definite pathogens (97%) had been reported by 24 hours and all 52 definite and possible pathogens by 36 hours.[10] Reducing empirical therapy from 48 to 24 hours with a formal time-out was applied to 196 of 414 newborns evaluated for possible early-onset sepsis at six units without a difference in the pre-specified safety endpoints.[11] Formal risk stratification moves the same lever: in an open-label cluster-randomised trial in ten Dutch hospitals enrolling 1,830 newborns of at least 34 weeks with at least one risk factor, antibiotics for suspected early-onset sepsis were started in 66 of 915 (7.2%) under the sepsis calculator against 243 of 915 (26.6%) under the categorical guideline, a difference of 19.4 percentage points between those two proportions against a cluster-adjusted absolute risk reduction of 19.0% as the trial reports it (95% confidence interval 11.3 to 26.7), with at least one harm criterion present in 64 of 915 (7.0%) against 134 of 915 (14.6%), relative risk 0.48 (95% confidence interval 0.36 to 0.63).[12]

Novelty and aim. Case reports of neonatal respiratory distress characteristically narrate the diagnostic sequence and close when serial reassessment resolves it. A search of PubMed and Google Scholar from inception to August 2026, combining terms for neonatal case reports with terms for procalcitonin reference intervals, blood-culture time to positivity and antibiotic stop rules, returned no report that instead audited a single late preterm admission against the derivation populations of its own biomarkers and against the published time-to-positivity distribution of the blood culture on which its own stop rule depended; the claim of novelty is limited to what that search retrieved. The aim of this report is to do exactly that: to set every measurement made in one admission beside the population in which the interval it was judged against was derived, to recompute every quantity the record states as arithmetic, to identify the point at which the respiratory diagnosis was revised and the antibiotic course was not, and to close with a numbered minimum data set naming, for the twelve measurements whose absence bore most directly on those decisions, the moment at which each must be obtained and the decision it would have changed.

2. Methods

Case design and reporting framework

This CARE-guided, single-patient retrospective case report was prepared from routine clinical records at a tertiary referral hospital in Padang, West Sumatera, Indonesia. The report describes the infant's course from birth through discharge.

Patient information and consent

Maternal and perinatal history, examination findings, laboratory and imaging results, respiratory support, medications, nutrition, and daily progress were abstracted from the de-identified clinical record. Written informed consent for publication, including the chest radiograph, was obtained from both parents as the infant's legal guardians. Direct identifiers were removed before analysis and publication.

Clinical record audit and analysis

Recorded values were transcribed without silently reconciling discordances. Respiratory indices, haematological ratios, bilirubin fractions, fluid and nutritional prescriptions, dosing denominators, and weight change were recomputed from the source values and compared with the populations in which the cited reference intervals and decision thresholds were derived.

Ethical considerations

The report describes routine clinical care and introduced no intervention, additional investigation, or change in management. The case was reviewed by the institutional health research ethics committee, which issued a written determination that ethics-committee approval was not required for this de-identified retrospective report.

3. Results

Pregnancy, labour and the delivery-room transition

The mother was 27 years old and G1P0A0H0. Antenatal care comprised 2 visits to a primary health centre and 5 to an obstetrician, 7 in all. She reported white vaginal discharge without pruritus or odour from the third trimester and completed a 5-day course of antibiotics for a urinary tract infection before delivery. No maternal fever was recorded at any point in pregnancy. Her weight rose from 60 kg before pregnancy to 80 kg at term; the record states the gestational weight gain as 18 kg, whereas the two recorded weights differ by 20 kg. Admission bloods showed haemoglobin 11.2 g/dL, leucocytes 7,800/mm^3, platelets 205,000/mm^3 and haematocrit 33%, with a negative hepatitis B surface antigen; elsewhere the same document gives a maternal leucocyte count of 10,930/mm^3 before delivery, and no sampling time is attached to either figure. Group B streptococcal screening was not performed. The maternal, perinatal and delivery-room record, with every quantity the source states more than once printed in both of its forms, is set out in Table 1.

Delivery was spontaneous and vaginal, in the active phase of the first stage, complicated by preterm premature rupture of membranes with oligohydramnios and a single live intrauterine fetus. The amniotic fluid is described as scant and mixed with blood in the history and as clear in colour and scant in volume in the summary. The latency from rupture of membranes to delivery is recorded only as longer than 12 hours; no interval in hours appears anywhere. Gestational age computed from the recorded date of the last menstrual period to the recorded date of birth is 36 weeks and 1 day, and the estimated date of delivery the record prints falls exactly 280 days after the recorded last menstrual period, so the two obstetric dates are internally consistent. Neither date

is reproduced here, because together with the computed interval they would reconstitute the date of birth.

The infant was male, with a birth weight of 3,000 g, a head circumference of 32.0 cm and a birth length given as 45.0 cm in the perinatal history and 44.0 cm at the admission examination and in the case analysis. Apgar scores were 6 at one minute and 9 at five. He grunted from birth with reduced tone. The Downes score at birth is recorded as 4 of 10, and the five component descriptors the record supplies – a respiratory rate of 60 to 80 per minute, mild retraction, cyanosis that resolved with supplemental oxygen, good and symmetrical bilateral air entry, and grunting audible on auscultation – sum to 4, so the recorded total is reproducible from its own components.

Table 1. The maternal, perinatal and delivery-room record.

Item	As the record states it	Where the record states it a second time	Recomputed here, or the reference position
Maternal age and parity	27 years, G1P0A0H0	stated once	-
Antenatal care	2 visits to a primary health centre and 5 to an obstetrician	stated once	7 visits in total
Maternal weight	60 kg before pregnancy, 80 kg at term	gestational weight gain stated as 18 kg	**20 kg from the two recorded weights**
Maternal leucocyte count	7,800/mm³ on admission	**10,930/mm³ before delivery**	no sampling time for either
Maternal haemoglobin, platelets, haematocrit	11.2 g/dL, 205,000/mm³, 33%	stated once	haemoglobin and haematocrit sit at the conventional lower limits for pregnancy (11.0 g/dL and 33 per cent) and the platelet count is within range
Maternal group B streptococcus	*never tested*	*no result exists*	**the single most consequential missing maternal datum**
Maternal intrapartum temperature	*never measured*	*no maternal temperature appears anywhere in pregnancy or labour*	**the record's only assertion of fever is neonatal, for hospital day 1, and the highest neonatal temperature recorded on any day is 37.0 °C**
Rupture of membranes	preterm premature, classified as longer than 12 hours	*the latency in hours is never recorded*	**latency enters published models as a threshold or as an adjustment covariate; a "longer than 12 hours" category supports neither**
Amniotic fluid	scant and mixed with blood	**clear in colour and scant in volume**	the colour is stated twice, differently
Gestational age by the last menstrual period	*a last menstrual period is recorded; the date is withheld here*	*an estimated date of delivery is recorded; the date is withheld here*	36 weeks 1 day; the recorded estimated date of delivery falls exactly 280 days after the recorded last menstrual period, so the two obstetric dates are internally consistent
New Ballard score	30, mapped in the record to 36–38 weeks; the four scorable physical descriptors are plantar surface (anterior transverse crease only, about 34 weeks), breast (stippled areola, 1–2 mm bud, about 36 weeks), eye / ear (thick cartilage, ear stiff, about 40 weeks), genitals (male) (rugae present, both testes descended, about 38 weeks)	*not recorded: the six neuromuscular items appear nowhere*	**30 maps to 36 weeks on the maturity grid, and the four recorded descriptors span 6 weeks between them**
Delivery	spontaneous vaginal, first stage active phase	stated once	-
Birth weight	3,000 g	stated once	between the 50th and 90th Fenton centiles
Birth length	45.0 cm (perinatal history)	**44.0 cm (admission examination and case analysis)**	the two values straddle the 10th Fenton centile
Head circumference	32.0 cm	stated once	between the 10th and 50th Fenton centiles
Apgar score	6 at one minute, 9 at five minutes	stated once	-
Downes score at birth	4 of 10	**6 in the case analysis**	the five recorded descriptors sum to 4
Lowest oxygen saturation in the delivery room	75% at three minutes	**55–70%, described as severe hypoxaemia**	no value below 75% appears in the observations
Capillary refill time	under 3 seconds at the STABLE assessment	under 2 seconds at the admission examination	both lie within the normal range
Mean arterial pressure on day 1	40 mmHg, beside a blood pressure of 65/35 mmHg	**45.0 mmHg, the conventional estimate from the same two numbers**	both clear the lower acceptable bound of 36 mmHg for this gestation, the printed value by 4 mmHg and the recomputed value by 9.0; the day-5 figure reproduces exactly and the day-3 figure to within 0.7 mmHg
Blood glucose and temperature at stabilisation	96 mg/dL and 36.9 °C	stated once	both within the reference interval

The third column is reserved for quantities the source document states more than once; where it does, every recorded value is printed rather than one being chosen. Red marks a value that disagrees with another statement in the same document, that its own components do not reproduce, or whose absence bears directly on a decision described here; grey marks a quantity the record does not contain.STABLE, the sugar-temperature-airway-blood pressure-laboratory-emotional support assessment used at this unit. Fenton centiles are the third-generation preterm growth reference; in 2,541 neonates the Fenton and INTERGROWTH-21st charts gave discordant birthweight classifications in 171 (6.7%).[13] Gestational age computed from the recorded date of the last menstrual period to the recorded date of birth. The New Ballard maturity grid assigns 36 weeks to a total of 30 and 38 weeks to a total of 35; the range printed in the record spans both grid points. Two comparisons of postnatal gestational-age scores against early ultrasound bear on that mapping: in 1,114 neonates the expanded New Ballard score overestimated gestation by 0.65 weeks[14], and in a separate study of 106 infants the same score showed a mean bias of only -0.14 weeks but limits of agreement wider than one week in either direction for every method tested, so no method could be relied on to place an individual infant's gestation within a week of the true value.[15] The conventional estimate of mean arterial pressure is (systolic + 2 × diastolic) / 3.

Continuous positive airway pressure was begun at the first minute of life at a positive end-expiratory pressure of 7 cmH_2O and a fraction of inspired oxygen of 0.21; oxygen saturation was not yet readable. The fraction of inspired oxygen was raised to 0.30 and saturation reached 75% by the third minute, at which point peripheral cyanosis had resolved and retractions had improved. Saturation rose to 90 to 95% by the fifth minute, allowing the inspired oxygen to be weaned back to 0.21, and reached 95 to 98% by the fifteenth minute. Blood glucose was 96 mg/dL and temperature 36.9 °C. Intramuscular vitamin K was given within the first hour. The whole admission, from the first minute to the fifth hospital day, is illustrated in Figure 1, which carries only what the record contains together with the four quantities recomputed in this report and marked as such.

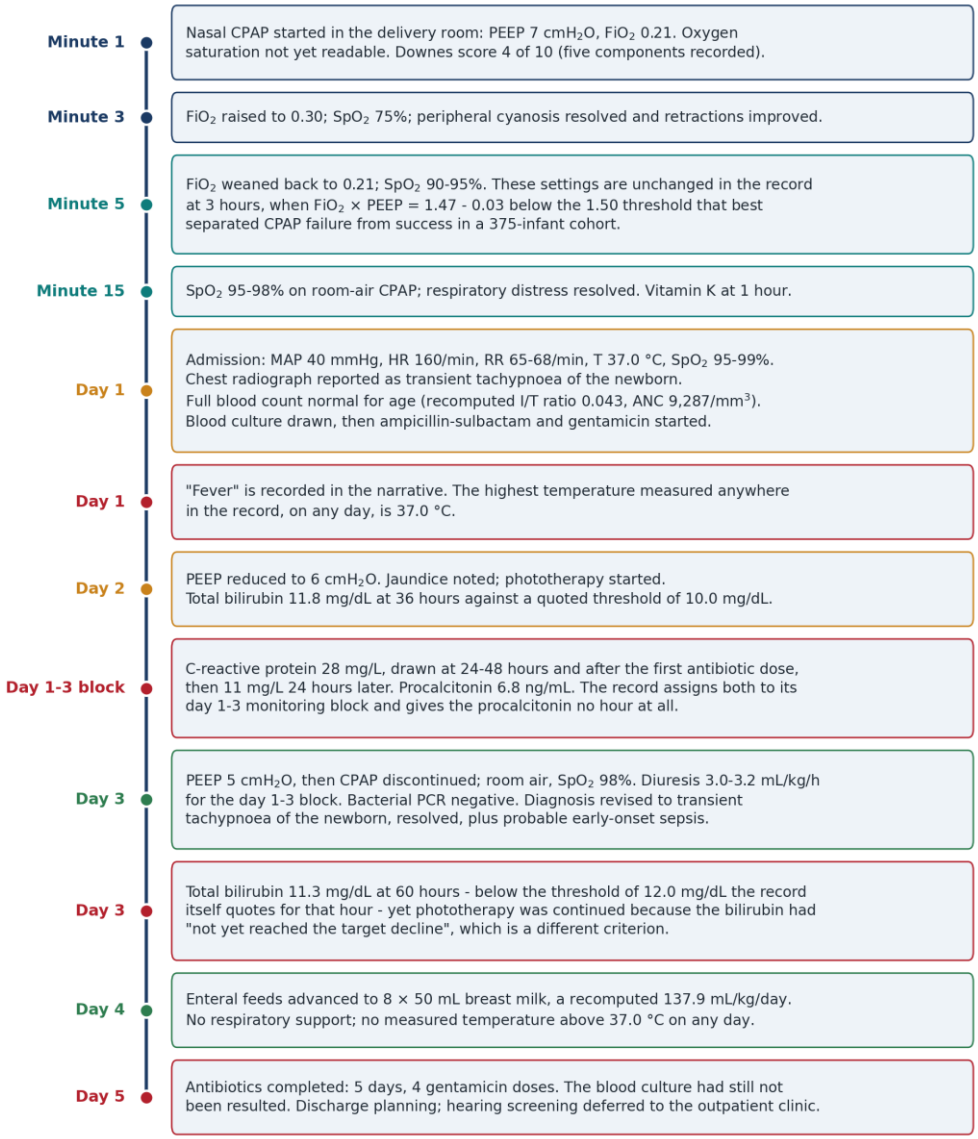

Figure 1. *The acute course, from the first minute of life to the fifth hospital day. Each entry carries what the record contains, together with four quantities recomputed here and marked as such: the product of the fraction of inspired oxygen and the positive end-expiratory pressure at three hours, the immature-to-total neutrophil ratio, the absolute neutrophil count and the enteral volume per kilogram. Routine items of the discharge plan that carry no time in the record – the vaccines, the newborn screening panel and the one-month blood count – are described in the outcome and discharge subsection of the Results and are not placed here. Colour marks the character of each entry rather than its severity: navy and teal for the delivery-room transition, amber for a new observation or a new treatment, green for an observation showing improvement, red for a point at which a measurement or a rule was applied outside the frame that makes it interpretable, and grey for routine care.*

Admission examination and the first investigations

At the admission examination the infant looked unwell and was less active than expected. Blood pressure was 65/35 mmHg with a mean arterial pressure of 40 mmHg, heart rate 160 beats per minute, respiratory rate 65 to 68 breaths per minute, axillary temperature 37.0 °C and oxygen saturation 95 to 99% on continuous positive airway pressure at a positive end-expiratory pressure of 7 cmH_2O and a fraction of inspired oxygen of 0.21. Weight was 2,950 g, length 44.0 cm, head circumference 32.0 cm, chest circumference 31.0 cm and abdominal circumference 32.0 cm. Nasal flaring and minimal epigastric retraction were present; breath sounds were bronchovesicular and symmetrical without crackles or wheeze; the cardiac examination was unremarkable; the liver was palpable a quarter of the way below the costal margin with a sharp edge and the spleen was not palpable; peripheral perfusion was good with warm extremities. All primitive reflexes were present.

