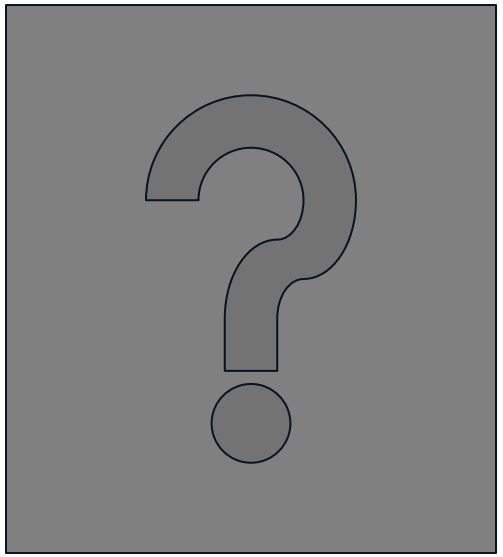
Infant Jaundice

Why does it occur and what can we do?

50-80% of Newborns today



What is jaundice?

- Yellow skin and eyes from buildup of bilirubin, which comes from RBC breakdown, and delayed clearance.

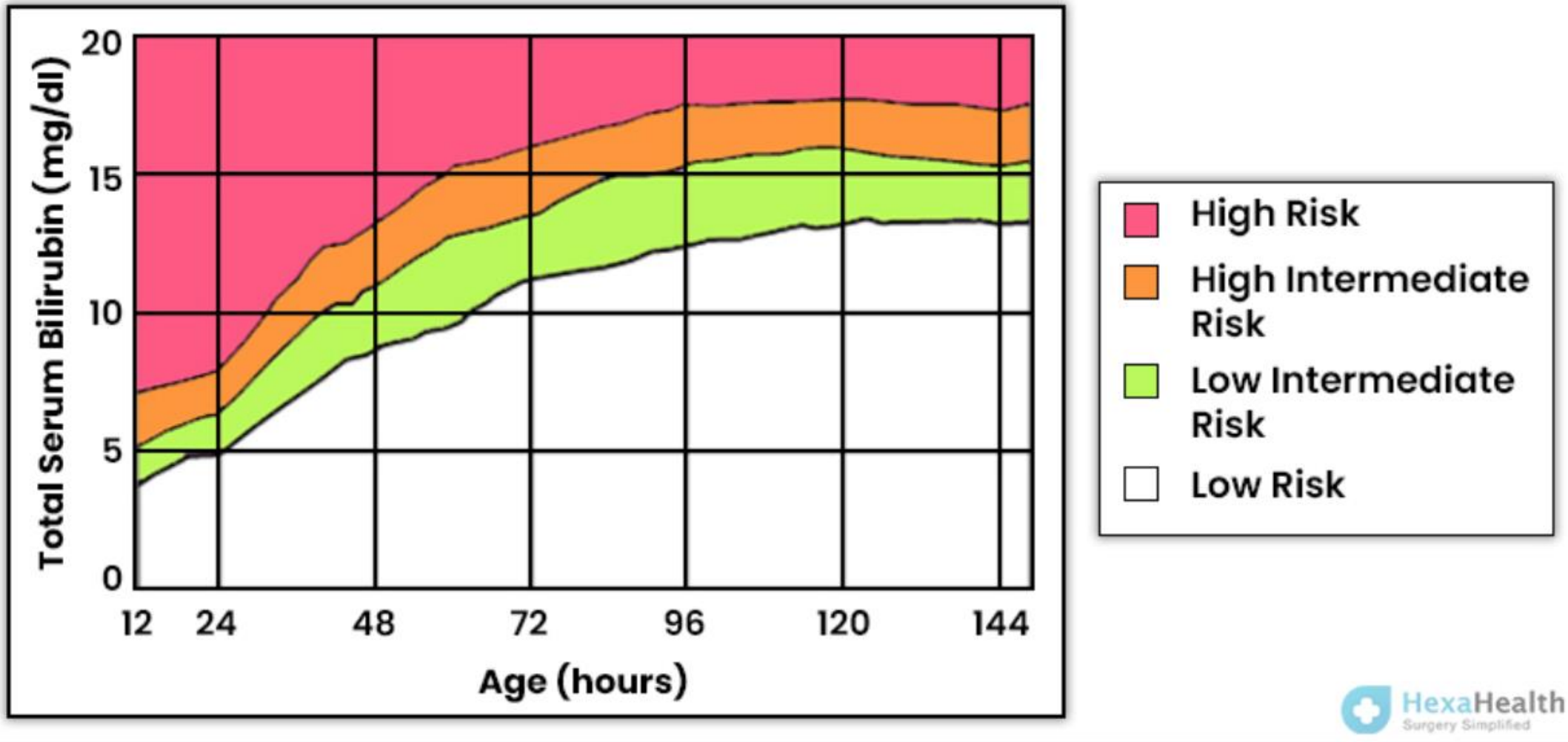
Types of infant jaundice

- **"Physiologic"**
  - "Breast milk jaundice"
    - After one week, not severe, will resolve but can take up to 3 months. (The etiology includes pregnane-3a,20β-diol is thought to inhibit bilirubin's conjugation, which in turn impedes bilirubin excretion.)
  - "Breast feeding jaundice"
    - Usually means the baby isn't feeding well, may be dehydrated, and isn't eliminating pigments via intestines and kidneys
  - Blood group incompatibility
  - Other severe disorders

When to seek medical help:disclaimer

- If occurs in the first day of life
- If severe or worsening rapidly
  - Beware of medical interventions. Can help and hinder.

Bilirubin Level in Newborn



Trend

- Aside from more deadly congenital causes of jaundice, infant jaundice is not reported to be common in medical texts before the 1900's
- Since 1990 on the rise globally (Zuo 2023) though mortality has declined.
- What is the cost of treatment?

Treatment

- Ancient Egypt, sun worship
- Essex UK report of a nurse working in premature ward, noted sunlight to decrease the yellow color in babies.
  - Lower bilirubin in test tube set in sunny windowsill.
- 1950's sunlight or full spectrum lights were used.
- After 1950, blue lights became the standard of care.
  - Many toxicities associated with this type of light.

Bilirubin

- Is actually an antioxidant, that has the capacity to dampen down oxidative stress. Getting rid of it using blue light may be effective and helpful in severe cases, but for everyone else, should be thoughtfully re-considered.

Yes, bilirubin is considered an antioxidant.

