Turkish National Pediatric Society
1958

5 November 2015

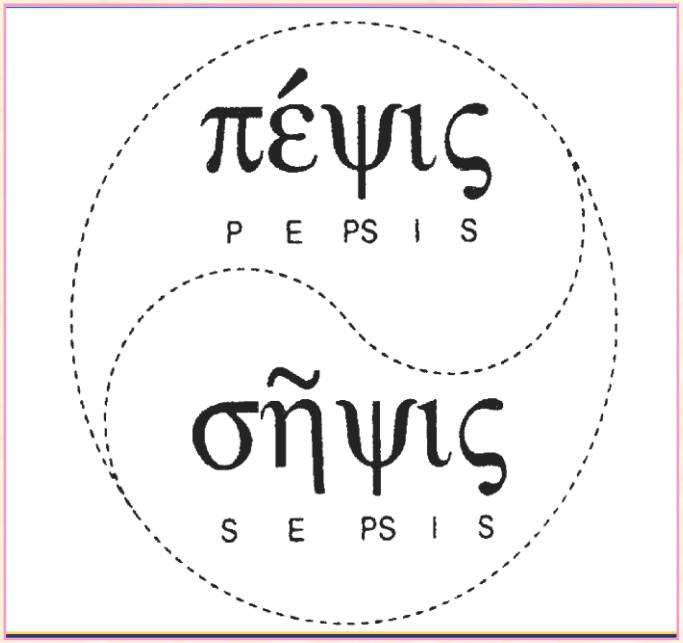
SIPO
Società Italiana Pediatria Ospedaliera

3rd ITALIAN-TURKISH-IRANIAN PEDIATRIC MEETING

Update in neonatal sepsis

Gennaro Vetrano Pediatrics/Neonatal Intensive Care Unit, Sacro Cuore di Gesù Hospital, Benevento, Italy

Sepsis in history

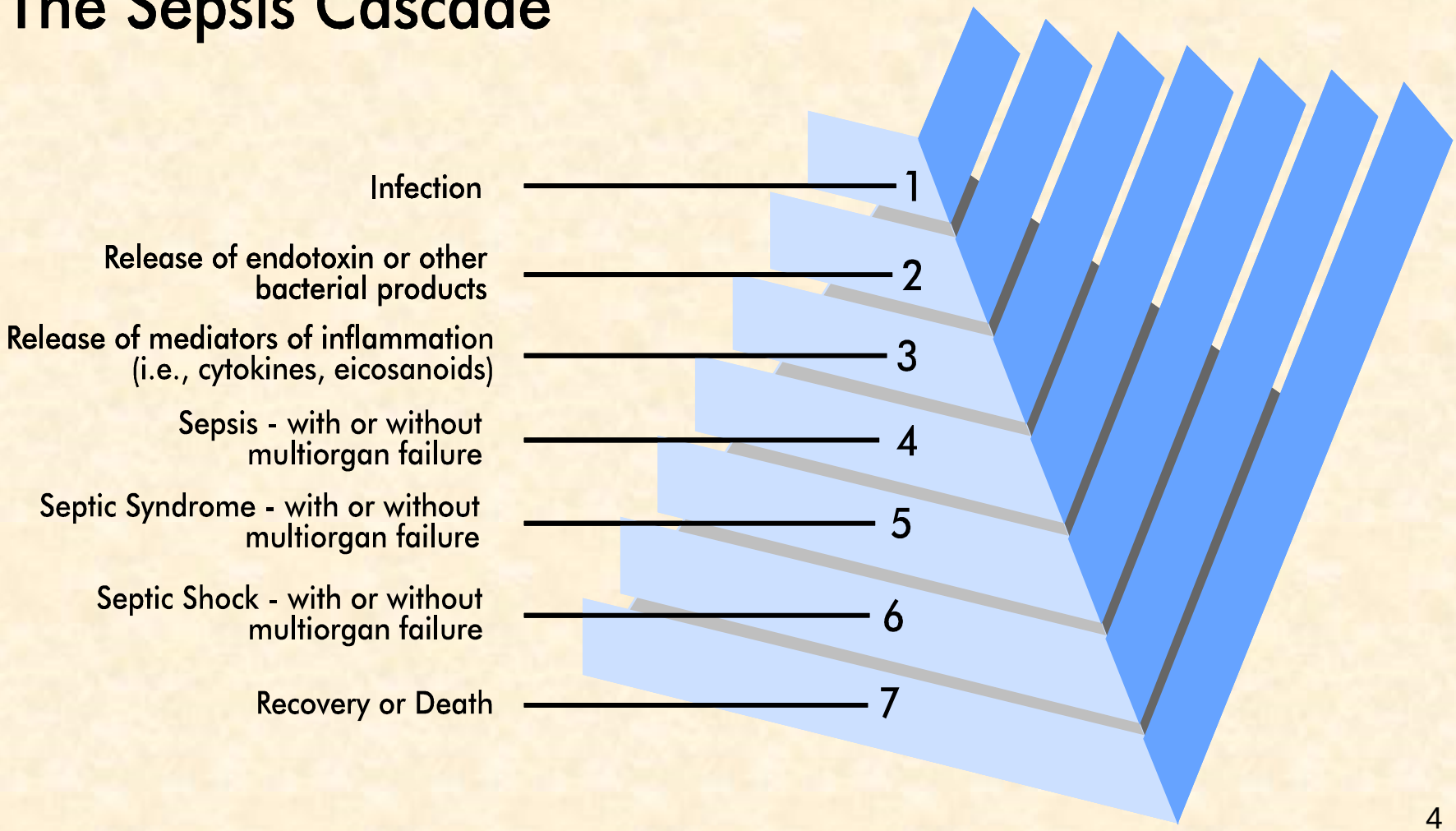


From the culture of ancient Greece
Sepsis (degradation) and pepsis (digestion)

DEFINITION OF NEONATAL SEPSIS

- Sepsis is defined as the clinical syndrome characterized by a host systemic inflammatory response to invading pathogens with onset in the first month of life
- DEFINED CLINICALLY
- DEFINED MICROBIOLOGICALLY (positivity of blood culture and/or liquor culture)

The Sepsis Cascade



INCIDENCE

- **1-8 / 1000 LIVE BIRTHS**
  13-27 / 1000 BORN WITH WEIGHT <1500 G AT BIRTH

- **Death rate: 13-25% (higher in preterm infants and in those with early fulminant disease)**

NEONATAL INFECTIONS

In the world, every year, 5,000,000 deaths occur in the neonatal period; of these over 2,000,000 are due to infections

- In developing countries the mortality from sepsis is approximately 60%

- In developed countries, mortality from sepsis is between 20 and 40%

- The data on mortality for sepsis in VLBW have not changed in the last 30 years -

- 33-66% of infants in NICUs have an infection; in 50% of cases sepsis

Haque, 2005

Classification by AGE OF ONSET

- Early onset sepsis (EOS)
- Late onset sepsis (LOS)

- Clinical relevance (vertical – during delivery for early ones) (horizontal - nosocomial or community sepsis for later ones)
- There is no consensus in the literature at what age are endpoint criteria (from 48 hours to the first 6 days after birth for early onset sepsis)
- Hospitals applying early discharges may expose infants to infections of the community, those who apply later discarges to nosocomial infections

EARLY NEONATAL SEPSIS

- The bacteria most frequently responsible for early onset sepsis are:
  Beta-Hemolytic Streptococcus Gr. B (GBS), (about 50% of the cases)
  -Escherichia Coli (about 20-40% of the cases)
  -other bacteria (about 10-30% of cases)

Early Human Development 88S2 (2012) S69–S74

Contents lists available at ScienceDirect

Early Human Development

journal homepage: www.elsevier.com/locate/earlhumdev

Early and late onset sepsis in very-low-birth-weight infants from a large group of neonatal intensive care units

C.P. Hornik[a,b], P. Fort[a], R.H. Clark[c], K. Watt[a,b], D.K. Benjamin Jr.[a,b], P.B. Smith[a,b,*], P. Manzoni[d], E. Jacqz-Aigrain[e], F. Kaguelidou[e], M. Cohen-Wolkowiez[a,b]

Table 3
Microbiology of early- and late-onset sepsis

	EOS		LOS	
	N (%)	Mortality (%)	N (%)	Mortality (%)
Gram-positive organisms	356 (34.3)	24.7	8984 (61.4)	10.6
CoNS	24 (2.3)	0	4133 (28.3)	9.4
Enterococcus spp.	17 (1.6)	20.0	1001 (6.8)	7.1
Group B *Streptococcus*	189 (18.2)	27.1	448 (3.1)	7.7
Listeria monocytogenes	13 (1.3)	25.0	1 (0.01)	100.0
Staphylococcus aureus	22 (2.1)	15.0	2258 (15.4)	10.8
Gram-negative organisms	604 (58.2)	28.0	3829 (26.2)	21.3
Enterobacter spp.	5 (0.5)	20.0	720 (4.9)	12.4
Escherichia coli	346 (33.4)	23.4	900 (6.2)	17.9
Haemophilus influenza	96 (9.3)	19.1	7 (0.1)	33.3
Klebsiella spp.	16 (1.5)	11.1	990 (6.8)	12.7
Pseudomonas spp.	12 (1.2)	30.0	300 (2.1)	35.0
Serratia spp.	7 (0.7)	42.9	363 (2.5)	14.8
Candida spp.	28 (2.7)	28.0	1528 (10.5)	28.8
Other	49 (4.7)	10.6	287 (2.0)	14.2
Total	1037 (100)	26.0	14,628 (100)	15.1

CoNS, coagulase-negative *Staphylococcus*; EOS, early-onset sepsis; LOS, late-onset sepsis.

