Delayed clamping causes Jaundice.

First draft.

"You see, Hilary, that's one reason why we clamp the cord immediately. If you leave it, you can get serious jaundice, which cases brain damage." Those words, said to me after I complained about an immediately clamped cord, rang through my head later, as the paediatrian stood there with the blood test results saying that he wanted to put my badly jaundiced baby "under lights". I had four words for him: "Over my dead body". I'd had enough of lies, betrayal, and being treated like an idiot.

So when David was born, I waited with interest to see whether or all that blood from the placenta, resulted in jaundice worse than Ian's. David's jaundice was milder, and cleared up far quicker than Ian's did. So much for the wisdom of the experts.

In 1993 this[1] caught my eye:

"Take neonatal jaundice. Babies with high levels of bilirubin in their blood look yellowish. Physicians put the babies under special lights that alter the bilirubin molecule so it can be excreted. But testing and treating neonatal jaundice exacts an emotional price on mother and baby and the cost is high.

"On night while my wife [Dr susan Niermeyer of the University of Colorado Health Sciences Centre] was cooking dinner, she wondered out loud, 'Why are so many babies jaundiced?' recalls anthropologist John Brett of the University of California at San Francisco.

"I said, 'Probably because they're supposed to be." "

He may be right. Bilirubin acts as a toxic avenger, sweeping up molecules that can damage lung, interesting, eye and other cells.

In older children and adults, enzyme systems do the biochemical housecleaning: in newborns, those systems are not up to it."

The Guardian, reporting the same item, said,

Dr Brett and Dr Niermeyer think this [lights] is at best pointless and at worst harmful. Bilirubin is extremely good at mopping up oxygen-based free radical – highly reactive molecules which can do a lot of damage if allowed to wander around on their own.

[1] "Medical Frontiers", 1993. "Scientists turn to the Flintstone diagnosis" New Zealand Herald, May 26, Section 2, page 4.

…believe that the high bilirubin levels in babies are a finely crafted evolutionary response to being pushed into the oxygen-rich air of the outside world after nine moths of cosseting in the womb. Any brain damage, they say, is a result of other disease that allow bilirubin to get into the brain."

The Economist, in their rendition said all of the above, but after the Guardian bit above, added:

"brain – a place where it has no right to be, and from which it is normally excluded."

If this is enough for you, read no more.

If you want chapter and verse, here goes:

Expanding on this in 1999[2] Dr Niermeyer says, ***"Jaundice of the newborn is one of the most common, complex, well-studied, and misunderstood phenomena in modern pediatric medicine. Despite thousands of studies spanning nearly 50 years, neonatal jaundice, or hyperbilirubinemia remains one of the most baffling and frustrating aspects of health in newborns. We suggest that the primary reason for this ongoing confusion is the inappropriate conceptualization of the role of bilirubin in the newborn period… bilirubin in the healthy newborn ceases to be a confusing and troubling aspect of the newborn period but rather and expected and valued part of the transition to extrauterine life if viewed from the stance of an evolutionary theory of medicine."*** (my emphasis)

If, as Niermeyer says, all newborns have bilirubin levels well above the adults norm, and the majority develop and get rid of visible jaundice within the first few weeks without a problem…, what is the problem?

How did "jaundice" become a "dangerous disease"? The whole issue of brain damage (kernicterus) was first concentrated on in the 50's with regard to Rh incompatibility, (probably caused by immediate cord clamping in Rh incompatible babies) and as part of that, the medical profession attempted to define what was normal. The guidelines which determined "sickness" in normal physiological jaundice were extrapolated from poorly controlled studies on a small number of sick babies with erythroblastosis fetalis. Yet there are pitifully few studies trying to figure out the physiological basis of jaundice in a healthy newborn with no underlying illnesses.

There is a huge difference between pathological jaundice, and physiological jaundice.

A baby with jaundice caused by abnormal biochemical processes, will have a skin colour more akin to a yellow green. These disoreder have names which will cross your eyes, like; tyrosinaemia; hypothyroidism; hepatitis syndromes like biliary artesia, cystic fibrosis, choledochal cyst and alpha-1 antitrypsin deficiency; rhesus incompatibility; PKU; Gilbert Syndrome; and G6PD deficiency. Other pathological causes are sepsis, disseminated intravascular coagulation and Crigler-Najjar syndrome.

