Supplement for: Antenatal and neonatal antecedents of executive dysfunctions in extremely preterm children.

Methods

The 10-year assessment and data analyses are described in the manuscript. Here we describe the antecedents we considered risk factors for the executive dysfunctions.

Demographic, pregnancy, and delivery variables

After delivery, a trained research nurse interviewed each mother in her native language following a structured procedure. Following discharge, the research nurse reviewed the maternal chart using a second structured data collection form to collect information about events after admission.

Maternal report of the sequence of events leading to preterm delivery served as the primary source of information for defining the initiator of preterm delivery. The six initiators of preterm delivery (preterm labor, pre-labor rupture of the fetal membranes, placental abruption, cervical insufficiency, preeclampsia, and delivery for fetal indications) are defined elsewhere.[1]

A course of antenatal adrenal corticosteroids given to enhance fetal lung maturation was considered complete if the gravida received two doses of betamethasone 24 hours apart and delivered at least 48 hours after the first dose, or if she received 4 doses of dexamethasone at 12 hour intervals. Neonatal data were collected from the newborn's medical record.

Newborn variables

Gestational age estimates were based on a hierarchy of the quality of available information. Most desirable were estimates based on the date of embryo retrieval or intrauterine insemination or fetal ultrasound before the 14th week (62%). When these were not available, reliance was placed sequentially on a fetal ultrasound at 14 or more weeks (29%), report of last menstrual period (LMP) without fetal ultrasound (7%), and gestational age recorded in the log of the neonatal intensive care unit (1%). The birth weight Z-score is the number of standard deviations the infant's birth weight is above or below the median weight of infants at the same gestational age in referent samples not delivered for preeclampsia or fetal indications.[2,3]

We collected all the physiology, laboratory and therapy data for the first 12 hours needed to calculate a SNAP-II™ score.[4]

Mode of ventilation was defined as the highest level of support on each day and ranged from no support, increased ambient oxygen in a hood, nasal cannula, nasal continuous positive airway pressure, and conventional mechanical ventilation to high frequency ventilation.[5] After the first week, this information was collected on days 7, 14, 21, and 28, and at 36 weeks post-menstruation. We did not record the specific devices used. We also recorded the number of days each infant received supplemental oxygen, CPAP, and conventional mechanical ventilation (including high frequency ventilation).

Information about blood gases after the first postnatal week was collected on days 7 and 14.[6] We classified the modal PaO_2 on postnatal days 7 and 14 as in the lowest quartile or in a

higher quartile. We also noted if the infant did not have a blood gas assessment on those days.

ELGANs were classified into three mutually exclusive respiratory dysfunction groups: those with consistently low FiO_2 (an $FiO_2 < 0.23$ on all days between 3 and 7 days of life and receiving $FiO_2 \leq 0.25$ on Day 14), those with pulmonary deterioration (PD) (an $FiO_2 < 0.23$ on any day between 3 and 7 days and receiving $FiO_2 > 0.25$ on day 14), and those with early and persistent pulmonary dysfunction (EPPD) (an FiO2 ≥ 0.23 on all days between 3 and 7 days of life and receiving $FiO_2 > 0.25$ on Day 14).[7] For individual infants, the FiO_2 assigned for each day of life was the mode FiO_2 for that day. Day 0 began at the time of birth and continued through 24 hours of age. Day 1 began at the end of the first 24 hours of age and ended at midnight of that calendar day. Thus, Day 1 varies in length. Day 2 through 7 began and ended at midnight.

Documented early bacteremia was defined as recovery of an organism from blood drawn during first week, and late bacteremia as recovery of an organism from blood drawn during weeks 2, 3 or 4.[8] Specific organisms were not identified. A diagnosis of a tracheal infection required the recovery of a pathogen from tracheal aspirate. An infection (whether blood, trachea or CSF) was identified as clinically suspected if the culture was negative and clinician treated the baby with antibiotics for 72 or fewer hours. Presumed infections were also culture-negative, but the infant received antibiotics for more than 72 hours.

The diagnosis of PDA was assigned by clinicians without uniformity of definition. We did record when the diagnosis was confirmed by echocardiography. Diagnoses of pneumothorax, pulmonary interstitial emphysema, and pulmonary hemorrhage were those made by the clinicians caring for the ELGAN.