The full blood count on the first day showed haemoglobin 20.0 g/dL, haematocrit 57.0%, leucocytes 13,460/mm^3, platelets 214,000/mm^3 and reticulocytes 5.77%. The differential count – basophils 0%, eosinophils 1%, band forms

3%, segmented neutrophils 66%, lymphocytes 18% and monocytes 12% – sums to 100. The absolute neutrophil count recomputed from those fractions is 9,287/mm³ and the absolute lymphocyte count 2,423/mm³, both within the reference band for the first hours of life. The immature-to-total neutrophil ratio is stated as 0.05 and recomputes to 0.043 from 3 band forms and 66 segmented neutrophils; a neutrophil-to-lymphocyte ratio of 3.6 appears in the record and recomputes to 3.83 if band forms are counted with the neutrophils and 3.67 if they are not. All three exceed 2.75, the value that maximised the area under the curve for that ratio in a 137-neonate Indonesian series – a curve whose area was 0.46, no better than chance – so nothing follows from crossing it.[16] The immature-to-total ratio sits far below the 0.20 threshold conventionally used. The peripheral smear showed no toxic granulation and no giant thrombocytes. The examination and the count, each value set beside its reference interval and beside what it does and does not support, are detailed in Table 2.

Two values in that count deserve to be named rather than passed over, and they are the haemoglobin of 20.0 g/dL and the haematocrit of 57.0%. Both sit in the upper part of the neonatal range, and in a comparative series of 64 infants with transient tachypnoea both ran significantly HIGHER in the less severely affected group rather than the more severely affected one, so in that series high-normal indices did not mark worse disease.[17] The haematocrit of 57.0% lies 8 percentage points below the venous threshold of 65% at which neonatal polycythaemia is defined, so this infant did not have polycythaemia; the sampling site is not recorded, and a capillary sample reads higher than a simultaneous venous one, which can only move the value further from the threshold rather than towards it. It is worth stating explicitly because polycythaemia is the one haematological condition that would have offered an alternative unifying explanation for respiratory distress and jaundice together: in a 21-year single-centre series, 51 of 53 term newborns meeting the polycythaemia definition (96.23%) were symptomatic and hyperbilirubinaemia was the commonest manifestation (69.81%).[18] That route to a unifying explanation is therefore closed, and the haematocrit row of Table 2 records how far from the definition the value sits. A second haematological route is not closed but is unlikely: both parents are recorded as blood group B, which excludes the maternal group O incompatibility that causes most ABO haemolytic disease, but the infant's own group, his rhesus status and a direct antiglobulin test are all absent from the record, and the reticulocyte count of 5.77% is within the range expected on the first day of life rather than raised.

Table 2. The admission examination and the day-1 full blood count, each value set beside the reference interval used at this unit and beside what the value does and does not support.

Measurement on hospital day 1	Recorded	Reference interval	What it does and does not support
Mean arterial pressure	40 mmHg	36–60 mmHg	within the interval, 4 mmHg above its lower bound; no inotrope was given or required
Heart rate	160 beats/min	100–180 beats/min	within range
Respiratory rate	**65–68 breaths/min**	40–60 breaths/min	tachypnoea, the presenting sign
Axillary temperature	37.0 °C	36.5–37.5 °C	**the narrative asserts fever on this day; this is the highest value recorded**
Oxygen saturation on CPAP	95–99% at PEEP 7 cmH_2O, FiO_2 0.21	90–100%	room-air oxygen from five minutes of life onward
Haemoglobin	20.0 g/dL	14–22 g/dL	upper part of the neonatal range
Haematocrit	57.0%	42–65%	8 percentage points below the 65% venous polycythaemia threshold; the sampling site is not recorded
Reticulocytes	5.77%	3–7%	within range for the first day of life
Leucocytes	13,460/mm³	5000–30000 /mm³	within range
Platelets	214,000/mm³	150000–450000 /mm³	within range
Differential count	band 3%, segmented 66%, lymphocyte 18%, monocyte 12%, eosinophil 1%, basophil 0%	sums to 100%	the six fractions sum to 100
Absolute neutrophil count	*not stated*	7800–14400 /mm³	recomputed as 9,287/mm³, within the reference band
Absolute lymphocyte count	*not stated*	2000–11000 /mm³	recomputed as 2,423/mm³
Immature-to-total neutrophil ratio	0.05	< 0.2	**recomputed as 0.043 from 3 bands and 66 segmented forms**
Neutrophil-to-lymphocyte ratio	3.6	the only published neonatal cut-off is 2.75[16]	**recomputed as 3.83 counting bands, or 3.67 counting segmented forms only**
Peripheral blood smear	no toxic granulation and no giant thrombocytes	-	no morphological marker of bacterial infection
Chest radiograph	reported as transient tachypnoea of the newborn	-	**the report places the infiltrates at the periphery; the case analysis calls them perihilar**
Lung ultrasound	*never performed*	*no result exists*	**the bedside test that separates the two diagnoses under consideration was not obtained**

Red marks a value outside its interval or in conflict with another statement in the record; grey marks a quantity the record does not contain.

CPAP, continuous positive airway pressure; PEEP, positive end-expiratory pressure; FiO_2, fraction of inspired oxygen. Absolute counts are the recorded leucocyte count multiplied by the corresponding differential fraction. The immature-to-total neutrophil ratio is the band count divided by the sum of the band and segmented counts; the single recomputed value of 0.043 sits well below the 0.20 threshold conventionally used. The only neonatal cut-off retrieved by the search described in the Introduction for the neutrophil-to-lymphocyte ratio is 2.75, which both readings here exceed – but it comes from a 137-neonate Indonesian series in which the neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios both performed no better than chance for neonatal sepsis (areas under the curve 0.46 and 0.47, P = 0.53 and P = 0.66), so no management follows from crossing it, and that series reports no cut-off for the immature-to-total ratio at all.[16] The polycythaemia threshold is a venous haematocrit of 65%; a capillary sample typically reads several points higher than a simultaneous venous sample, and the sampling site is not recorded here.

The chest radiograph

An anteroposterior chest radiograph was obtained on the first day. The report describes a midline trachea, a normal superior mediastinum, good lung expansion, a normal heart size with a cardiothoracic ratio below 60%, mild thickening of the horizontal fissure, bilateral diffuse radial pulmonary infiltrates extending to the peripheral lung fields, no reticulogranular opacity, smooth hemidiaphragms with sharp costophrenic angles and intact bony structures, and gives the impression of transient tachypnoea of the newborn. The image itself is reproduced in Figure 2, alongside a second panel marking the landmarks that can be identified at the resolution at which it survives in the source document.

Two things about that radiograph bear directly on what follows. The first is that the report and the narrative do not describe the same distribution: the report places the infiltrates as extending to the peripheral lung fields, while the case analysis in the same document calls them perihilar. The second is that the image is available only at a native raster of 384 × 272 pixels. Over the 2.62 in at which each panel of Figure 2 is printed that is about 147 pixels per inch, which is below the resolution at which fine parenchymal texture can be judged. We therefore do not re-adjudicate the reported infiltrates, and no annotation in the figure asserts them. That limitation is not incidental to the argument of this report: a single radiograph, read once, was allowed to sit against a clinical working diagnosis that contradicted it until the third hospital day, without being repeated and without any second imaging modality being brought to bear.

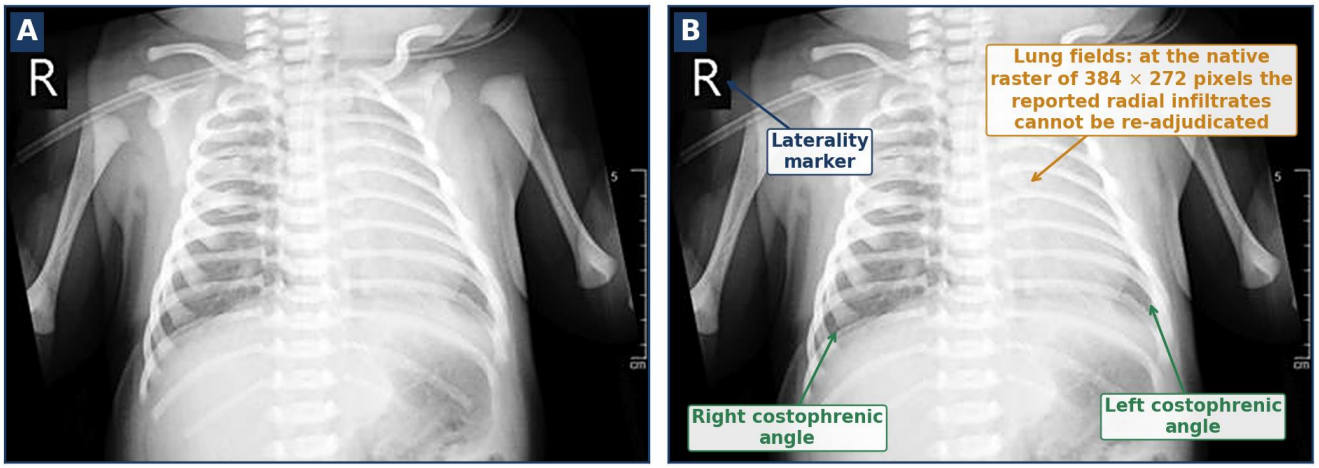

Figure 2. The chest radiograph obtained on the first day of life. ***(A)*** *The image as it appears in the source record, with contrast windowed to the 0.5th and 99.5th percentiles and no other processing.* ***(B)*** *The same image with the landmarks that can be identified at this reproduction resolution. The radiological report describes mild thickening of the horizontal fissure with bilateral diffuse radial infiltrates extending to the peripheral lung fields, no reticulogranular opacity, good expansion, a cardiothoracic ratio below 60% and sharp costophrenic angles, and gives the impression of transient tachypnoea of the newborn. The image is available only at a native raster of 384 × 272 pixels, which over the 2.62 in at which each panel is printed is about 147 pixels per inch; the parenchymal findings on which that impression rests therefore cannot be independently re-adjudicated here, and no annotation in panel B asserts them. The identity of the infant is not deducible from the image, and no burned-in text was present in the source. The tubing crossing the upper right hemithorax is the support circuit lying on the chest wall; it is not commented on in the report.*

Inflammatory markers, the blood culture and the molecular assay

A blood culture was drawn before the first antibiotic dose. Its inoculum volume is not recorded, no time of collection is given, and no result – positive or negative – appears anywhere in the record; on the fourth and fifth hospital days the plan still reads "waiting for blood culture results". A multiplex bacterial polymerase chain reaction was negative for all tested pathogens. C-reactive protein was 28 mg/L when first measured at 24 to 48 hours of life – that is, after antibiotics had been started – and 11 mg/L on a repeat 24 hours later, a fall of 60.7%. Procalcitonin was 6.8 ng/mL. The hour at which that procalcitonin sample was taken is not recorded anywhere in the document. The comparison detailed in Table 3 places each of these three results, together with the blood culture and the molecular assay, beside the population in which the reference interval or the published comparator it was judged against was derived, so that the frame each value carries can be read off the row rather than assumed.

Respiratory course

Respiratory support was weaned steadily. The positive end-expiratory pressure fell from 7 cmH_2O on the first day to 6 on the second and 5 on the third, at an unchanged fraction of inspired oxygen of 0.21 throughout, and support was discontinued on hospital day 3 with complete resolution of chest retraction and a saturation of 98% in room air. Respiratory rate fell from 65 to 68 breaths per minute on admission to 45 by the third day. Diuresis was 3.0 to 3.2 mL/kg/h for the day 1 to 3 monitoring block and 3.0 to 3.5 mL/kg/h for the day 4 to 5 block – the record reports observations by block rather than by day, so no single day carries its own figure – at or above the usual neonatal range of 1.0 to 3.0 mL/kg/h. The whole weaning sequence, with the hour or day at which each observation was made, is summarised in Figure 1.

Table 3. Each inflammatory marker measured in this infant set beside the population in which the interval it was judged against was derived.

Value in this infant	Comparator value, and the population in which it was derived	Where this infant's value falls
C-reactive protein 28 mg/L, drawn at 24–48 hours and after the first antibiotic dose	90th centile 7.60 mg/L and 97th centile 8.00 mg/L at 24 hours in the 36 PRETERM infants, against 10.80 and 12.00 mg/L in the 109 TERM infants, of one cohort of infants of at least 34 weeks screened for presumed early-onset sepsis who did NOT receive antibiotics[5]	**far above the 97th centile of the applicable preterm arm**
C-reactive protein 11 mg/L, 24 hours later	the same preterm arm of the same uninfected cohort[5]	**still above the preterm 97th centile of 8.00 mg/L, after a 60.7% fall in 24 hours**
C-reactive protein as a test	at a cut-off of 10 mg/L and drawn within 4 hours of the blood culture, sensitivity 41.7%, specificity 89.9%, positive likelihood ratio 4.12; drawn 24–72 hours after the culture, sensitivity rises to 89.5% but specificity falls to 55.7% and the likelihood ratio to 2.02, in 10,134 infants[6]	**the hour of the culture is not recorded, so neither sample can be assigned to a window; the second necessarily falls 24 hours or more after a culture drawn on day 1, in the window where the test discriminates least**
Procalcitonin 6.8 ng/mL, hour of sampling not recorded	upper 95% bound 4.39 ng/mL at 12–36 hours in 143 term samples and 4.44 ng/mL in 95 preterm samples, in a reference group from which infants with respiratory failure were EXCLUDED[8]	**above the bound, but the exclusion that defines this reference group is the condition this infant had**
The same value, 6.8 ng/mL	median 6.83 ng/mL at 12–36 hours in TERM neonates with respiratory failure and no bacterial infection[8]	0.03 ng/mL below that median
The same value, 6.8 ng/mL	median 9.56 ng/mL at 12–36 hours in PRETERM neonates with respiratory failure and no bacterial infection[8]	below that median
The same value, 6.8 ng/mL	median 49.82 ng/mL at 12–36 hours in preterm neonates WITH bacterial infection[8]	**roughly one seventh of the infected median**
The same value, 6.8 ng/mL	average peak 15.12 ng/mL at about 36 hours of life among 315 UNINFECTED very low birth weight preterm neonates, from 1,015 determinations[7]	**less than half the uninfected peak in that population**
Cord-blood procalcitonin was not measured	median 0.097 ng/mL, interquartile range 0.082 to 0.134, in 82 healthy newborns of more than 32 weeks[19]	*no baseline value exists for this infant*
Bacterial polymerase chain reaction, negative	sensitivity 14.8% for multiplex polymerase chain reaction against 7.4% for blood culture in 229 infants of whom 69% were preterm[20]	**a negative result excludes very little at this sensitivity**
Blood culture, never resulted	median time to positivity 21.0 hours, interquartile range 17.1–25.3, with 68% positive by 24 hours, 94% by 36 hours and 97% by 48 hours among 594 cultures growing pathogens within 72 hours of birth at 19 hospitals[9]	**the antibiotic course ran to 120 hours**
Blood culture volume, never recorded	median inoculum 1 mL, interquartile range 0.6–1.4, with 259 of 742 bottles (35%) below 0.9 mL[21]	*the yield of this culture cannot be assessed*

The point of the table is the second half of the middle column: a reference interval carries its derivation population with it, and three of the intervals available here were derived in populations that exclude this infant, differ from him, or are reported separately for an arm he does not belong to. Red marks a value that lies outside the interval that applies to him, or an interval that does not apply to him at all; grey marks a measurement the record does not contain.

