Birth asphyxia:
when the pieces of the puzzle don't fit

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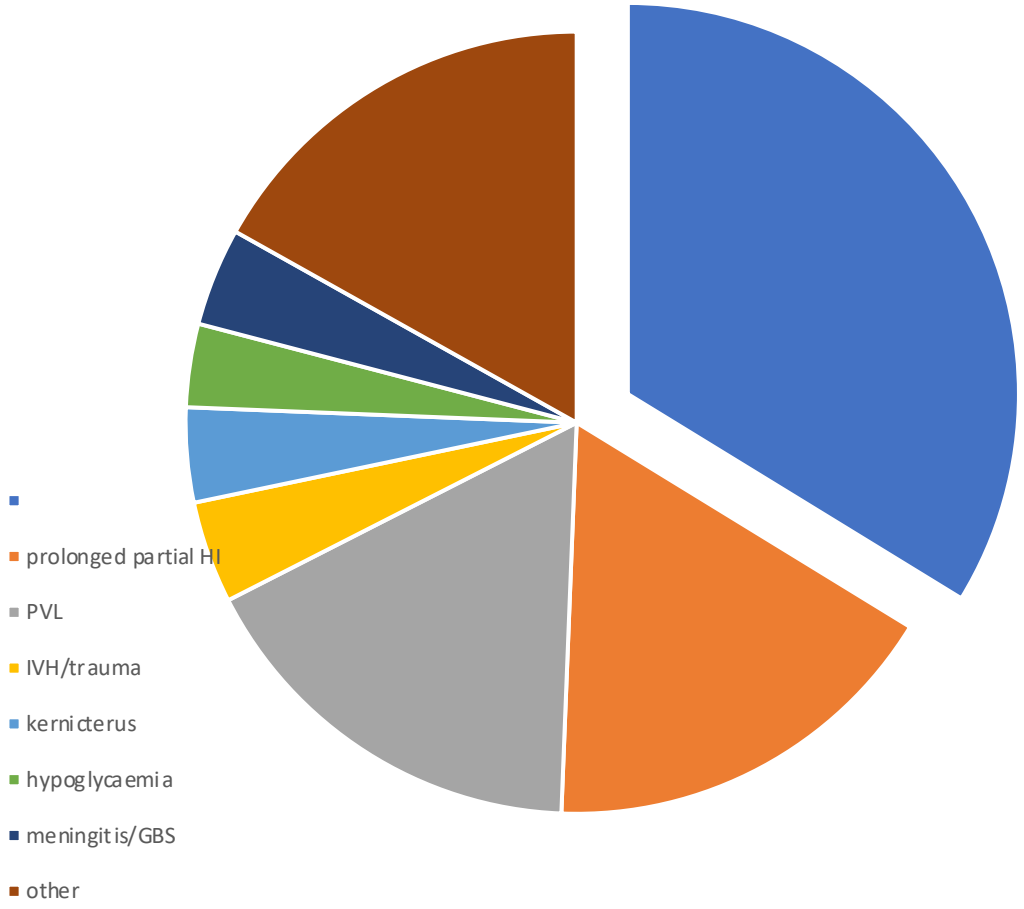
Objectives

To review the criteria for establishing the probability of a damaging intrapartum hypoxic ischaemic injury with a focus on acute profound hypoxic ischaemia.

To examine the criteria individually in order to consider exceptions:

- CTG changes
- cord blood acidosis
- Apgar score and resuscitation
- encephalopathy
- imaging changes
- type of disability

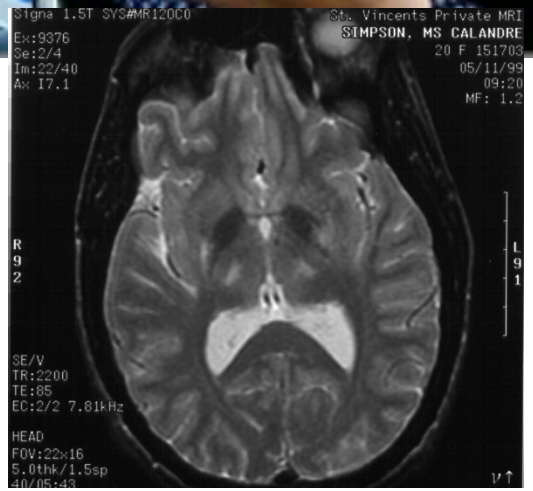
Analysis of over 3000 litigated cases



Acute profound HI
>1000 cases

775 settled; 405
for the Plaintiff

Smart, funny, trapped: at 21, Calandre gets her day in court



Calandre Simpson is an intelligent and perceptive young woman, trapped inside a crippled body.

At her birth 21 years ago, a court heard yesterday, she was "barely alive" when she was delivered by emergency caesarean after a doctor botched four or five attempts at using several types of forceps at St Margaret's Private Hospital, Darlinghurst.

During the delivery, which lasted about 40 minutes, Calandre's heart rate dropped from 140 to 80 beats a minute, and her brain was deprived of vital oxygen, rendering her with athetoid cerebral palsy.

Calandre, of Vaucluse, is suing the obstetrician, Dr Robert Diamond, in the NSW Supreme Court for undisclosed damages, claiming an experienced and competent doctor would have been able to deliver her properly using forceps.

Acute profound HI – typical case

- Fetal bradycardia < 80 bpm for more than 10 minutes immediately before birth
- Birth depression and need for resuscitation
- Cord blood acidosis
- Early neonatal encephalopathy with seizures (since 2010, cooled)
- MR imaging evidence of damage to the deep grey matter
- Cerebral palsy, often with learning disability

International consensus statement/ACOG criteria

Essential criteria:

- **evidence of a metabolic acidosis (fetal, cord or very early neonatal) with pH <7.0 and base deficit >-12 mmol/l;**
- **early onset of encephalopathy in infants of > 34 weeks**
- **CP of the spastic quadriplegic or dyskinetic type**
- **Exclusion of other identifiable aetiologies, such as trauma, coagulation disorders, infectious conditions or genetic disorders*.**

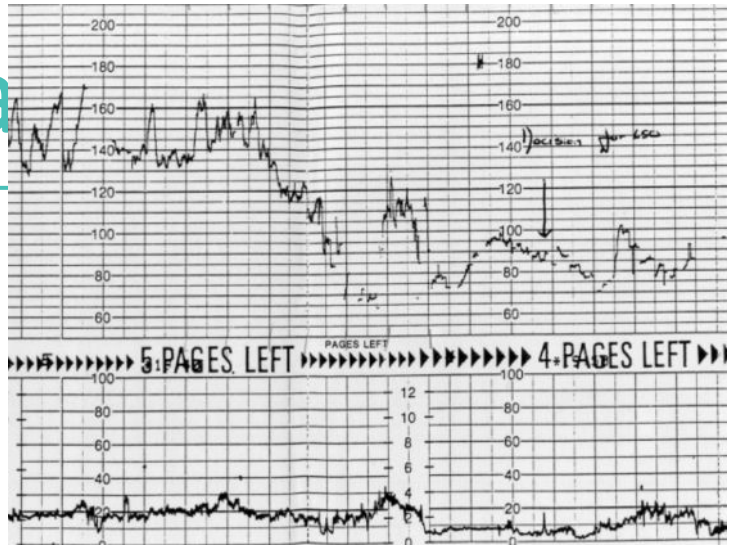
Source: MacLennan A et al BMJ 1999 319:1054-9