[2] Trevathan, W. 1999. "Evolutionary Medicine" June 17. ISBN-13: 978-0195103557 (Pages 7 – 23)

Yet people with Crigler-Najjar syndrome maintain bilirubin levels of 19 mg/dL for 50 years or more with no detectable damage to their nervous system.

The skin colour of normal physiological jaundice will appear as a more bronzy sun-tanned look. The original studies which decreed that breastfeeding "caused" jaundice, were done in hospital, in the days when babies were regimented on 3 – 4 hourly feed; it was assumed that mothers didn't have breastmilk until after several days, so babies were given glucose water, and formula, "to give the mother her rest", which of course, further delayed establishment of breastfeeding.

Ironically,(and empirically), when milk comes in fast, like mine does, a well-fed fully breastfed baby can showed exaggerated jaundice colour (and an abundant supply of wet nappies) which indicates that the laying down of good gut flora and plenty of "fluid" has increased the speed of bilirubin clearance. That is a positive physiological sign, which may be interpreted as a "worsening" of "disease".

However, one of the earliest signs of insufficient milk can also be exaggerated jaundice (with very few wet nappies), because the small amount of breast milk doesn't block de-conjugation of bilirubin.

The fact that most mammal species exhibit similar metabolic processes in their newborn, argues against bilirubin as being some aberrant toxic waste just waiting to cause brain damage. Yet that's what the medical profession believes, so they constantly test bilirubin levels, and when they get to a certain point, the baby is blindfolded and put under lights (phototherapy).

Phototherapy came about because of two observations[3]. The first was a "careless accidental exposure of some blood to sunlight which lead to the finding that bilirubin degraded to biliverdin when exposed to light." The second was the astute incidental observation by a nurse (Sister J. Ward, that the skin of jaundiced infants becomes bleached on exposure to sunlight, whereas unexposed skin does not.

Based on these two empirical observations, phototherapy was started. According to Niermeyer, phototherapy is detrimental to both a mother's confidence in herself and bonding. Mothers whose babies are treated seek more medical attention for their babies, and are more likely to stop breastfeeding. The mother becomes uncertain, defers to the system, and considers that her own body (breastfeeding) isn't up to the job.

The why's and what's of jaundice aren't explained to the mother, seemingly, because there is so much difference of opinion on what jaundice is all about, that it's easier to follow protocols, than give mothers some facts.

Babies who do get kernicterus and brain damage, are not thoroughly studied, looking at genetic bases for bilirubin expression, factors that permit bilirubin to cross the blood-brain barrier, underlying liver and metabolic disorders, sepsis … or the impact of immediate cord clamping on a wide range of physiological parameters in the newborn. Studies of jaundice outcomes should be done, but must have

[3] PMID: 11803408

proper controls of babies who closed their own cords, and were successfully appropriately breastfed on demand.

This is not merely and intellectually selfish idea for self-justification. Debate has arisen in medical literature of late, that phototherapy of babies for jaundice is linked with type 1 diabetes, asthma[4] and that children who have been put under lights, develop "considerably higher numbers of common and clinically atypical nevi[5]" (moles). The authors say, ***"In view of the immaturity of the skin and immune system in newborns, intensive neonatal phototherapy could markedly influence melanocytes and nevus developments."***

Is an increased risk of skin cancers, acceptable, if indeed bilirubin is a neonatal anti-oxidant scavenger of critical importance to good survival? You could say, it would be simpler to go back to using the sun, but ironically the phototherapy technicians[6] now decrees that ***"At present there is insufficient evidence to support exposure to sunlight for treating neonatal jaundice."***

If bilirubin is an antioxidant, and an oxygen free radical scavenger, how quickly does it take for a baby to raise its oxygen levels and what is the impact of that in the baby's body?