Values in the middle column are transcribed from the source abstracts with their denominators. The procalcitonin reference interval of 0.14 to 4.39 ng/mL was derived after excluding neonates with respiratory failure; this infant required continuous positive airway pressure throughout the window in which the sample was most likely drawn, so his membership of the excluded group is an inference from the treatment he received rather than a stated match – the source does not define respiratory failure or give the size of that group. The same publication reports the median for neonates who DID have respiratory failure without bacterial infection, and that median is 6.83 ng/mL in term and 9.56 ng/mL in preterm infants.[8] Because the hour of sampling is not recorded, the comparison above places the value on the 12–36 hour curve as an approximation: at an earlier hour it would sit further below those medians, and at a later hour it would lie on the falling limb of the physiological curve, where the 12–36 hour medians do not apply. The C-reactive protein centiles are 24-hour centiles and the first sample was drawn later than that, which is the point made in the C-reactive protein subsection of the Discussion.

One quantity in that sequence is worth recomputing. Among 375 moderate and late preterm infants who required continuous positive airway pressure within the first 24 hours of life, of whom 45 (12%) went on to fail and require intubation within 72 hours, the variables measured at three hours that best separated failure from success were the fraction of inspired oxygen, with an optimal threshold of 0.23, and the product of the fraction of inspired oxygen and the positive end-expiratory pressure, with an optimal threshold of 1.50; a product above that threshold at three hours multiplied the modelled risk 19-fold.[22] The record documents a fraction of inspired oxygen of 0.21 and a positive end-expiratory pressure of 7 cmH_2O across that interval – the settings and the reason recorded for each change are tabulated day by day in Table 4, and its note sets out why an interval of unchanged settings is what the three-hour reading is read from – so the three-hour product for this infant is 1.47.

Jaundice and phototherapy

Jaundice was first noted on the second hospital day. The monitoring entry describes it as extending to the thighs and labels it Kramer zone 4; the physical examination in the same entry records Kramer zone 2; and the case analysis calls it Kramer zone 3. Jaundice extending to the thighs is zone 3 on the conventional scheme, in which zone 4 denotes the arms and legs below the knees, so the descriptor and the label attached to it do not agree.

Total bilirubin was 11.8 mg/dL at 36 hours of life, with indirect 11.1 and direct 0.3 mg/dL; the two fractions sum to 11.4 mg/dL, which is 0.4 mg/dL below the printed total. Intensive phototherapy was started, against a threshold the record quotes as 10.0 mg/dL for the high-risk category at that age. Twenty-four hours later the total was 11.3 mg/dL at 60 hours, with indirect 10.6 and direct 0.7 mg/dL, and these two fractions sum exactly to the printed total. The threshold the

record quotes for that later hour is 12.0 mg/dL. The bilirubin had therefore fallen 0.5 mg/dL while the threshold against which it was being compared had risen 2.0 mg/dL, so that at 60 hours the measured value lay 0.7 mg/dL below the threshold quoted for that hour. The plan recorded on the same day nonetheless reads "continue intensive phototherapy, as bilirubin has not yet reached the target decline". The five hospital days, with the respiratory and bilirubin observations and the arithmetic or threshold check each day permits, are tabulated in Table 4.

Table 4. The five hospital days, with the respiratory, bilirubin and physiological observations the record contains and, in the final column, the arithmetic or threshold check that each day permits.

Hospital day	Respiratory support	Bilirubin at the hour shown (mg/dL)	Other recorded observations	The check performed here
1	CPAP, PEEP 7 cmH_2O, FiO_2 0.21	*not measured*	MAP 40 mmHg (recomputes to 45.0), HR 160/min, RR 65–68/min, weight 2,950 g	FiO_2 × PEEP at three hours = 1.47, which is 0.03 below the 1.50 threshold
2	CPAP, PEEP 6 cmH_2O, FiO_2 0.21	total 11.8 at 36 h; indirect 11.1, direct 0.3	jaundice noted, phototherapy started; threshold quoted as 10.0	**the fractions sum to 11.4, which is 0.4 below the printed total**
3	PEEP 5 cmH_2O, then support discontinued	total 11.3 at 60 h; indirect 10.6, direct 0.7	room air, SpO_2 98%, RR 45/min; diuresis 3.0–3.2 mL/kg/h for the day 1–3 block; CRP 28 then 11 mg/L and PCR negative, both assigned to that block	**total 11.3 is 0.7 below the quoted threshold of 12.0, yet phototherapy was continued; these two fractions do sum correctly to 11.3**
4	*none*	*not repeated*	feeds advanced to 8 × 50 mL; no measured temperature above 37.0 °C on any day	enteral volume recomputes to 137.9 mL/kg/day, 92.0% of the 150 mL/kg/day definition of full feeds
5	*none*	*not repeated*	weight 2,900 g; diuresis 3.0–3.5 mL/kg/h; antibiotics completed	cumulative weight loss 100 g, 3.3% of birth weight

Red marks a check the record does not pass; grey marks an observation the record does not contain.

CPAP, continuous positive airway pressure; PEEP, positive end-expiratory pressure; FiO_2, fraction of inspired oxygen; MAP, mean arterial pressure; HR, heart rate; CRP, C-reactive protein; PCR, polymerase chain reaction. The product of the fraction of inspired oxygen and the positive end-expiratory pressure at three hours, together with the fraction of inspired oxygen alone, were the two variables that best separated continuous positive airway pressure failure from success among 375 moderate and late preterm infants supported within the first 24 hours of life, of whom 45 (12%) failed.[22] The record documents a fraction of inspired oxygen of 0.21 and a positive end-expiratory pressure of 7 cmH_2O continuously from five minutes of life to the admission examination, so the three-hour value is read from that interval rather than from a separately timed observation. Diuresis above 3 mL/kg/h on days 3 and 5 is at or above the usual neonatal range and is the expected accompaniment of fetal lung-fluid clearance. The record groups its observations into a day 1–3 block and a day 4–5 block rather than reporting each day separately, so the diuresis and the biomarker values are placed here on the last day of the block to which the record assigns them.

Nutrition, growth and fluid balance

The day-1 prescription reads: total fluid 60 mL/kg/day, that is 180 mL/day; breast milk four times 5 mL then four times 10 mL, giving 60 mL/day and 40 kcal/day; and parenteral nutrition of 180 mL/day containing 1.0 g of protein at 11.0% glucose, giving 67 kcal/day, for 107 kcal/day in total. The two energy figures reproduce: 60 mL of breast milk at 0.67 kcal/mL is 40.2 kcal, and 180 mL of 11.0% glucose contains 19.8 g of glucose, which at 3.4 kcal/g is 67.3 kcal. The volumes do not. The enteral and parenteral components sum to 240 mL/day, which at the birth weight is 80 mL/kg/day, not the 60 mL/kg/day the same prescription states; the discrepancy is 60 mL/day. Delivered energy on that day was 36.4 kcal/kg and delivered protein 0.34 g/kg, against a customary target of 1.5 to 2.5 g/kg/day.

On hospital days 1 to 3 the infant received breast milk 8 times 30 mL, that is 240 mL/day or 81.4 mL/kg/day at the recorded weight, with parenteral nutrition to a total fluid intake of 100 mL/kg/day providing 187 kcal/day. Because the record groups days 1 to 3 into one block, hospital day 1 carries two enteral volumes – 60 mL/day in the prescription and 240 mL/day in the block summary – which follows from the block format rather than contradicting anything, since the first is what was written on the first day and the second what was reached by the third. The record prints that as 65 kcal/kg/day; at the weight recorded on the same day it is 63.4 kcal/kg/day, and the printed figure implies a weight of about 2,877 g, which the record never records. On days 4 to 5 feeds were advanced to 8 times 50 mL, that is 400 mL/day or 137.9 mL/kg/day, providing 268 kcal/day, which the record prints as 90 kcal/kg/day and which recomputes to 92.4 kcal/kg/day at the weight recorded on that day. That second per-kilogram figure implies a weight of about 2,978 g, close to the birth weight, so two consecutive entries use two different denominators.

Weight fell from 3,000 g at birth to 2,950 g on the first day and 2,900 g on the fifth, a cumulative loss of 100 g or 3.3% of the birth weight, well within the physiological range. The monitoring plan specified daily weighing; 4 weights exist for five days and two of them are identical, so the nadir was never established. Enteral feeding was tolerated throughout without abdominal distension, vomiting or other gastrointestinal complication, and bowel actions were yellow and soft, two to three times daily, with adequate urine output. The weight and energy trajectories, together with the respiratory, biomarker and bilirubin trajectories, are shown in Figure 3.

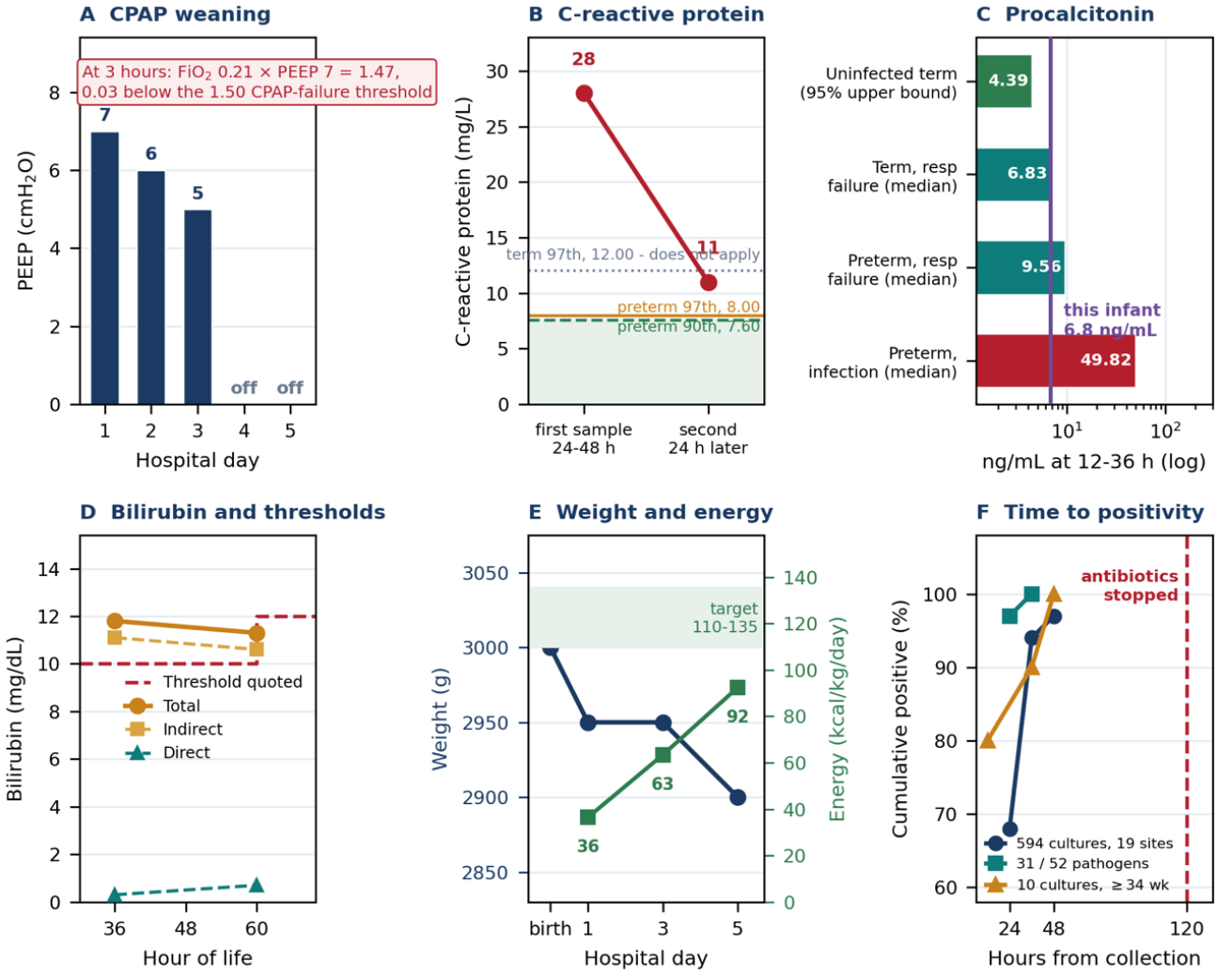

Figure 3. *Six panels: three trajectories from the recorded data, two comparisons of a recorded value against published reference distributions, and one panel of published time-to-positivity distributions with the hour at which this course was stopped marked on it.* ***(A)*** *Positive end-expiratory pressure fell by 2 cmH_2O across the first three hospital days at a constant fraction of inspired oxygen of 0.21, and support was then discontinued; the three-hour product of the two is annotated against the published failure threshold.* ***(B)*** *The two C-reactive protein values against the 90th and 97th centiles at 24 hours of the PRETERM arm of an uninfected reference cohort of infants screened for presumed early-onset sepsis who did not receive antibiotics; the term 97th centile is drawn in grey to show what reading the wrong arm would have looked like.[5] The first sample was drawn at 24 to 48 hours, later than the 24-hour reference, and the two samples are therefore plotted as first and second rather than at an hour the record does not give.* ***(C)*** *The single procalcitonin value against the four groups reported in the study from which its reference interval is taken; the uninfected term bar is the upper bound of a 95% range and the other three are medians, as labelled.[8]* ***(D)*** *Total, indirect and direct bilirubin at 36 and 60 hours against the phototherapy thresholds the record quotes; the total at 60 hours lies below the threshold quoted for that hour.* ***(E)*** *The four recorded weights, at birth and on days 1, 3 and 5 – the day-1 and day-3 values being identical – and the delivered energy on days 1, 3 and 5; the shaded band is the 110 to 135 kcal/kg/day range for a growing late preterm infant.* ***(F)*** *Cumulative blood-culture positivity by hour from three published series – 594 cultures at 19 hospitals, 31 then 52 pathogens in one level IV unit, and 10 positive cultures in infants of at least 34 weeks – with the hour at which antibiotics were actually stopped marked.[9,10,23]*

Antibiotic exposure and the stop rule

Empirical ampicillin-sulbactam 150 mg intravenously twice daily and gentamicin 15 mg intravenously every 36 hours were started on the first day after the blood culture was drawn. At the birth weight those doses are 100 mg/kg/day and 5 mg/kg/dose respectively, exactly the intended prescription; recomputed at the day-5 weight they are 103.4 mg/kg/day and 5.17 mg/kg/dose, both still within the intended range. The 36-hour gentamicin interval follows the unit's protocol for this postmenstrual age. Over the 5-day course, 4 gentamicin doses were given. No gentamicin trough or peak concentration and no serum creatinine were measured.

