Pediatric gastroenterology

Vasundhara Tolia*: Vasundhara Tolia is currently an Adjunct Professor of Pediatrics at Michigan State University School of Medicine in Lansing (MI, USA). Prior to that, she was a Professor of Pediatrics and Director of Pediatric Gastroenterology at Wayne State University (MI, USA) and Children's Hospital of Michigan (MI, USA), respectively. Dr Tolia attended the Medical College of Calcutta (Kolkata, India), completed a residency program and received postgraduate training in gastroenterology at Children's Hospital in Detroit (MI, USA). Dr Tolia is board certified in Pediatrics and Pediatric Gastroenterology. She has published over 150 articles in peer-reviewed journals, reviews and book chapters. In addition to being a researcher, educator, clinician and mentor, she has been on the Best Doctors' list and is an internationally sought speaker. She has lectured extensively throughout the world and she has held several editorial board positions. Dr Tolia has been a Fellow of the American College of Gastroenterology, American Gastroenterological Association, American Academy of Pediatrics and a member of the Society for Pediatric Research and the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition. She has received numerous grants and awards, including 'Woman of Distinction' from the Crohn's and Colitis Foundation of America.

Vasundhara Tolia speaks to Alisa Crisp, Assistant Commissioning Editor.

Q What led you to a career in pediatrics?

I like children, but I think that working with the different manifestations of diseases at different levels of development is what I find most fascinating about pediatric medicine. A simple urinary tract infection in a baby can cause vomiting, crying and fussiness but an older child can say 'I'm burning while peeing', so it's really more challenging. You are also dealing with a wide age range, right from premature babies up to adults. In the USA, the pediatric age is officially 21 years of age, although we start transitioning most patients over to adult care at 18 years of age when they start going to college. The diversity of manifestations of various diseases is very challenging and interesting to me.

Q What specifically do you find interesting about gastroenterology?

Pediatric gastroenterology is still a very young field – it's only about 40 years or so old – compared with many others. And even during my career span of 30 years as a pediatric gastroenterologist, there has been tremendous evolution in all aspects of the field. In particular, a major change has been a tremendous increase in the application of technology. Now, we do not hesitate to do the endoscopies and biopsies that we would not have thought about doing 30 years ago in routine practice. I find the combination of clinical acumen with technological findings and its applications in the management of the patient most interesting.

Providence Hospital, 16001 West Nine Mile Road, Southfield, MI 48075, USA; vasu.tolia@gmail.com

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Q Are there any particular individuals or events that played an important role in shaping your career?

I would like to start with an event, rather than an individual. I trained at Children's Hospital of Michigan (MI, USA), where the gastrointestinal division was not involved in research. So whenever I saw interesting cases, I would do a literature search and I published some case series and case reports. When I attended the first combined pediatric gastroenterology meeting of North America and Europe in New York City (NY, USA) in 1985, I looked around and saw my contemporaries presenting papers. Then I knew that I had to do something more than I was already doing. So I started looking for other collaborators in the hospital who were also interested in research. The chief of clinical pharmacology at that time, Dr Ralph Kauffman, currently at the University of Kansas (KS, USA), was very helpful in teaching me how to design studies, because I did not have much knowledge of statistics at that time, as my training had only been clinical. Therefore, from that point onwards, I would say that I was really inspired to do something more than I had been doing and since then I haven't stopped. Essentially, I nurtured myself to become a clinical investigator.

Q What achievement are you most proud of in your career?

Besides having been a mentor to all my fellows, I think that being the first pediatric endoscopist at Children's Hospital of Michigan and the creation of the state-of-the-art pediatric endoscopy unit there, I would consider one of my most significant achievements. Even after establishment of the unit, it is very important to keep abreast of technology; incorporating newer procedures and applying them in pediatrics has been one of my goals.

My role was to incorporate and apply techniques that are first performed in adults into children. We have to be sure that a technique is safe in adults first, before even thinking about doing it in children. For example, some of these new techniques include capsule endoscopy, enteroscopy, extended pH probe monitoring, impedance and small and large bowel manometry, among others. I usually started performing most of these techniques in clinical research protocols by designing clinical studies on pediatric patients. After establishing safety and efficacy, they can become mainstream procedures.

Q Is there a particular disease in pediatric gastroenterology that you find most interesting?