Bilirubin is a yellow pigment produced when red blood cells break down. It has been shown to have antioxidant properties, meaning it can protect cells from damage caused by free radicals.

Specifically, bilirubin can:

- Scavenge reactive oxygen species (ROS), such as peroxyl radicals.
- Protect lipids from oxidation.
- Inhibit the production of inflammatory mediators.

These antioxidant effects may contribute to the beneficial health effects associated with moderate levels of bilirubin, such as reduced risk of cardiovascular disease and certain types of cancer. However, excessively high levels of bilirubin can also be harmful.

Oxidative stress

- Terms: redox, oxidation, reduction, free radicals.
- Unpaired electrons can cause damage.
- Red blood cells are extremely susceptible to lipid peroxidation since they are rich in unsaturated membrane lipids, have rich supply of oxygen and transitional metal catalysts.
  - Giving unnecessary oxygen also problematic.
- Neonates have less capacity to deal with OS than adults.
  - More so in preterm babies.

What causes oxidative stress?

- Poison/inflammation/stress
  - Vaccines to mother
  - Infections in mother
  - Rough/stressful/chemical birth
  - Hep B vaccine to newborn
  - Vitamin K injection to newborn
  - Drugs to baby after birth
  - Immediate cord clamping
  - Blue light to baby for the “just in case” situations
  - Blue light to mother
  - nnEMF: mitochondrial quantum consequences

Prevent jaundice!

- Maternal redox status optimized
  - Circadian match:wake sleep sunlight and darkness
  - Eat real food with healthy oils and proteins.
  - Avoid all stress including **unnecessary medical threats**
- Blue light: phones/TV/LED
- Wifi at home
  - Ethernet is better for everyone
- Sunlight to mother all over body in appropriate doses
  - Skin type dependent
- Move away from densely populated 5G cities if possible

Antioxidants

- The problem is deeper than just some missing antioxidants, but sometimes antioxidants can intervene.