Medications were recorded if given on any day during the first 28 days and included methylxanthines (aminophylline, theophylline, caffeine), analgesics (i.e., morphine, fentanyl, or methadone), sedatives (i.e., lorazepam, midazolam, or chloral hydrate), and steroids (i.e., hydrocortisone and dexamethasone). We did not ask the research nurse who collected the data to identify the methylxanthine received. We subsequently confirmed that all but one of the participating centers used caffeine almost exclusively. We did not examine the dosages of any of the medications.

The newborn's chart was reviewed for receipt of blood products on post-natal days 7, 14, 21, and 28. These assessments were for those days only and not the intervening days. Thus, children who were identified as receiving a blood product definitely received a blood product, while some of those not so identified might have received a blood product during the interval between these sampling days.

After discharge, details were collected about the apparent need for respiratory care at 36 weeks post-menstrual age (PMA) along with discharge diagnoses. The diagnosis of bronchopulmonary dysplasia/chronic lung disease (BPD/BPD) was based on whether or not the child was receiving supplemental oxygenation at 36 weeks post-menstrual age. Note was also made of whether the infant was then on conventional mechanical ventilation. The child's necrotizing enterocolitis status was classified according to the modified Bell staging system.[9]

Participating ophthalmologists helped prepare a manual and data collection form, and then participated in efforts to minimize observer variability. Definitions of terms were those accepted by the International Committee for Classification of ROP [10]. In keeping with guidelines [11], the first ophthalmologic examination was within the 31st to 33rd post-menstrual week. Follow-up exams were as clinically indicated until normal vascularization began in zone lll.

Placentas

Delivered placentas were placed in a sterile exam basin and transported to a sampling room, where they were biopsied under sterile conditions. Eighty-two percent of the samples were obtained within 1 hour of delivery. The microbiologic procedures are described in detail elsewhere,[12,13] as are the histologic procedures.[14,15]

Results

Rather than go through each table individually, we grouped the findings by the executive dysfunction they are associated with.

Working memory (WM) limitation

The prevalence of working memory limitation was higher among children whose mother identified as Black, was less than 21 years old at the time of the delivery, was not married, and was eligible for government-provided medical-care insurance then. The prevalence of working memory limitation was also higher among children with the following characteristics than among their peers: recovery of Mycoplasma from the placenta parenchyma, no antenatal corticosteroid exposure, fetal indication for delivery, fetal growth restriction, had pulmonary deterioration or early and persistent pulmonary dysfunction, received an antibiotic during the first postnatal week as well as during the next 3 weeks, and developed pneumothorax, pulmonary hemorrhage, “surgical” necrotizing enterocolitis, and severe bronchopulmonary dysplasia (*i.e.*, dependencce on a mechanical ventilator as well as on supplemental oxygen). In addition, the prevalence decreased incrementally with the number of years of mother’s formal education, gestational age at birth, the lower the birth weight, and the SNAPPE II. Children whose mother sought conception assistance and children who received an antibiotic during the first postnatal week had a low prevalence.

Inhibition-inhibition (INI) limitation

The prevalence of an inhibition-inhibition limitation was higher among children whose mother had the following characteristics than among their peers: low age at the time of delivery, smoked cigarettes during the pregnancy, periodontal infection, consumed a non-steroidal anti-inflammatory drug, and did not have fever during this pregnancy. The prevalence was also high if the infant received an antibiotic during the first postnatal week as well as later during the first month, had pulmonary hemorrhage, “surgical” necrotizing enterocolitis, and severe bronchopulmonary dysplasia. In addition, the prevalence decreased with increasing birth weight, and was reduced among those whose placenta had fetal stem vessel thrombosis, and those who had early (postnatal week #1) bacteremia, and separately, late (postnatal weeks 2-4) bacteremia.