The stop rule the record sets on the third hospital day is explicit: "discontinue on day 5 if the blood culture remains negative". Antibiotics were stopped on day 5, and on that day the plan still records that the blood culture result was awaited. The rule was therefore never satisfied; the course ended because five days had passed. The antibiotic exposure, its dosing arithmetic, its monitoring and its duration are set out against the published comparators that bear on each in Table 5, and the relation between the accumulating evidence and the continuing exposure is illustrated in Figure 4.

Table 5. The antibiotic course, its dosing arithmetic, its monitoring and its duration, each set against the published comparator that bears on it.

Quantity	In this infant	Published comparator	Value in the comparator
Antibiotic regimen	ampicillin-sulbactam 150 mg twice daily and gentamicin 15 mg every 36 hours	a beta-lactam with an aminoglycoside is the standard first-line regimen; in a population-based French surveillance of 108 cases, 20 Escherichia coli isolates came from term and 15 from late preterm infants, and 5 of those 35 (14%) were resistant to both amoxicillin and gentamicin[24]	Escherichia coli caused 60% of late preterm cases in that surveillance
Dose per kilogram, computed on the birth weight	100 mg/kg/day and 5 mg/kg/dose	the same doses recomputed on the day-5 weight of 2,900 g	103.4 mg/kg/day and 5.17 mg/kg/dose
Gentamicin monitoring	*not recorded: no trough, no peak, no creatinine*	with standard dosing, trough concentrations lay outside the target range in 46.2% and peak concentrations in 46.0% of 335 neonates[25]	**about half of neonates miss target on standard dosing**
Gentamicin doses given	4 doses over 5 days	each dose of gentamicin, vancomycin or furosemide in the first 14 days carried an odds ratio of 1.25 (95% CI 1.14–1.38) for hearing loss among 57 cases and 180 matched controls born below 32 weeks – a population more preterm than this infant, and one in which the authors state the drug effect cannot be separated from the underlying illness[26]	**the screen for that harm was deferred to the outpatient clinic**
Duration	5 days, 120 hours	reducing empirical therapy from 48 to 24 hours with a formal time-out, in 414 newborns evaluated for possible early-onset sepsis at six units[11]	196 of 414 (47%) received the 24-hour course with no difference in the pre-specified safety endpoints
The stop rule as written	"discontinue on day 5 if the blood culture remains negative"	94% of cultures that will grow a pathogen have signalled by 36 hours and 97% by 48 hours[9]; all definite and possible pathogens had signalled by 36 hours in a level IV unit[10]	**the culture was never resulted, so the rule could not fire**
Days that the evidence would have avoided	**3.0 days against a 48-hour rule, 3.5 days against a 36-hour rule**	in 103 infants of at least 34 weeks, stopping in asymptomatic infants at 48 hours would have saved 217 antibiotic days, 31.1% of all days given[23]	217 days saved in one 5-year cohort
Where this course sits locally	5 days, culture-negative	median 9 days for culture-negative and 19 days for culture-proven early-onset sepsis, among the 242 suspected and 83 culture-proven cases identified from 2,509 neonates admitted within 72 hours to three Indonesian neonatal units; that case definition itself required five or more consecutive days of antibiotics[4]	shorter than that median, longer than the evidence supports
Where this course sits internationally	5 days	21,703 of 757,979 late preterm and term neonates (2.86%, 95% CI 2.83–2.90) received intravenous antibiotics in the first postnatal week, a median of 4 days (interquartile range 3–6) in those without early-onset sepsis[2]	58 neonates started and 273 antibiotic days for every case of early-onset sepsis
The class this admission belongs to	culture-negative, treated 5 days or more	culture-negative sepsis treated for 5 days or more occurred in 7,996 of 21,703 treated infants (37%), an incidence of 10.6 per 1,000 livebirths (95% CI 10.3–10.8)[3]	**21-fold more frequent than culture-proven early-onset sepsis**

Red marks a row in which the record falls short of what the comparator supports; grey marks a measurement the record does not contain.

CI, confidence interval. Doses were prescribed on the birth weight of 3,000 g and were not recomputed as the weight fell; at the day-5 weight the same prescription delivers 103.4 mg/kg/day of ampicillin-sulbactam and 5.17 mg/kg/dose of gentamicin, both still within the intended range. The 36-hour gentamicin interval is appropriate for this postmenstrual age. Rows 8 and 9 compare this single admission with cohort medians and row 10 with a cohort proportion; all three are offered to locate the course, not to claim that any individual course of this length is wrong.

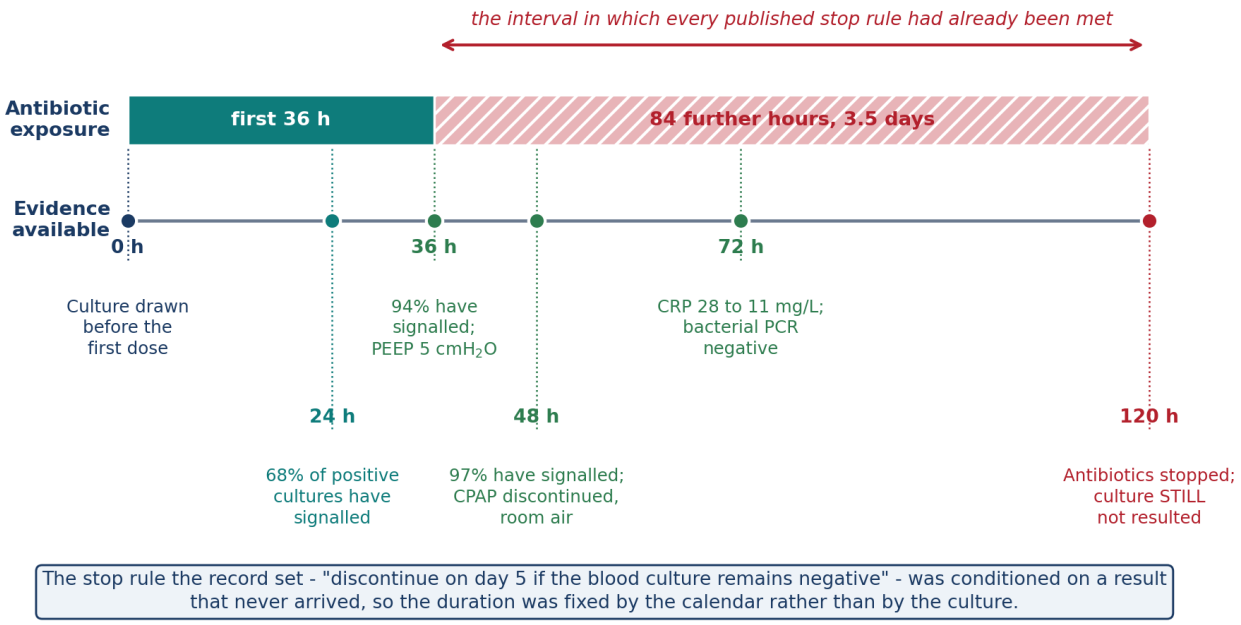

Figure 4. *The antibiotic course set against the evidence that accumulated beneath it. The upper bar is the exposure itself, divided at 36 hours; the lower track marks what was knowable at each hour. By 36 hours the published time-to-positivity distributions place the probability that a pathogen-growing culture has already signalled at 94%, the infant was weaning on continuous positive airway pressure, and by 72 hours C-reactive protein had fallen by 60.7% and the bacterial polymerase chain reaction was negative. The course nonetheless ran to 120 hours, because the stop rule the record set was conditioned on a culture result that never arrived.*

Outcome, diagnostic revision and discharge planning

The working diagnosis on the first day was respiratory distress of the newborn, suspected neonatal pneumonia with transient tachypnoea of the newborn as the differential, together with suspected early-onset sepsis and late preterm status. By the third day the assessment had been rewritten as respiratory distress due to transient tachypnoea of the newborn, resolved, together with probable early-onset sepsis, neonatal jaundice associated with preterm delivery, and late preterm status. The respiratory diagnosis was therefore revised – correctly, and on the strength of the clinical course – while the infective diagnosis was not merely retained but escalated in confidence, from suspected to probable, on a day when the C-reactive protein had fallen by 60.7%, the polymerase chain reaction had returned negative and respiratory support had been withdrawn.

The record states that the infant remained afebrile from the fourth day, although no temperature above 37.0 °C is recorded on any day, so there is no measured febrile period for him to have remained afebrile from. Enteral feeds were advanced to 137.9 mL/kg/day by day 4 and he was clinically stable at the close of the record. Hepatitis B vaccine was given on the first hospital day and oral poliovirus vaccine was planned for the day of discharge. Newborn hearing screening was not performed before discharge; the record states that it could not be completed during the admission because of limited resources and that the infant would be referred to the otorhinolaryngology clinic. Screening for congenital hypothyroidism and for glucose-6-phosphate dehydrogenase deficiency was planned for 48 to 72 hours of age and no result for either is recorded. Discharge planning included parental education, a repeat full blood count at one month to screen for anaemia of prematurity, and continued plotting of weight, length and head circumference on the Fenton chart. Figure 1 places the events of the acute course at the hour or day the record gives them; the routine items of the discharge plan listed in this paragraph carry no time in the record and are not placed there. The four red entries in that figure – the fever asserted but never measured, the two biomarkers assigned to a monitoring block rather than to an hour, the bilirubin that fell below its own quoted threshold while phototherapy continued, and the antibiotic course that outlived its own stop rule – are the points at which a measurement or a rule was applied outside the frame that makes it interpretable.

Internal discordances in the source record

Seventeen quantities are stated more than once in the source document with different values, or are stated in a form their own components do not reproduce. They are declared rather than silently reconciled, because a reader is entitled to know which numbers in this report rest on a single unambiguous statement and which do not. They comprise the birth length, the Downes score at birth, the lowest delivery-room saturation, the colour of the amniotic fluid, the maternal leucocyte count, the maternal gestational weight gain, the Kramer zone, the immature-to-total neutrophil ratio, the neutrophil-to-lymphocyte ratio, the bilirubin fractions at 36 hours, the day-1 fluid prescription, the energy per kilogram on days 1 to 3, the energy per kilogram on days 4 to 5, the distribution of the radiographic infiltrates, the mapping of the New Ballard score to a gestational age, the capillary refill time, and the day-1 mean arterial pressure. Seven are stated twice with two different values; the Kramer zone is stated three times with three; and the remaining nine are stated once in a form their own components, or the reference the record maps them to, do not reproduce. Where the two statements bracket a clinically meaningful boundary, both are printed and the boundary is named; where they do not, the discordance is recorded and the recomputed value is used. None of the seventeen, on the analysis set out in the biomarker, culture, risk-stratification, and stop-rule subsections of the Discussion, changes the conclusion reached about the antibiotic decision that is the subject of this report. Two of them do touch classifications the discussion uses, and both are named again where they are used: the two recorded birth lengths straddle the 10th Fenton centile, although the classification as appropriate for gestational age rests on the birth weight, which lies unambiguously between the 50th and 90th centiles, and the two recorded delivery-

room saturation nadirs sit on opposite sides of what would be called severe hypoxaemia. Those that concern the perinatal record are set out row by row in Table 1, those that concern the admission investigations in Table 2, and the bilirubin fractions in Table 4; the Kramer zone and the three nutritional discordances have no table row and are set out in the jaundice and nutrition subsections of the Results instead.

The parents' perspective

The parents were told on the first day that their son had respiratory distress, most likely pneumonia with transient tachypnoea as an alternative, and suspected early-onset sepsis related to prolonged rupture of membranes, and that intensive-care admission was needed for monitoring and respiratory support. They were counselled on completing the prescribed treatment, on exclusive breastfeeding, on hand hygiene, and on the signs that should bring the infant back urgently – poor feeding, fever or hypothermia, worsening respiratory distress, apnoea, cyanosis, lethargy or seizures. They were told that hearing screening is ideally done shortly before discharge, that it could not be arranged during this admission, and that it would be done through the outpatient clinic instead. On reviewing this manuscript the parents said that the part of the admission they had found hardest to follow was why the antibiotic was continued after they had been told their son was better, and they asked that the point be made plainly for other families; that request is one of the reasons this report is written the way it is.

4. Discussion

What the presentation could and could not distinguish

Grunting from birth in a late preterm infant born after prolonged rupture of membranes is compatible with both of the diagnoses that were entertained, and nothing in the presentation separates them. The five descriptors the record supplies – a respiratory rate of 60 to 80 per minute, mild retraction, cyanosis that resolved with supplemental oxygen, good and symmetrical bilateral air entry, and audible grunting – sum to a Downes score of 4, and nasal flaring, which was also present, belongs to the Silverman index rather than to this one. All of them measure the work of breathing rather than its cause. The modified Downes score is reproducible between observers: among 817 preterm infants scored concurrently and independently by a nurse and a physician across four tertiary units, the kappa statistic for the total was 0.89 and there was 98% concordance about the treatment threshold of 4.[27] A simplified version of the score, at a cut-off of 4 or more, predicted the receipt of surfactant among 168 infants weighing 2,000 g or less and of at least 25 weeks who were admitted on continuous positive airway pressure, with a sensitivity of 90.6% but a specificity of 52.2% and a positive predictive value of 46.6%.[28] Reproducibility and prognostic reach are not the same as aetiological discrimination, and neither of the two studies cited evaluates the score for aetiological discrimination at all. Acoustic analysis of the grunt itself has been attempted – 189 grunting segments from 38 infants yielded three spectral features related to the duration of hospital stay, with the harmonic ratio the most closely related – but that work is exploratory, uses expert ear grading as its reference and reports no accuracy figures.[29]

The maternal history pointed one way and the physiology pointed the other. Early-onset sepsis is not rare after preterm premature rupture of membranes: in a prospective three-centre cohort of 563 pregnancies with that complication, enrolled between 22 and 36+6 weeks and yielding 646 live-born neonates, the incidence was 29 of 646 (4.5%), and among the 26 neonates with microbiological samples the predominant organism was Escherichia coli in 14 (53.8%); that cohort had no unexposed comparator, so it gives an incidence rather than a relative risk, and oligohydramnios is not among its entry criteria.[30] Severity of oligohydramnios matters too: in 610 low-risk term pregnancies with incidental isolated oligohydramnios, a worse composite neonatal outcome occurred in 19.8% of those with the most severe reduction in amniotic fluid against 10.9% and 11.8% of the milder categories.[31] Against that, this infant's physiology was reassuring within minutes and stayed reassuring on the observations as the anamnesis records them: inspired oxygen returned to room air by the fifth minute of life and never rose again, and no saturation below 75% appears among them. The case analysis in the same document describes a nadir of 55 to 70% as severe hypoxaemia; that value appears nowhere in the observations, and if it were the true nadir the transition would have to be described differently. The maternal and perinatal profile listed in Table 1 records the severity of neither exposure: the oligohydramnios is described but never quantified by an amniotic fluid index, and the rupture latency is categorised rather than timed.

