

## Annual Report

1995 - 1996

### Chair's Report

This annual report represents a year of transition, with the leadership of the Department passing from Dr. Robert Haslam to myself. Thanks to Dr. Haslam's strong leadership, our dedicated staff, as well as the past and present commitment of the University of Toronto and of the Hospital for Sick Children, the Department of Paediatrics is currently strong and thriving. The Hospital for Sick Children is the "home base" for Canada's largest Department of Paediatrics, run by the University of Toronto. The Department's overall goal is to create, evaluate, disseminate, and utilize knowledge to improve the health of children in our city, province, country, and throughout the world, both now and in the future. In pursuit of this goal, one of our greatest strengths has been to engage in a variety of collaborations - local, regional, national, and international - which have helped stimulate research, strengthen clinical practice, and further the education of our future paediatric researchers and health care practitioners. These collaborations are the focus of this year's annual report. Two feature articles - one on cystic fibrosis and one on child abuse and neglect - provide an in-depth illustration of the importance of collaboration in solving medical and social problems. In addition, each division has provided a brief vignette highlighting some of its recent collaborative ventures, and indicated some of its achievements in the area of medical education.

The upcoming implementation of the Province of Ontario's Health Care Restructuring Commission's recommendations will have a significant effect on the location, though not the quality, of the Department's clinical care activities. Patient care by the Department has been traditionally provided almost exclusively within the walls of the Hospital for Sick Children. In recent years, however, increasing amounts of the Department's primary, secondary, and tertiary care are being offered within our partner hospitals affiliated with the Metropolitan Toronto Child Health Network, and this trend is expected to continue. The Department's clinical faculty will continue to provide the entire spectrum of paediatric care ranging from primary care to local children, to consultative general paediatrics and tertiary subspecialty care. Provincial and national quaternary care in such areas as bone marrow and solid organ transplantation, and innovative programs such as lung and blood gene therapy, will be focused exclusively at the Hospital for Sick Children.

Outstanding clinical care is inseparable from excellence in fundamental, translational, and clinical research. It is for this reason that a significant proportion of our full-time faculty have appointments as scientists within the Hospital for Sick Children Research Institute. This emphasizes our belief that, in order to create health care strategies to carry us into the next century, we have to focus not only on our present knowledge but on expanding that knowledge through research. Our role is to advance the care of all children, not only by caring for children with special problems but also by demonstrating leadership in education and in the discovery and improvement of health care strategies at all levels of paediatric care.

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### GENETIC JIGSAW

#### Unlocking the Secrets of CF Requires Worldwide Collaboration

In a typical class of grade-school children, chances are good that at least one child is carrying the genetic mutation responsible for cystic fibrosis. If that child later meets and marries another carrier, their offspring will have a one-in-four chance of inheriting the mutation from both parents - that is, of being born with the actual disease.

These odds - a one-in-twenty chance of being a carrier and approximately one in two-thousand of having the condition - make cystic fibrosis (CF) the most common fatal autosomal recessive disease in Caucasians. The condition is considerably less prevalent in people of African and Indian descent, and least common of all in the Oriental population.

At the heart of CF is an impairment in the body's ability to transport chloride across duct-lining cells, such as those found in the bronchi, nose, and reproductive tract. The protein that normally enables this chloride transfer is altered in people with CF, resulting in a less efficient (in some cases, completely inoperative) transfer mechanism. This leads to a salt and fluid imbalance in the body, and causes mucus to accumulate in various sites such as the lungs, liver, pancreas, and intestine.

At birth, people with CF may or may not exhibit multiple symptoms of the disease, and the severity of symptoms varies widely. Nevertheless, almost all CF sufferers have high levels of chloride in their sweat. In fact, diagnosis of CF is generally made on the basis of these levels. Eventually, most patients who have CF develop pancreatic insufficiency and progressive lung disease, although some forms of the disease are so mild that they may go unrecognized for a long time.

At the Hospital for Sick Children, CF research became a priority in the 1970s, gaining momentum toward the end of the decade with the establishment of a CF database, which later became the basis for a national database administered by the Canadian Cystic Fibrosis Foundation. As researchers at the Hospital started to analyze the information collected from the database, it soon became apparent that CF was, in some sense, more than a single disease. There were puzzling variations in symptoms - for instance, some patients had sufficient pancreas function to enable them to digest their food normally while others had pancreases that had essentially ceased to function as a digestive organ. Another finding was that patients with a well-functioning pancreas had milder disease symptoms onset of the lung problems that are often the cause of death in CF patients. Indeed, patients with preserved pancreatic function tend to live, on average, about twice as long (56 years) as those with pancreatic insufficiency (29 years).