* Added by ACOG in 2003, updated 2014

Secondary criteria

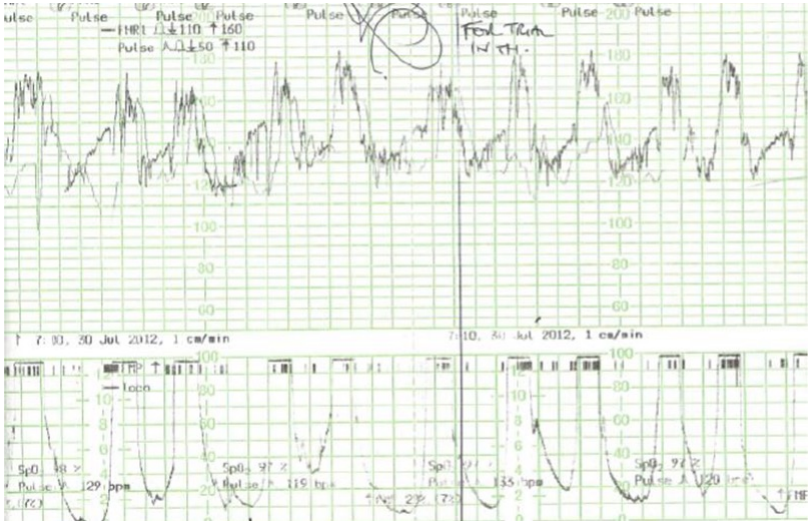
- sentinel hypoxic event occurring immediately before or during labour;
- fetal heart rate patterns consistent with an acute peripartum or intrapartum event
- sudden, rapid and sustained deterioration of CTG where the pattern was previously normal;
- Apgar <5 for >5 minutes;
- early evidence of multisystem involvement;
- early imaging evidence of an acute cerebral abnormality in a recognised pattern

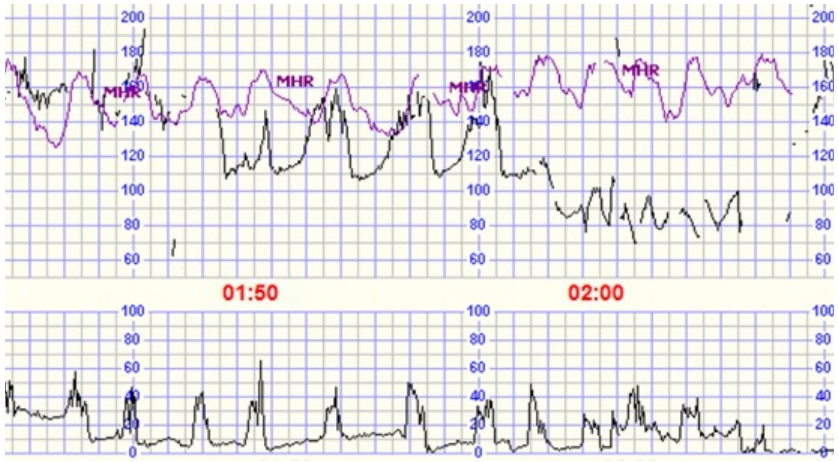
1. Fetal bradycardia



Bradycardia – usually <80 bpm for >10 minutes

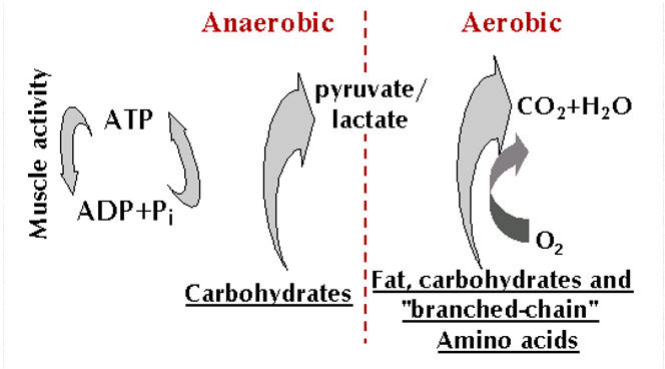
Very low Apgar with prior normal FH?
Think of maternal heart rate, doubling.





2. Cord blood acidosis

Why is metabolic acidosis so important?



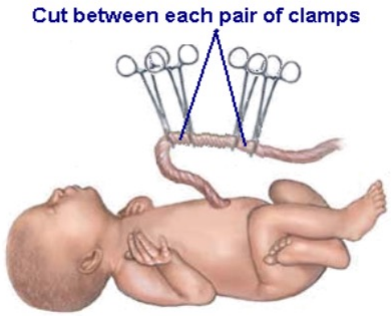
Aerobic metabolism

- ATP is the essential “energy currency” of all cells
- ATP is not stored
- Oxygen is required to make ATP

Anaerobic metabolism

- ATP is made from stored glycogen and lactic acid accumulates

Umbilical cord gases

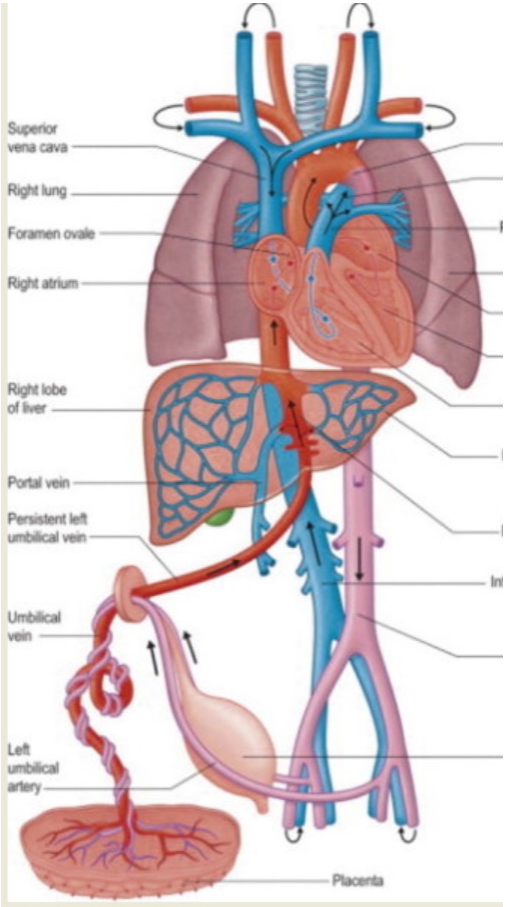


	Venous blood	Arterial blood
pH	7.25-7.45	7.18-7.38
H^+ ion concentration	56-36	64-43
PCO_2 mmHg	26.8-49.2	32.3-65.8
PCO_2 kPa	3.57-6.56	4.29-8.77
PO_2 mmHg	17.2-40.8	5.6-30.8
PO_2 kPa	2.29-5.44	0.75-4.1
HCO_3 mmol/L	15.8-24.2	17-27
Base deficit mmol/L	0 to 8	0 to 8

Data are mean ± 2 standard deviations. Lactate is < 5 mmol/L

From Pomerance JF 2012 Interpreting umbilical cord blood gases 2nd Edition: BNMG Pasadena http://www.cordgases.com

