

whereas, other risk factors, such as diabetes mellitus, neutropenia, corticosteroid therapy, and iron load, previously reported in older patients were virtually non-existent. No apparent underlying condition was found in 4 neonates (12%). The most common patterns of zygomycosis were disseminated (49%), gastrointestinal (24%), deeply extended (15%) and cutaneous (6%) disease. 15 (45%) cases were diagnosed by histology only and 18 (55%) by histology and culture. Among 18 culture-confirmed cases, *Rhizopus spp.* were isolated from 14 (78%) cases with mortality of 50%. Among 12 patients who were given antifungal therapy, 7 received an amphotericin B formulation only, while 5 received an amphotericin B formulation combined with other antifungal agents. However, 21 patients received no antifungal therapy. Overall mortality was 26/33 (79%) as compared to 56.4% for children >30 d and 52.8% for adults (CID 41:634, 2005; $p < 0.02$). Mortality was not significantly related with decade of publication, gender or race. Mortality was lower (2/7 or 29%) among patients who received an amphotericin B formulation than among neonates who received no antifungal therapy (21/21 or 100%, $p = 0.0002$); 16 (48%) neonates underwent surgery. With exception of two cutaneous cases that were both cured, all other patterns of zygomycosis carried a mortality rate $\geq 83\%$. **Conclusions:** *Zygomycosis* is an extremely serious infection in neonates with a high mortality and strong propensity to disseminate. Amphotericin B formulations significantly improve outcome.

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Parvovirus B19 and Myocarditis in an Infant

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Background: *Parvovirus B19* (PV B19) infection can cause a wide spectrum of disease syndromes. It is emerging as a new and important candidate for myocarditis and subsequent dilated cardiomyopathy (DCM) in immunocompetent and immunocompromised children.

The mechanism of PV B19 induced post natal myocarditis and subsequent DCM is different from that in other viral myocarditides and is characterized by infection of intracardiac endothelial cells of small arterioles and venules, with endothelial dysfunction, impairment of myocardial microcirculation, penetration of inflammatory cells and eventually myocyte necrosis. Recent data suggest that the cytokines interferon-gamma, tumor necrosis factor alpha and interleukin-6 and -8, which are observed

at high levels in PV B19-associated myocarditis in children in addition to microcirculatory dysfunction, contribute to myocardial damage and inflammation.

We report a case of life-threatening PV B19 DCM secondary to PV B19 myocarditis in immunocompetent toddler. The aim of this paper is to alert clinicians to the role of PV B19 in infant myocarditis and DCM.

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Lipopolysaccharide (LPS) Induced Priming of Human Newborn Polymorphonuclear Neutrophils (PMN) is Diminished due to Decreased Levels of MyD88 and Attenuated p38 Phosphorylation

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Background: Diminished response of polymorphonuclear neutrophils (PMN) to lipopolysaccharide (LPS) has been implicated in the increased susceptibility of human newborns to Gram-negative bacterial infections. LPS activates or primes PMN for a variety of host defense functions including enhanced production of oxidative radicals (respiratory burst), a process that is known to involve the Mitogen-Activated Protein (MAP) kinase p38.

Objectives: To determine the cell signaling pathways that may contribute to the attenuation of priming for newborn PMN.

Methods: PMN were isolated from newborn umbilical cord and adult blood. PMN lysates were separated on SDS PAGE and probed for MAP kinases, Toll-like Receptor-4 (TLR-4), Myeloid Differentiation Factor 88 (MyD88) using Western blotting. Functional activation was assayed after stimulation with LPS using flow cytometry to determine CD66b upregulation as an indicator of degranulation.

Results: We found that p38 phosphorylation in newborn PMN is attenuated in response to LPS stimulation even though adult and newborn PMN have similar amounts of p38 protein. The degree of attenuation in newborn PMN was dependent on the osmolarity of the medium. In addition, LPS-induced degranulation, a process that is p38 dependent, was also absent in newborn PMN. We also assessed LPS receptors on PMN and observed that while TLR-4 is present at similar levels on newborn and adult PMN, its downstream adaptor protein MyD88 was significantly diminished in newborn PMN compared to adult cells.