In 1989, a huge piece was added to the cystic fibrosis puzzle with the work of Dr. Lap-Chee Tsui at the Hospital for Sick Children, who cloned the CF gene and identified the most common CF-causing mutation, termed Delta F508. A worldwide cooperative venture, the 'CFgenotype consortium' soon followed, under Dr. Tsui's able leadership with new CF mutations being discovered almost daily. To date, close to 700 different CF mutations have been identified and catalogued. Certain types of CF mutation produce a slightly different form of the disease, which partially accounts for the enormously wide range in CF symptoms and severity. Unfortunately, the most common mutation, which occurs in about 60% of CF genes, produces one of the most severe forms of the disease.

In the wake of Dr. Tsui's groundbreaking work, the need arose for a more precise understanding of the relationship between mutation and disease. With this objective in mind, Dr. Durie, currently Head of the Hospital's Division of Gastroenterology and Clinical Nutrition, Dr. Mary Corey, a CF researcher at HSC, and Dr. Tsui, teamed up with researchers from other centres throughout the world to form the Genotype-Phenotype Consortium. During its seven years of existence, the consortium's mandate has been to study the connection between CF genotype (the type of mutation) and phenotype (the way the disease manifests itself). The consortium has always operated on an informal basis. Members of the group may set aside a time to meet during the annual North American cystic fibrosis convention, to typically, members inform each other about research projects they are working on or develop ideas for future projects, and collaborations.

According to Dr. Durie, the unstructured, collaborative relationship is in great part responsible for the group's success. "That way, there are almost no administrative requirements and we are able to concentrate on the important stuff - that is, the collaborative research," he says.

As hoped for, the consortium's work has resulted in a better ability to relate genotype to phenotype. "We now know that different mutations are specifically linked to different levels of pancreatic disease," explains Dr. Durie. "Patients with so-called mild mutations tend to have only slightly impaired pancreatic function, while patients with severe mutations have severe pancreatic insufficiency." This knowledge allows one to anticipate whether a particular patient is destined to have pancreatic problems. Furthermore, patients with mild mutations tend to have less severe manifestations of CF in other organs including the airways and the liver.

On the clinical front, the Hospital has long been recognized as one of the pioneering diagnosis and treatment centres for CF. It is often at HSC that children with "unexplained problems" first learn that they have CF. For instance, Dr. Durie recalls a young teenager from the U.S. being referred to him because of recurring stomach pains due to attacks of unexplained pancreatitis, an inflammation complication of the pancreas. Dr. Durie and his colleagues' knowledge of the association between this complication and CF led them to test for, and confirm the presence of, CF. "The patient might have gone on for the next five or ten years without any major problems. But problems particularly with respiratory disease would eventually surface, and knowing she had CF meant we were now able to keep an eye on her lung function," says Dr. Durie, adding that another advantage of making an early diagnosis in patients with mild disease is that their spouses can then be tested for the presence of the defective gene, which could influence family-planning decisions.

As early as 20 to 30 years ago, when many centres throughout the world were advocating a semi-starvation regimen for children with CF, CF caregivers at the Hospital under the leadership of the late Dr. Douglas Crozier were encouraging a high-fat and high-calorie diet for these children, on the grounds that such a diet could partly compensate for their impaired ability to digest food. It soon became apparent that patients who were treated at the Hospital seemed to grow normally and more importantly tended to have better lung function - and hence, a significantly longer lifespan - than the national or international norms. "It wasn't hard to put two and two together," says Dr. Durie. "The nutritional approach initiated at the Hospital many years ago has now become a standard procedure in Canada and throughout the world."

In addition to a calorie enriched diet, children with CF and pancreatic insufficiencies are given extra vitamins to compensate for their poor absorption of fat-soluble vitamins, and pancreatic enzymes extracted from pigs. This aggressive treatment results in a more normal growth pattern and a better long-term prognosis. In spite of these measures, however, some children with CF do not achieve proper growth and their diet has to be supplemented by tube feeding. A minor surgical procedure allows a permanent tube to be inserted into the patient's stomach, making it possible for the patient to be tube-fed in the home, generally while asleep. This too has become an internationally recognized procedure.

Typically, CF patients affiliated with the Hospital are seen about four times a year by a multidisciplinary team that keeps track of their physical and psychological development and carefully monitors their nutrition, adjusting it if necessary. Many of the children who receive this multifaceted treatment are able to lead a fairly normal lifestyle, says Dr. Durie. "By and large, they go to school, attend university, get jobs - although in many instances their lifespan is still much shorter."

