Published in final edited form as:
*J Pediatr*. 2009 August ; 155(2): 301. doi:10.1016/j.jpeds.2009.04.039.

# Complex role of mannose-binding lectin in infectious diseases

**I.C. Michelow, MD, DTM&H**[1,2], **L.M. Yantosca, BS**[1], **M. Karpel, BS**[1], and **E.V. Schmidt, MD, PhD**[1,2]

[1] Developmental Immunology, Department of Pediatrics, Massachusetts General Hospital, Boston, MA

[2] Harvard Medical School, Boston, MA

## To the Editor

The report of Martinson and Saulsbury (1) of a child with recurrent infections ascribed solely to mannose-binding lectin (MBL) deficiency appropriately highlights the important protective role of innate immunity against common childhood infections. However, the causative association in this case remains speculative because the relationship between two common events (respiratory infections and MBL insufficiency) may reflect chance alone. Evidence for MBL deficiency predisposing to infections often is limited by methodologic discrepancies in clinical studies. For example, there are no standard definitions of MBL “insufficiency” or “deficiency”; different assays are used to test MBL such as genotyping, binding to mannan and/or capacity to activate complement; MBL haplotypes are defined variably in terms of structural and promoter variants. MBL does appear to be primarily protective between 5 and 18 months of age when passively-acquired maternal antibodies are depleted and adaptive immunity is still immature (2); whereas in neonates, older children and adults (3–5), there is no consensus that isolated MBL deficiency confers susceptibility to infections although it appears to modify disease in patients with underlying disorders e.g. cystic fibrosis (6) or coexisting immunodeficiency (2). Because there is redundancy in the immune system, MBL deficiency is likely compensated by alternative defense mechanisms. However, a concurrent immune impairment may “unmask” the expression of MBL deficiency resulting in synergistic defects, a so-called “two-hit” model. It is intriguing that certain ethnic populations have a high prevalence of MBL variant alleles associated with MBL insufficiency which suggests that MBL polymorphisms have a selective advantage in certain milieux conceivably because some intracellular pathogens hijack the process of MBL-mediated opsonophagocytosis to enter host cells (7). Further meticulous research is needed to 1) define which MBL tests reliably predict immunocompromised status, 2) identify coexisting (possibly subtle) immunodeficiencies, and 3) define the role for prophylactic antibiotics and exogenous MBL, if any.

## References

1. Martinson HE, Saulsbury FT. Mannose-binding lectin deficiency in a child with recurrent infections. J Pediatr 2009;154:450–1.

Corresponding author: I.C. Michelow, Massachusetts General Hospital, 55 Fruit St, GRJ-1402, Boston, MA 02114, Tel: 617-726 2000, Fax: 617-724 3248, Email: E-mail: imichelow@partners.org.
Edited by SL and WFB

2. Koch A, Melbye M, Sorensen P, Homoe P, Madsen HO, Molbak K, et al. Acute respiratory tract infections and mannose-binding lectin insufficiency during early childhood. JAMA 2001;285:1316–21. [PubMed: 11255386]

3. Swierzko AS, Szala A, Cedzynski M, Domzalska-Popadiuk I, Borkowska-Klos M, Jopek A, et al. Mannan-binding lectin genotypes and genotype-phenotype relationships in a large cohort of Polish neonates. Hum Immunol 2009;70:68–72. [PubMed: 18957309]

4. Endeman H, Herpers BL, de Jong BA, Voorn GP, Grutters JC, van Velzen-Blad H, et al. Mannose-binding lectin genotypes in susceptibility to community-acquired pneumonia. Chest 2008;134:1135–40. [PubMed: 18641104]

5. Garcia-Laorden MI, Sole-Violan J, Rodriguez de Castro F, Aspa J, Briones ML, Garcia-Saavedra A, et al. Mannose-binding lectin and mannose-binding lectin-associated serine protease 2 in susceptibility, severity, and outcome of pneumonia in adults. J Allergy Clin Immunol 2008;122:368–74. [PubMed: 18582923]

6. Garred P, Pressler T, Madsen HO, Frederiksen B, Svejgaard A, Hoiby N, et al. Association of mannose-binding lectin gene heterogeneity with severity of lung disease and survival in cystic fibrosis. J Clin Invest 1999;104(4):431–7. [PubMed: 10449435]

7. Garred P, Harboe M, Oettinger T, Koch C, Svejgaard A. Dual role of mannan-binding protein in infections: another case of heterosis? Eur J Immunogenet 1994;21(2):125–31. [PubMed: 9098426]