An immediately clamped newborn baby hasn't yet developed its anti-oxidant enzyme system and in utero is about 45% oxygen saturated. This baby, doesn't reach 90% oxygen saturation until 10 minutes after birth. Caesarean babies take even longer. We don't know what the situation would be for an unclamped baby.

Within 15 minutes this immediately clamped baby is dealing with more than twice the amount of oxygen, in a circulatory system which is being re-educated. This increased oxygen will produce oxygen free-radicals, which could potentially damage protein, lipids and nucleic acids. Babies, both clamped and unclamped, develop jaundice. The enzymes superoxide dismutase, catalase and glutathione peroxidase are at much lower levels in newborns than in adults, and when these enzymes, and other antioxidant systems are at their lowest activity, bilirubin rises rapidly and falls slowly over several weeks.

A recent article[7] summarises this:

"Recently, some authors have suggested that unconjugated bilirubin is physiologically useful and can act as an antioxidant. During the oxidant stress, oxidants such as nitric oxide play an important role in the pathogenesis of human diseases, especially in the neonatal period. Neonates have limited antioxidant protective capacity against the circulating free radicals, and bilirubin is a potent antioxidant cytoprotectant. Increased oxidative stress in neonates may trigger hyperbilirubinemia and high serum bilirubin levels may protect the cells from oxidative damage."

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[4] PMID 18305267
[5] PMID 18536103
[6] PMID: 12697014
[7] PMID 18426853.

As I thought back to Ian, with his wonderfully bronze levels of jaundice which lasted over three weeks, and David's much milder and shorter form, there is no doubt in my mind, that jaundice has nothing to do with when the cord was clamped. To me, it's a programmed coping mechanism.

Many studies[8] have been done recently, which show that late clamping which markedly increases haematocrit, blood volume and tissue oxygen saturation, does not increase hyperbilirubinaemia, and there is no difference in either group.

The circumstance I believe caused Ian's more serious jaundice, were; Syntocinon[9] augmentation; and epidurals (especially bupivacaine which is what I was given). Those are just two amongst quite an array of drugs used during later, which can increase jaundice, supposedly through taking up space on the plasma sites which transport bilirubin to be excreted, leaving it free in the blood. However, I wonder how much "stress" aggressive management created inside him, "requiring" a higher anti-oxidant level of bilirubin, to meet his needs. By comparison, David's birth was a breeze and much more peaceful for both of us.

The study[10] which meshed Niermeyer's thoughts together in my mind, came out in 2004. This should be compulsory reading for neonatologists. In bird, reptiles and amphibians, the less toxic biliverdin is the end point of blood cell breakdown. In mammals, biliverdin is reduced to the seemingly more toxic "bilirubin". Sedlak asks the question, ***"Why have mammals evolved an energetically expensive and apparently unnecessary enzymatic step to converting the relatively innocuous biliverdin to the more toxic bilirubin? Moveover, why would nature develop a system that generates "elevated" bilirubin levels in a high proportion of all neonates?"*** Sedlak points out that looked at from the "why" point of view, biosynthesis of bilirubin does not seem to make sense.

But he said that if bilirubin protects against oxidation of lipids such as linoleic acid and vitamin A and had a greater antioxidant level than vitamin E, then maybe it does. If 10 nanomolar bilirubin can protect cultures from the oxidant stress of 10,000 times higher concentrations of hydrogen peroxide, that's worth having. When a molecule of bilirubin acts as an antioxidant, with biliverdin reductase, it is oxidized to biliverdin. Biliverdin reductase is an abundant and ubiquitous enzyme with a high turnover rate, so recycling biliverdin and bilirubin around and around, and using it as a cytoprotectant and antioxidant which is gradually degraded and later excreted, would ***"represent an elegant tour de force on the part of nature making use of bilirubin's antioxidant capacity but ensuring that tissues had low endogenous levels of bilirubin."*** He lists the many studies on various conditions in babies and adults where bilirubin protects from a vast array of disorders, and where people with high levels of bilirubin have a survival advantage.

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[8] Zaramella, P. et al 2008 "Early versus late cord clamping: Effects on peripheral blood flow and cardiac function in term infants." *Early Hum Dev.* Mar;84(3):195-200. PMID: 17513072.