CLINICAL MICROBIOLOGY REVIEWS, July 2004, p. 638–680
0893-8512/04/$08.00+0 DOI: 10.1128/CMR.17.3.638–680.2004

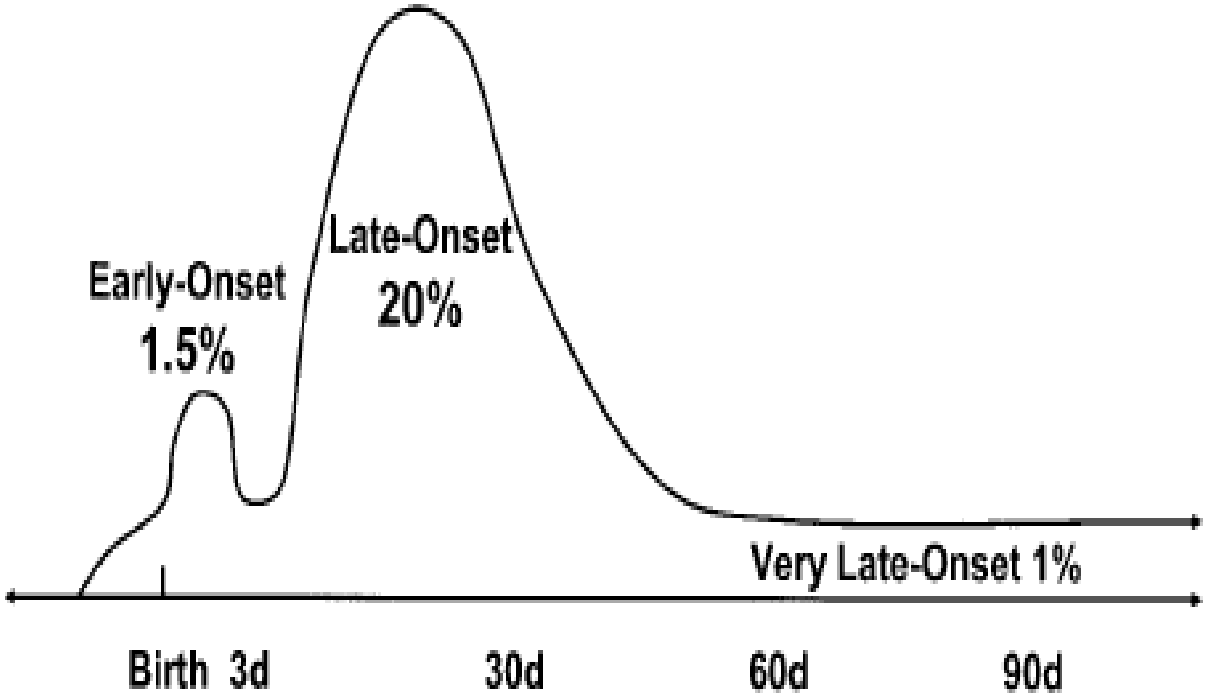


FIG. 1. Timing of bacterial and fungal sepsis in VLBW infants. Percentages indicate the approximate number of VLBW infants with septicemia. EONS usually occurs via ascent of organisms from the birth canal to the amniotic fluid, with or without rupture of amniotic membranes. LONS occurs with vertical and horizontal spread of organisms. While the vast majority of cases of sepsis in VLBW infants occur in the first 30 days of life, VLBW infants requiring prolonged intensive care are at risk for VLONS beyond 2 months of age.

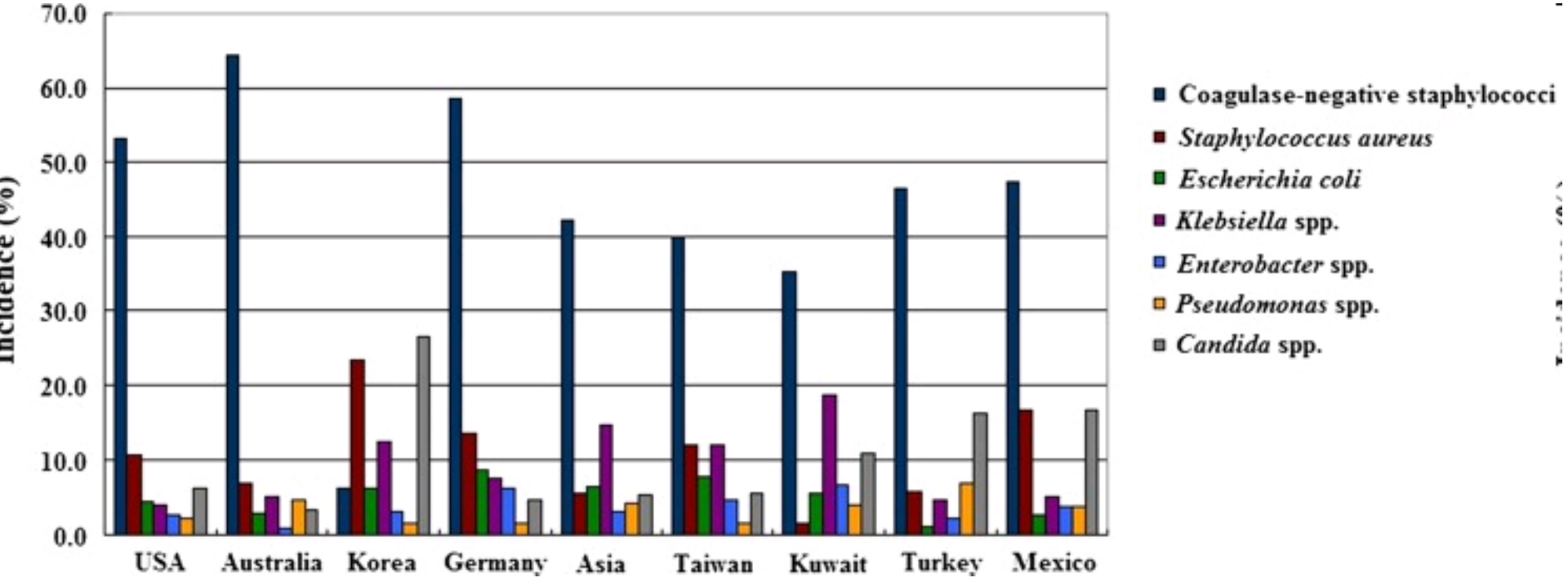
Arch Dis Child Fetal Neonatal Ed. 2015 May; 100(3): F257–F263.
Published online 2014 Nov 25. doi: 10.1136/archdischild-2014-306213
Ying Dong, Christian P Speer

Incidence of LOS by birth weight

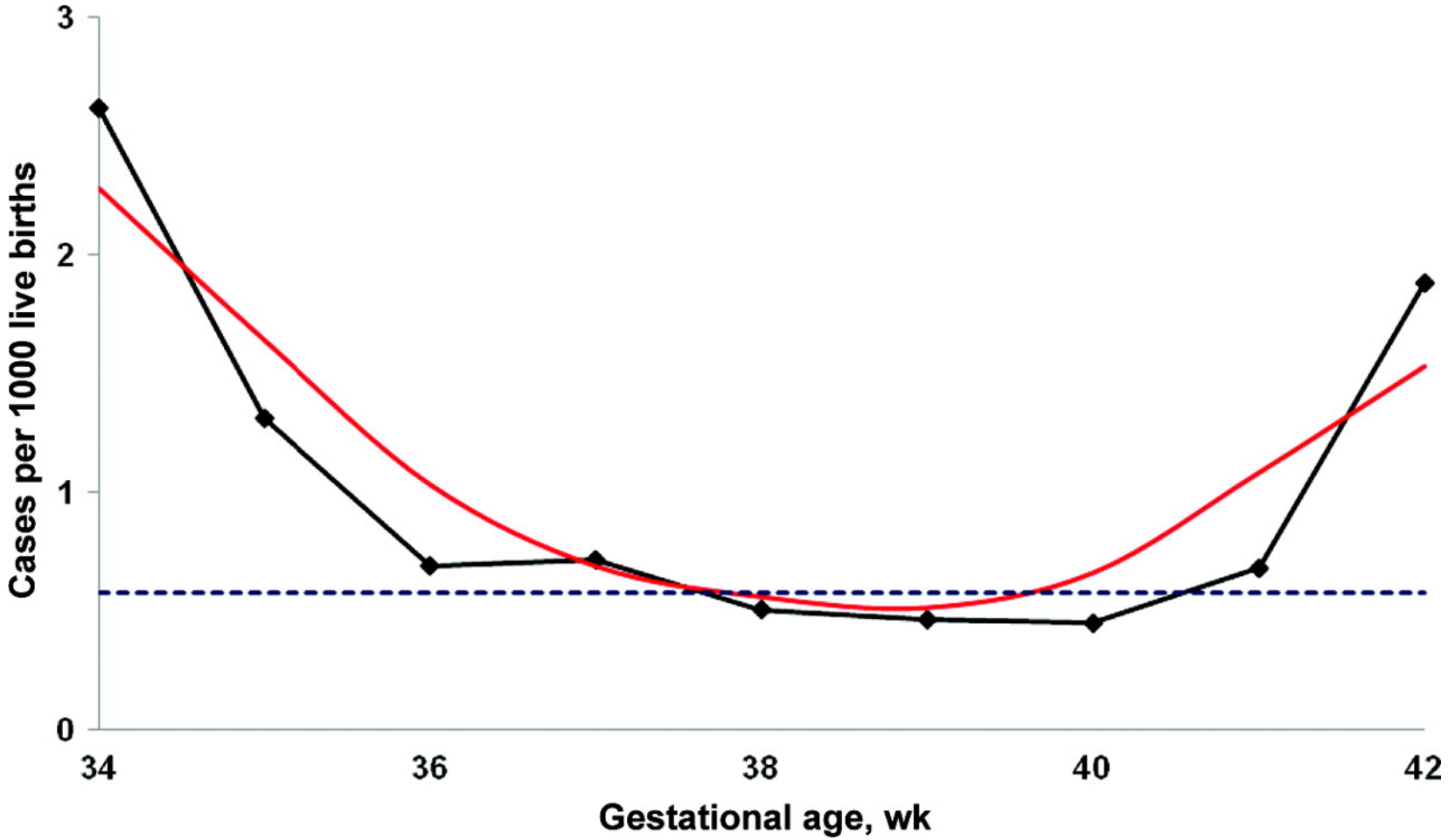
Reference	Birth weight (g)	No. of neonates	LOS, No. (%)
	400–500	223	146 (65.5)
Boghossian *et al*,USA	501–750	2680	1372 (51.2)
	751–1000	4030	1309 (32.5)
	1000–1499	1110	113 (10.2)
Vergnano *et al*, England	1500–2500	2945	66 (2.2)
	>2500	5340	88 (1.6)