Inhibition-switching (INS) limitation

The prevalence of an inhibition-switching limitation was higher among children whose mother had the following characteristics than among children whose mother did not have these characteristics/exposures: self-identification as Black, low age at the time of the delivery, not married, eligible for government-provided medical-care insurance, smoked during this pregnancy, was exposed to the smoke of others, did not have fever during this pregnancy, periodontal infection, and consumed a non-steroidal anti-inflammatory drug during the pregnancy. The prevalence was also relatively high among children born before the 27th week of gestation, had fetal growth restriction, had pulmonary deterioration or early and persistent pulmonary dysfunction, high measurements of P_aO_2 and PCO_2 on 2 of the first 3 postnatal days, received an antibiotic during the first postnatal week as well as later during the first month, received hydrocortisone, received a sedative, received packed cells or whole blood during 3 of the first 4 postnatal weeks, developed tracheal colonization, pneumothorax, pulmonary interstitial emphysema, pulmonary hemorrhage, “surgical” necrotizing enterocolitis, isolated intestinal perforation, retinopathy of prematurity, and severe bronchopulmonary dysplasia. The prevalence was also high among children who developed non-severe bronchopulmonary dysplasia, but not as high as among those who had severe bronchopulmonary dysplasia. In addition, the prevalence decreased incrementally with the number of years of mother’s formal education, the birth weight, while it increased with increasing SNAPPE II. Children whose mother sought conception assistance, and children who received surfactant and/or an antibiotic during the first postnatal week had a low prevalence, as did children who had early and/or late bacteremia.

Executive dysfunction composite (*i.e.*, Z-score ≤ -1 on all 3 assessments)

The prevalence of the executive dysfunction composite (identified as “All” at the top of the column before “Row total”) was higher among children whose mother had the following characteristics than among children whose mother did not have these characteristics/exposures: self-identification as Black, low age at the time of the delivery, not married, did not graduate from college (or equivalent) eligible for government-provided medical-care insurance, less than one year since previous pregnancy, was not trying to get pregnant, did not have fever during this pregnancy, had a periodontal infection, did not consume any medication, and consumed a non-steroidal anti-inflammatory drug during the pregnancy (*these 2 population characteristics really are compatible*). The prevalence was also high among children whose placenta harbored multiple organisms, including Mycoplasma species and normal vaginal flora, and among children delivered for fetal indications, were not exposed to antenatal magnesium, were born before the 27th week of gestation, had a high SNAPPE-II, high measurements of P_aO_2 on 2 of the first 3 postnatal days, and received an antibiotic during the first postnatal week. The prevalence was low among children whose mother sought conception assistance, or consumed aspirin during the pregnancy, or if the newborn was exposed to postnatal dexamethasone, and/or had early bacteremia.

Supplement table 1. Children classified by whether or not they had Z-scores ≤ -1 on each of three assessments of capabilities considered part of executive function.

Working Memory	Inhibition Inhibition	Inhibition Switching	N	Description
Isolated				
≤ -1			19	Isolated Working Memory
	≤ -1		97	Isolated Inhibition Inhibition
		≤ -1	79	Isolated Inhibition Switching
			230	Referent (no Z-score ≤ -1)
Sets of 2				
≤ -1		≤ -1	28	
≤ -1	≤ -1		15	
	≤ -1	≤ -1	141	
All				
All ≤ -1			169	All Working Memory
	All ≤ -1		360	All Inhibition Inhibition
		All ≤ -1	355	All Inhibition Switching
≤ -1	≤ -1	≤ -1	107	All 3

Supplement table 2. Row percents of maternal demographic characteristics of children classified by a Z-score ≤ -1 on the executive dysfunction listed at the top of each column.

Maternal characteristic		Executive dysfunction				Row total
		WM	INI	INS	All	
"Racial" identity	White	18	45	44	10	480
	Black	39	37	71	29	163
	Other	27	47	39	15	71
Hispanic	Yes	29	52	54	17	65
	No	23	50	49	15	649
Maternal age, Years	< 21	33	60	61	22	89
	21-35	23	49	49	14	473
	> 35	20	48	44	14	154
Years of Education	≤12 (HS)	32	58	60	20	273
	>12 to <16	25	45	52	17	169
	≥ 16 (College)	15	46	38	8	274
Single?	Yes	34	57	63	24	270
	No	17	46	42	10	416
Self supported?	Yes	21	48	47	13	484
	No	28	50	56	18	222
Public insurance	Yes	32	58	61	22	225
	No	20	47	44	12	491
Pre-pregnancy Body Mass Index (BMI)	<18.5	28	53	45	19	53
	18.5,<25	19	47	47	12	354
	25,<30	27	54	52	19	135
	>30	27	52	55	15	148
Total row percent		24	50	50	15	
Maximum column N		169	360	355	107	716

Supplement table 2a. Row percents of maternal socio-demographic characteristics. This table documents the inter-relatedness of these socio-demographic characteristics

		Government-provided insurance				
		Yes		**No**		
		Single		**Single**		
		Yes	**No**	**Yes**	**No**	Row N
"Racial" identity	White	14	5	10	71	480
	Black	49	10	21	20	163
	Other	47	8	10	38	71
Years of Education	≤12 (HS)	51	9	13	27	273
	>12 to <16	21	8	18	53	169
	≥ 16 (College)	3	2	9	87	274
Colum N		180	48	90	401	716

Supplement table 3. Row percents of maternal pregnancy characteristics of children classified by which executive dysfunction(s) they had.