https://x.com/DrJackKruse/status/1916505491053695486

Antioxidant vitamins and hyperbilirubinemia in neonates

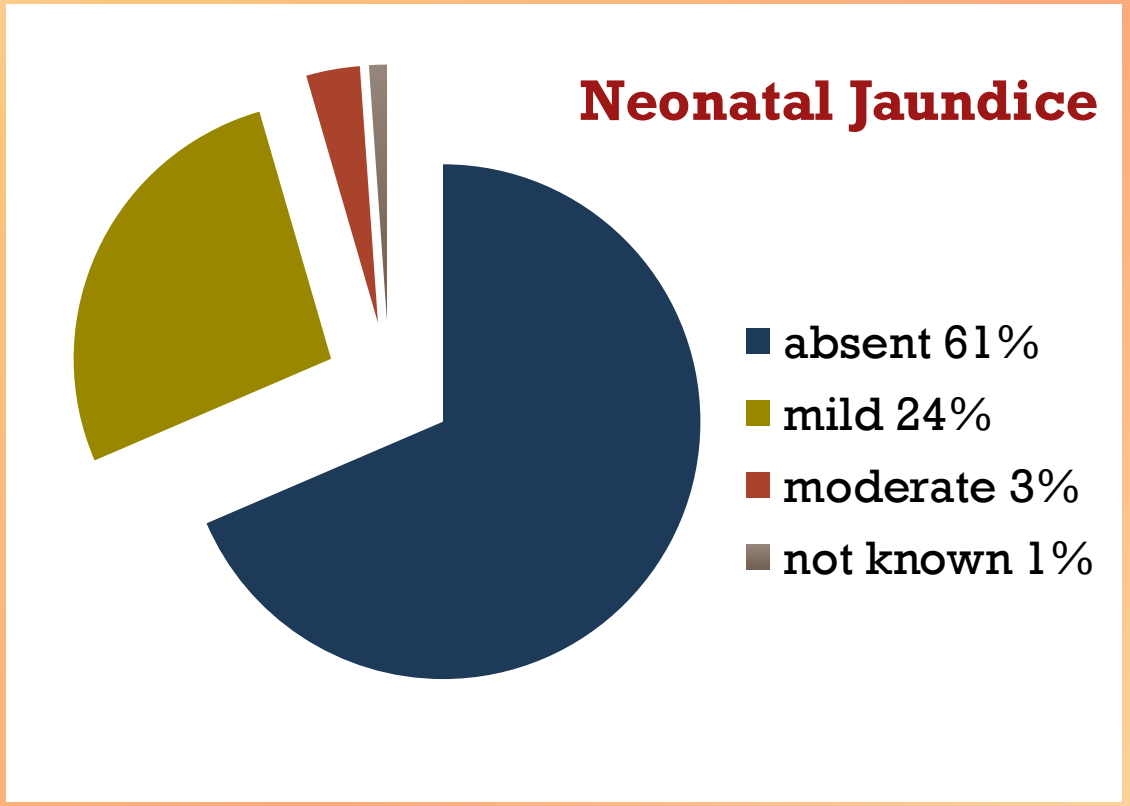
Parameters	Neonates without hyperbilirubinemia (n=119)		Neonates with hyperbilirubinemia (n=11)		P value (95% CI)
	Mean (SD)	Median (Range)	Mean (SD)	Median (Range)	
Vitamin C (µmol/l)	132 (36)	127.7 (56-250)	87 (22)	89.4 (62-124)	0.0001 (0.4500,1.0501)
Vitamin E (µmol/l)	10.4 (5)	9.1 (4-40)	7.5 (2)	6.3 (5-14.8)	0.001 (0.500,1.700)
Bilirubin (µmol/l)	65 (24)	58.1 (15-100)	238 (56)	246.2 (143-306)	0.0001 (-12.400,-8.370)

Abdul-Razzak 2007. PMID: 19675711

Prevention of jaundice: Vitamin C during pregnancy

- 89 pregnant women during first trimester of pregnancy
- 1 Gram Vit C orally, every other day over six months

"The physiological jaundice of the newborn, which is reported in 80-85% of cases (Anselmino and hoffmann: Ylppo: Fujimore) and was, therefore observed to a more or less degree, only 27.5%"



Garbelli 1957. PMID: 13420320

The effect of vitamin C supplementation in the last month of pregnancy on neonatal bilirubin levels; A double-blind randomized clinical trial

M Khadem Al-Hosseini [1], S T Rahideh [1], A Saadati [2], N Rahmati [3], F Azadeh [4], L Janani [5], F Shidfar [6]

Affiliations + expand

PMID: 32444041 DOI: 10.1016/j.ctim.2020.102359

Abstract

Objectives: Jaundice is a typical condition in the neonatal period, particularly in the Asian continent. Drowsiness and disruption of breastfeeding, behavioral and neurological disorders, hearing loss and mental retardation are the results of impairment in controlling it. The increase in oxidant substances can stimulate the heme oxygenase enzyme and increase the conversion of heme to bilirubin. In some studies, vitamin C levels in the blood of infants with hyperbilirubinemia were lower than in healthy infants.

