

Division of Critical Care Medicine

| DIVISION PROFILE | |
|---|-------------|
| Number of Faculty | 11 |
| Number of Fellows | |
| Clinical Fellows | 8 |
| Number of Other Students (full and part-time) | 2 |
| Number of Support Personnel | 22 |
| Annual Total Grant Support (direct) | \$1,375,176 |
| Annual Total Industry Contracts (direct) | \$97,857 |
| Number of Peer Reviewed Publications | 29 |
| Patient Encounters | |
| Inpatient | 5,965 |

FACULTY LISTING

Hector R. Wong, MD, Associate Professor of Pediatrics, Division Director

George Benzing, III, MD, Emeritus Professor of Pediatrics

Richard Brill, MD, Professor of Clinical Pediatrics, Associate Chief of Staff; Director, Pediatric Intensive Care Unit; Medical Director, Patient Transport Services

Paul Gardner, PhD, Research Assistant Professor of Pediatrics

Brian Jacobs, MD, Professor of Clinical Pediatrics, Director, Technology and Patient Safety

Neil Kooy, MD, Associate Professor of Clinical Pediatrics

Ann Marie LeVine, MD, Associate Professor of Pediatrics

Kristen Page, PhD, Research Assistant Professor of Pediatrics

Mark Rowin, MD, Assistant Professor of Clinical Pediatrics

Thomas Shanley, MD, Associate Professor of Pediatrics

Basilia Zingarelli, MD, PhD, Research Associate Professor of Pediatrics

OVERVIEW

The Division of Critical Care Medicine provides comprehensive and state-of-the-art clinical care for all critically ill children admitted to Cincinnati Children's Hospital Medical Center (CCHMC). In-house coverage and consultation is available 24 hours per day. The Pediatric Intensive Care Unit (PICU) consists of 25 intensive/intermediate care beds, all of which are located on the 6th floor of the hospital tower. In addition, the Division of Critical Care Medicine administers all transports to and from CCHMC. Staff from the Division of Critical Care Medicine also provides medical coverage for the Cardiac Intensive Care Unit at CCHMC. Dr. Mark Rowin provides 12 weeks of clinical service in the PICU located in Children's Medical Center in Dayton.

All medical patients admitted to the PICU are primarily managed by members of the Division of Critical Care Medicine. We actively seek consultation and co-management strategies with other medical subspecialty groups at CCHMC and community physicians. Surgical patients admitted to the PICU are co-managed by members of the Division of Critical Care Medicine and the respective surgical services. We serve a diverse group of patients and are capable of expertly providing advanced support for all forms of organ system failure including respiratory, cardiovascular, neurologic, hepatic, renal, and hematologic failure.

The Division of Critical Care Medicine has active and productive research programs in both basic science and clinical science. All of the 7 clinical faculty have active research programs. In addition, there are 3, PhD-level, full-time research faculty within the Division, and 12 research support personnel. Our basic research approaches range from molecular biology to large animal physiology to drug development. Specific basic research programs and interests include lung inflammation, immune modulation, ischemia-reperfusion, nitric oxide biochemistry, pulmonary hypertension, and heat shock protein biology. Specific clinical research programs and interests include vascular thrombosis, status asthmaticus, respiratory failure, pulmonary

hypertension, septic shock, nutrition, and genomics. Research activities are widely supported through various granting agencies and industry contracts.

The Division of Critical Care Medicine has an ACGME-accredited training program in Pediatric Critical Care Medicine. This 3 to 4 year program provides subspecialty training for pediatricians seeking certification in Pediatric Critical Care Medicine. The program includes extensive clinical and research training. A portion of the research training is funded through a NIH training grant. Six fellows are currently in the program, while 14 other fellows have graduated and are currently practicing in major PICUs throughout the country and abroad. In addition to the Pediatric Critical Care Medicine Fellowship Program, the division provides research training for various post-doctoral, graduate, and undergraduate students.



Left to Right: N. Kooy, A.M. LeVine, B. Zingarelli, H. Wong, K. Page, R. Brill

HIGHLIGHTS

At the recent Society of Critical Care Medicine Congress (February 2004, Orlando, FL) fellows from the Division of Critical Care Medicine presented 7 first author abstracts and received 4 individual awards for their work.