The umbilical arterial pH is always lower than the venous pH



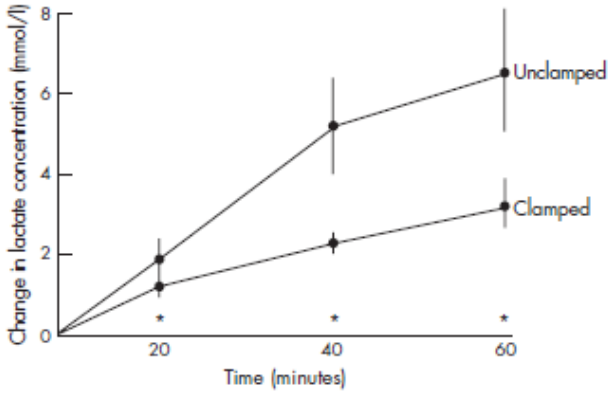
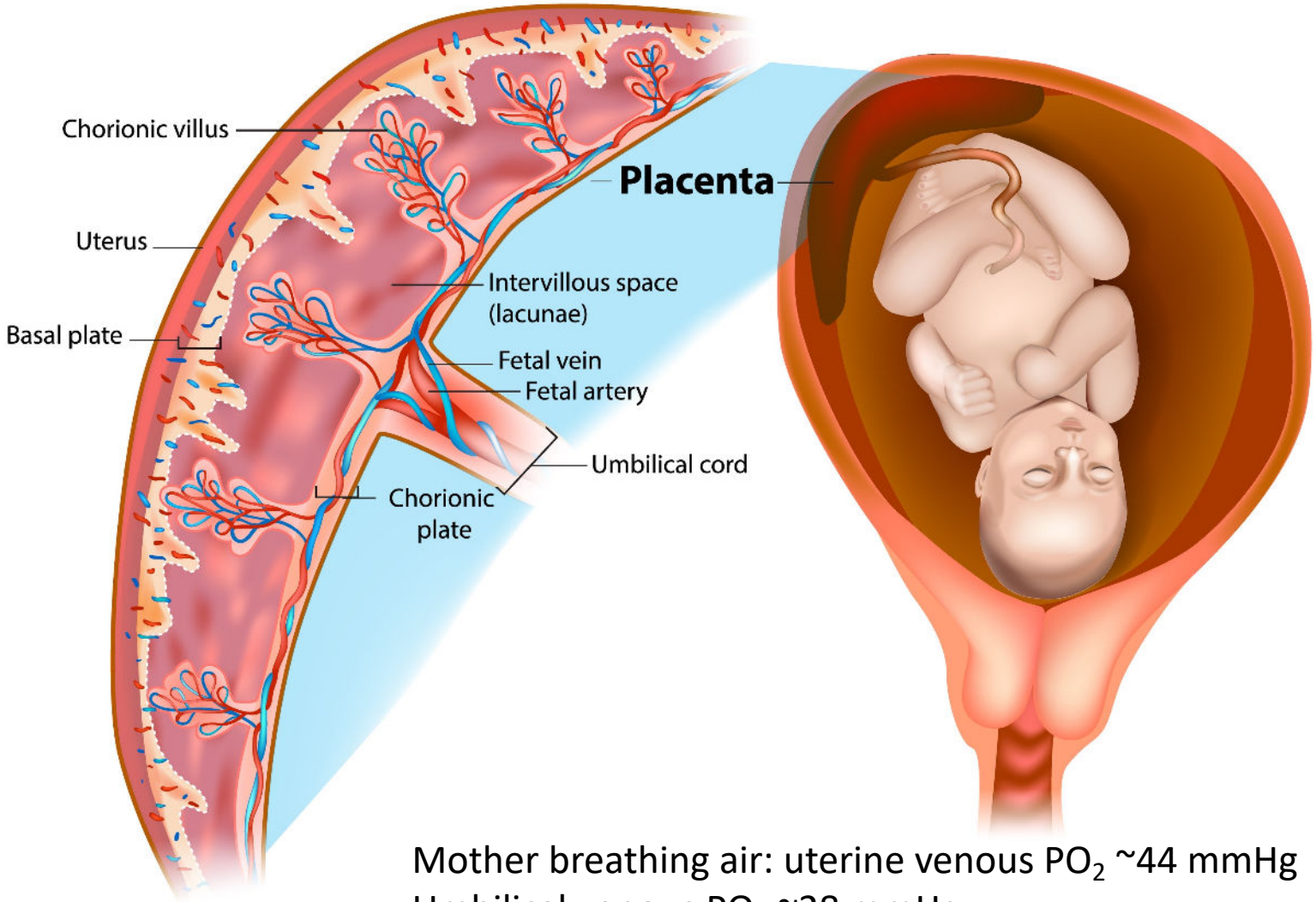


Figure 2 Change in arterial lactate concentration observed in clamped and unclamped vessels. Data are mean (SEM). *Significant difference between magnitude of change in clamped versus unclamped samples at corresponding time point ($p<0.05$).

no significant change in pH and blood gases in arterial blood in a clamped vessel stored at room temperature for up to one hour; but lactate increases

Armstrong, L. & Stenson, B. 2006,
Archives of Disease in Childhood, vol. 91, no. 5, pp. 342-345 *with permission*.



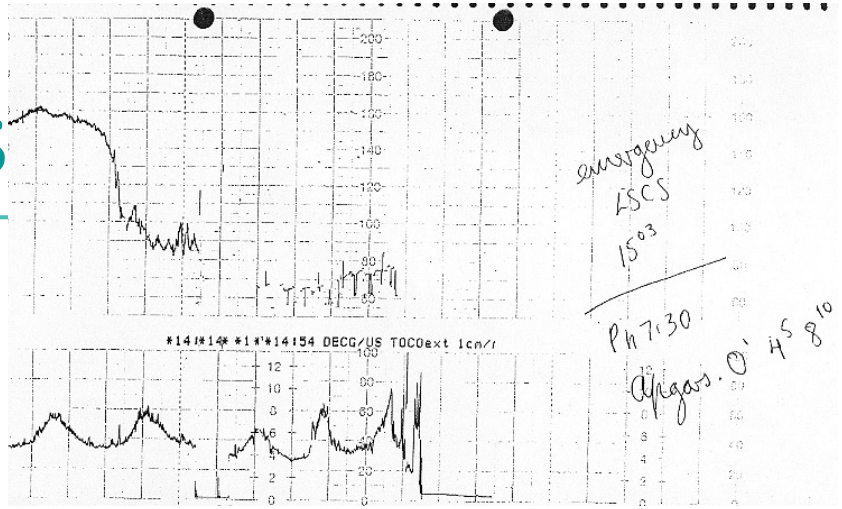
Mother breathing air: uterine venous PO_2 ~44 mmHg
Umbilical venous PO_2 ~28 mmHg

Mother in 100% oxygen: Umbilical arterial PO_2 <40 mmHg

Umbilical venous PO_2 cannot be higher than ~90 mmHg and usually less than 50

Adobe stock image, with subscription

Paradoxical results



Umbilical arterial pH can be significantly lower than the venous pH in cord occlusion

Check all the values if available; same vessel sampled twice

Use the appropriate normal ranges (labour?)

Check for internal inconsistency, unphysiological levels (e.g high oxygen)

Was the sample correctly processed?

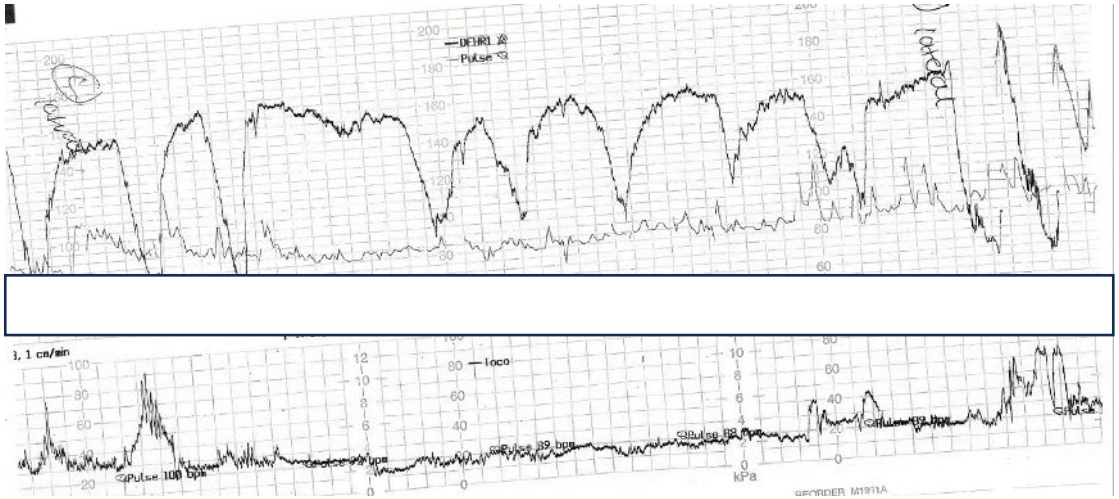
Look at the early neonatal values, lactate if available