Currently, the Hospital's CF clinic maintains close ties with a similar clinic at Wellesley Hospital, recognized as a leading treatment centre for adults with CF. Dr. Durie and Dr. Pencharz at HSC run weekly consultation clinics for patients with gastrointestinal or nutritional difficulties, and provide direction for doctors, at one or the other site. The close association between the two centres also makes it easier to follow young CF patients into adulthood, and thus gain a better understanding of the progression of the disease throughout the life cycle.

As with all genetic disorders, the last frontier in the treatment of CF would be to actually correct the basic defect by inserting normal genes or gene products into the appropriate cells of affected people. "Because of the prevalence and devastation of CF, research on gene therapy has been more intensive than with any other genetic disease," notes Dr. Durie. In the meantime CF researches throughout the world are

evaluating ways of circumvention the CF defect virus pharmacological approaches. According to Dr. Durie, it may not be too long before some or many of these brave-new-world techniques finds clinical applicability. "Give us five to fifteen years," he says, "and we may have some things figured out."

In the meantime, most children with CF have to live with significant medical problems and the expectation of a relatively short life. Given this reality, one might expect these children to become listless and despairing. Nothing could be further from the truth, says Dr. Durie. "If one can generalize about a group of individuals affected by a similar condition - and in this case, one definitely can - CF patients are an incredible bunch of kids. They and their families refuse to give up hope, even when the stresses they experience threaten to overwhelm them. As a group, they have had a most dramatic influence on my life."

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### **Looking Out for the Little Ones**

The Hospital for Sick Children's SCAN Program reaches out into the community to do battle with the problem of child abuse and neglect.

A couple of summers ago, a nine-year-old girl and her father went on a trip to visit her uncle and his family in a small town in Ontario. One evening, the girl told her father that there was blood on her shorts. His first thought was that his daughter had started to menstruate. He took her to a local physician (unlikely to have a neighborhood clinic in a small town) who agreed with the father's opinion - nine years old was certainly early for a menstrual period, but not unheard of.

When the father brought his daughter home and relayed the information to her mother, she pointed out that their daughter had developed none of the signs of impending puberty, such as hair under the armpits or the beginning of breasts. She suspected that, rather than having started her period, the child had been abused. In fact, the girl told her that she had been touched. "Impossible", said the father. He couldn't fathom either his brother or his teenage nephew being capable of such a thing. The mother accused her ex-husband of being too loyal to his family to see the evidence in front of him.

This is where the Hospital's SCAN (Suspected Child Abuse and Neglect) Program came into the picture. The girl and her mother were referred to SCAN for an assessment, and the girl was given a careful physical examination by the Program's trained professionals. What they found was that the child had injuries in her genital area that were consistent with having been abused. After investigation, the case went to court, and the young girl's cousin was found guilty of having sexually molested her.

"It's easy to point a finger at the girl's father for his head-in-the-sand attitude, but it's important to remember that such an attitude is not necessarily evidence that he doesn't have his daughter's best interests at heart," explains Dr. Marcellina Mian, paediatrician and director of the SCAN Program. "It's very common for caregivers of abused children to think it impossible for someone they know so well, such as their spouse or brother or best friend, to abuse one of their children," she adds.

The SCAN Program was started at the Hospital in 1973, in response to a growing recognition of the problem of child abuse and neglect. Annual referrals have increased from 115 during the first year of operation to as high as 1000 in the 1990s. In the 1970s, the majority of referrals dealt with physical abuse and neglect. When sexual abuse came to the foreground as a major societal problem in the 1980s, the proportion of referrals for sexual abuse rose steadily, surpassing the physical abuse and neglect referrals by 1984.

The SCAN Program is set up as a multidisciplinary team of three doctors and social workers, an art therapist and two nurses, whose combined role is to provide assessments for children and adolescents who are suspected of having been abused or neglected, and, in cases where actual abuse or neglect has occurred, to provide comprehensive treatment programs for these children. Referrals to SCAN come from

a variety of sources within and occasionally outside the province, including Children's Aid, the police, family doctors, community hospitals, educators, neighbours, and even caregivers themselves. In fact, most children referred to SCAN are accompanied by at least one of their parents.