The antenatal determinants that separate a late preterm infant who will need support from one who will not are only partly captured by the four factors this record counts. Among 86 late preterm infants of 34 to 36+6 weeks, of whom 35 developed respiratory distress syndrome and 51 did not, male sex, placental abnormality, intrauterine distress, premature rupture of membranes and gestational diabetes were each independently associated with respiratory distress syndrome, while birth weight, gestational age and gravidity did not differ between the two groups at baseline and were not reported as entered into the model; the report gives P values only and no odds ratios, so the magnitude of each association cannot be quoted.[32] The effect of rupture of membranes on the infant is likewise entangled with maturity: in a retrospective comparison, infants born after preterm premature rupture of membranes had lower birth weights, lower gestational ages, higher maternal infection rates, longer hospital stays and a higher complication rate ($P < 0.001$ for each), but because they were also smaller and less mature the association is confounded by gestation and the report gives no adjusted estimates.[33] Histological chorioamnionitis is common after rupture but not universal: among 17,146 pregnancies screened, 726 (4.23%) had preterm prelabour rupture of membranes, and 160 of the 286 analysed cases developed histological chorioamnionitis, with an antepartum prediction model reaching an area under the curve of 0.785 in derivation and 0.710 in validation.[34] No placenta was sent for histology in this admission, so the investigation that would have confirmed or excluded histological chorioamnionitis – the mechanism by which rupture is supposed to act – was never obtained; nor was a vaginal sample taken at delivery, from which a metagenomic score predicted early-onset sepsis with an area under the curve of 0.75 (95% confidence interval 0.61 to 0.90) in a 310-neonate subset – while vaginal culture alone did not, its adjusted odds ratio of 1.6 (95% confidence interval 0.5 to 5.0) crossing unity.[30]

The delivery-room trajectory read against a published failure index

The most informative single number in the first hours was not a laboratory result. Among 375 moderate and late preterm infants supported with continuous positive airway pressure within 24 hours of birth, 45 (12.0%) failed and required intubation within 72 hours; those who failed had a fraction of inspired oxygen at three hours of 34.4 ± 15.9%

against 22.8 ± 4.1% in those who succeeded and a fraction-of-inspired-oxygen by positive-end-expiratory-pressure product of 1.8 ± 0.9 against 1.1 ± 0.3, and the thresholds that best predicted failure were 0.23 for the fraction of inspired oxygen and 1.50 for the product.[22] This infant's product at three hours was 1.47, and his inspired oxygen was 0.21, both on the success side of both thresholds.

That observation must be stated with its margin, because the margin is small. A product of 1.47 is only 0.03 below the threshold of 1.50. At a positive end-expiratory pressure of 7 cmH_2O, the fraction of inspired oxygen that would place this infant exactly on the threshold is 0.214, which is 0.4 percentage points of inspired oxygen above the value recorded. A blender set half a percentage point differently, or a three-hour observation timed slightly differently, would have moved this infant across the line. The honest reading is therefore not that the index predicted the outcome, but that it placed this infant on the favourable side by a margin narrower than the precision with which inspired oxygen is recorded, and that a threshold derived from group data cannot adjudicate a single infant. What did adjudicate it was the trajectory: a positive end-expiratory pressure that fell by 2 cmH_2O over two days at constant inspired oxygen, and support withdrawn on day 3. The weaning sequence is plotted in panel A of Figure 3. The day-by-day sequence, with the recomputed three-hour index and the arithmetic check each day permits, is tabulated in Table 4.

The accompanying diuresis of 3.0 to 3.2 mL/kg/h in the day 1 to 3 block and 3.0 to 3.5 mL/kg/h in the day 4 to 5 block, at or above the usual neonatal range, is the physiological signature of the mechanism transient tachypnoea proposes. Delayed clearance of fetal lung fluid depends on the postnatal switch of the pulmonary epithelium from secretion to absorption through the epithelial sodium channel and the sodium-potassium adenosine triphosphatase; in 70 term newborns sampled at 2 minutes, 1 hour and 24 hours, the expression of those transporters changed markedly within the first hour after birth and was lower in infants delivered by elective caesarean section without labour, correlating with cord-blood noradrenaline.[35] A parallel line of evidence implicates the perinatal glucocorticoid surge: in 37 late preterm and term neonates with transient tachypnoea delivered by elective caesarean section without labour and 40 controls, mean cord cortisol was 131.36 against 233.32 nmol/L (P = 0.0001; odds ratio 3.7, 95% confidence interval 1.40 to 9.53), and cord cortisol correlated inversely with the duration of tachypnoea (r = -0.678) and with the respiratory rate (r = -0.535).[36] Both of those comparisons were made in infants delivered by elective caesarean section without labour, and this delivery was spontaneous and vaginal, so the mechanism they describe is offered as a candidate rather than as one demonstrated in a population that includes this infant. The airway sodium-transporter assay is a research technique and was not available here; cord cortisol is not, and it was simply not measured – on the same cord specimen that would have carried the baseline procalcitonin discussed below. Neither needed to be measured for this admission to be managed correctly; the point is that a brisk diuresis coinciding with the withdrawal of distending pressure is what the fluid-clearance account predicts, and it is what the record shows.

Within transient tachypnoea itself, severity is partly predictable, and the markers that predict it were not the ones measured here. Among 64 infants with transient tachypnoea divided by Silverman score into 34 with a score below 7 and 30 with a score of 7 or more, the more severely affected group needed more nasal continuous positive airway pressure and longer oxygen therapy (P = 0.001) and had higher platelet counts, higher absolute and relative nucleated red cell counts and higher right ventricular systolic pressures (P < 0.05 for each), with the nucleated red cell count per 100 white cells the strongest independent predictor (odds ratio 7.065, 95% confidence interval 1.258 to 39.670, P = 0.026) – a very wide interval on a small sample.[17] Notably, haemoglobin and haematocrit in that series were significantly HIGHER in the less severely affected group, which is worth recording here because this infant had a haemoglobin of 20.0 g/dL and a haematocrit of 57.0% and mild disease. A separate line of work suggests that the oxidative burden of transient tachypnoea falls with treatment: in late preterm and term neonates, total oxidant status, oxidative stress index and total antioxidant status all changed significantly after continuous positive airway pressure, and disulfide fell from 26.2 (19.2 to 31.7) to 19.5 (15.5 to 28.75) after treatment (P = 0.001), although that study reports no sample size and had no untreated control group.[37]

Procalcitonin read outside its derivation population

The single value most often invoked to keep an infective label alive in this situation is the procalcitonin, and here it was 6.8 ng/mL. The record does not say which result drove the decision to continue; what it does say is examined in the antibiotic stop-rule subsection of the Discussion. Read against the interval most commonly quoted for neonates – a 95% range of 0.14 to 4.39 ng/mL at 12 to 36 hours in term samples – it is elevated. But that interval was derived in a reference group from which neonates with respiratory failure were deliberately excluded, and the same publication reports, separately, that the median at 12 to 36 hours in neonates who did have respiratory failure without bacterial infection was 6.83 ng/mL in term and 9.56 ng/mL in preterm infants, against 49.82 ng/mL in preterm infants with bacterial infection.[8] This infant's value of 6.8 ng/mL sits 0.03 ng/mL below the term respiratory-failure median, below the preterm respiratory-failure median, and at roughly one seventh of the preterm infected median. The exclusion that defines the reference interval is respiratory failure, and this infant required continuous positive airway pressure from the first minute of life and throughout the window in which the sample was most likely drawn. That source does not define respiratory failure or report the size of its respiratory-failure group, so his membership of it is an inference from the treatment he received rather than a stated match; it is nonetheless the more defensible of the two available frames, because the alternative is an interval built by excluding infants like him. Panel C of Figure 3 places the value against all four of those groups on one axis.

The physiological surge compounds the problem. Among 315 uninfected very low birth weight preterm neonates contributing 1,015 determinations, procalcitonin rose after birth to an average peak of 15.12 ng/mL at about 36 hours of life before falling.[7] That population is more premature than this infant, so the peak cannot be transferred directly; the relevant inference is narrower and more robust, namely that a single procalcitonin drawn somewhere in the first three days of life, without its hour recorded, cannot be placed on an age-specific curve with the precision the curve demands. The record assigns the sample to its day 1 to 3 monitoring block, so the comparison above is an approximation, and one that favours the reading offered here: on either limb of a curve that peaks at about 36 hours the age-appropriate comparator is lower than the 12-to-36-hour medians, so at any other hour the same value would sit nearer to or above them rather than below. For comparison, cord blood taken immediately after birth in 82 healthy newborns of more than 32 weeks had a

median procalcitonin of 0.097 ng/mL (interquartile range 0.082 to 0.134), unaffected by gestational age, sex, mode of delivery, birth weight, prolonged rupture of membranes or maternal fever[19] – a baseline against which a rise could have been read, had one been taken. None was.

The corollary is a specific recommendation rather than a general caution. A procalcitonin ordered in a neonate with respiratory distress should carry its hour of life on the request form, and the interval printed on the report should be the one derived in neonates with respiratory failure, not the one derived after excluding them. Where the laboratory cannot supply the second interval, the clinician should supply it, because the difference between 4.39 ng/mL and 6.83 ng/mL is the difference between a value that reads as abnormal and one that reads as expected. Table 3 is constructed to make that substitution explicit for every marker measured in this admission.

C-reactive protein without the hour that would make it interpretable

The first C-reactive protein was 28 mg/L, drawn at 24 to 48 hours of life and after the first antibiotic dose. Which reference it should be read against is itself the question this report is about. At 36 weeks and 1 day this infant belongs to the preterm arm of the reference cohort, not the term arm, and the two arms of that cohort do not have the same centiles: the 90th and 97th centiles at 24 hours were 7.60 and 8.00 mg/L in the 36 preterm infants against 10.80 and 12.00 mg/L in the 109 term infants.[5] Read against the applicable preterm arm, both of this infant's values lie above the 97th centile – 28 mg/L by a wide margin and 11 mg/L still above 8.00 mg/L – whereas read against the term arm the second value would have looked merely borderline. Choosing the wrong arm would have made the fall look more complete than it was, and it is the same class of error this report identifies in the procalcitonin. It is also unremarkable in a different sense: among healthy term infants without sepsis born after prolonged rupture of membranes, the median C-reactive protein at 36 hours was 4 mg/L but individual values reached 92 mg/L, and infants who received antibiotics had higher concentrations at every time point than those who did not ($P < 0.001$) despite none having sepsis.[38]

The greater difficulty is when the sample was taken. Drawn within four hours of the blood culture, a threshold of 10 mg/L gave a sensitivity of 41.7%, a specificity of 89.9% and a positive likelihood ratio of 4.12 in a two-unit cohort of 10,134 admitted infants; drawn 24 to 72 hours after the culture, the sensitivity rose to 89.5% while the specificity fell to 55.7% and the likelihood ratio to 2.02.[6] Those windows are measured from the blood culture, and the hour at which this culture was drawn is not recorded, so neither sample can be assigned to a window with certainty. What can be said is bounded on one side: the culture was taken on the first hospital day, the first C-reactive protein at 24 to 48 hours of life and the second a further 24 hours after that, so the second sample necessarily falls 24 hours or more after the culture – in the late window, where the test is most sensitive and least specific, and where an elevated value carries the least information about whether infection is present. The first sample cannot be placed at all, which is a defect of the record rather than a property of the test. The same investigators compared periods with and without routine C-reactive protein use and found early-onset sepsis evaluation fell from 74.5% to 50.5%, antibiotic initiation from 65.0% to 50.8% and antibiotic prolongation in the absence of sepsis from 17.3% to 7.2%, with no difference in the rate or timing of sepsis detection, transfer or in-hospital mortality.[6] A national analysis of 572 neonatal units found the same association at unit level. Units were grouped by the proportion of sepsis evaluations in which a C-reactive protein was drawn within three days of birth, in fixed bands rather than in quartiles; compared with low-use units, in which fewer than a quarter of evaluations included the test, high-use units, in which at least three-quarters did, continued antibiotics beyond three days more often (25% against 10%, adjusted risk ratio 1.95, 95% confidence interval 1.54 to 2.48) with no difference in mortality within seven days of birth (adjusted risk difference -0.02%, 95% confidence interval -0.04% to 0.0008%).[39]

What the two C-reactive protein values in this admission do carry is direction. A fall from 28 to 11 mg/L in 24 hours, a decline of 60.7%, is the trajectory of an inflammatory response that is resolving, and it occurred alongside a falling respiratory rate, a falling positive end-expiratory pressure requirement and a negative molecular assay. Panel B of Figure 3 plots that fall against the uninfected reference centiles. The information needed to stop was present; what was missing was a rule that could act on it.

A useful way to see how little an isolated elevated C-reactive protein adds is to compare it directly with a structured risk estimate. Among 382 newborns worked up for equivocal symptoms, of whom 373 (97.6%) ultimately had no sepsis, the calculator's specificity was 83.9% against 76.1% for C-reactive protein, and the correlation between the maximum C-reactive protein and the calculator-derived risk, though statistically significant ($P < 0.01$), was weak (Pearson coefficient 0.27); applying the calculator would have reduced sepsis workups by 82.5% and antibiotic treatment by 83.4%.[40] Those reductions are modelled rather than observed, and with only nine cases of sepsis in the cohort the sensitivity of either approach is essentially unestimable – but the weakness of the correlation is the point that transfers: the biomarker and the risk estimate are measuring substantially different things, and treating the biomarker as a proxy for the risk is a category error. The two C-reactive protein comparisons – against the applicable preterm centiles and against the timing of the sample – are set out in the first three rows of Table 3, which pairs each measured value with the population in which the interval it was judged against was derived. The calculator comparison is not in that table, because the calculator is not a reference interval.

The negative molecular assay and the culture that never resulted

A multiplex bacterial polymerase chain reaction returned negative. The record's own interpretation of that result – that it does not exclude the diagnosis – is correct, and the published performance of these assays supports it: in a prospective study of 229 infants at risk of neonatal sepsis, of whom 69% were preterm, the sensitivity of a multiplex polymerase chain reaction was 14.8% against 7.4% for blood culture, with more false positives from contamination.[20] A proof-of-principle molecular culture study of 40 clinical samples found one organism the peripheral blood culture missed, two contaminants and 37 samples negative by both methods, returning results within 4 hours against 36 to 72 hours for conventional culture.[41] A negative molecular result therefore neither confirms nor refutes; it is the timing, not the verdict, that these assays improve.

The blood culture is the more consequential absence. It was drawn correctly, before the first antibiotic dose. But its inoculum volume was not recorded, and volume is the determinant of yield that a neonatal unit can actually control: among 742 cultures from 292 neonates the median inoculum was 1 mL (interquartile range 0.6 to 1.4) and 259 bottles (35%) held less than 0.9 mL, with night-shift collection associated with lower volumes ($P = 0.006$).[21] Even in a unit

with an explicit 1 mL per bottle guideline, clinicians reported at least 1 mL in 96.9% of evaluations while direct weighing of 544 evaluations found 93.4%, and very low birth weight infants evaluated more than seven days after birth had the highest proportion of inadequate inocula at 14.4%.[42] Without the volume, the negative predictive value of this culture can be bounded only by those population distributions and not estimated for this bottle; that same study found no difference in sample volume between culture-negative sepsis, sepsis rule-outs and bloodstream infection (P = 0.5), which it describes as an absence of evidence in a modest sample rather than proof that volume is unrelated to yield.[21] The unrecorded volume is therefore not a clerical omission but a missing premise. The last three rows of Table 3 give the culture, its unrecorded volume and the molecular assay their published comparators, and the haematological panel reproduced in Table 2 is, with the chest radiograph, one of only two investigations of the first day that returned a result at all – and even that panel prints two derived ratios its own components do not reproduce.