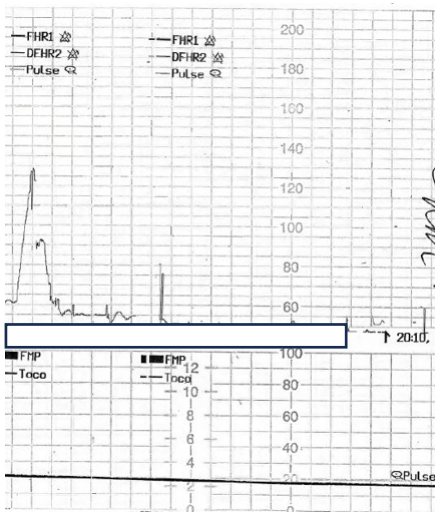
Occasionally complete cord occlusion = normal results

Blood Gas Values		
pH	7.318	
pCO_2	8.32	kPa
pO_2	4.04	kPa
Acid Base Status		
$cHCO_3^-(P,st)_c$	27.6	mmol/L
ABE_c	4.4	mmol/L
SBE_c	5.3	mmol/L
Oximetry Values		
ctHb	9.5	g/dL
sO_2	53.5	%
FO_2Hb	52.5	%
FCOHb	0.6	%
FHHb	45.6	%
FMetHb	1.3	%
Electrolyte Values		
cNa^+	133	mmol/L
cK^+	4.8	mmol/L
cCa^{2+}	1.38	mmol/L
cCl^-	98	mmol/L
Metabolite Values		
cGlu	6.3	mmol/L
cLac	2.7	mmol/L
ctBil	18	µmol/L
Hct_c	29.5	%
Temperature Corrected Values		
pH(T)	7.318	
$pCO_2(T)$	8.32	kPa
$pO_2(T)$	4.04	kPa
Oxygen Status		
ctO_{2c}	7.0	Vol%
$p50_c$	3.84	kPa

Example

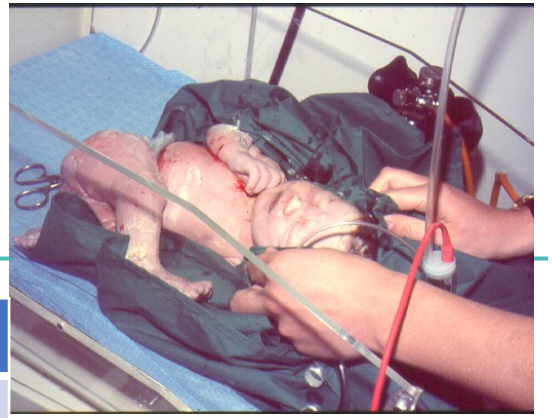
- Initial failed induction over 3 days, offered CS
- Then ROM and syntocinon
- CTG pathological, synt reduced, to theatre for trial
- Cord pH 7.37, BE -2 and 7.45 BE -2. Apgar 1,3,4





Baby pH after resuscitation 6.85, BE -20, lactate 16 ; HIE, cooled, MRI=BGT

3. Apgar scores



	Score	0	1	2
A	Appearance	Pale or blue	Body pink Extremities blue	pink
P	Pulse rate	absent	<100	>100
G	Grimace (reflex)	Nil	Some	cry
A	Activity (tone)	Limp	Some flexion	Well flexed, active
R	Respiration	Absent	Weak	normal

The score is reasonably robust although there is interobserver variability.

Check who calculated the score, and when, and does the narrative fit?

Was the heart rate measured using a stethoscope on the chest?

Was there a need for suction of meconium, etc?

Apgar scores should not go down

Time	comment
0630	Decelerations on CTG
0635	Birth. Apgar 5/6; blue, heart rate <60, grimacing and trying to cry; tone normal (score 2) Cord pH 7.36 base deficit 3.3
0640	Apgar score 1, B&M, chest compressions
0645	Heart rate 40
0655	Response after 4 doses of adrenaline

Dispute about the arrival time of the registrar, and the drug timings

In 851/1018 APA cases 1 min Apgar ≤3; ~30 SUPC - 85% approx

Terminal apnoea

V

Primary apnoea ?

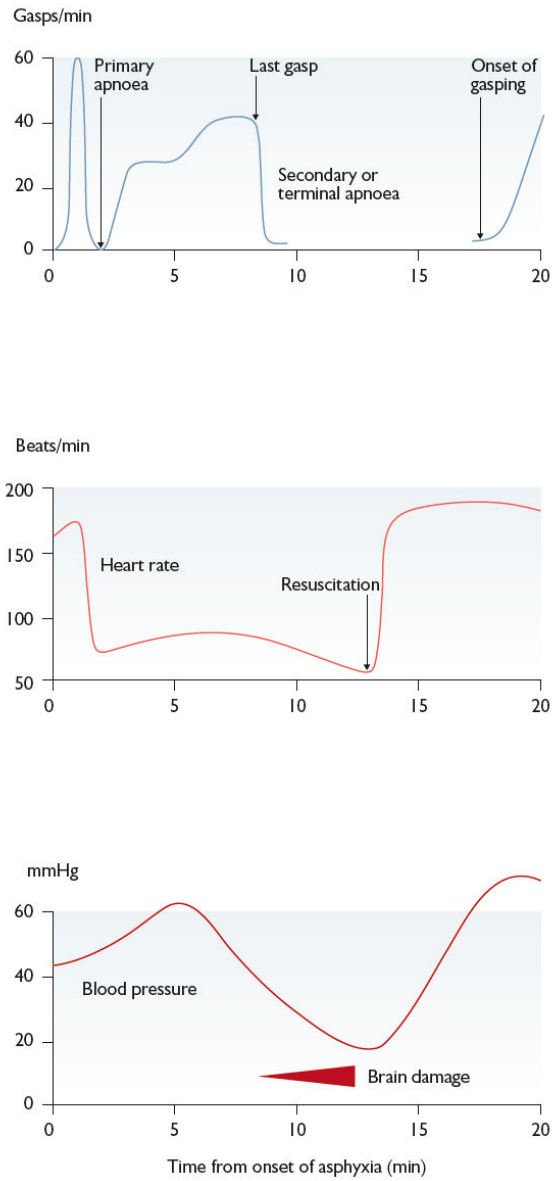


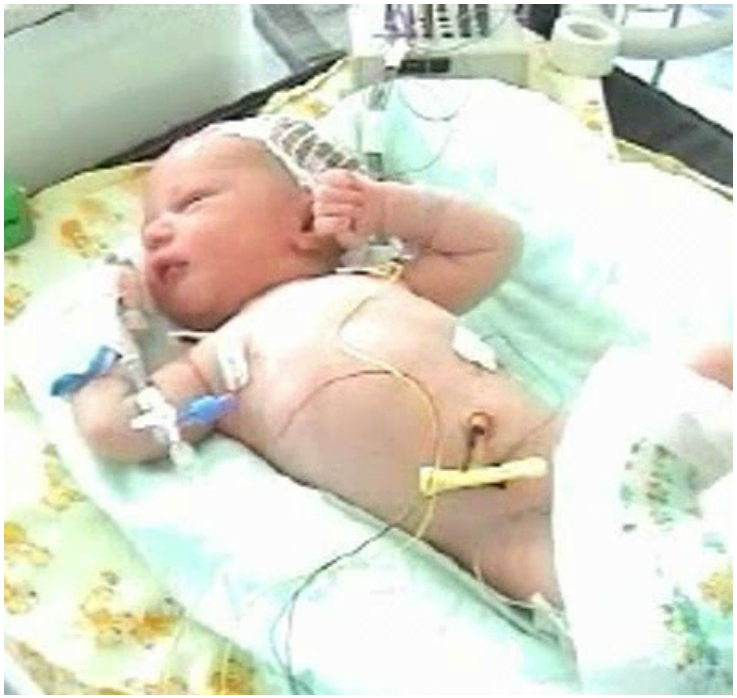
Fig 2 modified from Dawes et al J Physiol, as in Rennie Textbook of Neonatology 5th edition

4. Encephalopathy

- Seizures are the hallmark of encephalopathy, but mild encephalopathy can be present without seizure
- Frequent structured clinical examinations help to document the course and severity of encephalopathy
- In hypoxic ischaemic encephalopathy the condition evolves; seizures emerge after 12h, the baby's neurological state deteriorates and then improves
- Not all encephalopathy is HIE