Exposures and characteristics		Executive dysfunction				Row total
		WM	INI	INS	ALL	
Smoked during pregnancy	Yes	24	60	56	14	93
	No	23	48	48	15	609
Passive smoke exposure	Yes	28	59	61	19	165
	No	22	47	46	14	533
1st pregnancy	Yes	26	49	49	16	300
	No	22	51	50	14	400
Years since last pregnancy	< 1	29	56	53	21	75
	1-2	18	50	48	9	113
	2+	22	49	50	14	208
Conceived using birth control	Yes	29	50	53	19	103
	No	23	50	48	14	595
Trying to get pregnant	Yes	19	45	45	11	408
	No	30	57	55	21	292
Conception assistance	Yes	16	43	38	9	171
	No	26	52	53	17	529
Due date changed	Yes	25	54	53	14	135
	No	23	49	48	15	560
Illnesses this pregnancy						
Fever	Yes	19	35	40	7	43
	No	24	51	50	15	656
Vaginal/cervical infection	Yes	22	53	51	15	96
	No	24	49	49	15	603
Urinary tract infection	Yes	24	47	54	18	98
	No	22	50	49	14	601
Peridontal	Yes	30	80	80	20	10
	No	24	49	49	15	689
Medications						
Any medication	Yes	24	49	49	14	618
	No	31	60	52	20	81
Aspirin*	Yes	23	49	41	10	39
	No	24	50	50	15	658
NSAID*	Yes	27	67	61	20	49
	No	23	49	48	14	648
Acetaminophen*	Yes	19	49	48	12	371
	No	29	51	51	18	326
Antibiotic*	Yes	25	46	52	14	208
	No	23	52	48	15	490
Total row percent		24	50	49	15	
Maximum column N		165	351	347	103	702

* infants may be in more than one category

Supplement table 4. Row percents of placenta characteristics of four groups of children classified by which learning limitations they had.

Placenta characteristics		Executive dysfunction				Row total
		WM	INI	INS	ALL	
# of species isolated	0	24	49	51	15	329
	1	20	47	47	14	167
	≥ 2	29	55	53	20	154
Aerobe	Yes	26	53	53	18	208
	No	23	48	48	15	442
Anaerobe	Yes	23	51	47	17	182
	No	25	50	52	15	468
Mycoplasma	Yes	33	56	59	20	64
	No	23	49	49	15	586
Skin organisms*	Yes	21	49	43	15	124
	No	25	50	52	16	526
Vaginal organisms†	Yes	29	54	49	21	108
	No	23	49	51	15	542
Total row percent		24	50	50	15	
Maximum column N		157	324	327	103	650
Chorionic plate inflammation[1]	Yes	25	56	49	18	128
	No	23	47	49	14	527
Chorion/decidua inflammation[2]	Yes	25	51	49	16	228
	No	23	47	49	14	426
Fetal stem vessel infiltration[3]	Yes	22	51	50	16	163
	No	24	48	49	14	489
Umbilical cord vasculitis	Yes	26	54	50	17	111
	No	22	49	48	14	534
Fetal stem vessel Thrombosis	Yes	27	39	52	15	33
	No	23	50	49	15	618
Infarct	Yes	21	49	49	14	118
	No	24	50	49	15	541
Increased syncytial Knots	Yes	29	50	48	18	135
	No	22	49	49	14	527
Decidual hemorrgage/ fibrin deposition	Yes	22	46	47	15	110
	No	24	50	50	15	541
Total row percent		24	49	49	15	
Maximum column N		156	327	324	97	662

* *Corynebacterium sp, Propionebacterium sp, Staphylococcus sp*

† *Prevotella bivia, Lactobacillus sp, Peptostrep magnus, Gardnerella vaginalis*

1 stage 3 and severity 3

2 grades 3 and 4

3 grades 3, 4 and 5

Supplement table 5. Row percents of delivery characteristics of four groups of children classified by which executive dysfunction(s) they had.