Two further pieces of information that were available in this admission were never used in this way. The first is the full blood count itself. Among 1,103 neonates with pneumonia, of whom 330 also had sepsis, a low platelet-to-neutrophil ratio was independently associated with sepsis, and the incidence of sepsis was 43.9% in the low-ratio group against 15.9% in the high-ratio group (P < 0.01), with an area under the curve of 0.76 (95% confidence interval 0.73 to 0.80); the study reports no cut-off value and no group denominators, so it cannot be applied to an individual infant, but it illustrates that the count already drawn carries information about the very distinction being made.[43] The second is that the two strongest risk factors for neonatal pneumonia among low birth weight neonates – a birth weight below 1,600 g against 2,200 g or more (odds ratio 7.112, 95% confidence interval 1.650 to 30.651) and small-for-gestational-age status (odds ratio 2.598, 95% confidence interval 1.152 to 5.859), in 90 cases and 50 controls drawn from 230 low birth weight admissions – were both absent in this infant, who weighed 3,000 g and was appropriate for gestational age.[44] The confidence interval on the first of those odds ratios is extremely wide and no clinical decision should rest on it; the relevance here is the direction of the absent risk, not its magnitude.

Risk stratification, and what the four minor factors actually contribute

The record justifies empirical treatment by counting four minor maternal risk factors: prolonged preterm premature rupture of membranes, late preterm gestation, maternal vaginal discharge and maternal urinary tract infection. Each is real. What the count omits is the set of factors that were absent, and those absences carry more weight in every published model than the four that were present. There was no maternal intrapartum fever measured at any point, so fever was neither documented nor excluded; no clinical chorioamnionitis was recorded and no placenta was sent for histology, so histological chorioamnionitis was likewise neither confirmed nor excluded, in a condition where 160 of 286 pregnancies with preterm prelabour rupture in one series had it[34]; no known group B streptococcal colonisation, because no screening was done; and no intrapartum antibiotic prophylaxis, because the maternal antibiotic course treated a urinary tract infection before delivery and is not the same exposure. The highest maternal intrapartum temperature is one of the continuous inputs the neonatal early-onset sepsis calculator requires, alongside gestational age and the duration of rupture, so without it the calculator cannot be run at all; in the contemporary re-derivation of that calculator across 412,595 infants of at least 35 weeks with 113 cases, the updated model raised sensitivity from 0.76 (95% confidence interval 0.63 to 0.85) to 0.80 (95% confidence interval 0.68 to 0.89), a difference that was not statistically significant (P = 0.15), while recommended empirical antibiotic use rose from 3.5% to 3.7% (P < 0.0001); the authors compute that each additional case identified comes at the cost of 158 additional infants treated.[45]

The relevant comparison is not between models but between strategies. In 754 neonates of at least 34 weeks with risk factors for or symptoms compatible with early-onset sepsis, retrospectively applying the sepsis risk calculator or structured clinical observation instead of the laboratory screening actually used would have reduced laboratory testing from 56.8% to 9.9% and 22.4% respectively, admissions from 11% to 6.9% and 7.9%, and antibiotic use from 8.6% to 6.7% and 6.4% (all P < 0.01); 13 patients had sepsis and all but one – an asymptomatic Enterococcus faecalis bacteraemia – would have been detected by either strategy.[46] In a contemporary single-centre cohort of 184 infants of at least 34 weeks with at least one risk factor, of whom 43 (23%) had clinical signs and 1 (0.5%) was culture-positive, the local biomarker-augmented protocol treated 25 (14%), while categorical risk assessment would have recommended antibiotics for 46 (25%) and the sepsis risk calculator for 36 (20%).[47] The single most directly applicable study asked exactly the question this admission raises – whether sepsis evaluation and empirical antibiotics are mandatory for every neonate admitted with respiratory distress – and found that after an antimicrobial stewardship protocol, empirical treatment of neonates with respiratory distress fell from 95% to 41% with no cases of early-onset sepsis missed.[48] That study is a single-centre before-after series whose report states neither its total sample size nor the denominators behind either percentage, so "no missed cases" is an absence of events in an unknown denominator and cannot bound the residual risk.

Two further considerations belong here. First, the low-risk delivery characteristics under which no case of early-onset sepsis has yet been observed were absent: in 7,549 infants evaluated within 72 hours of birth from 53,575 births, 1,121 (14.8%) had all of caesarean delivery without labour or membrane rupture and no antepartum concern, and none of them had early-onset sepsis.[49] Zero events in 1,121 bounds that risk rather than estimating it, but the direction is clear, and this infant had none of those characteristics, so starting treatment was defensible. Second, the organism the empirical regimen most needed to cover in a late preterm infant is Escherichia coli, not group B streptococcus: in a population-based surveillance of 108 cases in infants of at least 34 weeks, Escherichia coli caused 60% of cases in late preterm infants, early-onset sepsis was six times more frequent in late preterm than in term infants, and 5 Escherichia coli strains (14%) were resistant to both amoxicillin and gentamicin.[24] The decision to start was right. The decision that requires examination is the decision to continue. The empirical regimen chosen, and the organisms it does and does not cover, are given in the first row of Table 5.

How much antibiotic exposure a deliberately low-risk late preterm and term population still attracts is itself instructive. In a review of 1,187 late preterm and term infants born by caesarean section with rupture of membranes of less than ten minutes – about as low a risk of ascending infection as it is possible to construct – an early blood culture was obtained from 234 (19.7%) and 170 (14.3%) were treated with antibiotics, and there were no cases of culture-proven early-

onset sepsis at all.[50] The infants who were treated were younger, smaller, more often diagnosed with respiratory distress and more often admitted to intensive care (P < 0.0001 for each), which is to say that in that practice it is the infant's own respiratory presentation, not the maternal risk profile, that drives the decision to treat. That is exactly what happened here, and it is not by itself a criticism; the criticism is that the same presentation was allowed to keep driving the decision after it had resolved.

The stop rule that could not fire

The rule the record sets is "discontinue on day 5 if the blood culture remains negative". It is conditioned on an event – the arrival of a negative culture report – that never happened. The consequence is that the course was not stopped by the culture but by the calendar, and the difference is not semantic. A rule of the form "stop at 36 hours unless the culture has signalled" fires on the passage of time, which is guaranteed; a rule of the form "stop on day 5 if the culture is negative" fires on the arrival of a report, which is not. Figure 4 sets the exposure against the evidence that accumulated beneath it.

The evidence points the same way in every setting, though not to the same number. Among 594 cultures growing a pathogen within 72 hours of birth at 19 hospitals, 68% had signalled by 24 hours, 94% by 36 hours and 97% by 48 hours, with a median time to positivity of 21.0 hours.[9] In a level IV unit, 30 of 31 definite pathogens (97%) had been reported by 24 hours and all 52 definite and possible pathogens by 36 hours.[10] In a single unit's 151 clinically relevant positive cultures the overall median was 17 hours (interquartile range 12 to 23), and all 13 early-onset cultures resulted within 24 hours.[51] In 103 infants of at least 34 weeks admitted over five years with suspected early-onset sepsis there were ten positive cultures, in which the time to positivity was under 12 hours in 80%, under 36 hours in 90% and under 48 hours in all of them; the mean time to positivity of pathogens was 17.7 ± 12.5 hours against 80.5 ± 55.8 hours for contaminants (P = 0.003), and discontinuing therapy in asymptomatic infants at 48 hours would have saved 217 antibiotic days, 31.1% of all days given.[23] A spread from 68% to 100% at the same hour is not consistency; the three series that report that hour rest on denominators of 594, 31 and 13, while a fourth of only 10 positive cultures reports at 12, 36 and 48 hours instead. The largest series is the most conservative of them, which is why a 36-hour rule is defensible on it. Panel F of Figure 3 plots three of those cumulative distributions against the hour at which this course was actually stopped.

Implementing that earlier rule has been done and audited. Reducing empirical therapy from 48 to 24 hours with a formal time-out was applied to 196 of 414 newborns evaluated for possible early-onset sepsis across six units, with no difference in the pre-specified safety endpoints of a positive blood or cerebrospinal fluid culture within seven days of discontinuation, or of overall and sepsis-related mortality.[11] The factors that prolong therapy when it is prolonged are known: among 131 neonates of at least 32 weeks with a negative blood culture, 47 (35.9%) received three days or more, and the reasons clinicians recorded were clinical appearance (38.3%), an elevated C-reactive protein (36.2%) and skin colour (10.6%).[52] All three were arguably operative in this admission: the infant looked unwell at the admission examination, the C-reactive protein was 28 mg/L when first drawn, and a jaundice whose Kramer zone the record labels three different ways was being treated from day 2 onward. Each has been examined above. Table 5 places this course beside the published comparators for each of its components, and Figure 4 shows how much of it fell after the point at which every published stop rule had already been met.

The cost of the extra days is not nothing. Stopping at 48 hours rather than at 5 days would have removed 3.0 days of exposure; stopping at 36 hours would have removed 3.5 days. In a randomised trial of 147 infants of at least 36 weeks treated with broad spectrum antibiotics for suspected early-onset sepsis for an average of 48 hours, gut microbial community composition and the antimicrobial resistance gene profile were both altered immediately after treatment (R^2 9.5% and 7.5%, adjusted P = 0.001 for both), with a decreased abundance of Bifidobacterium and increased Klebsiella and Enterococcus compared with 80 untreated infants drawn from a separate healthy birth cohort rather than randomised; the differences narrowed over 12 months but composition remained measurably different (R^2 1.1%, adjusted P = 0.03).[53] In a population-based cohort of 14,572 children of whom 10,220 (70%) received at least one antibiotic prescription in the first two years, early exposure was associated with childhood-onset asthma, allergic rhinitis, atopic dermatitis, coeliac disease, overweight, obesity and attention deficit hyperactivity disorder, with hazard ratios ranging from 1.20 to 2.89.[54] In 6,510 very preterm infants at low risk of early-onset sepsis, exposure of five to seven days was associated with moderate to severe bronchopulmonary dysplasia or death (adjusted odds ratio 1.23, 95% confidence interval 1.01 to 1.50).[55] None of those associations can be transferred to a single late preterm infant given four doses of gentamicin, and this report does not do so; they are cited to establish that the extra days have a cost direction, not to quantify a harm in this patient.

Better markers for the stopping decision are being sought. The most developed candidate, presepsin, is not yet ready to carry the decision alone. In a multicentre prospective cohort of 333 infants started on antibiotics for suspected early-onset sepsis, of whom 169 were preterm, presepsin measured at the moment of suspicion had an area under the curve of 0.60 (95% confidence interval 0.50 to 0.70) in term infants and 0.84 (95% confidence interval 0.73 to 0.95) in preterm infants, where a cut-off of 645 pg/mL gave a sensitivity of 100% and a specificity of 54%; the authors state explicitly that with 65 term and 15 preterm cases no firm conclusion can be drawn.[56] Until such a marker is validated, the stopping decision rests on the culture and the clinical course. The clinical course was available here well before day 5; the culture result, which on the published distributions should have been reportable by 36 hours, never was.

The test that was never done

The clinical question this admission was built around – transient tachypnoea or pneumonia – has a bedside answer that takes minutes and no radiation, and it was never sought. Among 160 newborns with suspected lung disease, of whom 142 were finally diagnosed with lung disease, lung ultrasound distinguished transient tachypnoea of the newborn with 100% accuracy and neonatal pneumonia with 96.8%, with an overall sensitivity of 95.77%, a specificity of 77.77% and a kappa of 0.846 against the final clinical diagnosis – a reference standard that may itself have been informed by the ultrasound, and a specificity computed on the 18 newborns in whom lung disease was excluded, so that each of them moves it by more than five percentage points.[57] In a prospective cross-sectional study of 100 neonates of at least 28 weeks, lung ultrasound agreed with chest radiography on pneumonia in 97.5% of radiograph-positive and 95% of radiograph-negative cases, and on respiratory distress syndrome in 94.7% and 100%, with 98.5% total agreement between the two. The comparator there was radiography

rather than an independent standard, so those are figures for agreement between two index tests and not for accuracy, and the report gives no per-diagnosis denominators.[58] A prospective multicentre study of 135 neonates with pathogen-confirmed pneumonia found the extent of pulmonary consolidation diagnosed severe disease with a sensitivity of 83.3% and a specificity of 85.2%, while noting explicitly that ultrasound cannot identify the pathogen.[59]

Ultrasound also speaks to the two respiratory decisions this admission actually made. In 130 newborns of at least 36 weeks with postnatal respiratory distress scanned at 30 and 60 minutes, a lung ultrasound score above 5, an inspired oxygen fraction above 0.21 and respiratory acidosis at 30 minutes were associated with needing continuous positive airway pressure for an hour or longer, in a model with an area under the curve of 0.87 and good interrater reliability (intraclass correlation 0.76 to 0.77) developed and evaluated in the same 130 infants and, by the authors' own statement, awaiting independent validation; the double lung point and pleural line abnormalities were frequently seen.[60] For the other end of the course, in 41 infants born below 32 weeks with previous respiratory distress syndrome – not a population this infant belongs to – a lower score in the seven days before an attempt was associated with successful discontinuation of continuous positive airway pressure (odds ratio 0.46, 95% confidence interval 0.23 to 0.91, P = 0.025), and adding the score to clinical variables raised the cross-validated area under the curve from 0.85 to 0.90.[61] A score obtained at the bedside also tracks the clinical score clinicians already use: among 100 neonates with respiratory distress, the lung ultrasound score correlated with the Downes score (Pearson coefficient 0.712, P < 0.001) but not with the chest radiograph score.[62] A retrospective pilot analysis of cardiopulmonary ultrasound in term and late preterm infants with transient acute respiratory distress identified seven sonographic phenotypes and suggested that up to half had signs of raised pulmonary vascular resistance, though it reports no sample size and the phenotypes remain hypotheses.[63]

The practical argument for adopting it is not only diagnostic. Introducing lung ultrasound as the first-line study in a neonatal unit reduced the proportion of infants undergoing chest radiography was 71.2% in 104 infants against 100% in 73 historical controls, and the radiation dose 4.47 against 5.54 microgray per infant; the comparison is uncontrolled for secular change in practice across the four years it spans, and the report gives neither counts nor P values.[64] In this admission a single radiograph was obtained, read once, never repeated, and left standing in contradiction to the working respiratory diagnosis until that diagnosis was revised on the third day. That examination is the eighth of the twelve measurements set out in Table 6, each listed there with the moment at which it must be obtained and the decision in this admission it would have changed. The strength of that claim should be stated with the studies' own caveats: in the 160-newborn series the reference standard was the final clinical diagnosis, which may itself have been informed by the ultrasound, and the disease-specific accuracies of 100% rest on case numbers the report does not state[57]; in the 135-neonate multicentre study the authors state explicitly that ultrasound cannot identify the pathogen and that their accuracy figures grade severity within confirmed pneumonia rather than detect it.[59] The ultrasound would very probably have resolved the contradiction on the first morning; it would not have resolved it with certainty. The image presented in Figure 2 is the only imaging this admission produced, and row 8 of Table 6 records the test that was never performed.