Design: In this double-blind clinical trial study, 144 healthy pregnant women aged 20-40 years who were in 34th weeks of gestation were randomly divided into intervention, and control groups and until the end of pregnancy, they took a 500 mg tablet of vitamin C or placebo (Preparation of starch) daily. Demographic information, dietary intake, and physical activity level of the participants were also evaluated. The total blood bilirubin level was measured on the fifth day after birth using a sample of the neonatal heel. Statistical analysis was performed using SPSS software version 22. In this study P-value < 0. 05 was considered significant.

Results: Of the 144 participants, 128 of them completed the intervention. There was no significant difference between the two groups at the level of vitamin C intake through diet, and anthropometric indices, but the total bilirubin level in the neonates of the two groups was statistically different (P = 0.02).

Conclusion: Vitamin C supplementation in the last month of pregnancy had a significant effect on neonatal bilirubin level and decreased it significantly.

What can blue light to infant do?

- Growth plate damage in rats
- Mutagenic/gametocidal in rats
- Alter circadian genes
- SIADH
- Myeloid leukemia
- Change in cytokines
- Cardiorespiratory changes
- Blood flow and kidney function
- DNA damage
- Eye damage

J Pediatr (Rio J). 2007 Jul-Aug;83(4):319-22. doi: 10.2223/JPED.1645. Epub 2007 Jul 11.

Total oxidant/antioxidant status in jaundiced newborns before and after phototherapy

Ali Aycicek [1], Ozcan Erel

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PMID: 17625638 DOI: 10.2223/JPED.1645

Abstract

Objective: To assess the effect of phototherapy on serum oxidant and antioxidant status in hyperbilirubinemic full-term newborns.

Method: Thirty-four full-term infants from 3 to 10 days of age exposed to phototherapy were studied. The serum antioxidant status was assessed by measuring the total antioxidant capacity (TAC) and individual antioxidant components: vitamin C, uric acid, albumin, thiol contents and total bilirubin. The oxidant status was assessed by determining the total oxidant status (TOS), oxidative stress index (OSI) and individual oxidant components: malondialdehyde (MDA), and lipid hydroperoxide levels.

Results: Vitamin C, uric acid, total bilirubin and MDA concentration were significantly lower, whereas serum TOS, lipid hydroperoxide and OSI levels were significantly higher after phototherapy ($p < 0.05$). There were significant positive correlations between serum total bilirubin and MDA ($r = 0.434$, $p = 0.001$).

Conclusions: Although the MDA level was reduced after phototherapy, phototherapy has a negative impact on numerous parts of the oxidant/antioxidant defense system in jaundiced full-term newborns, exposing them to potential oxidative stress.

"The conclusion is that phototherapy has a negative effect on several parts of the oxidant/antioxidant system in newborns with hyperbilirubinemia, exposing them to possible oxidative stress."
Aycicek

Ali Aycicek

Tabela 1 - Comparação dos parâmetros séricos oxidantes e antioxidantes antes e depois da fototerapia em recém-nascidos ictéricos. Os dados são expressos como média ± DP

	Antes da fototerapia (n = 57)	Após a fototerapia (n = 49)	p*
CAT (mmol equiv. de Trolox /L)	1,54±0,31	1,48±0,13	0,281
Total – grupo SH (mmol/L)	0,42±0,01	0,43±0,01	0,165
Vitamina C (mg/dL)	2,1±1,3	1,3±0,6	0,029
Ácido úrico (mg/dL)	5,0±2,7	3,7±1,4	0,027
Albumina (mg/dL)	3,8±0,5	3,9±0,5	0,580
Bilirrubina total (µmol/L)	17,1±2,5	13,8±2,3	< 0,001
EOT (µmol equiv.de H_2O_2 /L)	11,34±5,9	16,34±7,4	0,002
MDA (µmol/L)	2,46±0,36	1,98±0,33	< 0,001
Hidroperóxido lipídico (µmol H_2O_2/L)	6,11±2	7,37±2,8	0,025
IEO (unidade arbitrária)	0,07±0,03	0,11±0,05	0,002

CAT = capacidade antioxidante total; EOT = estado oxidante total; IEO = índice de estresse oxidativo; MDA = malondialdeído.
* Teste *t* para amostras pareadas.

Editorial > J Pediatr (Rio J). 2007 Jul-Aug;83(4):293-6. doi: 10.2223/JPED.1674.