Pregnancy characteristic		Executive dysfunction				Row total
		WM	INI	INS	ALL	
Antenatal steroid course	Complete	23	51	50	15	450
	Partial	19	47	50	13	183
	None	35	54	49	18	83
Pregnancy complication	PTL	22	49	46	13	328
	pPROM	24	52	51	17	157
	PE	26	51	57	17	90
	Abruption	25	52	51	12	84
	Cervical Insufficiency	19	50	50	16	32
	Fetal Indication	40	48	56	24	25
Magnesium sulfate	None	26	59	53	20	225
	Tocolysis	22	46	48	13	397
	Seizure prophylaxis	26	46	51	13	89
Cesarean	Yes	25	49	49	15	482
	No	20	53	50	15	234
Duration of labor, hours	0	26	47	54	16	163
	≤ 12	26	51	48	18	166
	> 12	21	52	48	13	387
Duration of membrane rupture, hours	< 1	25	49	52	15	416
	1-24	26	53	44	15	121
	> 24	20	51	47	15	179
Fever*	Yes	*17*	54	54	14	35
	No	23	50	50	15	657
Highest WBC*	Yes	28	49	49	16	144
	No	22	51	50	15	558
Total row percent		24	50	50	15	
Maximum column N		169	360	355	107	716

* within the interval from before delivery to 48 hours post delivery

Supplement table 6. Row percents of characteristics at the time delivery of four groups of children classified by which executive dysfunction(s) they had.

Characteristic of the infant		Executive dysfunction				Row total
		WM	INI	INS	ALL	
Sex	Male	24	49	48	16	342
	Female	23	51	51	14	374
Multiple gestation	Yes	23	48	47	13	255
	No	24	52	51	16	461
Gestational age, Weeks	23-24	30	50	55	18	127
	25-26	25	50	53	17	327
	27	19	50	43	11	262
Birth weight, grams	≤750	29	56	56	19	236
	751-1000	22	49	50	14	325
	> 1000	18	43	37	10	155
Birth weight Z-score*	< -2	40	58	65	20	40
	≥ -2,< -1	26	50	50	17	90
	≥ -1	22	50	48	14	586
Head Circumference Z-score*	< -2	35	67	58	21	48
	≥ -2,< -1	31	51	53	21	154
	≥ -1	20	49	48	12	483
Total row percent		24	50	50	15	
Maximum column N		169	360	355	107	716

* External standard (Yudkin et al., 1987)

Supplement table 7. Row percents of postnatal characteristics of four groups of children classified by which executive dysfunction(s) they had.

Postnatal factor		Executive dysfunction				Row total
		WM	INI	INS	ALL	
SNAPPE-II	< 30	18	49	43	12	310
	30-44	24	47	51	14	230
	45+	33	58	61	22	163
Lowest Q lowest MAP[§]	Yes	26	50	52	14	145
	No	23	50	48	15	558
Vasopressor [¶]	Yes	24	52	52	13	147
	No	23	50	49	15	569
Highest Q MAP variability [†]	Yes	22	52	45	15	159
	No	24	49	50	15	544
Lowest Q lowest P_aO_2*	Yes	24	45	53	15	119
	No	24	52	52	14	464
Highest Q highest P_aO_2*	Yes	30	58	65	20	122
	No	22	49	46	13	461
Lowest Q lowest PCO_2*	Yes	24	58	57	19	123
	No	24	49	48	13	460
Highest Q highest PCO_2*	Yes	24	54	62	15	133
	No	24	50	46	14	450
Lowest Q lowest pH*	Yes	22	48	54	14	125
	No	24	52	49	15	458
Lowest Q P_aO_2 day 7	Yes	*17*	*34*	55	10	58
	No	23	55	55	14	235
	Unknown	25	50	46	16	423
Lowest Q P_aO_2 day 14	Yes	22	42	53	11	36
	No	22	55	55	15	121
	Unknown	24	50	48	15	559
Tracheal colonization[††]	Yes	25	52	60	12	138
	No	23	50	47	15	575
Early bacteremia (wk 1) [††]	Yes	19	38	38	*7*	42
	No	24	51	50	15	673
Late bacteremia (wks 2-4) [††]	Yes	24	48	46	14	442
	No	23	55	56	15	269
Mech ventilation, day 7[MV]	Yes	25	50	52	15	412
	No	22	51	46	16	303
Mech ventilation, day 14[MV]	Yes	26	51	55	16	392
	No	21	50	44	13	319
Mech ventilation, day 21[MV]	Yes	27	53	57	17	381
	No	20	47	41	13	326
Mech ventilation, day 28[MV]	Yes	28	53	55	18	321
	No	20	49	46	13	377
Total row percent		24	50	50	15	
Maximum column N		169	360	355	107	716