Arch Dis Child Fetal Neonatal Ed. 2015 May; 100(3): F257–F263.
Published online 2014 Nov 25. doi: 10.1136/archdischild-2014-306213
Ying Dong, Christian P Speer

Major causative pathogens of neonatal late-onset sepsis and their incidence by geographical areas.



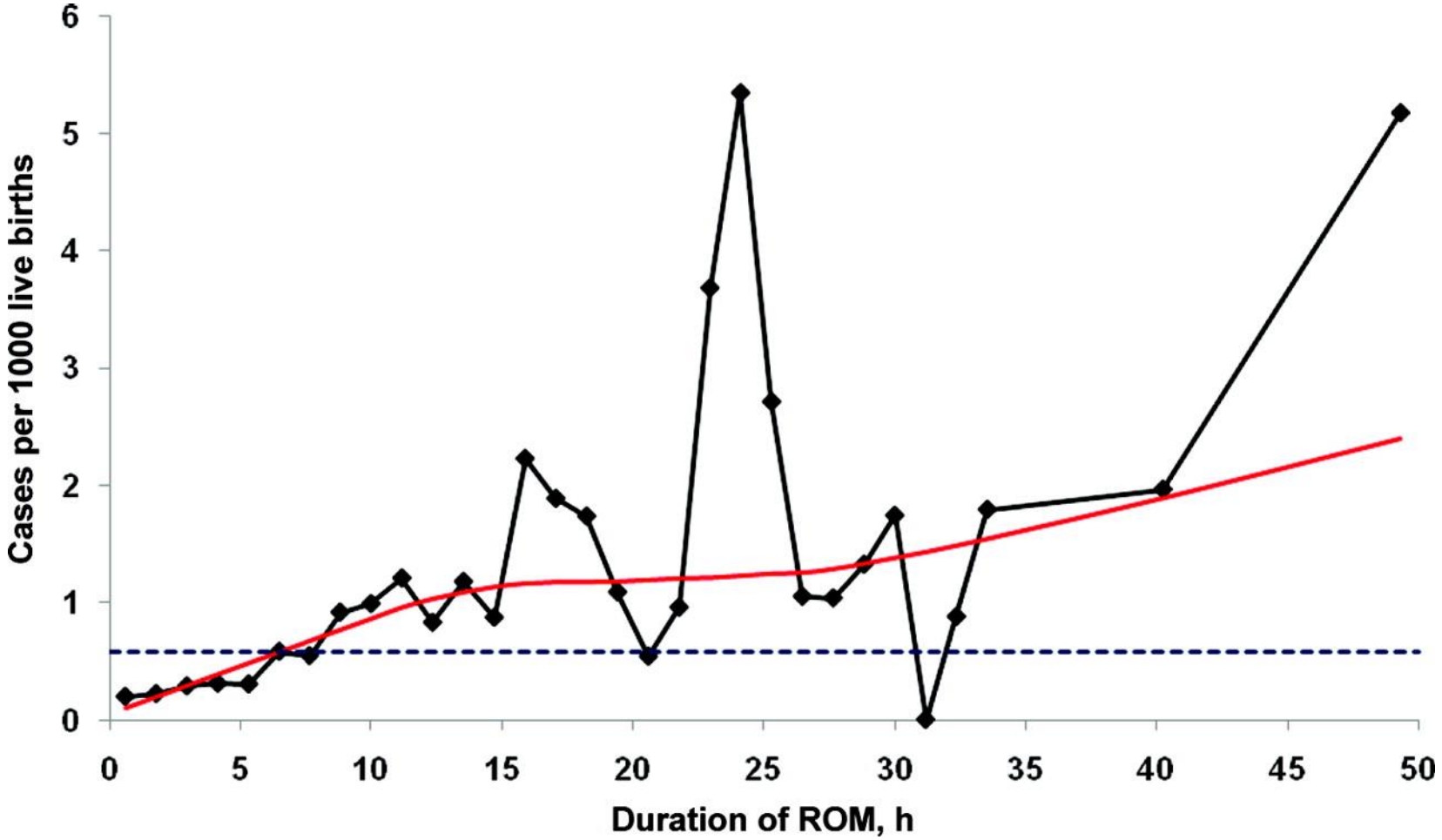
Rate of sepsis according to gestational age.



Karen M. Puopolo et al. Pediatrics 2011;128:e1155-e1163

PEDIATRICS®

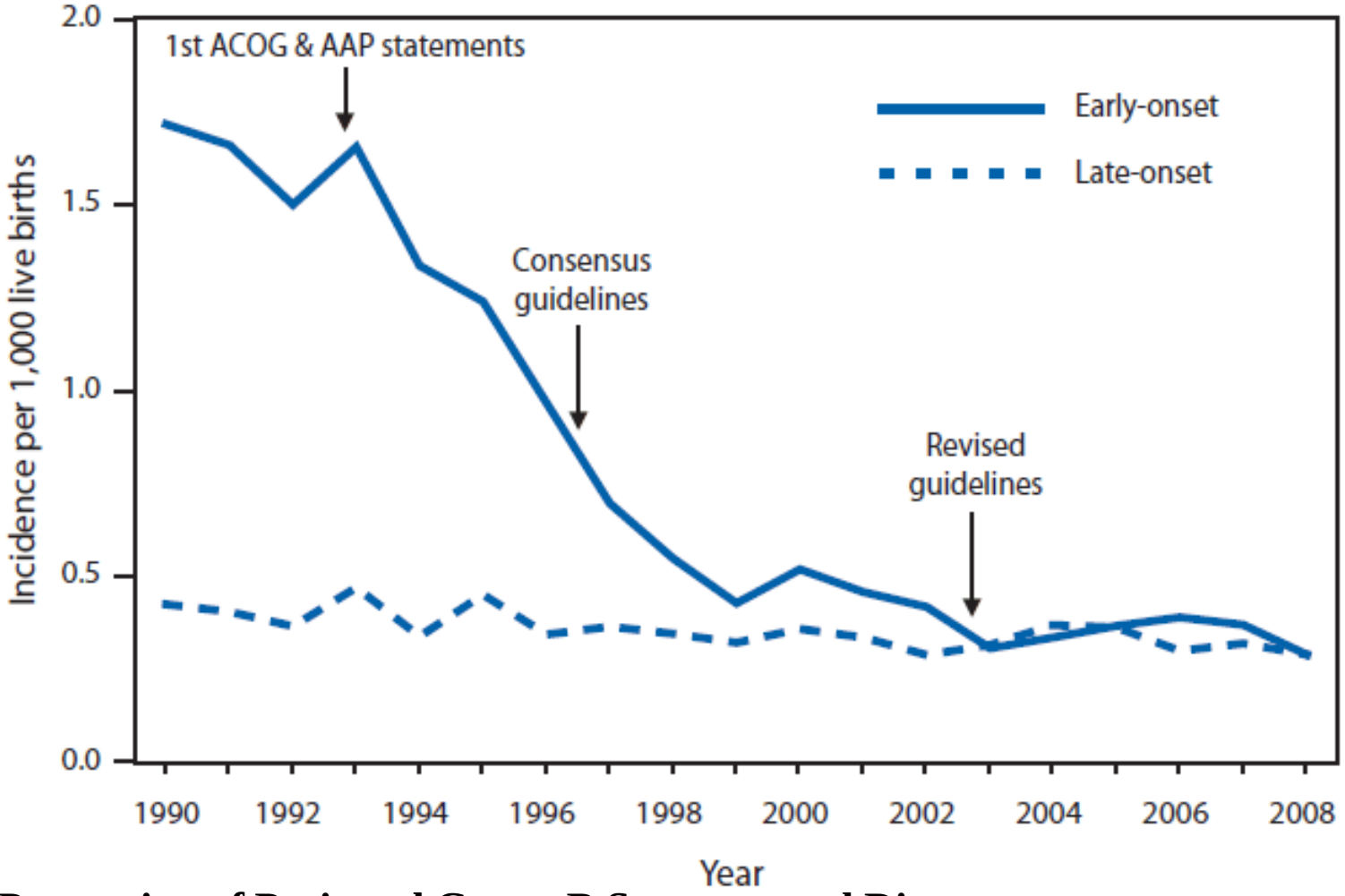
Rate of sepsis according to duration of ROM. ROM was measured to the nearest 0.1 hour and took on values from 0 to 226.4 (inclusive); ROM times of >50 hours were rare, and times between 30 and 50 hours were sparse.