Turn off the lights and the oxygen, when not needed: phototherapy and oxidative stress in the neonate

Augusto Sola

PMID: 17676233 DOI: 10.2223/JPED.1674

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
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eRA COMMONS USER NAME	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Instituto Esquiu-Buenos Aires, Argentina	B.S.	1966	English, Biology
University of Buenos Aires, Argentina	M.D.	1973	Medicine

A. Positions and Honors

Professional Experience:

1974-1976 Pediatric Resident, University of Massachusetts, Worcester, MA
1976-1977 Senior chief of Pediatrics, University of Massachusetts, Worcester, MA
1977-1978 Neonatal Fellow, University of Massachusetts, Worcester, MA
1978-1979 Research Fellow, CVRI, Neonatology, UCSF, San Francisco, CA
1980-1987 Assistant Professor of Pediatrics, University of Buenos Aires
1987-1991 Professor of Pediatrics, University of Buenos Aires
1984-1991 Director of Neonatology, University of Buenos Aires
1991-1994 Associate Professor of Pediatrics and Director, Neonatal Clinical Services, University of California, San Francisco, CA
1995-1997 Professor of Pediatrics and Director, Neonatal Clinical Services, University of California, San Francisco, CA
1997-2001 Director, Neonatology, Cedars-Sinai Medical Center, Los Angeles, CA
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Professor, Pediatrics, UCLA School of Medicine, Los Angeles, CA
2001-2004 Co-Director of Emory Regional Perinatal Center, Emory Univ School of Medicine, Atlanta, GA
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2001-2006 Professor of Pediatrics, Obstetrics/Gynecology, Emory Univ School of Medicine, Atlanta, GA (tenure)
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- Absence of evidence is not evidence of absence.
- The more we study, the more we become aware of our own ignorance.
- It is surprising how little is known about the damage caused by phototherapy and its probable mechanisms, and that so little attention has been paid to the possible adverse effects of such a frequently applied therapy. Who could have imagined that exposing healthy full-term newborns to just 48 hours of phototherapy soon after birth could cause metabolic disturbances in their underdeveloped and still poorly functioning defenses against oxidative stress?

"Phototherapy increases oxidative stress"

- Lower vit C
- Lower GSH
- Lower albumin

Dahiya 2006. PMID: 23105589

Indian Journal of Clinical Biochemistry, 2006, 21 (1) 157-160

ANTIOXIDANT STATUS IN NEONATAL JAUNDICE BEFORE AND AFTER PHOTOTHERAPY

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ABSTRACT

Phototherapy has been related to increased oxidative stress and lipid peroxidation. In the present study, thirty full term jaundiced neonates with appropriate weight were analyzed before and after completion of phototherapy for malondialdehyde (MDA), reduced glutathione (GSH), total thiols, vitamin C and superoxide dismutase (SOD) levels in hemolysate and albumin levels in plasma. These parameters were analyzed in cord blood samples of 20 healthy neonates as control. It was observed that levels of MDA were elevated significantly ($p<0.001$) in patients as compared to controls and that the levels increased significantly after phototherapy ($p<0.001$). Levels of SOD were also found to be increased significantly as compared to controls and the levels rose after phototherapy ($p<0.001$). On the other hand, the levels of non-enzymatic antioxidants such as GSH, total thiols and vitamin C were significantly low ($p<0.001$) as compared to controls and the levels decreased significantly after phototherapy ($p<0.001$). The plasma albumin levels also were found to be decreased significantly after phototherapy ($p<0.01$). Therefore, phototherapy increases oxidative stress and should be used with care.

Table 2. Levels of MDA, Total Thiols, Reduced Gluatathione, Vitamin C and SOD in controls and patients (pre and post-phototherapy) of neonatal jaundice

	Controls (Mean ± SD) Range	Before Phototherapy (Mean ± SD) Range	After Phototherapy (Mean ± SD) Range
MDA (nM/gHb)	3.37 ± 0.516 (2.59-4.60)	4.62 ± 0.58* (3.65-5.85)	5.63 ± 0.72* ** (4.08-6.85)
Total Thiols (M/gHb)	68.21 ± 7.38 (58.10-88.20)	47.46 ± 10.22* (36.88-65.20)	43.04 ± 6.27* ** (30.32-59.65)
Reduced Glutathione (M/gHb)	29.65 ± 4.88 (18.39-36.90)	14.83 ± 2.75* (11.61-21.12)	11.72 ± 2.86* ** (9.64-21.0)
Vitamin C (mg/gHb)	0.841 ± 0.16 (0.592-1.180)	0.445 ± 0.09* (0.296-0.640)	0.351 ± 0.07 * ** (0.22-0.51)
SOD (EU/gHb)	1377.90 ± 432.67 (1449-1625)	2212.57 ± 397.79* (1600-3020)	2580.27 ± 683.56* ** (1980-3890)