§ Lowest MAP: lowest MAP recorded in the first 24 hours, in the lowest quartile for gestational age

¶ Vasopressor: treatment for hypotension in the first 24 hours, using any vasopressor (dopamine, dobutamine, epinephrine)

† Labile MAP: labile blood pressure, defined as the upper quartile of the difference in the lowest and highest MAP

* extreme quartile for gestational age on two of the first three postnatal days

†† Definite, i.e., culture proven

MV Includes conventional mechanical ventilation and high frequency ventilation

Supplement table 8. Row percents of medications administered during the first postnatal month to four groups of children classified by which executive dysfunction(s) they had.

Medications and therapies		Executive dysfunction				Row total
		WM	INI	INS	ALL	
Surfactant, week 1	Yes	24	50	50	14	630
	No	23	56	49	19	86
Methylxanthine,15+ days	Yes	22	50	45	15	453
	No	26	51	58	14	263
Any hydrocortisone	Yes	28	52	60	17	86
	No	23	50	48	15	630
Any dexamethasone	Yes	20	54	48	*9*	54
	No	24	50	50	15	662
Any analgesic	Yes	24	50	51	16	482
	No	22	50	47	13	234
Any sedative	Yes	25	50	60	16	177
	No	23	50	46	14	539
PDA treatment	Yes	23	51	50	14	416
	No	24	49	49	16	300
Transfusion †	Yes	25	51	54	16	382
	No	22	50	44	13	333
Antibiotic, week 1	Yes	24	51	50	15	699
	No	*12*	*29*	41	*0*	17
Antibiotic, week 2-4	Yes	25	53	52	16	537
	No	19	42	41	12	177
Total row percent		24	50	50	15	
Maximum column N		169	360	355	107	716

† packed cells or whole blood during 3 of the first 4 postnatal weeks

Supplement table 9. Row percents of postnatal characteristics and diagnoses of four groups of children classified by which executive dysfunction(s) they had.

Diagnostic & classification entities		Executive dysfunction				Row total
		WM	INI	INS	ALL	
Lowest quartile growth velocity	Yes	23	50	52	*10*	160
	No	24	51	50	17	535
Patent ductus arteriosus	Yes	24	51	49	15	468
	No	23	49	50	16	248
Pneumothorax	Yes	31	48	61	17	54
	No	23	50	49	15	662
Pulmonary interstitial Emphysema	Yes	27	46	61	16	106
	No	23	51	48	15	610
Pulmonary hemorrhage	Yes	33	71	71	25	24
	No	23	50	49	15	692
Respiratory group classification	EPPD[†]	24	51	53	12	276
	PD[††]	27	51	54	19	264
	Low FiO_2	*18*	49	*39*	13	156
Necrotizing enterocolitis (Bell stage)	< IIIb	23	50	49	14	674
	IIIb	43	65	56	35	23
	Isolated perf[P]	21	47	58	16	19
ROP: stage	3-5	24	49	55	15	117
	< 3	23	51	47	15	528
ROP: plus disease	Yes	27	53	58	17	59
	No	23	50	49	15	646
ROP: pre-threshold[‡‡]	Yes	24	53	58	16	74
	No	23	50	49	15	631
BPD/CLD	Severe [S]	32	60	75	25	53
	Mild/Moderate [M]	25	48	53	14	285
	No	21	51	43	14	371
Total row percent		24	50	50	15	
Maximum column N		169	360	355	107	716

[V] Alone or with other lesions
[*] 1000*((wt28-wt7)/wt7)/21; units: g/kg/day
[§] Pulmonary interstitial emphysema
[†] Early and persistent pulmonary dysfunction
[††] Pulmonary deterioration
[S] On ventilator as well as oxygen at 36 weeks post-menstrual age
[M] On oxygen, but not on ventilator at 36 weeks post-menstrual age
[§§] Includes less severe disease
[P] Isolated intestinal perforation
[‡‡] Satisfied ET-ROP criteria for ablative surgery (pre-threshold disease)

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