Karen M. Puopolo et al. Pediatrics 2011;128:e1155-e1163

PEDIATRICS®

Incidence of early- and late-onset invasive group B streptococcal (GBS) disease --- Active Bacterial Core surveillance areas, 1990--2008, and activities for prevention of GBS disease



Prevention of Perinatal Group B Streptococcal Disease
Revised Guidelines from CDC, 2010: Jennifer R. Verani, Lesley McGee, Stephanie J. Schrag. *Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases*

Virulence. 2014 Jan 1; 5(1): 170–178.

Neonatal sepsis

An old problem with new insights

Birju A Shah and James F Padbury

Microbial pathogens and risk factors associated with neonatal sepsis

Neonatal sepsis	Microbial pathogens	Risk factors
Early-onset	• Group B streptococci • *Escherichia coli* • *Streptococcus viridans* • Enterococci • *Staphylococcus aureus* • *Pseudomonas aeruginosa* • Other gram-negative bacilli	• Maternal Group B streptococcal colonization • Chorioamnionitis • Premature rupture of membranes • Prolonged rupture of membranes (> 18 h) • Preterm birth (< 37 weeks) • Multiple gestation
Late-onset	• Coagulase-negative Staphylococci • *Staphylococcus aureus* • *Candida albicans* • *Escherichia coli* • *Klebsiella pneumoniae* • Enterococci • *Pseudomonas aeruginosa* • Group B streptococci	• Prematurity • Low birth weight • Prolonged indwelling catheter use • Invasive procedures • Ventilator associated pneumonia • Prolonged antibiotics

Clinic

- Body temperature
- Change of behavior
- Skin
- Gastrointestinal symptoms
- Cardiopulmonary symptoms
- Metabolic symptoms

LABORATORY

- EXAMS CULTURAL

DEFINITIONS OF SEPSIS AND FOCAL INFECTIONS IN VERY-LOW-BIRTH-WEIGHT INFANTS

- **The isolation of an organism from a blood culture of a newborn with clinical symptoms of infection is the common definition of sepsis**
- In case of Staphylococci coaug. neg., many recent studies require the isolation of the same organism from two blood cultures or from a single blood culture with other laboratory evidence of sepsis, as a high value of CPR

Blood culture
Positivity criterion
Days of positivity

- 1 day
- 2 days
- 3 days
- 4 o more days

The positivization time can be inversely proportional to the pathogenic role of the microorganism

More than one bottle positive > probability of true bacteremia

New scenarios in the microbiological diagnosis of sepsis

Journal of Molecular Diagnostics, Vol. 7, No. 5, November 2005

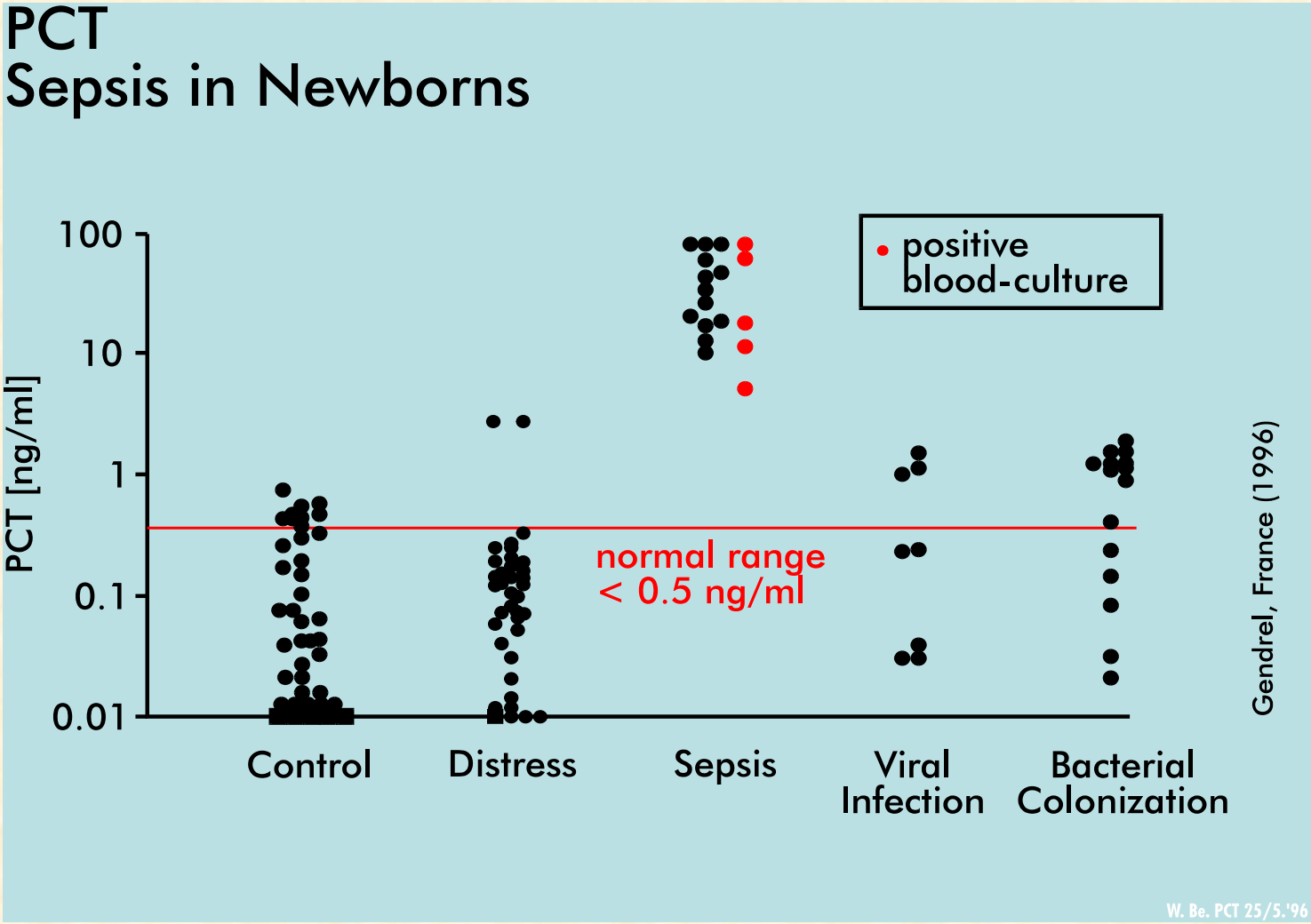
Real-Time Polymerase Chain Reaction for Detecting Bacterial DNA Directly from Blood of Neonates Being Evaluated for Sepsis

Jeanne A. Jordan*† and Mary Beth Durso†

From the School of Medicine, Department of Pathology, University of Pittsburgh, Pittsburgh, Pennsylvania; and Magee-Women's Research Institute,† Pittsburgh, Pennsylvania*

biomarkers of sepsis

PCT, Sepsis in Newborns



Virulence. 2014 Jan 1; 5(1): 170–178.

Neonatal sepsis

An old problem with new insights

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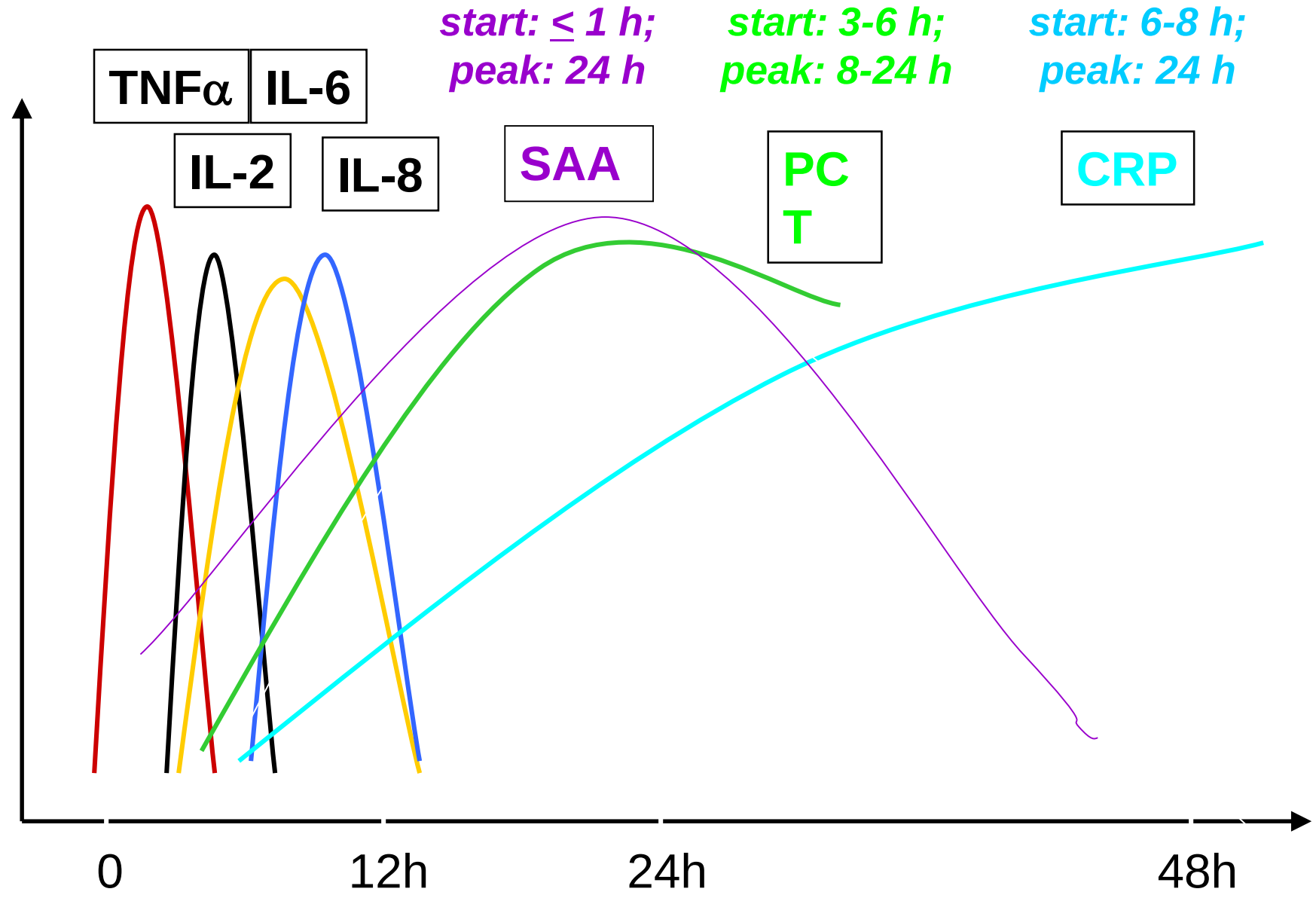
Diagnostic performance of adjunctive tests of neonatal sepsis