Recognition of encephalopathy

- Changed sleep-wake cycling
- Altered level of consciousness
- Lowered reactivity
- Altered muscle tone
- Altered reflexes
- seizures



Modified Sarnat score

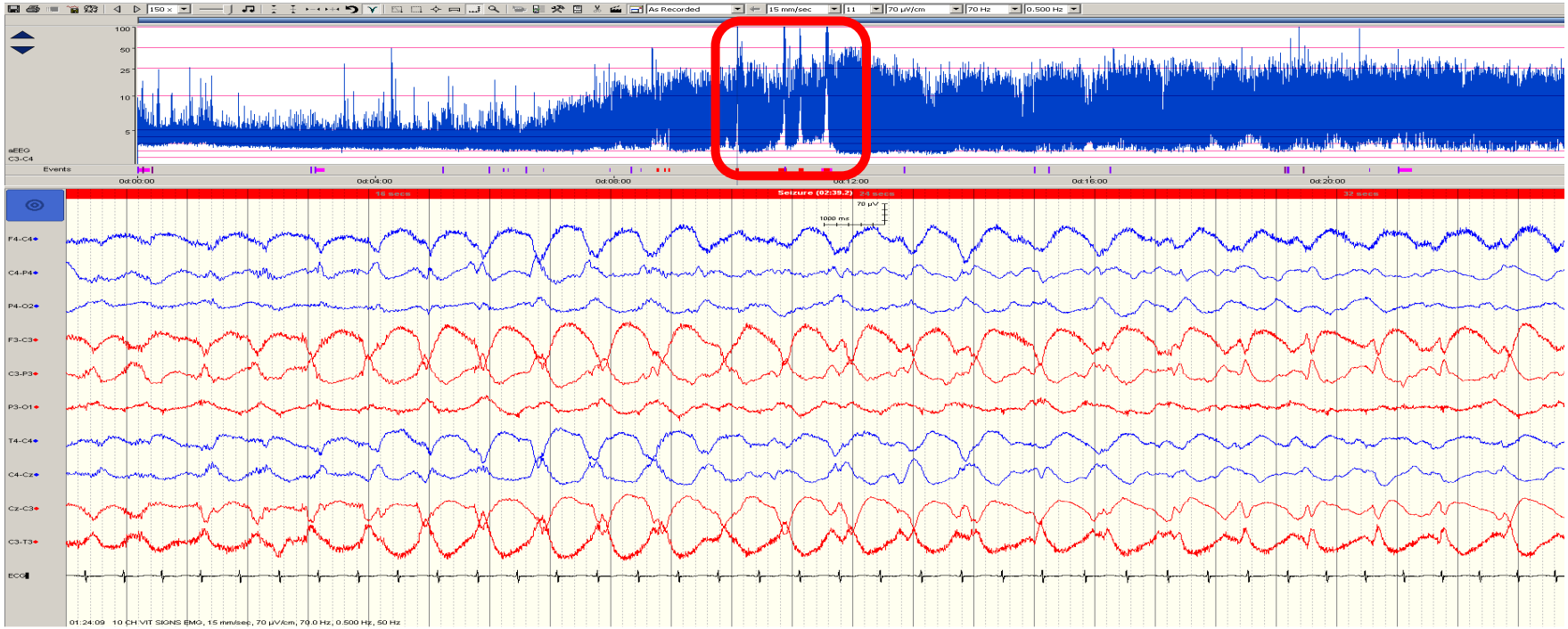
Domain	Stage1	Stage2	Stage3
Seizures	None	Common focal or multifocal seizures	Uncommon (excluding decerebration) Or frequent seizures
Level of consciousness	Normal hyper alert	Lethargic Decreased activity in an infant who is aroused and responsive Can be irritable to external stimuli	Stuperose/ comatose Not able to rouse and unresponsive to external stimuli
Spontaneous activity when awake or aroused	Active Vigorous does not stay in one position	Less than active Not vigorous	No activity whatsoever
posture	Moving around and does not maintain only one position	Distal flexion, complete extension or frog – legged position	Decerebrate with or without stimulation (all extremities extended)
tone	Normal – resists passive motion Hypertonic, jittery	Hypotonic or floppy, either focal or general	Completely flaccid like a rag doll
Primitive reflexes	Suck: vigorously sucks finger or ET tube Moro – Normal extension of limbs followed by flexion	Suck: weak Moro: incomplete	suck: completely absent Moro: completely absent
Autonomic system	Pupil – normal size Reactive to light Heart rate normal >100 Respirations - normal	Pupils – constricted <3mm but react to light Heart rate: bradycardia (<100 variable up to 120) Respirations: periodic irregular breathing effort	Pupils: fixed dilated, skew gaze not reactive to light Heart rate: variable inconsistent rate, irregular, may be bradycardic Respirations: completely apnoeic requiring positive pressure ventilation

Training in neurological examination

http://hopefn3.org/members/

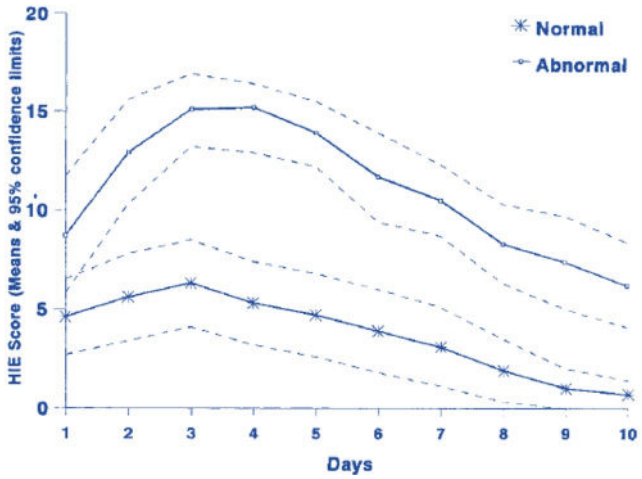
HIE – EEG Evolution……3 hours after delivery