Jaundice: a threshold crossed downward, and a phototherapy course that continued

Indirect hyperbilirubinaemia developing after 24 hours in a late preterm infant establishing feeds is expected, and treating it was reasonable. Two features of the way it was managed are worth setting out. The first is arithmetic: the fractions at 36 hours sum to 11.4 mg/dL against a printed total of 11.8 mg/dL, while the fractions at 60 hours sum exactly. The second is the direction of the comparison. Between the two measurements the total fell 0.5 mg/dL while the threshold the record quotes rose from 10.0 to 12.0 mg/dL, so that the second value lay 0.7 mg/dL below the threshold quoted for its own hour. The plan on that day nevertheless reads that phototherapy should continue because the bilirubin had not reached the target decline. A target decline is not the same criterion as a treatment threshold, and mixing them is how a course of phototherapy outlives its indication. Panel D of Figure 3 shows the two measurements against the two thresholds the record quotes. Both measurements, both quoted thresholds and both arithmetic checks are recorded in Table 4.

Two further observations follow. The direct fraction rose from 0.3 to 0.7 mg/dL while the indirect fraction fell; both values remain within the normal range, and the rise is therefore not evidence of the cholestatic picture that sepsis would produce, so the attribution of the jaundice partly to "concurrent probable sepsis" is unsupported by the fractions themselves. And the thresholds quoted – 10.0 mg/dL at 36 hours and 12.0 mg/dL at 60 hours for the high-risk category – correspond to the pre-2022 convention. After the 2022 revision of the American Academy of Pediatrics thresholds, phototherapy use across a network of eight hospitals and more than 22,000 newborns of at least 35 weeks fell from 3.9% to 2.1% (P < 0.001), and total serum bilirubin measurements fell 23% from 712 to 551 per 1,000 newborns (P < 0.001), with no observed increase in readmissions for phototherapy.[65] We do not claim that this infant would have gone untreated under the current convention, because the record does not state which risk factors were applied; we note only that the same numbers would today be read against higher lines. Bilirubin binding adds a further caution: among 132 healthy term and late preterm infants, unbound bilirubin correlated with total serum bilirubin overall but not above 12 mg/dL, and post-phototherapy values were similar to pre-treatment values.[66] Risk models for phototherapy in this population are driven largely by feeding and delivery variables; in 8,242 neonates the best model reached an area under the receiver operating characteristic curve of 0.911, with mode of delivery, daily formula intake, breastfeeding frequency, maternal body mass index and maternal white cell count as the strongest predictors.[67] Item 12 of **Table 6** is the screening result that would have completed this account and that the record never reports.

Nutrition, growth and the arithmetic that does not close

Enteral feeding was started early and advanced without intolerance, which is the correct approach and one that non-invasive respiratory support does not contraindicate. The unit recorded full enteral feeds on day 4, by its own criterion. For context, two randomised trials in the same population report almost identical timings: in the factorial DIAMOND trial of 532 infants born at 32+0 to 35+6 weeks, time to full enteral feeding was 5.8 ± 1.5 days with taste and smell exposure and 5.7 ± 1.9 days without (P = 0.59), and neither parenteral amino acids nor milk supplementation altered body fat at four months (adjusted mean differences -0.20, 95% confidence interval -1.32 to 0.92, P = 0.72, and 0.65, 95% confidence interval -0.45 to 1.74, P = 0.25).[68] In a blinded

randomised trial of 201 infants born at 32+0 to 36+6 weeks with a birth weight of at least 1,500 g, mean time to full enteral feeds was 5.7 ± 2.6 days on donor milk and 5.8 ± 3.4 days on formula (adjusted mean difference -0.07, 95% confidence interval -0.90 to 0.76), although infants given donor milk regained birth weight more slowly (10.7 ± 5.7 against 8.4 ± 4.4 days; hazard ratio 0.65, 95% confidence interval 0.47 to 0.88).[69] In a non-randomised cohort of very low birth weight infants – a population more preterm than this one – rapid enteral advancement combined with non-invasive ventilation did not impede that support, and a head-circumference difference persisted to two years (P = 0.034) in the 74.4% of the cohort followed up, with no difference in mental or psychomotor developmental indices.[70] Measured against the 150 mL/kg/day definition both randomised trials used, however, this infant was at 137.9 mL/kg/day on days 4 to 5, which is 92.0% of that target – so the honest comparison is that this admission is comparable to, rather than faster than, the 5.7 to 5.8 days those trials report.

The arithmetic of the prescription is a different matter, and it is worth setting out because it is invisible to reading and obvious to recomputation. The day-1 prescription states a total fluid intake of 60 mL/kg/day, that is 180 mL/day, while its own components – 60 mL enteral and 180 mL parenteral – sum to 240 mL/day, which is 80 mL/kg/day at the birth weight and 81.4 mL/kg/day at the weight recorded on the same day. The two energy figures on that day both reproduce from the volumes given to the nearest whole kilocalorie – 40.2 printed as 40 and 67.3 printed as 67 – which means the volumes were used to compute the energy and the stated total was written separately. Delivered protein on day 1 was 0.34 g/kg/day against a customary target of 1.5 to 2.5 g/kg/day, and delivered energy 36.4 kcal/kg/day. By days 4 to 5 the infant was receiving 137.9 mL/kg/day of breast milk, 92.0% of the 150 mL/kg/day definition of full feeds used in both trials cited above – a definition whose other limb is exclusive breast-feeding, which he had already met, so the two limbs do not agree here – providing 92.4 kcal/kg/day – 84.0% of the lower bound of the 110 to 135 kcal/kg/day range for a growing late preterm infant, a shortfall of 17.6 kcal/kg/day. Panel E of Figure 3 plots that energy trajectory against the target band alongside the weight.

The per-kilogram figures the record prints do not use a consistent denominator. On days 1 to 3, 187 kcal/day is printed as 65 kcal/kg/day, which implies a weight of about 2,877 g; on days 4 to 5, 268 kcal/day is printed as 90 kcal/kg/day, which implies about 2,978 g. Neither implied weight is the weight recorded on the corresponding day. The practical remedy is simple and belongs in any unit's charting: print the weight used for the calculation next to the per-kilogram figure. The same discipline would have exposed the day-1 fluid discrepancy at the bedside rather than in a later audit. The daily observations against which those figures should have been checked are listed in Table 4.

Composite scores whose components are not documented

Two composite scores in this record invite reconstruction from what the record contains, and they behave differently. The Downes score of 4 can be reconstructed: its five descriptors are all present and they sum to 4. The New Ballard score of 30 cannot. That instrument has twelve items, six physical and six neuromuscular; the record documents 4 scorable physical descriptors and none of the six neuromuscular items – posture, square window, arm recoil, popliteal angle, scarf sign and heel-to-ear. Worse, the four physical descriptors that are recorded do not agree with each other: an anterior transverse plantar crease only corresponds to about 34 weeks on the maturity grid, a stippled areola with a 1 to 2 mm bud to about 36 weeks, rugae with both testes descended to about 38 weeks, and thick, stiff ear cartilage to about 40 weeks – a spread of 6 weeks across four items of the same instrument. The record then maps a total of 30 to "36–38 weeks", whereas the maturity grid assigns 36 weeks to a total of 30 and 38 weeks to a total of 35, so the printed range spans two grid points.

The reassurance in this instance is that the dating does not depend on the score. Gestational age computed from the recorded last menstrual period is 36 weeks and 1 day, and the New Ballard total of 30 maps to 36 weeks, so the two estimates differ by 1 day and the classification as late preterm is secure whichever is preferred. That agreement is fortunate rather than guaranteed. Against early-trimester ultrasound in 1,114 neonates, the expanded New Ballard score overestimated gestation by 0.65 weeks, the Parkin score by 0.68 weeks and the Eregie score by 0.32 weeks, with the Eregie score achieving the highest validity at 79.6%.[14] A prospective comparison in 106 infants with a median gestation of 34 weeks found mean biases of -0.14 weeks for the Ballard score and 0.06 weeks for an unstructured clinical assessment, but wide limits of agreement, and none of the methods tested met the pre-specified standard of placing gestation within one week of the true value.[15] The classification of birth weight is similarly chart-dependent: among 2,541 neonates, 171 (6.7%) were classified differently by INTERGROWTH-21st and Fenton charts, with agreement falling from a kappa of 0.88 in preterm to 0.71 in full-term categories.[13] A composite score should therefore be charted item by item, not as a total, and a report of gestational age should name the method that produced it. Both estimates, and the four physical descriptors the record supplies, are given in Table 1, and the recomputed haematological indices in Table 2. Item 9 of Table 6 is the set of neuromuscular descriptors that would have made the printed total reproducible.

Diagnostic revision, discharge and what happens after the record ends

The respiratory diagnosis in this admission was revised, and revised correctly. That is worth naming, because the commoner failure runs the other way. In a multicentre retrospective review of 882 randomly selected children admitted non-electively to four academic paediatric intensive care units, 13 (1.5%) had a diagnostic error within seven days of admission; infections and respiratory conditions were the commonest missed diagnoses, and the commonest missed opportunities were failure to consider the diagnosis despite a suggestive history and failure to broaden diagnostic testing, each present in 69% of the errors.[71] Diagnostic uncertainty on admission was associated with error (odds ratio 9.67, 95% confidence interval 2.86 to 44.0), while the association with atypical presentation had a confidence interval that crosses one (odds ratio 4.58, 95% confidence interval 0.94 to 17.1) and should not be quoted as significant despite the source describing it so. This admission did broaden its testing and did revise its diagnosis. What it did not do was withdraw the label it had stopped needing, and a retained diagnosis is a diagnostic error of a quieter kind: it carries forward into the discharge summary, into the next admission's history, and into the antibiotic decisions that a future clinician will make on the strength of a documented episode of probable early-onset sepsis. Figure 1 shows the day on which the respiratory diagnosis was revised and the day on which the antibiotic course finally ended, and the gap between them is the subject of this report.

The follow-up this infant needs is therefore not only the respiratory and audiological surveillance already planned.

Late preterm and term infants readmit at a measurable rate in a predictable window: among 5,408 infants of at least 36 weeks discharged from a well-baby nursery, 219 (4.0%) were readmitted within the first 28 days at a mean age of 13.3 ± 7.1 days, and the leading causes as that report prints them were respiratory tract infection (29.58%), jaundice (13.70%) and urinary tract infection (9.59%) – the second and third of which resolve exactly on a denominator of 219 while the first does not.[72] The two commonest causes are precisely the two conditions this admission treated, so the counselling given to the parents about when to return is the intervention with the clearest yield among the discharge interventions available, though no comparative data rank it against any other. Beyond the neonatal period, transient tachypnoea is not entirely benign: in a matched analysis of 645 children with transient tachypnoea against 187,809 without, emergency-department visits for asthma were 2.05 times more frequent (95% confidence interval 1.46 to 2.89, P < 0.001) by six years of age.[73] The same report gives a 38% increase in asthma diagnoses (95% confidence interval 1.18 to 1.51, P < 0.001); a third estimate, for short-acting beta-agonist prescriptions, carries a confidence interval of 1.1 to 2.89 that is not internally consistent with the stated 28% increase and is therefore not reproduced here. That study was conducted in term infants and its groups were markedly unequal in size, so the magnitude does not transfer to a late preterm infant; the direction is enough to justify asking about wheeze at the routine visits rather than waiting for it to be reported. The exposures that generated both of them are recorded in Table 1.

What this admission did well

It would misrepresent the record to present it only as a list of shortfalls, and several decisions in it were exactly right. Continuous positive airway pressure was started at the first minute of life rather than after a period of observation, and inspired oxygen was titrated down as soon as saturation allowed rather than left elevated; the infant was in room air from the fifth minute. The value of early distending pressure in this population is supported by a multicentre randomised trial in which 20 minutes of prophylactic continuous positive airway pressure after caesarean birth reduced the need for respiratory support at 30 minutes (odds ratio 0.4, 95% confidence interval 0.2 to 0.9) and unplanned neonatal intensive care admission (odds ratio 0.35, 95% confidence interval 0.1 to 0.9) among 115 late preterm infants, although the duration of support in the first week did not differ[74] – a trial in caesarean births, so it applies to this vaginally delivered infant only by analogy. Vitamin K was given within the first hour, which matters: in a nationwide cohort of 2,020,302 Swedish live births of at least 35 weeks, the 24,089 infants with no record of intramuscular vitamin K had higher adjusted odds of bleeding (1.52, 95% confidence interval 1.27 to 1.81) and of intracranial bleeding (2.91, 95% confidence interval 2.13 to 3.96) in infancy.[75] The blood culture was drawn before the first antibiotic dose. Enteral feeding was begun early and advanced without complication. The gentamicin dose and interval followed the unit's protocol for this postmenstrual age, and neither is in question here. And the respiratory diagnosis was revised, on the third day, on the strength of the clinical course rather than of any single test – which is the right basis for revising it.

The five-day course also sits below a local median, though not a clean comparator. In three Indonesian neonatal units the median duration for culture-negative early-onset sepsis was 9 days and for culture-proven disease 19 days, with gram-negative organisms accounting for 85 of 94 isolates (90.4%).[4] Across low- and middle-income settings the picture is one of escalation rather than restraint: in a prospective cohort of 3,204 infants with clinical sepsis at 19 sites in 11 countries, 206 different empirical combinations were started in 3,141 of them, 728 of 2,880 initial regimens (25.3%) were escalated, and mortality was 350 of 3,204 (a rate that report prints as 11.3%, 95% confidence interval 10.2 to 12.5, where the two counts themselves give 10.9%).[76] Where culture-proven sepsis does exist, the direction of travel is also towards shorter courses: a randomised non-inferiority trial in eight centres found 2 of 125 relapses on a seven-day course against 6 of 130 on a fourteen-day course (risk difference -3.0%, 99.5% confidence interval -9.2% to +3.1%), with a shorter hospital stay by a median of 4 days, although the trial stopped early at an interim analysis with far fewer participants than planned.[77] Judged against its own setting, this admission was conservative. Judged against the time-to-positivity evidence, it was 3.0 days longer than a 48-hour rule and 3.5 days longer than a 36-hour rule would have allowed. Both statements are true, and the second is the one that can be acted on. Both readings are given side by side in row 8 of Table 5, the days each rule would have saved are in row 7, and the interval they disagree about is the shaded portion of Figure 4.

A minimum data set

Almost everything that made this admission hard to adjudicate was a measurement that was either not taken, or taken without the one attribute that makes it interpretable. A fever was asserted on hospital day 1, and no temperature recorded on that day or on any other reached the threshold; on the maternal side no temperature appears at all. A rupture-to-delivery interval was categorised and never timed. A procalcitonin was measured and never dated. A culture was drawn and its volume never recorded, and its result never reported. A radiograph was taken once and never repeated, while the one modality that would have settled the question was never used at all. Table 6 sets out twelve such items, each with the moment at which it must be obtained and the decision in this admission that it would have changed. Nothing in the list requires equipment beyond the assays this unit already runs – a full blood count, C-reactive protein, procalcitonin, a blood culture and the newborn screening panel – together with a thermometer, a clock, scales, an ultrasound probe and an otoacoustic-emission device.