Conclusion: Although the mechanism of PMN priming by LPS is not fully understood, our results suggest that MyD88 and p38 phosphorylation are

important pathways in the process and contribute to attenuated response of newborn PMN to LPS in vitro.

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Infection and Distribution Patterns of Beta and Gamma Herpesviruses in Waldeyer's Ring Tissue

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Background: The lymphoid tissue of the oropharynx acts as a portal of entry and exit and as reservoir for the human beta and gamma herpesviruses (HHV) following primary infection and establishment of latency.

Objective: To elucidate frequencies and quantities of the human beta HHV (HHV-5, -6, -7) and gamma HHV (HHV-4, -8) in adenoids and palatine tonsils.

Methods: We determined the presence and the quantities of HHV-4, -5, -6, -7 and -8 in autologous adenoids and palatine tonsils from children undergoing three-tonsillectomy for medical reasons using in-house established quantitative polymerase chain reaction assays with lower detection limits ranging between 2 and 10 HHV DNA copies/ μ g DNA.

Results: HHV-4 (Epstein-Barr virus) was detected in 80% of the organs from 30 children, HHV-5 (cytomegalovirus) in 63%, and HHV-6 and HHV-7 in 77% each. HHV-8 was not detected. If detectable in a patient, HHV-4 was found in 73% in both adenoid and tonsils, HHV-5 in 23%, HHV-6 in 40%, and HHV-7 in 53%. The number of DNA copies of a given HHV in autologous adenoids and tonsils significantly correlated for HHV-4 and HHV-7 ($p=0.04$ and $p=0.0007$, respectively), but not for HHV-5 and HHV-6. The HHV DNA levels correlated between HHV-5 and HHV-6 in adenoids and tonsils ($p=0.01$ and $p=0.02$, respectively) and between HHV-5 and HHV-7 in tonsils ($p=0.04$), but not between other HHV.

Conclusions: The different correlations of quantitative contents in autologous adenoids and tonsils suggest for HHV-5 and HHV-6 infection and distribution patterns distinct from those of HHV-4 and HHV-7.

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Randomized Controlled Trial of Oral vs. Sequential Intravenous/Oral Cephalosporins in Dimercaptosuccinic Acid (DMSA) Scintigraphy-documented Acute Pyelonephritis in Children

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Background: No study has assessed the efficacy and safety of oral antibiotics in children with DMSA-documented pyelonephritis.

Objectives: To compare efficacy and safety of oral versus sequential intravenous/oral cephalosporin treatment of acute pyelonephritis in children.

Methods: 235 children aged 6 months to 16 years with a febrile urinary tract infection – rectal temperature $>38^\circ$, C-reactive protein (CRP) >10 mg/L, and bacterial growth in cultures from urine collected by catheter – were prospectively randomly assigned to receive either intravenous ceftriaxone (50 mg/kg once daily) for 3 days, followed by oral ceftibuten (9 mg/kg once daily) for 11 days or oral ceftibuten for 14 days. A first DMSA scintigraphy to detect acute renal lesions was performed within 5 days. Micturition cystogram and 2nd DMSA were performed after 6 weeks and 6 months, respectively. Exclusion criteria were complex renal malformations and septical appearance.

Results: 150 children (64%; 132 females (f) and 18 males (m); median age 25 months, range 6–189) had acute renal lesions on DMSA. 71 (47%; 61 f, 10 m; median age 20 months) were given ceftriaxone/ceftibuten, 79 (53%; 71 f, 8 m; median age 27 months) ceftibuten. One patient from the oral regimen only had to be switched to intravenous therapy due to repeated vomiting. The 2nd DMSA showed persistent lesions (scars) in 33 children (46%; 29 f, 4 m) treated with ceftriaxone/ceftibuten versus 19 (24%; 18 f, 1 m) treated with ceftibuten ($p=0.004$).

Conclusions: In children with DMSA-documented pyelonephritis, oral antibiotic therapy for 14 days with once daily ceftibuten is effective, safe and convenient, and resulted in significantly less renal scars than sequential intravenous/oral cephalosporin therapy.