The Program holds several clinics every week, with about 4 or 5 physical assessments per clinic. The physical assessment consists of a head-to-toe examination of the body, including the private parts. A nurse explains the process to children before they have the exam, which, although noninvasive, may be a disconcerting and possibly frightening experience. One of the instruments used in the assessment is a colposcope which utilizes a bright light and magnification. This device, held about a foot away from the body, allows the examiner to get a better view of areas that are difficult to examine unaided, such as the hymen. An even more useful feature of the colposcope is its ability to take photographs that can later be used for further scrutiny, consultation with colleagues, or legal evidence.

In cases where it is not clear that suspicions of abuse are warranted, children can be seen at a Brief Assessment Clinic, designed to provide a rapid means to cue recall of abuse in a non-leading manner. It includes a psychosocial interview of the parents and a physical examination of the child followed by an art-therapy interview which can facilitate the expression of a child's memories of traumatic events without being immediately recognizable to the child as a vehicle for disclosure. When the Brief Assessment process cannot determine if abuse has occurred, a recommendation for further evaluation is made.

Full assessments include in-depth psychosocial evaluation of the child(ren) and parents, and interviews with people involved in the care of the child, such as the grandparents, teacher, or significant others (or parents' new partners), and can take up to three months. Treatment services include short-term crisis counselling and long-term treatment programs for both victims and their families.

While the word "neglect" may not have as ominous connotations as "abuse," the problem is every bit as serious, according to Dr. Mian. She cites three common types of neglect: failure to provide adequate nutrition, failure to create a safe environment, and failure to provide stimulation. Neglectful parents may have social or mental health problems such as depression or drug-addiction. "For instance, a mother addicted to crack cocaine may leave her baby alone in a crib for several hours while she goes out on the street in search of her drug." More commonly, neglectful parents simply lack the ability to provide appropriate care for their children. SCAN does not operate as a finger-pointing operation whose aim is to uncover wrongdoing at every corner. In fact, a significant proportion of claims are disproved rather than confirmed, according to Dr. Mian. She attributes this to the heightened awareness of abuse in today's society and the resultant, and sometimes excessive, concern that people have about some children's statements or behaviour. However, she points out that although "abuse is at times overreported in this day and age, it's still better to expose some false claims than to miss real cases," and notes that "we're all relieved if a suspicion of abuse turns out to be unfounded." One recent case of this sort involved an infant boy who was brought to the Hospital's emergency department with a large bump on his head. His skull was x-rayed, and the child was found to have a skull fracture. The boy's parents were unable to account for the fracture - they were certain their son hadn't fallen, been dropped, or otherwise bumped his head - and stated that they hadn't been away from him in the past few days. The family was referred to SCAN for a more comprehensive assessment of the situation.

"Whenever we have discrepancy between a physical finding, such as a skull fracture, and the explanation for this finding, such as "I'm sure my child didn't hit his head" or "It happened when he fell onto the carpet from a couch," we have a case of possible abuse or neglect, which requires closer examination," Dr. Mian explains.

Upon detailed questioning from SCAN personnel, the parents recalled that they had attended to some personal business and had left the child with a friend. The parents then questioned their friend, who insisted that nothing had happened to the baby in her presence. The SCAN team was now prepared to investigate the possibility of abuse by a parent, although they felt this was unlikely given the cooperativeness and genuine distress shown by the parents. The problem was solved the next day, when

the friend called the parents and admitted that she had indeed dropped the baby and been too afraid to tell them what happened.

The SCAN Program has forged strong ties to community agencies all over Ontario and even out of province. Collaborative relations are also maintained with the police, Crown and defense attorneys. Indeed, SCAN personnel are routinely called in to give expert opinions in court. SCAN also functions as an educational program, holding many presentations both within HSC and in the community, including colposcopy rounds five times a year to provide training for physicians and offering a yearly seminar at the University of Toronto on the Shaken Baby Syndrome. Graduate students from various faculties and practicing professionals from various disciplines have spent time with SCAN to learn how to respond to the problem of child abuse. In addition, SCAN staff are available to talk about specific cases to doctors in community hospitals.

In the near future, SCAN will be hosting a two-day conference on child abuse aimed at a heterogeneous group of professionals including doctors, social workers, nurses and lawyers. It will have an entirely Canadian faculty, which Dr. Mian believes "will give the event a special relevance to Canadian healthcare professionals."

Dr. Mian came by her vocation after she graduated from medical school and went to work in a small community hospital where the medical director had a special interest in child abuse and neglect. "Although some people would not want to deal with this type of work, I found it gratifying and learned its special skills" she recalls. After many years of experience in her chosen field, what continues to lift Dr. Mian's spirits is how well most children are able to cope with their circumstances. "I'm always impressed anew by children's natural resilience," she says. "Even with their distressing personal histories, many of these kids do amazingly well."