Brian Jacobs, MD, was the primary author of a multi-disciplinary, institutional application that led to a Nicholas E. Davies Award of Excellence presented by Healthcare Information and Management Systems Society (HIMSS).

The division's training program underwent a formal ACGME site visit in April 2004. The site visitor had no deficiencies to report and we fully expect re-accreditation of our training program in November 2004.

Sue Poynter, MD, received a Procter Scholarship and will join the faculty in August 2004.

Fiscal year 2004 was the busiest with regard to admissions to the PICU (1638 admissions). It is expected that the PICU admission rate and census will continue to grow over the next several years.

Tom Shanley, MD, became Director of Critical Care Medicine at the University of Michigan.

An endowed chair of critical care medicine was established during fiscal year 2004.

Dr. Wong was selected to Best Doctors in the subspecialty of Pediatric Critical Care Medicine.

TRAINING

| | | |
|---------------------|------|--|
| Patricia Abboud, MD | PL-4 | Wright State University School of Medicine |
| Jennifer Kaplan, MD | PL-5 | Orlando Regional Healthcare |
| Michael Vish, MD | PL-5 | Wayne State University School of Medicine |
| Craig Hallstrom, MD | PL-6 | University of Mississippi |
| Marianne Nimah, MD | PL-6 | S.U.N.Y. Health Sciences Center |
| Will Parilla, MD | PL-6 | Albany Medical Center |
| Rajesh Aneja, MD | PL-7 | S.U.N.Y.-Buffalo |
| Sue Poynter, MD | PL-7 | CCHMC |

GRANTS, CONTRACTS AND INDUSTRY AGREEMENTS

Grant and Contract Awards

Annual Direct/Project Period Direct

| | | |
|--|---------------------|---------------------|
| Brilli, R | | |
| Hypothermia for Pediatric Cardiac Arrest Planning Grant | | |
| National Institutes of Health (University of Michigan subcontract) | | |
| | 07/01/03 – 06/30/05 | \$6,712/\$13,424 |
| Gardner, P | | |
| Flavochemoglobin-Catalyzed Nitric Oxide Dioxygenation | | |
| National Institutes of Health | | |
| R01 GM 65090 | 07/01/01 – 06/30/06 | \$126,280/\$640,623 |
| Jacobs, B | | |
| Transfusion Requirements in Pediatric Intensive Care Units | | |
| Canadian Institute of Health Research (Sainte Justine Hospital) | | |
| | 11/01/03 – 10/31/05 | \$3,500/\$7,000 |
| Page, K | | |
| Cockroach-Induced Pro-Inflammatory Responses in Humans | | |
| American Lung Association | | |
| RG-068-N | 07/01/02 – 06/30/04 | \$35,000/\$70,000 |
| Poynter, S | | |
| The Role of Lysozyme in Airway Host Defense | | |
| National Institutes of Health (Yale University subcontract) | | |
| K12 HD 00850 | 07/01/02 – 06/30/04 | \$100,500/\$195,250 |
| Rowin, M | | |
| Characterization of Betal on Granulocytes | | |
| National Institutes of Health | | |
| K08 AI 01809 | 07/01/01 – 06/30/05 | \$100,750/\$433,000 |
| Shanley, T | | |
| PP2A Regulation of the JNK MAPK Pathway | | |
| National Institutes of Health | | |
| R01 GM 066839 | 01/01/03 – 12/31/07 | \$175,000/\$875,000 |
| Wong, H | | |
| The Heat Shock Response and Cytoprotection | | |
| National Institutes of Health | | |
| R01 GM 61723 | 06/01/03– 05/31/07 | \$200,000/\$800,000 |

Genomic Analysis of Pediatric SIRSNational Institutes of Health
R01 GM 064619

08/01/03 – 07/31/06

\$407,434/\$1,155,692

Zingarelli, B

Role of PPAR and Agonists in Septic ShockNational Institutes of Health
R01 GM 067202

07/01/03 – 06/30/07

\$220,000/\$880,000

Current Year Direct**\$1,375,176****Industry Contracts**

Jacobs, B

| | |
|------------------------------------|----------|
| Genentech, Inc. | \$3,596 |
| HDC Corporation | \$5,775 |
| ONY, Inc. | \$4,620 |
| Siemens Medical Solutions USA, Inc | \$75,000 |