HIE – EEG Evolution….12 hours - seizures



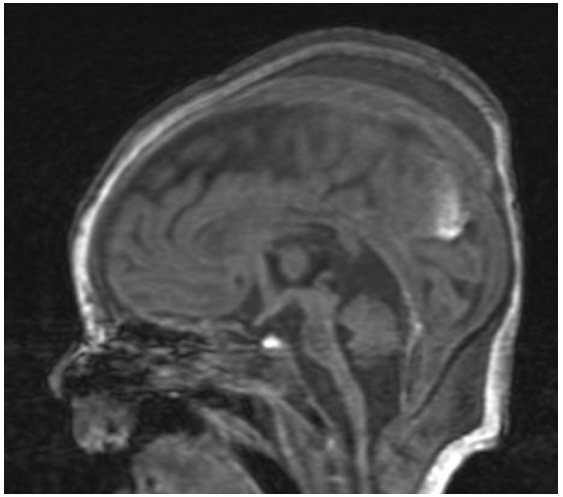
Thompson score – evolution and outcome

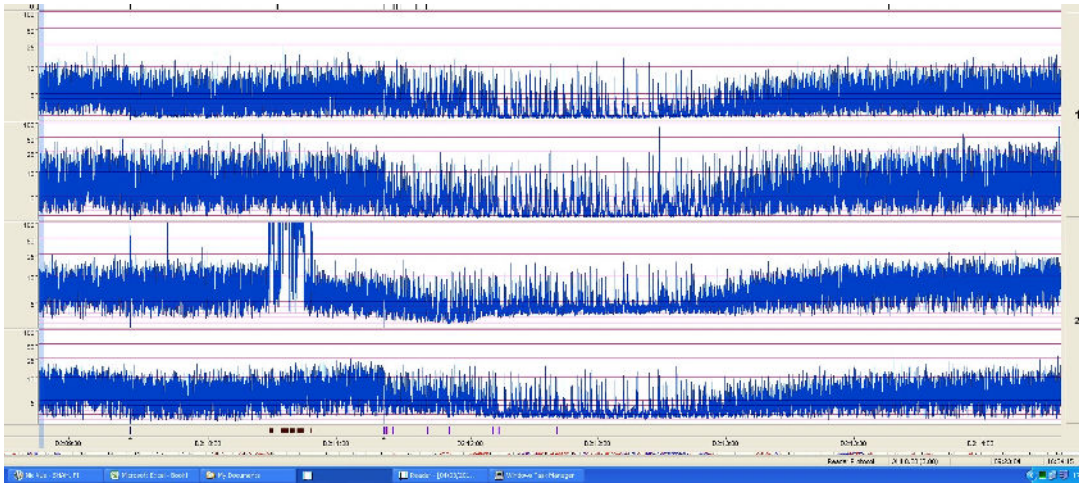
Sign	Score 0	1	2	3
Tone	Normal	Hyper	hypo	flaccid
conciousness	Normal	Hyperalert	Lethargic	comatose
Fits	None	< 3 per day	>2 per day	
Posture	Normal	Fisting	Distal flexion	decerebrate
Moro	Normal	Partial	absent	
Grasp	Normal	Poor	absent	
Suck	Normal	Poor	Absent	
respiration	Normal	Hypervent	Brief apnoea	IPPV
Fontanelle	Normal	Full not tense	tense	



Modified from Thompson et al Acta Paed Scand 1997;86:757-761

Atypical course - Cerebral malformation





Term baby; maternal swine flu at 4-6 weeks, polyhydramios, reduced FM

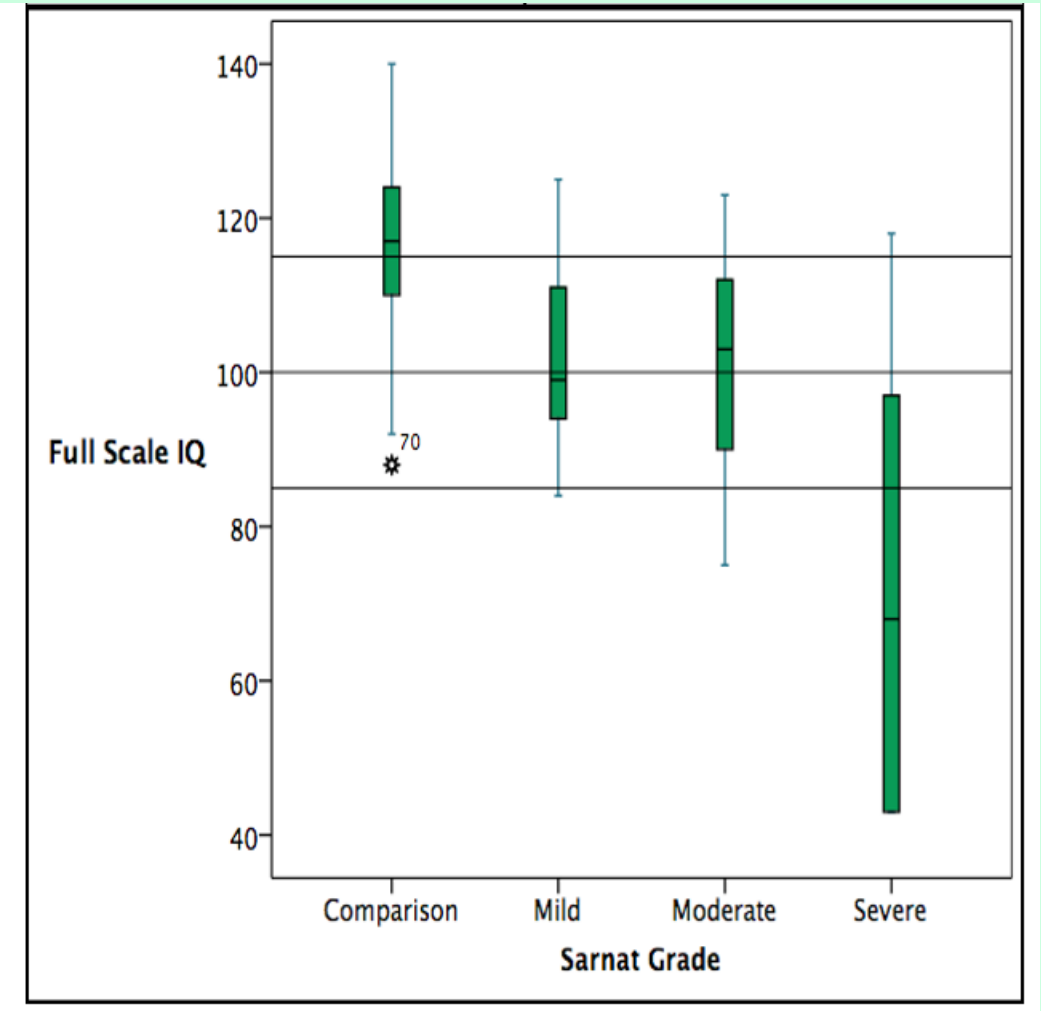
CTG Late decelerations, meconium liquor + maternal GBS; floppy at birth, cord pH 6.8, Apgar 2^{1} 5^{5} 5^{10}

Transferred for cooling; cranial US no oedema, EEG deteriorating, poor RE

Further neurometabolic & imaging investigations performed

Muscle biopsy - low levels mitochondrial NADH ubiquinone reductase and cytochrome oxidase – probable pontocerebellar hypoplasia type 6

Outcome by grade of encephalopathy



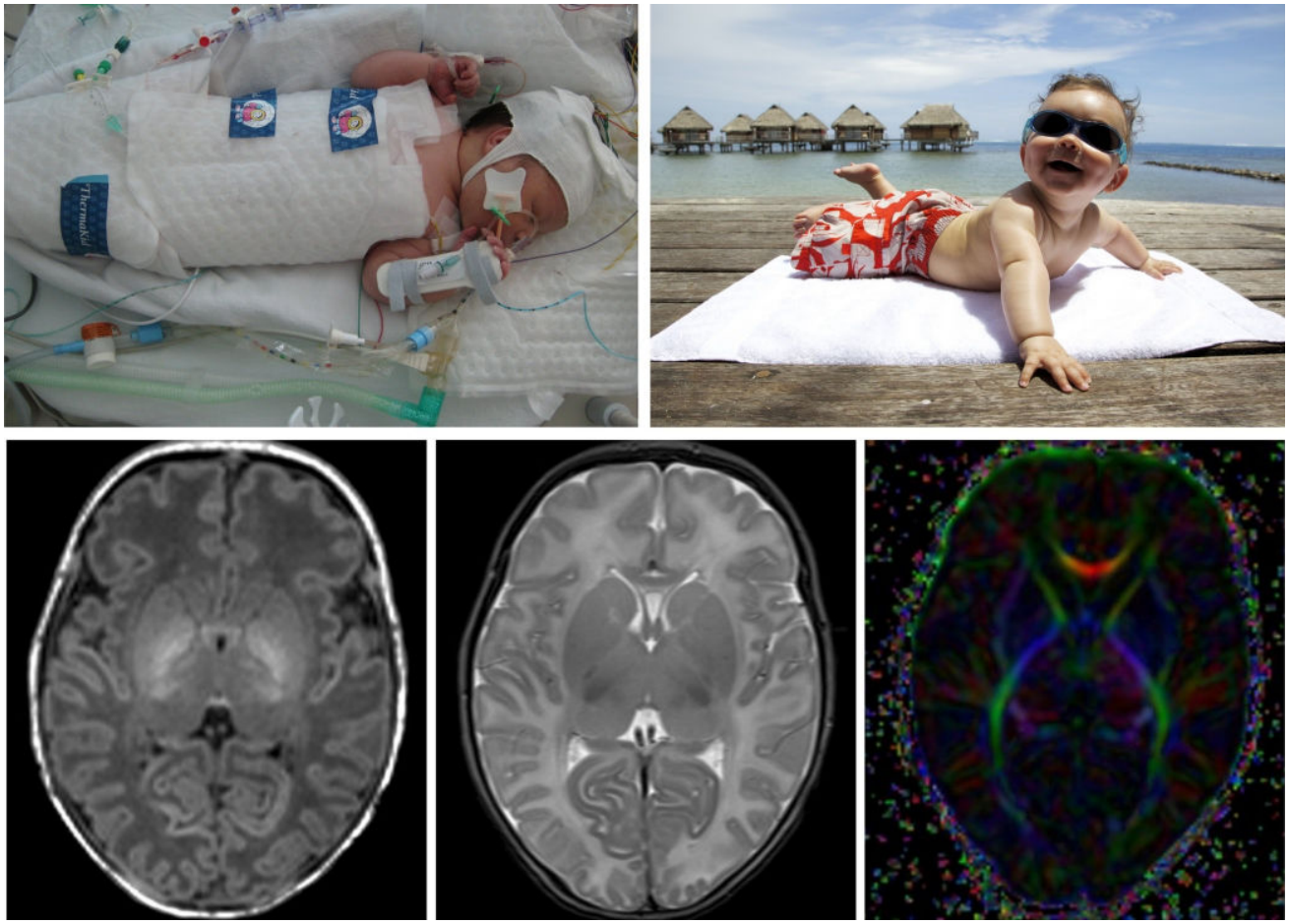
Grade 1 HIE – 75% were normal
Grade 2 HIE – 46%
Grade 3 or 4 – 21%