Diagnostic test	Sensitivity (%)	Specificity (%)	PPV[a] (%)	NPV[b] (%)	Likelihood ratio (+)	Likelihood ratio (−)
WBC[c]	44	92	36	94	5.5	0.60
I:T ratio[d]	54.6	73.7	2.5	99.2	2.07	0.61
Platelets[e]	22	99	60	93	2.72	0.78
CRP[f]	70–93	78–94	7–43	97–99.5	3.18–15.5	0.07
PCT[g]	83.3	88.6	83.33	88.57	6.9	0.188
IL-6[h]	87	93	76	97	12.42	0.14
IL-8[i]	91	93	91	97	13	0.10
TNF-α[j]	75	88	67	51	6.25	0.28
IAIP[k]	89.5	99	95	98	89.5	0.106


start: ≤ 1 h;
peak: 24 h
start: 3-6 h;
peak: 8-24 h
start: 6-8 h;
peak: 24 h
TNFα
IL-6
IL-2
IL-8
SAA
PC
T
CRP
0
12h
24h
48h

Fanos et al. Italian Journal of Pediatrics 2014, 40(Suppl 1):A11
http://www.ijponline.net/content/40/S1/A11

ITALIAN JOURNAL OF PEDIATRICS

MEETING ABSTRACT Open Access

Metabolomics in the diagnosis of sepsis

Vassilios Fanos[1*], Mauro Stronati[2], Diego Gazzolo[3], Giovanni Corsello[4]

From 70th Congress of the Italian Society of Pediatrics, Joint National Meeting SIP, SICuPP, SITIP
Palermo, Italy. 11-14 June 2014

Table 1 Metabolomic studies that have analyzed the metabolic profiles of septic patients and of experimental animals (From ref. 6, mod.)

Author	Population study	Sample	Metabolomic analysis	Metabolite alterations
Fanos et al. 2014	9 septic newborns vs 16 control newborns	Urine	GC-MS 1H NMR	Lactate, glucose, maltose, ribitol, ribonic acid, pseudo-uridine, 2,3,4 trihydroxybutiric acid, 2-ketpgluconic acid, 3,4 hydroxybutanoic acid, 3,4,5 trihydroxypentanoic acid <(GC-MS) Acetate, acetone, citrate, creatinine, glycine, lactate, lysine, glucose (1H-NMR)
Mickiewicz et al. 2013	60 septic shock vs 40 SIRS vs 40 control pediatric patients	Serum	1H-NMR	2-hydroxybutyrate, 2-hydroxyisovalerate, lactate, glucose, 2-oxoisocaproate, creatine, creatinine, histidine, and phenylalanine
Schmerler et al. 2012	74 SIRS vs 69 septic vs 16 control human adults	Blood	LC-MS/MS	Acylcarnitines and glycerophosphatidylcholines
Mickiewitz et al. 2014	39 septic shock adult patients vs 20 ICU control patients	Serum	1H-NMR	Isobutyrate, phenylalanine, 2 hydroxyisovalerate, myoinositol, acetylcarnitine, creatine, lactate, valine, arginine, methanol, glucose, glycine
Liu et al. 2010	40 septic vs control rats	Plasma	UPLC–Q-TOF-MS	Hypoxanthine, indoxyl sulfate, glucuronic acid, gluconic acid, proline, uracil, nitrotyrosine, uric acid and trihydroxy cholanoic acid
Lin et al. 2009	40 septic vs 20 control rats	Serum	1H NMR	Lactate, alanine, acetate, acetoacetate, hydroxybutyrate and formate
Izquierdo-Garcìa et al. 2011	14 septic vs 14 control rats	Lung tissue, BALF and serum	1H NMR	Alanine, creatine, phosphoethanolamine and myoinositol

The main messages from the published studies are as follows. Metabolomics is able to early diagnose the infection (in some cases in preclinical conditions). Metabolomics is able to predict the outcome in single individuals . Metabolomics appears to be a promising and useful instrument also in the diagnosis of sepsis. In the next future some easy tools, like urinary dipsticks, with the discriminant metabolites will be available in clinical settings, bedside.

Virulence. 2014 Jan 1; 5(1): 170–178.

Neonatal sepsis

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- Non-culture dependent methods based on proteomics, in situ hybridization, gene arrays, mass spectroscopy, and polymerase chain reaction (PCR) methods to screen blood for bacteria, and other supplemental diagnostic tests based on evaluation of the immune system, **are being evaluated to help resolve ambiguities in these situations.**

PREVENTION OF SEPSIS

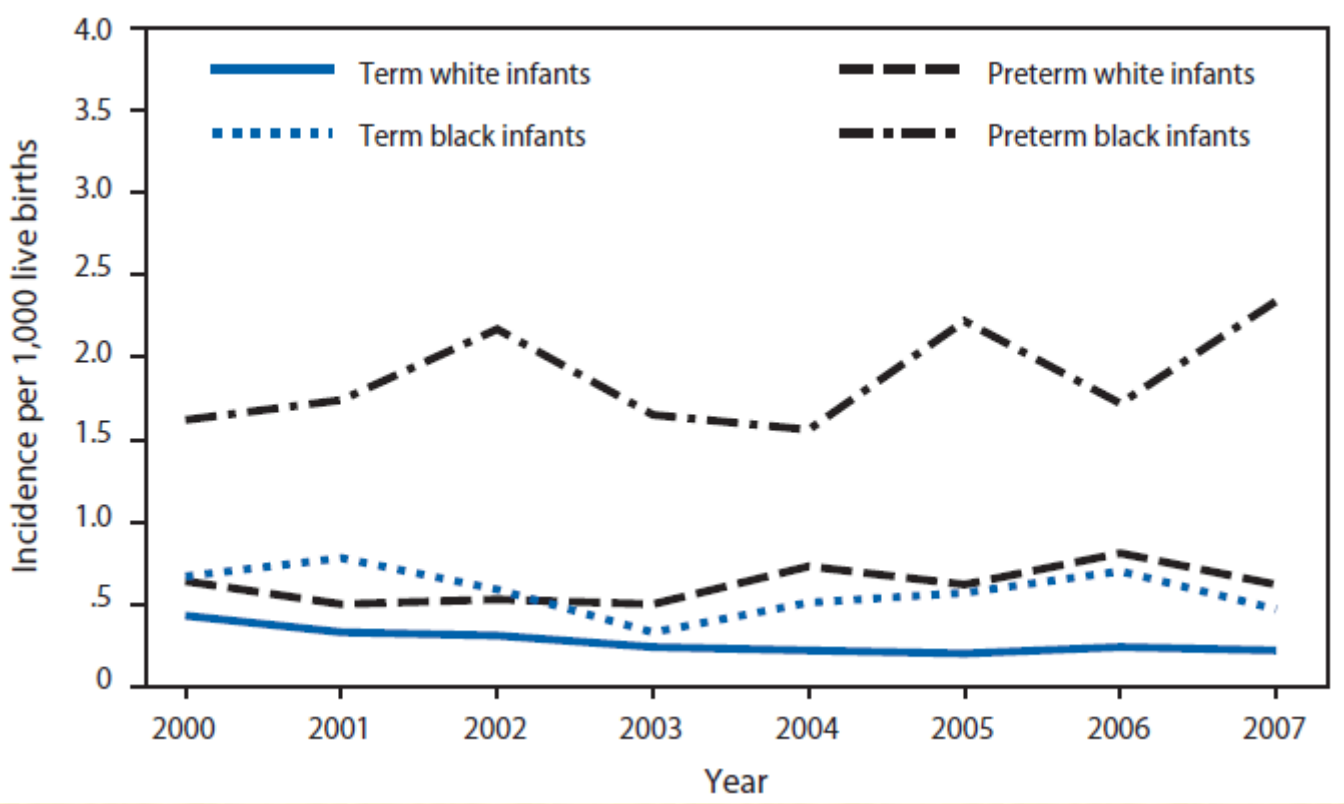
Prevention of Perinatal Group B Streptococcal Disease: Revised Guidelines from CDC, 2010