Two of the twelve deserve emphasis because they close loops this admission left open. Item 5 is the hour at which the blood culture was declared negative, for the reason set out in row 5 of that table; recording it costs nothing. Item 11 is the pre-discharge hearing screen. Four gentamicin doses were given, and in a case-control study of 57 children with hearing loss and 180 matched controls born below 32 weeks, each dose of gentamicin, vancomycin or furosemide in the first 14 days carried an odds ratio of 1.25 (95% confidence interval 1.14 to 1.38) and each day of medication exposure an odds ratio of 1.23 (95% confidence interval 1.1 to 1.37), although the authors state explicitly that the contributions of the drugs and of the underlying illness cannot be separated.[26] Where the resource exists, the exposure can be avoided in the susceptible infants who are successfully tested: a point-of-care test for the mitochondrial m.1555A>G variant returned a genotype in 26 minutes in 751 neonates across two units, identified three carriers who all avoided aminoglycosides, and did not delay the time to antibiotics, although 424 of the antibiotic-treated infants (80.6%) were successfully tested and the rest were not.[78] The variant is rare – no carrier was found among 479 maternal samples in one biobank series, in which 15.9% of mothers and 13.9% of neonates had

aminoglycoside exposure, and a series with no carrier in it yields no prevalence estimate[79] – so the screen that matters most for most units remains the audiological one, performed before the infant goes home rather than after. Both items appear in Table 5 as well, where the gentamicin exposure is set beside the published risk per dose, and the interval that Figure 4 shades is the interval during which those doses continued to accumulate.

Table 6. A twelve-item minimum data set for a late preterm neonate started on antibiotics for suspected early-onset sepsis.

	Measurement	Moment at which it must be obtained	Why it would have changed what was done
1	*Maternal intrapartum temperature – never recorded*	at least hourly from rupture of membranes until delivery	The highest maternal intrapartum temperature is one of the continuous inputs the neonatal early-onset sepsis calculator requires, alongside gestational age and the duration of rupture; without it the calculator cannot be run.[45] No maternal temperature appears anywhere in this record; the only assertion of fever is neonatal, for hospital day 1, and no neonatal temperature above 37.0 °C is recorded on any day.
2	**Latency from rupture of membranes to delivery, in hours**	recorded at delivery	A published intra-amniotic infection score built from gestational age, maternal white cell count and C-reactive protein reaches an area under the curve of 0.92 in derivation and 0.86 in validation[80], and a separate model of histological chorioamnionitis uses a latency threshold of 48 hours[34]. A latency recorded only as "longer than 12 hours" cannot be entered into the second, and the first cannot be computed here because no maternal C-reactive protein was measured.
3	*Maternal group B streptococcus status – never recorded*	on the routine antenatal schedule	Group B streptococcus and Escherichia coli account for most early-onset sepsis, and their relative frequency differs between term and late preterm infants.[24,81] No screening result appears.
4	**Blood-culture inoculum volume and collection time**	at the moment of collection, before the first antibiotic dose	Thirty-five per cent of 742 neonatal bottles held less than 0.9 mL, and night-shift collection was associated with lower volumes.[21,42] Without the volume, a negative culture cannot be weighed.
5	*The hour at which the blood culture was declared negative – never reported*	at 36 and at 48 hours from collection	By 36 hours 94% and by 48 hours 97% of cultures that will grow a pathogen have signalled.[9,10] A negative report at 36 hours is an actionable result; the absence of a report is not.
6	**A pre-antibiotic C-reactive protein**	with the blood culture, before the first dose	Within four hours of the culture the test has a positive likelihood ratio of 4.12; drawn 24 to 72 hours later the ratio falls to 2.02.[6] Both samples here were drawn at or beyond that later window, and neither before the first dose.
7	**Procalcitonin with its hour of life recorded**	at a stated postnatal hour, interpreted on an age-specific curve	Procalcitonin rises physiologically after birth to an average peak of 15.12 ng/mL at about 36 hours in uninfected very low birth weight preterm neonates, and the widely used reference interval excludes infants with respiratory failure.[7,8] An untimed value cannot be placed.
8	*Lung ultrasound – never performed*	at the bedside within the first hours of respiratory distress	In 160 newborns lung ultrasound distinguished transient tachypnoea with 100% accuracy and pneumonia with 96.8%[57]; in 100 neonates its score correlated with the Downes score.[62] It is the single bedside test that answers the question this admission was built around.
9	*The six neuromuscular items of the New Ballard score – never recorded*	within 12 hours of birth, with the six physical items	The record prints a total of 30 and documents only four physical descriptors, which point to four gestations spanning 6 weeks.[14] The total cannot be reconstructed from what the record contains.
10	**Daily weight**	every day, as the unit's own monitoring plan specified	4 weights exist for five days and two of them are identical, so the nadir was never established. Time to full enteral feeds, defined in both trials as 150 mL/kg/day or exclusive breast-feeding, was 5.7 to 5.8 days in two randomised trials of moderate and late preterm infants[68,69]; this infant was at 137.9 mL/kg/day on days 4 to 5, computed on the day-5 weight because no day-4 weight exists, which is 92.0% of the volumetric limb of that definition.
11	**Hearing screen**	before discharge, not after it	Four gentamicin doses were given; in a case-control study of infants born below 32 weeks, each dose of gentamicin, vancomycin or furosemide in the first 14 days carried an odds ratio of 1.25 for hearing loss, an association the authors state cannot be separated from the severity of the underlying illness.[26] A point-of-care genotype that avoids the drug in susceptible infants returns in 26 minutes.[78]
12	*Glucose-6-phosphate dehydrogenase result – never reported*	before phototherapy is stopped	Phototherapy was given for indirect hyperbilirubinaemia in a late preterm infant and the screening test planned for 48 to 72 hours is never reported. Risk models for phototherapy in this population are driven by feeding and delivery variables, of which mode of delivery, breastfeeding frequency and the maternal white cell count are recorded here while daily formula intake and maternal body mass index are not.[67]

Each item names the measurement, the moment at which it must be taken for it to be interpretable, and the decision it would have changed in this admission. Red marks an item that was partly recorded or recorded at the wrong moment; grey marks an item that is absent from the record altogether.

The list is derived from this single admission and is offered as a checklist rather than as a validated instrument; it names the twelve measurements whose absence bore most directly on the decisions described here and is not an exhaustive inventory of everything this record omits. Items 1, 2 and 3 are obstetric and must be captured before the infant is born; items 4 to 8 are decided in the first hours; items 9 to 12 belong to the admission as a whole. Beyond the assays this unit already runs – a full blood count, C-reactive protein, procalcitonin, a blood culture and the newborn screening panel – nothing in the list requires equipment other than a thermometer, a clock, weighing scales, an ultrasound probe and an otoacoustic-emission device.

Limitations

This is a single case, described retrospectively from a clinical record that was not written for this purpose, and no causal claim of any kind can be drawn from it. The central finding – that the respiratory diagnosis was revised and the antibiotic course was not – is an observation about one admission and is not offered as evidence about practice in general. The blood culture result is unknown. The time-to-positivity literature describes only cultures that did grow, so it cannot be used to infer that this one did not; the absence of a report is uninformative in both directions, which is itself the point of the antibiotic stop-rule subsection of the Discussion. The argument of this report does not require the culture to have been negative, only that it had not been reported when the decisions were made. The procalcitonin comparison rests on a single value whose hour of sampling is not recorded, which is itself the point being made, but it means the comparison in Table 3 assumes the 12 to 36 hour window, which is the window in which physiological procalcitonin is highest. An hour outside it cuts the same way in both directions: on the rising limb before the peak at about 36 hours, and again on the falling limb after it, the age-appropriate comparator is lower than the 12 to 36 hour medians, so the same value would sit nearer to or above them rather than below. The assumed window is therefore the one most favourable to the reading offered here, not a conservative one. The publication from which that interval comes states neither its country nor its setting, does not define respiratory failure, and gives no size for its respiratory-failure group.

The three-hour continuous positive airway pressure index is read from a period during which the record documents unchanged settings rather than from a separately timed three-hour observation, and its margin below the published threshold is 0.03 in the units of the product itself, which at the recorded positive end-expiratory pressure corresponds to a difference of 0.0043 in the fraction of inspired oxygen – less than half the 0.01 at which that fraction is charted; the index is presented as a description, not as a prediction. The chest radiograph survives only at 384 × 272 pixels, so the reported parenchymal findings cannot be independently re-adjudicated, and Figure 2 is presented with that stated. Seventeen items are recorded in the source either more than once with different values, or stated once in a form their own components do not reproduce. Most do not alter the argument, but their presence means some of the values reported here rest on a single unverified statement; two of them – the birth length and the lowest delivery-room saturation – straddle a boundary the discussion uses, and both are named where they are used. Finally, several of the comparator studies cited were conducted in populations that differ from this infant: the procalcitonin peak of 15.12 ng/mL comes from very low birth weight preterm neonates[7], the antibiotic-exposure and bronchopulmonary dysplasia association comes from infants below 32 weeks[55], the ototoxicity case-control study also comes from infants below 32 weeks[26], and the long-term asthma association after transient tachypnoea comes from term infants[73]. Each is cited for the direction of an effect or the existence of a reference frame and not for a magnitude transferable to this infant. Two more belong on that list: the continuous-positive-airway-pressure weaning score comes from infants born below 32 weeks with previous respiratory distress syndrome[61], and the rapid-advancement feeding cohort from very low birth weight infants[70]. The unequal groups and term population of the asthma study are set out where it is cited, in the diagnostic-revision and discharge subsection of the Discussion, and are not restated here. Figure 2 is presented at the largest printed width at which the image does not become visibly interpolated.

5. Conclusion

A late preterm male neonate born after prolonged preterm premature rupture of membranes grunted from birth, was stabilised on continuous positive airway pressure within one minute, returned to room air by five minutes, was weaned off support on the third day and was in room air, feeding and clinically stable at the close of the record. Every element that pushed the diagnosis towards infection was either a test read outside the frame in which it was derived or outside the window in which it is informative, or a risk factor counted without its counterweight: a procalcitonin of 6.8 ng/mL reported with no reference interval beside it, and interpretable only against an interval derived after excluding neonates with respiratory failure, when the median for neonates who have respiratory failure without infection is 6.83 ng/mL in term and 9.56 ng/mL in preterm infants; a C-reactive protein drawn 24 to 48 hours after birth and after the first antibiotic dose, in the window where the test is least specific, and reported without any reference interval beside it, when the arm of the reference cohort that applies to a late preterm infant has lower centiles than the term arm against which such a value is ordinarily read; and four minor maternal risk factors counted without the unmeasured factors – an intrapartum temperature never taken, a placenta never examined, a group B streptococcal screen never performed – being counted against them.

Every element that could have settled the infective question was either not obtained or not acted on. The respiratory question was settled by the clinical course, and that was acted on, on day 3. No lung ultrasound was performed, although it has been reported to distinguish transient tachypnoea from pneumonia at the bedside within minutes. No blood-culture volume was recorded and no culture result was ever reported, although 94% of cultures that will grow a pathogen have signalled by 36 hours. The stop rule the record set was conditioned on that report, so it could not fire on its own terms; the course nevertheless ended after 5 days, with no reason for stopping recorded and no culture result available at any point – 3.0 days longer than a 48-hour rule and 3.5 days longer than a 36-hour rule would have allowed. The respiratory diagnosis was correctly revised on day 3; the infective diagnosis was escalated from suspected to probable on the same day, while the C-reactive protein was falling by 60.7%, the molecular assay was negative and respiratory support was being withdrawn.

Three things follow for practice. First, write stop rules that fire on the passage of time, not on the arrival of a report: "stop at 36 hours unless the culture has signalled" is a rule that always executes, and "stop on day 5 if the culture is negative" is not. Second, when a neonatal biomarker is ordered, record the hour of life on the request and read the result against the interval derived in infants with the same physiology, because for procalcitonin the difference between the interval derived after excluding respiratory failure and the median measured within it is the difference between an abnormal result and an expected one. Third, obtain the test that answers the question being asked: the whole of this admission turned on a distinction that bedside lung ultrasound distinguished with an accuracy of 96.8% for pneumonia and 100% for transient tachypnoea in a single 160-newborn series whose reference standard was the final clinical diagnosis and whose disease-specific denominators are not stated, and it was never done. The twelve-item minimum data set in Table 6 names the twelve measurements

whose absence bore most directly on the decisions described here, the moment at which each must be taken, and the decision it would have changed. Figure 1 marks the hour or day of every one of those failures that has one: the asserted fever, the two undated biomarkers, the bilirubin threshold crossed downward and the antibiotic course that outlived its own stop rule. The three obstetric items precede the timeline; the lung ultrasound, the undocumented neuromuscular items of the maturity score, the daily weights and the newborn screening results carry no hour in the record and are therefore not placed on it.

Declarations

Ethics approval

This report describes routine clinical care delivered in 2026 and involved no intervention, no additional investigation and no change to management. In accordance with institutional policy on single-case reports, the case was reviewed by the Health Research Ethics Committee of Dr. M. Djamil General Hospital and the Faculty of Medicine, Universitas Andalas, which issued a written determination that ethics-committee approval was not required for a de-identified retrospective description of care already given; the determination reference is reproduced in full in the accompanying ethics approval statement. Written informed consent for publication, including publication of the chest radiograph reproduced as Figure 2, was obtained from both parents as the infant's legal guardians; a copy of the signed form is available to the editorial office on request.

Consent for publication

Written consent for publication of this de-identified case, including all tables and figures and the radiographic image, was obtained from both parents. A copy of the signed consent form is available to the editorial office on request. All directly identifying information has been removed: the infant's name, medical record number and dates of birth and admission do not appear, the admission date is reduced to the month and the year, and every interval is expressed as an hour or a day of life. The radiograph carries no burned-in identifying text and shows no facial features.

Data availability

All data supporting the findings are contained within the article. The underlying clinical record is held at Dr. M. Djamil Hospital, Padang, and cannot be shared publicly because it contains identifying information. Every derived quantity reported here – the absolute neutrophil and lymphocyte counts, the immature-to-total neutrophil ratio, the neutrophil-to-lymphocyte ratio, the product of the fraction of inspired oxygen and the positive end-expiratory pressure, the mean arterial pressure, the bilirubin fraction sums, the delivered fluid, energy and protein per kilogram, the weight loss and the weights implied by the printed per-kilogram figures – is reproducible from the values printed in Tables 1 to 6 and in the nutrition subsections of the Results and Discussion, together with the reference sources cited in the table notes. One exception is unavoidable: the gestational age computed from the last menstrual period rests on two calendar dates that de-identification requires be withheld, so only the computed interval is reported.

Conflict of interest

The authors declare no financial or non-financial conflicts of interest related to this manuscript.

Clinical trial registration

Not applicable. This is a retrospective single-patient case report and not a clinical trial.

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Author contributions

Contributions are stated in the CRediT taxonomy. **DR:** conceptualization, investigation, data curation, formal analysis, visualization, writing – original draft, project administration. **EY:** conceptualization, methodology, validation, supervision, writing – review and editing. **BSP:** methodology, validation, resources, supervision, writing – review and editing. All authors meet the four ICMJE criteria for authorship, have read and approved the final manuscript, and agree to be accountable for all aspects of the work.

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Use of artificial intelligence

No artificial intelligence (AI) tools were used in the preparation of this manuscript.

CARE guideline statement

This report was prepared in accordance with the CARE guideline for case reports and its explanation and elaboration document.[82] A completed CARE checklist with measured page references accompanies the submission, and the parental perspective required by item 12 of that checklist appears in the parents' perspective subsection of the Results.

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