No difference autism/ADHD

35% mild HIE at 24 h needed support at school v 3% controls

personal communication
from Prof Deirdre Murray – see Early EEG grade and outcome Pediatrics 2016:138 (4) e 201659

Cooling -the biggest single neonatal therapeutic advance in over 50 years



British Association for Perinatal Medicine:

Therapeutic Hypothermia for neonatal encephalopathy - A framework for practice 2020

A. Infants ≥36 completed weeks gestation admitted to the NICU with at least one of the following:

· Apgar score of ≤5 at 10 minutes after birth

· Continued need for resuscitation, including endotracheal or mask ventilation, at 10 minutes after birth (see notes below)

· Acidosis defined as any occurrence of:

- pH ≤7.00
- Base deficit ≥16mmol/l

in any cord or baby gas sample within 60 minutes of birth

Infants that meet criterion A will be assessed for whether they meet the neurological abnormality entry criteria (B) by trained personnel:

B. Moderate to severe encephalopathy, consisting of altered state of consciousness (lethargy, stupor or coma)

AND at least one of the following:

· hypotonia

· abnormal reflexes including oculomotor or pupillary abnormalities

· absent or weak suck

· clinical seizures

Infants that meet criteria A & B will be assessed by aEEG (read by trained personnel):

C. At least 30 minutes duration of amplitude integrated EEG recording that shows abnormal background aEEG activity or seizures. (see notes below) There must be one of the following:

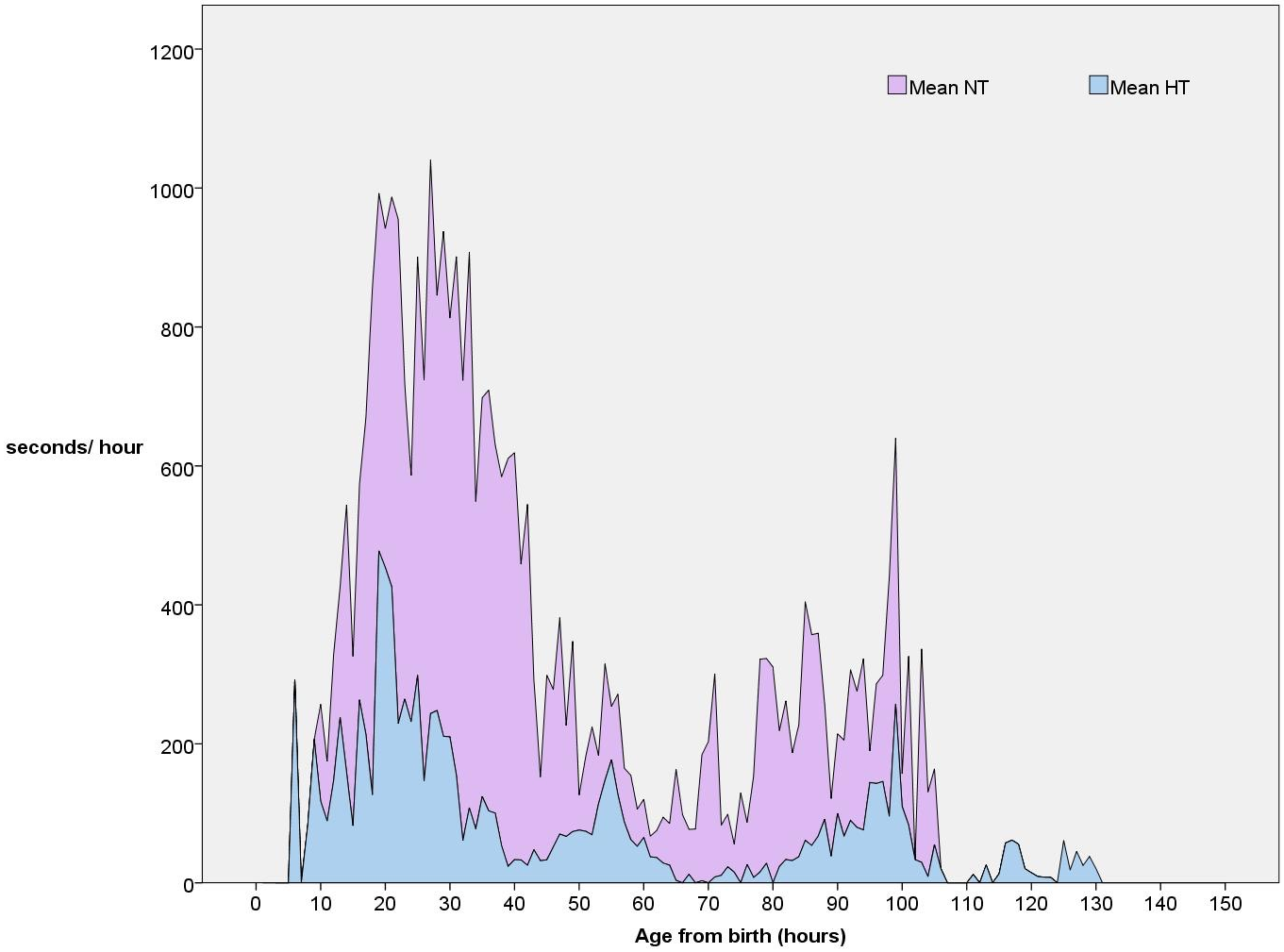
· normal background with some seizure activity