Brilli, R

| | |
|-----------------------------|---------|
| Lilly Research Laboratories | \$8,866 |
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Current Year Direct Receipts**\$97,857****TOTAL****\$1,473,033****PUBLICATIONS**

1. **Brilli R.** Adrenal insufficiency, steroids, and pediatric septic shock. In: Randolph AG, editor. 2004 Current Concepts in Pediatric Critical Care Course. Des Plaines, IL: Society of Critical Care Medicine; 2004. p. 181-189.
2. Barton P, Kalil AC, Nadel S, Goldstein B, Okhuysen-Cawley R, **Brilli RJ**, Takano JS, Martin LD, Quint P, Yeh TS, Dalton HJ, Gessouron MR, Brown KE, Betts H, Levin M, Macias WL, Small DS, Wyss VL, Bates BM, Utterback BG, et al. Safety, pharmacokinetics, and pharmacodynamics of drotrecogin alfa (activated) in children with severe sepsis. *Pediatrics* 2004;113(1 Pt 1):7-17.
3. Haupt MT, Bekes CE, **Brilli RJ**, Carl LC, Gray AW, Jastremski MS, Naylor DF, Pharm DM, Md AS, Wedel SK, Md MH. Guidelines on critical care services and personnel: Recommendations based on a system of categorization of three levels of care. *Crit Care Med* 2003;31(11):2677-83.
4. Kurachek SC, Newth CJ, Quasney MW, Rice T, Sachdeva RC, Patel NR, Takano J, Easterling L, Scanlon M, Musa N, **Brilli RJ**, Wells D, Park GS, Penfil S, Bysani KG, Nares MA, Lowrie L, Billow M, Chiochetti E, Lindgren B. Extubation failure in pediatric intensive care: a multiple-center study of risk factors and outcomes. *Crit Care Med* 2003;31(11):2657-64.
5. Nimah M, **Brilli RJ**. Coagulation dysfunction in sepsis and multiple organ system failure. *Crit Care Clin* 2003;19(3):441-58.
6. **Gardner PR**, Gardner AM, Hallstrom CK. Dioxygen-dependent metabolism of nitric oxide. *Methods Mol Biol* 2004;279:133-50.
7. Ullmann BD, Myers H, Chiranand W, Lazzell AL, Zhao Q, Vega LA, Lopez-Ribot JL, **Gardner PR**, Gustin MC. Inducible defense mechanism against nitric oxide in *Candida albicans*. *Eukaryot Cell* 2004;3(3):715-23.
8. Everman DB, Nitu ME, **Jacobs BR**. Respiratory failure requiring extracorporeal membrane oxygenation after sodium phosphate enema intoxication. *Eur J Pediatr* 2003;162(7-8):517-9.