Recommendations and Reports

November 19, 2010 / 59(RR10);1-32

Prepared by Jennifer R. Verani, MD, Lesley McGee, PhD, Stephanie J. Schrag, DPhil
Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases

Incidence of early-onset invasive group B streptococcal disease, stratified by race and term --- Active Bacterial Core surveillance areas, 2000--2007



Late-onset neonatal sepsis: recent developments
Ying Dong,1 Christian P Speer2
Arch Dis Child Fetal Neonatal Ed 2015;100:F257–F263

Prevention of neonatal LOS

infection control protocols

remains to be the cornerstone of LOS prevention. By implementing bundles of evidence-based strategies, namely hand hygiene, full-barrier precautions, 2% chlorhexidine skin antiseptics, avoidance of the femoral route and prompt removal of unnecessary catheters, combined with cultural and behavioural support

Arch Dis Child Fetal Neonatal Ed. 2015 May; 100(3): F257–F263.
Published online 2014 Nov 25. doi: 10.1136/archdischild-2014-306213

Theoretical mechanisms of currently explored feeding strategies to prevent neonatal LOS

Explored strategy	Theoretical mechanisms
Probiotics	↑ the intestinal mucosal barrier to prevent the translocation of bacteria
	Competitive exclusion of potential pathogens
	Produce bacteriocins that kill pathogens
	↑ immunoglobulin A mucosal responses
	Modulation of host immune reactions to microbial products
Early enteral trophic feeding	↑ enteral nutrition and gut maturation
	Prevent the atrophy of gastrointestinal mucosa
	↑ the establishment of healthy gut microflora
	↓ the use of parenteral nutrition by facilitating full enteral feeding
	↑ gut mucosal immunity
Lactoferrin	Antimicrobial effect by iron chelation
	Immunomodulatory function through cytokine production
	↑ the growth of probiotic bacteria
	↑ the growth and differentiation of enterocytes
	↓ the formation of reactive oxygen species

Late-onset neonatal sepsis: recent developments
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Prevention of neonatal LOS

Probiotics

•Although theoretically promising, the use of probiotics in clinical trials has revealed inconsistent results with regard to the prevention of nosocomial sepsis, and meta-analyses showed that probiotics did not significantly reduce the incidence of sepsis as compared with the controls. The lack of effect may be largely due to the heterogeneity among trials in terms of probiotic administration protocol (strains, dosage, frequency and duration), and **more studies are required to determine the efficacy and safety of probiotics in infants.**

Late-onset neonatal sepsis: recent developments
Ying Dong,1 Christian P Speer2
Arch Dis Child Fetal Neonatal Ed 2015;100:F257–F263

Prevention of neonatal LOS

Lactoferrin

•LF, a major protein in human milk, performs multiple functions as an important component of innate immune defence against infections. Bovine lactoferrin (BLF) has been shown to significantly decrease the incidence of neonatal LOS as compared with placebo controls. When combined with probiotics, BLF further enhanced its prophylactic effect on LOS, emphasising the synergistic action of LF and other antimicrobial agents. However, there was a small number of preterm infants included in these trials, and further studies are warranted to fully assess the effectiveness and safety of LF in neonates by addressing its optimal dosage, duration of treatment and possible combination with probiotics. **The prophylactic use of LF cannot be recommended as routine yet**.

Oral lactoferrin for the prevention of sepsis and necrotizing enterocolitis in preterm infants

Mohan Pammi, Steven A Abrams

Cochrane Database of Systematic Reviews 2015

- **Authors' conclusions**
- **Implications for practice**
- We found moderate- to low-quality evidence to suggest that oral lactoferrin prophylaxis decreases late-onset sepsis, NEC ≥ stage II, and "all-cause mortality" in preterm infants without adverse effects. Low-quality evidence indicates that lactoferrin in combination with probiotics decreases late-onset sepsis and NEC ≥ stage II in preterm infants without adverse effects. **Although oral lactoferrin holds great promise in the prevention of neonatal sepsis and NEC, questions regarding optimal dosage and type (bovine or human recombinant lactoferrin), or whether it should be regulated as a food additive or as a medication, remain.**
- **Implications for research**
- Completion of all ongoing trials and registered trials will result in data from more than 6000 preterm neonates and will enhance the quality and applicability of evidence for oral lactoferrin prophylaxis in preterm infants. Effects of exclusive maternal milk feeding and addition of probiotics to lactoferrin supplementation should also be clarified. Clinical randomized trials evaluating lactoferrin prophylaxis should assess not only short-term beneficial effects, but also long-term neurodevelopmental and pulmonary outcomes.

Updated 06 September 2014

Late-onset neonatal sepsis: recent developments
Ying Dong,1 Christian P Speer2
Arch Dis Child Fetal Neonatal Ed 2015;100:F257–F263

Prevention of neonatal LOS

Early enteral trophic feeding with breast milk

•Therefore, breast milk has been given priority over formula in the introduction of enteral trophic feeding due to its benefits on the promotion of neonatal immune functions. **It is demonstrated that human milk feeding started within the first 72 h after birth was associated with an approximately threefold reduction in the risk of LOS.** Despite numerous studies, multiple factors of the feeding protocol, such as the time of initiation, method of administration and advance rate still remain controversial, and further trials are needed for protocol optimisation.

Late-onset neonatal sepsis: recent developments
Ying Dong,1 Christian P Speer2
Arch Dis Child Fetal Neonatal Ed 2015;100:F257–F263

Prevention of neonatal LOS

Immune replacement therapy

•Intravenous immunoglobulins (IVIG), which can enhance opsonic activity, complement activation, antibody-dependent cytotoxicity and neutrophil phagocytosis, showed no prophylactic effect on neonatal sepsis. It is noteworthy, that IVIG treatment of neonates with suspected or proven sepsis also failed to reduce the mortality in a large multicentre trial. Moreover, INH-A21, a specific antistaphylococcal immunoglobulins against *S. epidermidis* and *Staphylococcus aureus*, demonstrated no significant effect to prevent neonates against sepsis despite its theoretical value.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Multicenter, Randomized Trial of Prophylactic Fluconazole in Preterm Neonates

Paolo Manzoni, M.D., Ilaria Stolfi, M.D., Lorenza Pugni, M.D., Lidia Decembrino, M.D., Cristiana Magnani, M.D., Gennaro Vetrano, M.D., Elisabetta Tridapalli, M.D., Giuseppina Corona, M.D., Chiara Giovannozzi, M.D., Daniele Farina, M.D., Riccardo Arisio, M.D., Franco Merletti, M.D., Ph.D., Milena Maule, M.D., Fabio Mosca, M.D., Ph.D., Roberto Pedicino, M.D., Mauro Stronati, M.D., Michael Mostert, M.D., and Giovanna Gomirato, M.D., for the Italian Task Force for the Study and Prevention of Neonatal Fungal Infections and the Italian Society of Neonatology

N ENGL J MED 356;24 WWW.NEJM.ORG JUNE 14, 2007

CONCLUSIONS

- Prophylactic fluconazole reduces the incidence of colonization and invasive candida infection in neonates weighing less than 1500 g at birth.
- The benefit of treating candida colonization is unclear.

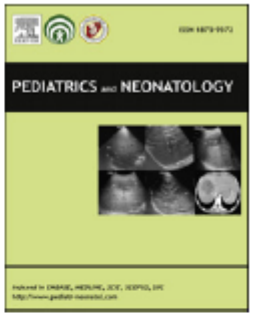
n engl j med 356;24 www.nejm.org june 14, 2007

Pediatrics and Neonatology (2012) 53, 83–89

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: http://www.pediatr-neonatol.com



REVIEW ARTICLE

Strategies for the Prevention of Neonatal Candidiasis

Eugene Leibovitz*

Pediatric Emergency Medicine Department, Soroka University Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel

Conclusions

Fluconazole prophylaxis was shown, in carefully performed, randomized, placebo-controlled studies, to reduce Candida spp. colonization and IFI rates without emergence of drug resistance and without adverse effects during extended periods of time. Fluconazole prophylaxis administered to preterm neonates with birth weight <1000 g and/or 27 weeks' gestation or less has the potential of reducing and potentially eliminating IFI and Candida-related mortality.

MANAGEMENT

- As the signs and symptoms of neonatal sepsis are nonspecific, early diagnosis and prompt treatment remains a challenge.
- In order to decrease the widespread, prolonged use of unnecessary antibiotics and improve the outcome of the infants with sepsis, reliable identification of sepsis at an earlier stage is paramount.