[9] PMID: 12552319.

[10] Sedlak, T.W., et al. 2004. "Bilirubin Benefits: Cellular protection by a Biliverdin Reductase Antioxidant Cycle." Pediatrics. Jun;113(6): 1776-82, PMID: 15173506.
http://pediatrics.aappublications.org/cgi/reprint/113/6/1776?ck=nck

He also points out that in babies, serum bilirubin are 100 to 1000 times higher than intracellular values, but that 99% of that is bound to plasma and not available for intracellular action, but would be likely to have a direct therapeutic action in coping with oxidative stimuli wherever blood flows, but also feeding tissues. The tissue bilirubin would most likely function in diseases of specific organs. He also pointed out that scientists knew little about how bilirubin moved in and out of cells.

The whole article argued that bilirubin was a plausible survival strategy, and finished the article with the comment that, ***"uric acid was once regarded solely as a toxic metabolite responsible for gout, whereas it is now increasingly appreciated as an antioxidant. Similarly physiologic antioxidant roles for bilirubin, may detoxify its traditional nefarious reputation."***

So why is it so important to find out just what bilirubin does; why all mammals use it, and why physiological jaundice affects the majority of babies?

If you are going to look at what causes brain injury and such lesions as neonatal encephalopathy, you have to take into consideration that[11]: ***"Since oxygen free radicals are considered important in the genesis of ongoing injury following hypoxia-ischemia, therapies targeting the destruction of oxygen free radical have been developed…. Neuroprotection has only been shown when these agents have been administered several hours before the hypoxic-ischemic insult."***

Is that what bilirubin, the ultimate antioxidant is for? Yet most paediatricians consider physiological jaundice a toxic evil to be removed as fast as possible.

Cord clamping in this context is important, because while cord clamping doesn't affect whether or not a baby gets jaundice, not cord clamping is proven to protect babies from free radical brain damage:

"A recent randomized trial in brain hemodynamics demonstrated that delayed clamping (by 60 – 90 sec) improved cerebral oxygenation in the first 24 hours of life.. delaying cord clamping by 30 – 120 s seems to be associated with a lesser need for transfusion and less intraventricular haemorrhage. [12]***"***

Another study [13]***says that the additional blood in preterm infants obtained by delayed cord clamping " helps stabilize cerebral blood flow, autoregulation, increase oxygen delivery to vulnerable tissues, prevent ischemia, and cytokine release, and provide additional stem cells to establish adequate immunocompetence". It also prevented late onset sepsis. "Delayed clamping of the umbilical cord… improved oxygen delivery to the tissues in increasing system blood volume. Increased blood volume was advocated to facilitate pulmonary adaptation with decrease for medical interventions particularly mechanical ventilation… this reserve potentially reduces the risk of hypoxic ischemic events to the brain..placentofetal transfusion may be beneficial to reduce the risk of disturbed cerebral***

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[11] PMID 15693398.

[12] Zaramella, P. et al 2008 "Early versus late cord clamping: Effects on peripheral blood flow and cardiac function in term infants." *Early Hum Dev.* Mar;84(3):195-200. PMID: 17513072.

[13] PMID: 17332197.

oxygenation. Our study demonstrates an increased tissue oxygenation in the neonatal brain after delayed cord clamping."

I find it hard to believe that delayed, or no cord clamping, ONLY does that in preterm babies!

And at the BMJ, the debate goes on[14]with many doctors calling for a halt to the barbaric practice of immediate cord clamping.

How could a baby be better set up for survival, than all the blood in the cord and placenta to increase oxygen levels, prevent brain damage etc, with an added dollop of bilirubin to mop up free radicals caused by the required increase in oxygen use.

What a unique system, designed specifically to bridge mammalian babies over that time period when their own antioxidant systems haven't yet got up to speed, and optimum survival of healthy babies without any pathological disease, is the name of the game.

Lights, anyone?

[14] http://www.bmj.com/cgi/eletters/335/7615/312 and http://www.bmj.com/cgi/eletters/334/7602/1027-f