9. **Jacobs BR**. Central venous catheter occlusion and thrombosis. *Crit Care Clin* 2003;19(3):489-514, ix.
10. **Jacobs BR**, Schilling S, Doellman D, Hutchinson N, Rickey M, Nelson S. Central venous catheter occlusion: a prospective, controlled trial examining the impact of a positive-pressure valve device. *JPEN J Parenter Enteral Nutr* 2004;28(2):113-8.
11. Parilla NW, **Jacobs BR**. Central venous catheters in the pediatric intensive care unit: access versus infection. *Pediatr Crit Care Med* 2003;4(4):491-2.
12. **Jacobs BR**. Central venous catheter occlusion and thrombosis. In: Randolph AG, editor. 2004 Current Concepts in Pediatric Critical Care Course. Des Plaines, IL: Society of Critical Care Medicine; 2004. p. 21-32.
13. Uc A, **Kooy NW**, Conklin JL, Bishop WP. Peroxynitrite inhibits epidermal growth factor receptor signaling in Caco-2 cells. *Dig Dis Sci* 2003;48(12):2353-9.
14. Wheeler DS, **Kooy NW**. A formidable challenge: the diagnosis and treatment of viral myocarditis in children. *Crit Care Clin* 2003;19(3):365-91.
15. **Page K**, Strunk VS, Hershenson MB. Cockroach proteases increase IL-8 expression in human bronchial epithelial cells via activation of protease-activated receptor (PAR)-2 and extracellular-signal-regulated kinase. *J Allergy Clin Immunol* 2003;112(6):1112-8.
16. **Rowin ME**, Patel VV, Christenson JC. Pediatric intensive care unit nosocomial infections: epidemiology, sources and solutions. *Crit Care Clin* 2003;19(3):473-87.
17. Odoms K, **Shanley TP**, **Wong HR**. Short-term modulation of interleukin-1beta signaling by hyperoxia: uncoupling of I kappa B kinase activation and NF-kappa B-dependent gene expression. *Am J Physiol Lung Cell Mol Physiol* 2004;286(3):L554-62.
18. **Shanley TP**, **Wong HR**. Molecular genetics in the pediatric intensive care unit. *Crit Care Clin* 2003;19(3):577-94.
19. Lorts A, Pearl JM, **Shanley TP**. Bouncing back from inhaled nitric oxide. *Pediatr Crit Care Med* 2004;5(3):294-5.
20. Lorts A, **Shanley TP**. Myocardial depression in sepsis. In: Randolph AG, editor. 2004 Current Concepts in Pediatric Critical Care Course. Des Plaines, IL: Society of Critical Care Medicine; 2004. p. 169-180.
21. Nemeth ZH, **Wong HR**, Odoms K, Deitch EA, Szabo C, Vizi ES, Hasko G. Proteasome inhibitors induce inhibitory kappa B (I kappa B) kinase activation, I kappa B alpha degradation, and nuclear factor kappa B activation in HT-29 cells. *Mol Pharmacol* 2004;65(2):342-9.
22. Sheehan M, **Wong HR**, Hake PW, **Zingarelli B**. Parthenolide improves systemic hemodynamics and decreases tissue leukosequestration in rats with polymicrobial sepsis. *Crit Care Med* 2003;31(9):2263-70.
23. Wheeler DS, Catravas JD, Odoms K, Denenberg A, Malhotra V, **Wong HR**. Epigallocatechin-3-gallate, a green tea-derived polyphenol, inhibits IL-1 beta-dependent proinflammatory signal transduction in cultured respiratory epithelial cells. *J Nutr* 2004;134(5):1039-44.
24. **Zingarelli B**, Hake PW, Burroughs T, O'Connor M. Parthenolide, an inhibitor of NF-kappa B, reduces the inflammatory response in hemorrhagic shock in the rat. In: Faist E, editor. 6th World Congress on Trauma, Shock, Inflammation and Sepsis - Pathophysiology, Immune Consequences and Therapy. Munich: Medimond International Proceedings; 2004. p. 193-198.
25. Guyton K, **Zingarelli B**, Ashton S, Teti G, Tempel G, Reilly C, Gilkeson G, Halushka P, Cook J. Peroxisome proliferator-activated receptor-gamma agonists modulate macrophage activation by gram-negative and gram-positive bacterial stimuli. *Shock* 2003;20(1):56-62.
26. **Zingarelli B**, Hake PW, O'Connor M, Denenberg A, Kong S, Aronow BJ. Absence of poly(ADP-ribose)polymerase-1 alters nuclear factor-kappa B activation and gene expression of apoptosis regulators after reperfusion injury. *Mol Med* 2003;9(5-8):143-53.
27. **Zingarelli B**, Sheehan M, Hake PW, O'Connor M, Denenberg A, Cook JA. Peroxisome proliferator activator receptor-gamma ligands, 15-deoxy-Delta(12,14)-prostaglandin J2 and ciglitazone, reduce

systemic inflammation in polymicrobial sepsis by modulation of signal transduction pathways. *J Immunol* 2003;171(12):6827-37.

28. **Zingarelli B**. Peptidoglycan is an important pathogenic factor of the inflammatory response in sepsis. *Crit Care Med* 2004;32(2):613-4.
29. **Zingarelli B**, Hake PW, O'Connor M, Denenberg A, **Wong HR**, Kong S, Aronow BJ. Differential regulation of activator protein-1 and heat shock factor-1 in myocardial ischemia and reperfusion injury: role of poly(ADP-ribose) polymerase-1. *Am J Physiol Heart Circ Physiol* 2004;286(4):H1408-15.