Choice and Duration of Antimicrobial Therapy for Neonatal Sepsis andMeningitis

Sindhu Sivanandan, Amuchou S. Soraisham, and Kamala Swarnam *University of Calgary, Calgary, AB, Canada*

- **In summary, based on current available evidence, the combination of ampicillin and gentamicin is an appropriate choice for empirical therapy of EOS in neonates, where GBS and *E. coli* continue to be the predominant organisms. In developing countries, empiric antibiotic therapy should be based individualized for each hospital or region.**

Hindawi Publishing Corporation
International Journal of Pediatrics
Volume 2011, Article ID 712150, 9 pages

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Management of Neonates With Suspected or Proven Early-Onset Bacterial Sepsis

Richard A. Polin and the COMMITTEE ON FETUS AND NEWBORN
Pediatrics 2012;129;1006; originally published online April 30, 2012;
DOI: 10.1542/peds.2012-0541

- Recent data suggest an association between prolonged empirical treatment of preterm infants (≥5 days) with broad-spectrum antibiotics and higher risks of late onset sepsis, necrotizing enterocolitis, and mortality.
- To reduce these risks, antimicrobial therapy should be discontinued at 48 hours in clinical situations in which the probability of sepsis is low

Choice and Duration of Antimicrobial Therapy for Neonatal Sepsis andMeningitis

Sindhu Sivanandan, Amuchou S. Soraisham, and Kamala Swarnam *University of Calgary, Calgary, AB, Canada*

- In summary, there is inadequate evidence from randomized trials in favor of any particular antimicrobial regimen for the empirical treatment of suspected LOS.
- Vancomycin and third-generation cephalosporin (e.g., cefotaxime) should be considered for LOS in a neonate presenting with cardiorespiratory instability and in areas where MRSA is prevalent.

Hindawi Publishing Corporation
International Journal of Pediatrics
Volume 2011, Article ID 712150, 9 pages

Choice and Duration of Antimicrobial Therapy for Neonatal Sepsis andMeningitis

Sindhu Sivanandan, Amuchou S. Soraisham, and Kamala Swarnam *University of Calgary, Calgary, AB, Canada*

- **Duration of Antimicrobial Therapy for Proven Bacterial Sepsis without Meningitis**
- **Klein recommend 10 days of therapy for culture-proven sepsis with minimal or absent focal infection (Klein JO. Bacterial sepsis and meningitis. In: Remington JS, Klein JO, editors. *Infectious Disaeses of the Fetus and Newborn Infant*. 6th edition. Philadelphia, Pa, USA: WB Saunders; 2006. pp. 247–295)**
- **In summary, pending further evidence, it is reasonable to treat for 10–14 days with appropriate antimicrobial agents in infants with blood-culture-proven sepsis. However, in selected situations (neonates ≥32 weeks gestation and ≥1500 grams, who become asymptomatic within 5 days of appropriate therapy), we can consider stopping antibiotics at 7–10 days, provided appropriate followup can be ensured.**

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International Journal of Pediatrics
Volume 2011, Article ID 712150, 9 pages

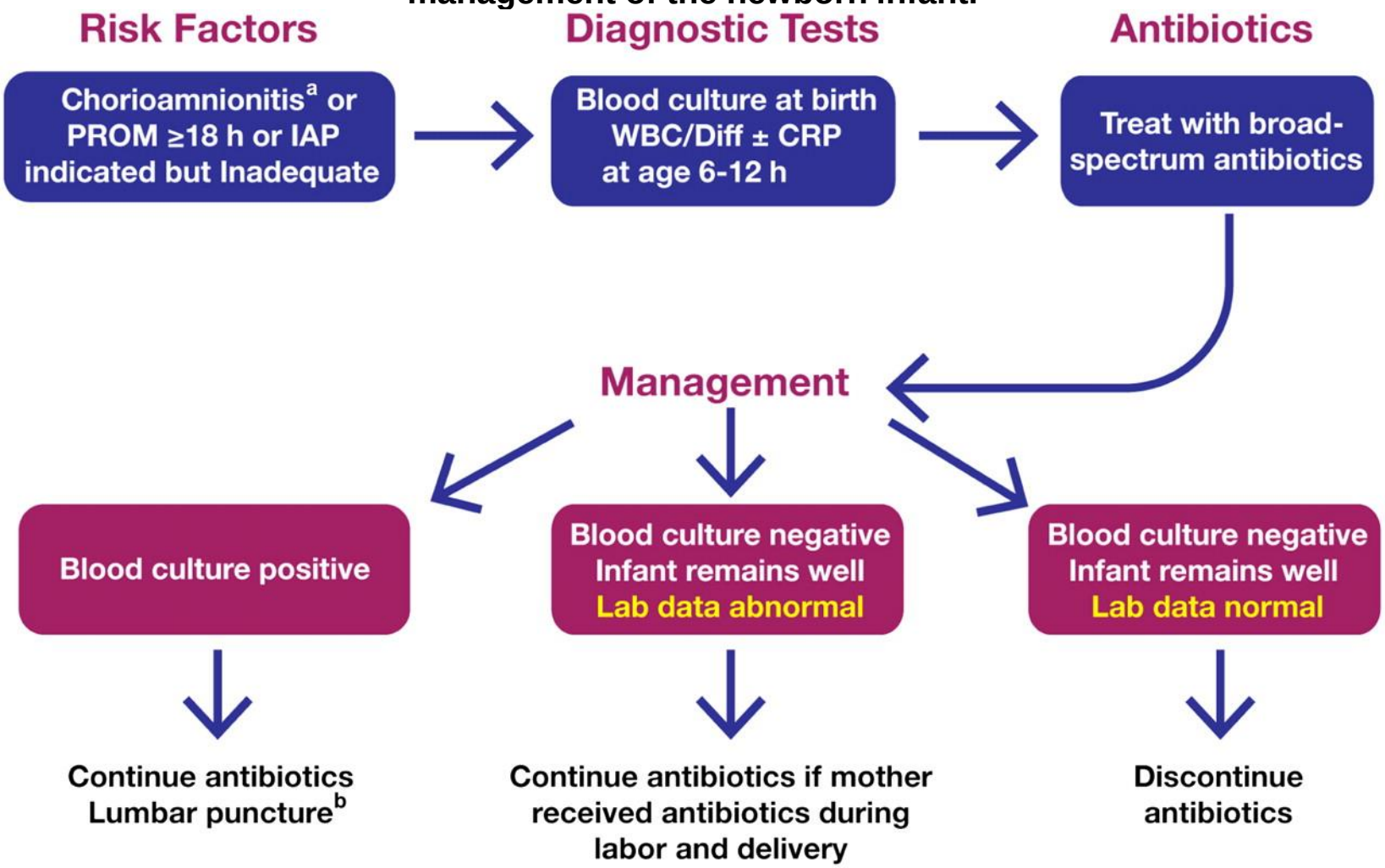
Choice and Duration of Antimicrobial Therapy for Neonatal Sepsis andMeningitis

Sindhu Sivanandan, Amuchou S. Soraisham, and Kamala Swarnam *University of Calgary, Calgary, AB, Canada*

- **Antimicrobial Choice and Duration of Therapy for Neonatal Meningitis**
- In summary, combination of ampicillin and cefotaxime or ampicillin and aminoglycoside is appropriate for treatment of suspected early-onset neonatal meningitis. For suspected late-onset meningitis, a combination of vancomycin plus a third-generation cephalosporin is recommended while awaiting CSF culture and susceptibility results. The duration of antimicrobial therapy for neonatal meningitis should be 14 to 21 days for GBS, ≥21 days for *L. monocytogenes* meningitis, and minimum of 21 days for Gram-negative meningitis.

Hindawi Publishing Corporation
International Journal of Pediatrics
Volume 2011, Article ID 712150, 9 pages

Evaluation of asymptomatic infants <37 weeks' gestation with risk factors for sepsis. aThe diagnosis of chorioamnionitis is problematic and has important implications for the management of the newborn infant.



Richard A. Polin, and the COMMITTEE ON FETUS AND NEWBORN Pediatrics 2012;129:1006-1015

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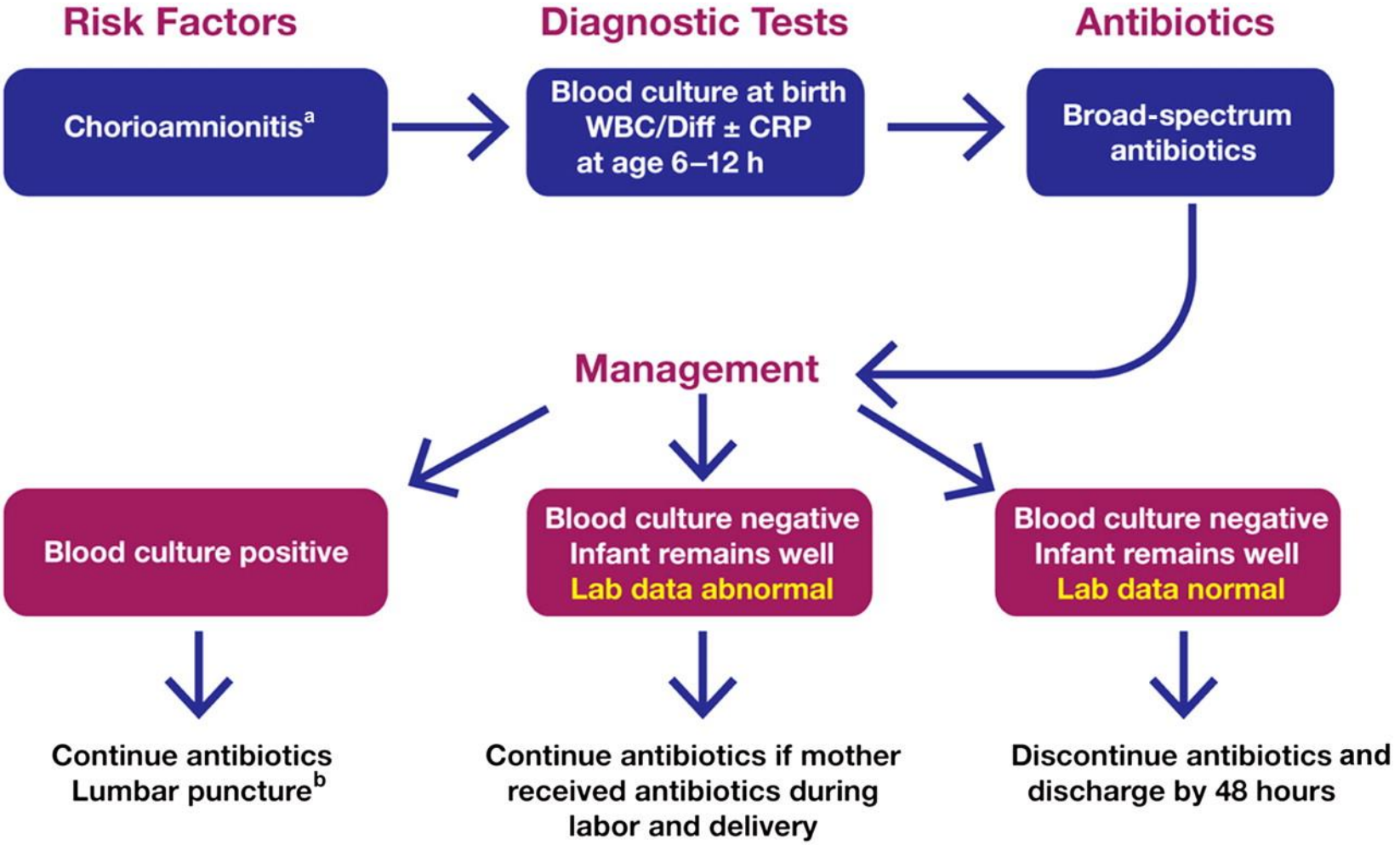
Evaluation of asymptomatic infants ≥37 weeks' gestation with risk factors for sepsis. aThe diagnosis of chorioamnionitis is problematic and has important implications for the management of the newborn infant.



