EDITORIAL

Breaking the "One Disease One Organism" Myth

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Community acquired pneumonia (CAP) in pediatric patients is caused either by *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Mycoplasma pneumoniae* or *Chlamydia trachomatis* [1]. Establishing an etiological diagnosis is quite difficult as collection of an appropriate sample in children is not only tedious but also because most of the implicated organisms are fastidious and difficult to culture. Non-compartmentalization of infectious diseases in younger children also makes it difficult to locate the exact focus of infection. On top of this, cost and non-availability of some molecular techniques for accurate diagnosis of these infections burdens the pediatricians towards taking conjectural decisions, thereby leading to abuse of antimicrobial drugs.

It is also important to reconsider Robert Koch's "*one organism, one disease*" dogma. In infectious disease syndromes, there is infrequently a single unifying etiology, especially in samples from non-sterile sites like throat swab [2]. Ideally, to establish a true causal relationship, the organism should be isolated from sterile fluids/sites such as blood or CSF. In a recent study from Northern India, it was found that majority of children with CAP had multiple pathogens, and those organisms were associated with nasopharyngeal carriage, thereby indicating a causal relationship in most cases [3]. In this study, the pathogen(s) and mortality could not be correlated. As rightly mentioned by Singh, *et al*. [4], in their study published in this issue of *Indian Pediatrics*, the nasopharyngeal carriage of an organism does not necessarily correlate with the etiology of the pneumonia, but it is definitely a risk factor for CAP. While the rate of carriage may range from 9% to 40%, the prevalent serotype must also be known. Another study from Northern India detected pneumococcal nasopharyngeal carriage of 6.5% with serotype 19 being most common [5].

In their study, Singh, *et al*. [4] have observed high nasopharyngeal carriage rates for common respiratory pathogens. There is a need to compare these rates with those in healthy children. It also raises a need to assess the efficacy of pneumococcal vaccination against nasopharyngeal colonization. A recent study from Southern India assessed nasopharyngeal carriage rate in healthy under-five school-going children to be about 28%, with the serotype 19 being the commonest [6]. A previous study from Northern India assessed pneumococcal carriage of around 47% and 53% in urban and rural under-five healthy school-going children [7]. The consensus on antimicrobial susceptibility from these studies is to avoid co-trimoxazole, as most pneumococcal isolates have demonstrated maximum resistance to this drug.

Since the inclusion of the pneumococcal vaccines PCV10 and PCV13 in the IAP recommended immunization schedule [8], we may need to re-assess the predominant serotypes in the nasopharyngeal carriage in the community. Kumar, *et al.* [6] reported 21% bacterial isolates belonging to serotype 10 in their study; this serotype is not covered by any of the conjugate vaccines currently available in the Indian market. This may require upgrading the currently available vaccines as has been done in the past [9]. Future research may include analyzing the effect of vaccines on herd immunity, and on reducing the nasopharyngeal carriage of pathogens.

Funding: None; *Competing interest*: None stated.

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EDITORIAL

Hunting for Mutations in Indian Patients with Hunter Syndrome

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Hunter syndrome, also known as mucopolysaccharidosis type II, is an X-linked lysosomal storage disease predominantly affecting the central nervous system, bones, heart and lungs in a progressive manner. Affected individuals also have coarse facial features and joint contractures, but the severity of all manifestations is highly variable. Supportive care was the only therapeutic option until recently when enzyme replacement therapy became available. Hematopoietic stem cell transplantation is another treatment option for these patients. As is true for most genetic diseases, the exact incidence and prevalence rates for this condition in India is not known, though it is expected that India has one of the largest burden of genetic disorders [1]. Enzyme replacement therapy is very expensive at present and is beyond the reach of most. Prenatal diagnosis is an option considered by many Indian families for this condition.

As a practicing clinical geneticist and researcher, I often find that mutation data are scarce for Indian patients, even for common genetic conditions. Databases for normal sequence variations also highly under-represent the Indian scenario. This under-representation puts clinicians and researchers in a very tough situation to decipher the pathogenicity of DNA sequence variations that they encounter during diagnostic testing and research. Most often, we end up extrapolating data from rest of the world and apply it to our population, which is not ideal.

Identifying mutations in a genetic disease not only helps us confirm the diagnosis, but it also enables definitive prenatal diagnosis for the families. In this issue of *Indian Pediatrics*, Narayanan,*et al*. [2] present the clinical profile and mutation spectrum of Indian patients with Hunter syndrome. Though the number of study children is very small, this is probably the way to begin addressing these rare genetic disorders in our country. Several earlier publications have suggested that Indians might have unique or private mutations for monogenic disorders [3-5]. Further, India being the second most populous country in the world, provides a great opportunity for creation of disease-specific mutation databases. In fact, we now have some publications describing the largest series of patients with mutations in the genes studied [3,6-9]. Genetic studies on lysosomal storage diseases are now facilitated by the National Task Force on Lysosomal Storage Diseases established by the Indian Council of Medical Research, New Delhi. I hope these efforts culminate in much needed mutation data for Indians with these genetic conditions thus facilitating their diagnosis, management and prevention.

Funding: None; *Competing interest*: The author is a member of National Task Force on Lysosomal Storage Disease, funded by ICMR and Department of Health Research.

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