I find all of pediatric gastroenterology interesting, mainly because once I had started the fellowship program, I had to find many topics to study to involve the fellows (the postgraduate trainees who come to specialize in pediatric gastroenterology). I have to get them involved in doing research, so I have probably touched on all aspects of the field. The diseases that I have personally studied the most have been gastroesophageal reflux disease (GERD), inflammatory bowel diseases (IBD) and *Helicobacter pylori* infection.

Q Your current work is on GERD. Can you give me a bit of background on this disease and what it involves?

This is a disease that might span the lifetime of an individual. Whether the disease is becoming more prevalent or whether we are more aware of it is really a matter of debate, but we are diagnosing it more and finding a need to intervene in more cases. Right from infants and babies into older children and teenagers, this disease is prevalent, and it is challenging to take care of it because the evolution and natural history of the disease is not the same at all ages. When it occurs after 2–3 years of age, it can be an ongoing issue. It might come and go, with waxing and waning symptoms. Once you take an individual off the treatment, the symptoms generally recur in a few months, unless the parents and children are very conscientious in managing the disease through conservative management, mainly lifestyle modifications. It becomes a chronic disease and it is very frustrating for the patients and children to come back and say it's back again. I feel that teaching them to handle it is an art. In addition to this, there is a major concern in the pediatric age group about taking medications and their potential long-term side effects. Another key part of managing the disease is knowing about the safety of the medications and making the parents feel comfortable with using a treatment as necessary. The parents and children have to understand that this is not a one-time occurrence and that the disease is

going to keep coming back and they may need to drastically modify their lifestyle, which is not easy. You can imagine that a teenager going to a party is going to want some soda and pizza or to indulge in cakes and pastries, and if many of those foods bring on an increase in symptoms, they need to know how best to manage it so they can maintain a good quality of life and still keep their symptoms under control.

Q Are there any other complications in specifically treating children with this disease?

One of the major complications in treating children with the disease is the chronicity; the fact that ongoing symptoms lead to the disease. Sometimes the disease can be silent or children may underplay their symptoms. However, the patients can have significant endoscopic findings, such as erosions with minimal symptoms. This is particularly an issue in developmentally handicapped children, because they are not always expressive and cannot say what is happening to them. Progression of the disease, of course, occurs in otherwise normal children too. Luckily, complications, such as Barrett's esophagus, occur very infrequently in children. This is an example of the difference between children and adults – we do not have to worry about Barrett's esophagus as much as in adults. However, symptoms related to other organs, such as the respiratory tract and exacerbation of asthma, can be part of the problem in children.

Q Are there any exciting treatments that are currently in clinical trials in the field of pediatric gastroenterology?

Reflux disease research is currently focusing on GABA receptor agonists to improve reflux symptoms by decreasing inappropriate lower esophageal sphincter relaxation. I am not aware of other treatments in the pipeline. There is some very exciting research going on in the IBD area, for example, the role of microbes and antimicrobial agents, the genetics of the disease and gene expression, efficacy and safety of treatments in the long term, especially the biological agents and, the study of racial differences and the phenotypic presentation of IBD. For many other conditions, especially symptomatic problems, such as constipation, abdominal pain and reflux, we are resorting to developing screening questionnaires, whereby through their use, the physician has a better idea about what sort of category to classify the symptoms into and what would fit best as far as evaluation and management is concerned. The development of those questionnaires and including them in clinical trials is also interesting; IBD is obviously a disease that has significant morbidity and we still need to find ways to control it better.

Q Are there particular diseases within pediatric gastroenterology that you feel we are still far from understanding?

We need to try to control the pandemic of pediatric obesity much better. Being a gastroenterologist, nutrition is a major part of our field of practice, so preventive measures to deal with obesity, making individuals aware of lifestyle management (exercise and healthy eating) is very important. This has to be carried out on a family basis, because you cannot just treat the child and expect the parents not to be involved. One of the challenges in pediatrics is that half the time you are treating the parent rather than the child. The parents are naturally concerned about the health of the child, and so you have to really reassure the parent and ensure that they stay on top of management of the disease, otherwise it becomes very challenging to handle. Besides pediatric obesity, another disease that we don't yet understand enough is nonalcoholic steatohepatitis, which is also becoming more and more prevalent. It usually manifests initially with elevated transaminases on laboratory testing. That is another condition that we really do not have a good understanding of as yet.

I think another disease that is coming to the forefront and we are seeing more of is eosinophilic esophagitis, which can mimic GERD but is associated with aeroallergies and food allergies. Sometimes we cannot identify a specific allergen. The disease causes swallowing difficulty, reflux-type symptoms, fussiness and, in babies, another spectrum of the disease can be rectal bleeding. Eosinophilic esophagitis is also a big challenge to manage and we do not really have a good understanding of the pathophysiology of this particular disease yet.