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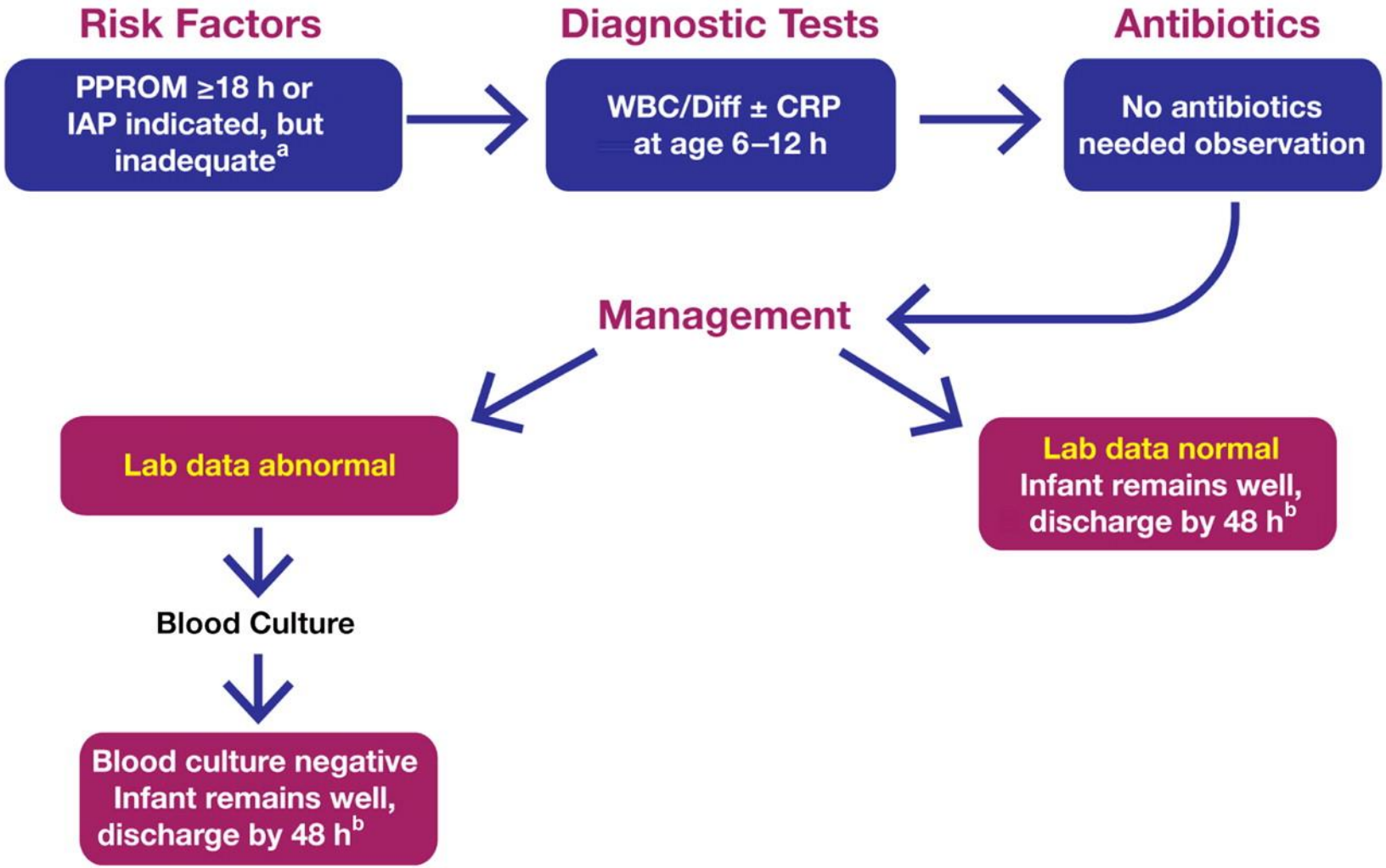
Evaluation of asymptomatic infants ≥37 weeks' gestation with risk factors for sepsis (no chorioamnionitis). alnadequate treatment: Defined as the use of an antibiotic other than penicillin, ampicillin, or cefazolin or if the duration of antibiotics before d...



Richard A. Polin, and the COMMITTEE ON FETUS AND NEWBORN Pediatrics 2012;129:1006-1015

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Management of Neonates With Suspected or Proven Early-Onset Bacterial Sepsis

Richard A. Polin and the COMMITTEE ON FETUS AND NEWBORN

Pediatrics 2012;129;1006; originally published online April 30, 2012;
DOI: 10.1542/peds.2012-0541

1. Neonatal sepsis is a major cause of morbidity and mortality.
2. Diagnostic tests for early-onset sepsis (other than blood or CSF cultures) are useful for identifying infants with a low probability of sepsis but not at identifying infants likely to be infected.
3. One milliliter of blood drawn before initiating antimicrobial therapy is needed to adequately detect bacteremia if a pediatric blood culture bottle is used.
4. Cultures of superficial body sites, gastric aspirates, and urine are of no value in the diagnosis of earlyonset sepsis.
5. Lumbar puncture is not needed in all infants with suspected sepsis (especially those who appear healthy) but should be performed for infants with signs of sepsis who can safely undergo the procedure, for infants with a positive blood culture, for infants likely to be bacteremic (on the basis of laboratory data), and infants who do not respond to antimicrobial therapy in the expected manner.
6. The optimal treatment of infants with suspected early-onset sepsis is broad-spectrum antimicrobial agents (ampicillin and an aminoglycoside). Once the pathogen is identified, antimicrobial therapy should be narrowed (unless synergism is needed).
7. Antimicrobial therapy should be discontinued at 48 hours in clinical situations in which the probability of sepsis is low.

Pedicino *et al. Italian Journal of Pediatrics* 2015, **41**(Suppl 1):A28
http://www.ijponline.net/content/41/S1/A28

ITALIAN JOURNAL OF PEDIATRICS

MEETING ABSTRACT Open Access

The best diagnostic approach for systemic neonatal infections

Roberto Pedicino[1*], Carmela Paciullo[1], Manuela Bedetta[2]

From XXI Congress of the Italian Society of Neonatology
Palermo, Italy. 24-26 September 2015

Conclusions

•In the last 20 years, few results has been reached in reducing mortality due to neonatal infections despite the increased amount for general care and the effort expended on research. **Actually, the best diagnostic approach seems still to rely on clinical examination, culture and hematological parameters (leukocytes count, neutrophils count, C-Reactive Protein and Procalcitonin).**

•Promising prospects may be offered in the future from human genetic studies, for all the biological results (proteomics, metabolomics and transcriptomics) that they promise to reveal.

Tzialla *et al. Italian Journal of Pediatrics* (2015) 41:27
DOI 10.1186/s13052-015-0117-7

ITALIAN JOURNAL OF PEDIATRICS

REVIEW Open Access

Antimicrobial therapy in neonatal intensive care unit

Chryssoula Tzialla[1*], Alessandro Borghesi[1], Gregorio Serra[2], Mauro Stronati[1] and Giovanni Corsello[2]

Future strategies

Appropriate antibiotic policies

Development of innovative treatments

Discovery of new antibiotics

and in addition… all the above may be superfluous if the following criteria are not applied

- meet specific criteria of organization
- providing to maintain an adequate ratio nurses/beds
- avoid overcrowding and understaffing
- make easily available devices for hand washing
- organize meetings for training/provide to caregivers regular feedback of performance data
- plan continuous monitoring and a surveillance system of the rate of nosocomial infections

Thank you for your attention

ilginiz için teşekkürler

با تشکر از توجه شما