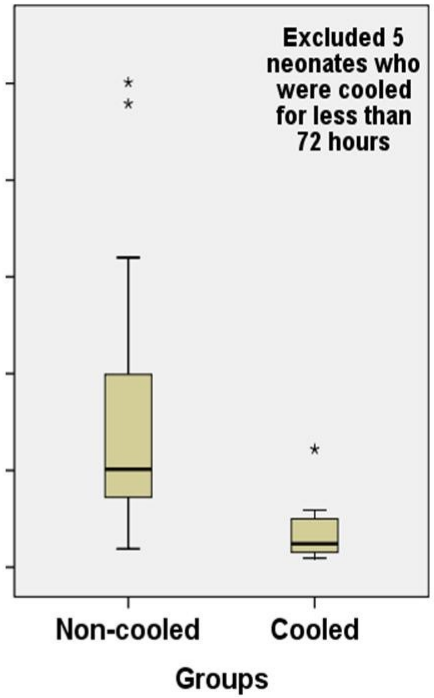
· moderately abnormal activity

· suppressed activity

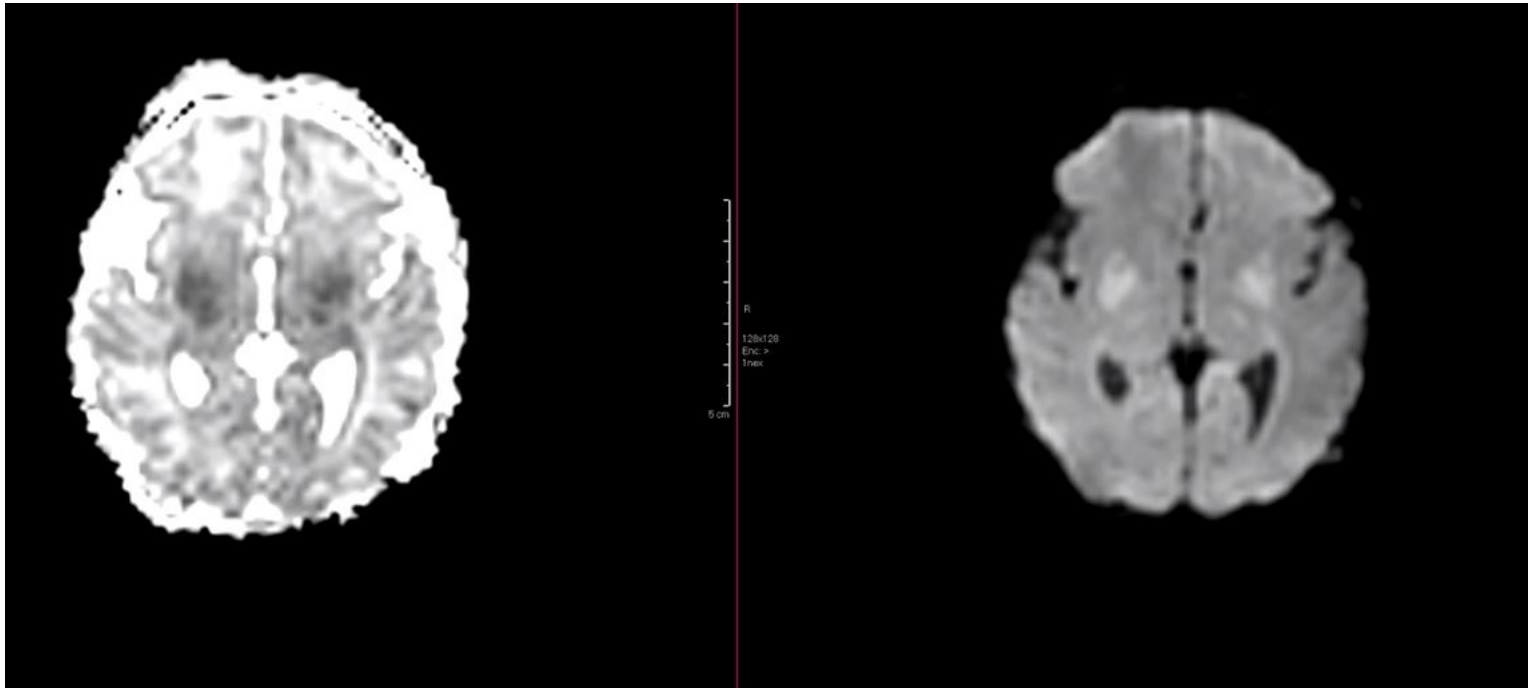
· continuous seizure activity

Seizures reduced in cooled babies





5. Imaging



DWI - Water sensitive sequences, peak at 3-5 days

“pseudonormalise” after 7-10 days

More normal MRIs after cooling, but function not always normal

62 cooled babies with MRI 2005-2011

35/62 had normal MRI

Of these 35, 26 had normal development (74%)

7 moderate delay (20%) – mainly cognitive

2 severe delay (6%)

Rollins et al Ped Neurol 2014 50(5) p 447-451

6. Type of disability

- Dyskinetic tetraplegic CP with or without learning difficulties
- Learning difficulties without cerebral palsy
- Memory problems (“developmental amnesia”)
- Executive function problems
- Social communication disorders, with and without learning difficulty

Dyskinetic tetraplegic cerebral palsy

Uncontrolled movements

Varying muscle tone

Difficulty swallowing and speaking (bulbar palsy)

Learning difficulties with no CP

	Cooled (163)	Not cooled (162)	P value
Dead	47 (29%)	49 (30%)	0.81
No disability	65/96 (68%)	37/45 (45%)	0.002
CP	21/98 (21%)	31/86 (36%)	0.03

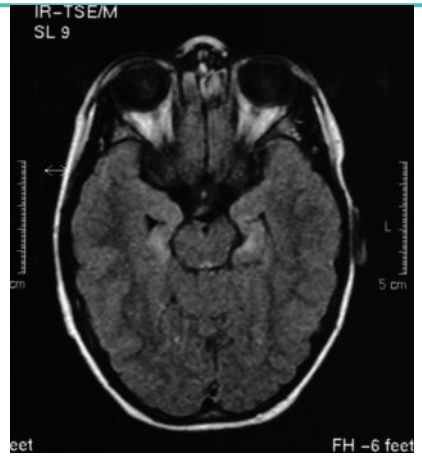
Among those who could be tested, there was no significant difference with respect to IQ scores on a continuous scale, or scores of working memory. There were differences in the score of attention/executive function.

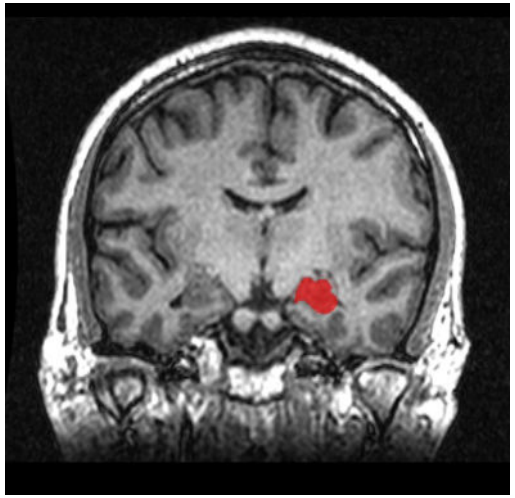
The US data are similar, with attention-executive function problems in 4% of cooled survivors compared to 13% of non-cooled (p=0.19).

Data extracted from Azzopardi et al NEJM 2014;371 pp140-149; Shankaran et al NEJM 2012;366:2085-2092

Atypical outcomes; example

2nd twin; cord prolapse; em CS
Apgar score 1 and 4 early neonatal pH 6.98
Seizures, not cooled (old case)
No physical disability at all
MRI – hippocampal damage
Borderline IQ , memory and executive function problems





De Haan et al Human memory development and its dysfunction after early hippocampal injury
Trends in Neuroscience 2006;29:374-381

Kasdorf et al Pediatric Neurology 2014;51:104-8

Grossman et al Archives Disease in Childhood fetal and neonatal edition 2023;108:F295-F301

Atypical outcomes; example

Cord prolapse at time of forceps – em CS
Apgar scores 3,5 but score 2 for HR
Cord pH 6.89, 7.11
Not cooled – crying with normal tone
No encephalopathy normal MRI
Social communication disorder. Boy. Family history of ASD

Modabbernia 2017 Environmental risk factors for autism: an evidence based review Mol Autism 8:13

Gardener 2011 Perinatal and neonatal risk factors for autism: a comprehensive meta-analysis Pediatrics 128:344-355

Conclusion

The spectrum of outcomes which are recognised to occur after perinatal hypoxic ischaemia has widened considerably, particularly since the introduction of therapeutic hypothermia.

Damaging acute profound HI in the immediate run-up to delivery is associated with birth depression, metabolic acidosis and an evolving encephalopathy.

The fewer the pieces fit into the jigsaw, the less likely that causation will be established - I have not addressed timing.

Thank you