Take home message for newborn jaundice

- Avoid the problem as described above.
- Don't use blue light treatment if not necessary. Don't give oxygen to baby if not required.
- If bilirubin is mildly elevated, give vitamin C, sunlight, and mother's milk. Mother vitamin C and sunlight, avoid blue light.
- If bilirubin is moderately elevated, make sure it is not rising rapidly, give vitamin C, sunlight, and mother's milk. Mother vitamin C and sunlight, avoid blue light.
- If bilirubin is >15 evaluate more closely, make sure it is not rising, and do as above.
- If >20 need intensive medical care. But why not use antioxidant therapy alongside full spectrum light. (hospital will not use sunlight)

An experienced midwife's comments

- *We shouldn't be taking bloods for SBR testing based on color alone, although this is common practice. We all understand that this is a normal neonatal transition from life in utero to life on the outside. We should be assessing the baby holistically. Is the baby waking for feeds and has good tone, or sleepy and floppy. Are we having frequent enough feeds.*

- *While the baby is processing this bilirubin then it is a good idea to have them feeding 3 hourly, monitor their output. If they are having plenty of wet diapers and the occasional dirty diapers in the first week then they are processing it. Expect that you might see yellow whites of the eyes as well and urates in the daipers. This is normal and part of the excretion process.*

- *Encourage nutritional support for the mother and exposure to sunlight during the day for both mother and baby.*

- *Following birth given additional vitamin c – my recommendation is 2500mg twice a day to help aid her recovery.*

- *In all my years of practice (34yrs) I have only had a handle of the breast feeding jaundice hang around beyond the time of discharge from my care at 6 weeks.*
  Most babies will have cleared it within 2-3 weeks.

No, the American Academy of Pediatrics (AAP) does not recommend vitamin C for infant hyperbilirubinemia, as it is not a standard or recommended treatment for the condition. The primary treatments for high bilirubin levels are phototherapy and exchange transfusion. While some studies suggest that vitamin C may have antioxidant benefits and potentially lower bilirubin levels, these findings are not part of the AAP's official treatment guidelines for neonatal hyperbilirubinemia.

Why vitamin C is not a recommended treatment:

Lack of established evidence:

The AAP's official guidelines do not list vitamin C as a treatment option, focusing instead on evidence-based methods like phototherapy.

Inconclusive research:

While some research has explored vitamin C's role in reducing oxidative damage related to hyperbilirubinemia, the results are not definitive enough to support it as a recommended intervention for infants.

Focus on established treatments:

The established treatments for significant hyperbilirubinemia are well-known and effective, such as phototherapy.

No, the American Academy of Pediatrics (AAP) does not currently recommend antioxidants for infant hyperbilirubinemia; while some studies have explored vitamin E and zinc sulfate for their potential antioxidant effects, the AAP's official guidelines focus on established treatments like phototherapy, and there is no consensus on the efficacy of antioxidant therapy, with some research showing no significant benefit or potential risks, such as toxicity from high zinc levels.

Why the AAP doesn't recommend antioxidants

Lack of clear benefit:

Many studies have failed to show a significant difference in bilirubin levels or the need for treatment between infants receiving antioxidant therapy and those receiving a placebo.

Potential risks:

High levels of zinc, in particular, can lead to toxicity, especially when combined with intensive phototherapy, making supplementation a concern.

Established treatments:

The AAP's guidelines for managing hyperbilirubinemia emphasize proven methods such as visual assessment of jaundice, transcutaneous bilirubin (TcB) measurement, total serum bilirubin (TSB) testing, and treatments like phototherapy and exchange transfusions.

Yes, there are studies investigating antioxidants like vitamin C and E for infant jaundice, showing mixed results; some studies suggest potential benefits by reducing oxidative stress and bilirubin levels, while others find limited or no significant difference compared to traditional treatments alone. Vitamin C supplementation during the late stages of pregnancy also showed a significant decrease in neonatal bilirubin levels. However, more research is needed to establish definitive therapeutic roles, as vitamin C and E levels have been observed to be lower in jaundiced infants, and the effectiveness of direct supplementation in treating existing jaundice is still under investigation.