Q How do you think we can improve our understanding or treatment of these diseases?

Allergy evaluation is definitely necessary for the management of eosinophilic esophagitis after the diagnosis has been established by endoscopy and biopsy. If you can identify a particular allergen

or substance then you need to remove that from the child's environment or diet. However, if you cannot find an allergen then we have to look at other treatments. We have performed a trial with a biological agent but it did not show significant benefit to be accepted as a therapeutic agent. Instead, we have been using topical steroids in a cyclical fashion. We use the steroids for a few months until resolution of symptoms and withdraw treatment by tapering. We then repeat the treatment again when the symptoms recur; we always want to minimize the use of steroids as much as possible because of the potential side effects in the long term. We still need to learn a lot about this disease by collecting tissues, studying the genetics, and using long-term observational registries. In pediatrics, multicenter studies must be carried out because the number of patients in any of these entities in one particular center is not very high, so it is not possible to conduct quick trials. Whenever you do multicenter studies, there has got to be uniformity of criteria for diagnosis, interpretation of results and management. Otherwise one center may be doing something entirely differently from another center, and it becomes very difficult, such as comparing apples and oranges. We therefore really need to have good studies and proper leadership to understand more about most of the pediatric diseases.

Q You mentioned *H. pylori*, is this a condition that we are coming to know more about or is there still a lot that we need to understand?

Overall, I believe that the incidence of *H. pylori*, is decreasing. We were at the peak of research 20 years ago in this disease. Since then, the natural history of the disease has been altered, particularly with the use of better therapy. In the pediatric age group, antibiotics are frequently used for other infections in the body and some of them, although not all, can influence the resistance patterns of the bacteria.

When I was studying *H. pylori*, one of the main things I was focusing on was antibiotic resistance. We were doing cultures and studying antibiotic sensitivity and how to treat the disease if the first-line treatment did not work. Screening the rest of the family is also important if the infection is persistent because it is spread by close contact. We found that the infection can spread to or from other members of the family; unless they are all treated at the same time, there is no hope to eradicate it. In the pediatric age range, *H. pylori* is often only found when we carry out an endoscopy on the children, which we only do when the children are symptomatic. In endoscopy, we may see normal findings, hypertrophic nodular gastritis or ulcers. If *H. pylori* is detected, it is treated. I would not write this off as an incidental finding on discovering this infection if an individual was having abdominal pain, which is the reason for performing the endoscopy. There is a theory about *H. pylori* not causing abdominal pain, but I would say that those data are confusing it with functional abdominal pain, which is located in the periumbilical area. *H. pylori* can cause epigastric abdominal pain. Overall, I believe that the impetus to study *H. pylori* at the moment has decreased compared with previously. This is not because we know all about it, but its incidence appears to be declining. It might be one of those infectious diseases that we are going to conquer in the long run.

Q How do you think the field of pediatric gastroenterology or pediatrics in general will evolve in the next 10 years?

I think that we will focus much more on the genetics of the disease, including pharmacogenomics. For instance, I have carried out some questionnaire studies in children proven to have GERD from endoscopy and biopsies. We did questionnaires with parents and grandparents and found that in 42% of these children, a first-degree relative, such as a sibling or a parent, had GERD and 12% of patients had three generations in the family, even grandparents, with the disease. There were also some with Barrett's esophagus. Family history may therefore play a role in this condition. While we know that it is not an autosomal dominant or recessive disease, where you can specify the chance of a child developing the disease, when you see a family history of multiple members of the family with the disease, there is a higher chance of not only the child having the disease, but also for it to be persistent. In addition, genetic anticipation may occur. So we need to be focusing on evaluating family history carefully. With early screening and the use of conservative measures, we can try to manage these conditions better.

Once the diseases are diagnosed, I think better therapeutic measures and improved safety and efficacy, as well as safe management, is going to be the focus over the next decade.

I think that the biggest challenge to the field of pediatrics itself is improving preventive care, which is really going to become key in the long term. This includes developing vaccines and using pharmacogenomics, where we can understand how the body is going to react to a particular medicine before using it. I think that prevention is obviously better than allowing the disease to occur and have to treat it by the use of genomic medicine, and intervention even while the baby is *in utero*, as soon as a treatable condition is diagnosed. I think that early identification of conditions for better management and preventing progression is where we need to focus most.

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V Tolia has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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